Asian Institute of Research

Journal of Health and Medical Sciences

Vol. 5, No.4 December 2022

ASIAN INSTITUTE OF RESEARCH

Connecting Scholars Worldwide

ASIAN INSTITUTE OF RESEARCH
Connecting Scholars Worldwide

Mental Model of Mothers of Adolescent Girls and Health Service Providers on HPV Vaccination in Urban Slum Areas of Dhaka, Bangladesh: A Mixed-Method Study

Fariha Haseen[1], Hridi[1], Sadia Akter Sony[2], Dilip Kumar Basak[3], Md Monirul Islam[4], Sharlin Akther[5], Syed Shariful Islam[1]

[1] Department of Public Health and Informatics, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh
[2] Toronto Metropolitan University, Toronto, Canada
[3] BioDev Serviced, Dhaka, Bangladesh
[4] Rural Reconstruction Foundation, Jashore, Dhaka, Bangladesh
[5] Bangladesh Business & Disability Network, Dhaka, Bangladesh

Correspondence: Fariha Haseen, Department of Public Health and Informatics, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh. Email: farihahaseen@bsmmu.edu.bd/far_haseen@yahoo.com. Contact no +8801711066908

Abstract
Background: The study aimed to explore the perception of mothers of adolescent girls and health service providers in urban slums toward HPV vaccination. Methodology: A cross-sectional mixed-method study in the slums of Rayer Bazaar, Kamlapur and Mohakhali was conducted. The quantitative part included a household survey of mothers (n=150) and service providers (n=30) through a semi-structured pre-tested questionnaire and qualitative interviews included in-depth interviews (IDI) with mothers (n=10) and key-informant interviews (KII) with service providers (n=10). Results: Around 96% of mothers had never heard of HPV, and 98% were unaware that the virus's transmission could be halted. Only 3.3% of mothers were aware that HPV can cause cervical cancer, although, during IDI, it was seen that the majority of mothers said that cervical cancer is a communicable disease. Nearly 98% of mothers wanted their daughters to get vaccinated. Service providers had a good understanding of HPV, HPV vaccine, and cervical cancer. All service providers during KII agreed that if they had received adequate training on HPV vaccination and cervical cancer, they could have treated their patients better. Conclusion: The findings of this study have important implications for the design and advocacy of HPV immunization programs in Bangladesh.

Keywords: HPV Vaccination, Cervical Cancer, Mothers, Service Providers, Bangladesh

1. Introduction

Globally, cervical cancer ranks 4th among all gynaecological cancers and in Bangladesh it ranks 2nd among all gynaecological cancer. The crude incidence and mortality rate estimates for cervical cancer in Bangladesh are 10.2 and 6.1 per 100 000, respectively (Globocan, 2020). Early identification and timely screening are challenging in slum areas due to a lack of knowledge about cervical cancer among the general public and healthcare professionals, as well as restricted access to healthcare facilities. The awareness is crucial and it allows people to better grasp the issue by gaining knowledge and, as a result, changing their attitudes. This empowers them to identify problem areas and make the necessary improvements (Chandana et al.,2020). The Government of Bangladesh has developed a National Strategy for Cervical Cancer Prevention and Control (2017-2022). The goal of this strategy is to improve cervical cancer prevention and control activities to reduce the incidence, prevalence, morbidity and death from cervical cancer and to promote women's good health which is in alignment with Sustainable Development Goals 3, 5 and 10 (DGHS, MoH&FW, 2017). The WHO Secretariat modelled the health and socioeconomic impacts of cervical cancer by achieving the 90-70-90 targets by 2030 in 78 low- and lower-middle-income. This model proposes that 90% of girls are fully vaccinated with HPV by the age of 15, 70% of women screened with the high-performance test by the age of 35, and then again by the age of 45 and 90% of women with cervical cancer receive treatment (WHO, 2020).

Slums are home to about one-third of the world's urban population. From 689 million in 1990 to 880 million in 2014, the population increased significantly, and by 2030, it is projected to double (Singh et al., 2018). Every day, at least 1500 new migrants arrive in Dhaka, making it one of the world's megacities with the fastest rate of expansion. The majority of these new immigrants settle in slums, contributing to an alarming yearly growth rate of more than 7%. (Adams et al., 2015). These slum residents are socially and economically impoverished. They frequently have poor nutrition, low income, lack of knowledge about health issues and preventive behaviour; and limited access and utilization of health care services. The unhealthy surroundings of the slum provide fertile ground for several infectious diseases as well as perilous living conditions render harmful practices such as poor menstrual hygiene practices, child marriage, hence early and multiple childbearing. (Hridi et al., 2022) all of which makes the women and adolescent girls of the slum prone to a preventable yet life-threatening condition – cervical cancer (Haseen et al.,2020).

The first infection of the Human Papillomavirus often occurs soon after first sexual intercourse, so early age at sexual intercourse is a substitution for the early age of exposure to HPV, this is because the adolescent cervix is vulnerable to HPV infection. Early age at marriage also results in multiple pregnancies, which can cause injury to cervical tissue leaving it vulnerable to infections. (Chandana et al.,2020). Studies conducted in the slums of Dhaka found that the mean marriage age in slums was 13.6 years. Because the living conditions of adolescents and their families in the slums are sometimes unsafe, they were married off early. Adolescent girls do not usually visit facilities if they have menstrual problems or during pregnancy. Girls do not foster good menstrual hygiene. All of these make adolescent girls and women in slums more susceptible to HPV infections and eventually cervical cancer if not treated (Hridi et al.,2022 & Haseen et al.,2020).

HPV immunization is most effective when given before the sexual debut and HPV infection. Girls aged 9 to 13 years old are recommended to be vaccinated against HPV using effective, economical, and equitable delivery systems, according to World Health Organization (WHO) recommendations. It is more cost-effective to vaccinate a single age cohort within the intended age range (WHO, 2018). In Bangladesh, the Expanded Program on Immunization (EPI) is one of the well-established and successful programs aimed at lowering child and maternal morbidity and mortality from vaccine-preventable diseases. Even during the recent pandemic, it was seen that Bangladesh was able to achieve the target set by the WHO for COVID-19 vaccination with the Ministry of Health and Family Welfare (MOH&FW) by successfully inoculating 70% of the country's population with two full doses (WHO, 2022).

The fact that sexual contact is the primary mode of transmission of vaccine-preventable HPV serotypes appears to be concealed from vaccine recipients, their parents/guardians, or teachers. The failure to reveal the mode of transmission of the virus against which the girls are being immunized creates ethical problems. In some cases,

incomplete information may be presented to avoid societal controversies for the greater good. In the case of vaccination, which primarily serves a practical purpose, it may be argued that complete information may impede vaccine adoption. Several low- and middle-income countries (LMICs) have reported that promoting the HPV vaccine's anti-cancer role to the public while ignoring its genuine significance in preventing sexually transmitted HPV infection is associated with high vaccination coverage. (Salwa & Abdullah Al-Munim, 2018 and Haseen & Sony, 2017).

With support from the Global Alliance for Vaccines and Immunizations (GAVI), the EPI Program of Directorate General of Health Services (DGHS) piloted the introduction of HPV vaccination in Gazipur, Bangladesh in 2016 for two years. The aim of the piloting was to examine the implementation capacities with the intention that if the experience is positive GAVI, UNICEF, WHO and other stakeholders will support the Government of Bangladesh for the nationwide rollout of the HPV vaccine. (Haseen & Sony, 2017). The 2-years implementation experience was good with minimal challenges. Even though Bangladesh is in a good position to start its nationwide HPV vaccination, public awareness and acceptance of the vaccine are critical to including a novel vaccine in a national immunization program. Although HPV infection is common and its repercussions can be severe, the majority of people have little or no knowledge about it. Previous research has also found that women lacked information regarding HPV preventive techniques. This was especially true for those from lower socioeconomic backgrounds (Haseen et al., 2020). Attitudes and cultural factors linked with HPV infection and cervical cancer might influence infection rates, preventative approaches such as vaccine uptake, and the cost, morbidity, and mortality associated with HPV-related diseases. The vaccine policy will be more widely accepted as people's perceptions of the danger of HPV infection and the advantages of immunization improve (Ezenwa, 2013).

Studies found parental acceptance was higher if a physician recommended immunization (Markowitz et al., 2013). Parental decisions to vaccinate their adolescent children were enabled by various factors such as awareness of the serious consequences of HPV infection, vaccine efficacy, personal knowledge of someone with cancer, and whether they believed that their children were at risk for acquisition of HPV infection or chance of developing cervical cancer (Madhivanan et al., 2014). Adolescents expect parental help when making immunization decisions. Furthermore, most mothers of adolescent girls are eager to discuss immunization with their daughters. In this light, the opinions of both parents and adolescents are recognized to be analyzed jointly for the acceptability of HPV vaccines (Tsu et al., 2014).

City corporations and NGOs provide primary healthcare services in urban slums. Slum dwellers usually sought treatment at pharmacies for general health issues or from homoeopaths and traditional healers for diseases like hepatitis, and STIs/RTIs, and they prefer inexpensive home births by traditional birth attendants despite knowledge of the high-quality maternity services (Adams et al., 2015). Therefore, the knowledge and attitude of health service providers in slums are crucial, because they play critical roles in disease prevention and health promotion by teaching these vulnerable populations through culturally relevant health education and promotion initiatives (Ebu et al., 2021). The study conducted in Gazipur found that HPV Vaccine was accepted more by the community as the health workers and/or teachers had a good relationship with parents, and they were able to follow up effectively with families who asked for more information. It also ensured the presence of girls during both doses of the vaccine (Haseen et al., 2017).

Parents and health service providers are the critical gatekeepers of adolescents and thus it is plausible to assume that when mothers and health service providers are well informed, they may have positive perceptions about HPV vaccination. This study aimed to assess mothers' knowledge of HPV and their willingness to vaccinate their adolescent daughters against HPV as well as to understand the perception of health service providers regarding HPV, cervical cancer and vaccination in the urban slums of Dhaka. This study is important because there is a paucity of research examining mothers' perspectives and health service providers' awareness of HPV vaccination in Dhaka's urban slums. Herein we present findings that would be useful to administrators and managers to plan the advocacy activities during the introduction of HPV vaccine in the national immunization program.

2. Methods and materials

The cross-sectional study was conducted in the slums of Rayer Bazaar, Kamlapur and Mohakhali of Dhaka city along with health centres in these slums. Ward number 20 of Mohakhali slum and ward number 34 of Rayer Bazar slums of Dhaka North City Corporation (DNCC) and ward no 8 of Kamlapur TT para slum of Dhaka South City Corporation (DSCC) were purposively selected to meet a selection of our participants and sample size. We selected a mixed-method approach for this study, linking common themes across the survey and semi-structured interviews.

For the survey with mothers, sampled households were chosen from a list of pre-prepared slum households, where a mother has an adolescent daughter, using simple random sampling. A lottery method was used to select a mother from each household. Data were collected through face-to-face interviews in Bangla in a private setting at household with informed written consent. With a separate questionnaire service providers were interviewed, who were giving services from the health facilities situated in the slum areas. Data were collected through face-to-face interviews in Bangla in their free time with informed written consent. The completed questionnaires were entered into a database in SPSS version 23. Descriptive statistics were replaced.

For the qualitative interviews, purposive sampling was used. In total ten mothers of adolescent girls from the slum for in-depth interviews (IDIs) and ten service providers who provide services to slum people for the key informant interviews were purposively selected. The interviews were carried out in Bangla with informed written consent. In-depth interviews were performed in a private environment at the household and key informant interviews (KIIs) were done in the respective workplace of service providers. During the interview, informed written consent was taken, notes were taken and interviews were recorded with voice recorders and then transcribed. Data were manually coded. All the transcripts were reviewed and themes were generated based on the analysis plan. Thematic analysis was used for this research (Barun and Clarke, 2006). Data validity was ensured by triangulation, which was again verified by comparing the data from the IDI and KII. The study got ethical approval from the Institutional Review Board of BSMMU.

3. Results

3.1 Sociodemographic characteristics of the participants

One hundred and fifty mothers and thirty service providers participated in the survey and ten mothers and ten service providers took part in the qualitative interviews. The average age of the mothers of female adolescents was 36.54 years. Around 53.3% of mothers had no education. Most of the mothers (59.3%,) were housewives and around 26% of them were house helpers. The mean age at marriage of these mothers was 16.67 years.

As for the service providers, their average age was 35.7 years. Approximately 10% of the service providers were medical doctors and around 3% of them had a specialized degree in gynaecology and obstetrics. Around 43.3% of service providers were paramedics/nurse/midwife/assistant nurse/medical assistant/SACMO.

3.2 Knowledge of mothers of adolescents and service providers on HPV

Knowledge of mothers of adolescents during the survey:

Around 96% of the mothers never heard about HPV. Only 4% of the mothers thought this virus produced diseases like cervical cancer; another 2% thought this virus was transmitted from one person to another. Only 1% said the virus was transmissible through intimate partners and 1.3% said through sexual intercourse. Approximately 98% of mothers did not know that HPV was transmissible and 98% of them were not aware that this transmissibility could be halted. Almost 66% of mothers wanted information about HPV from a specialized physician, for instance, an obstetrician and gynaecologist, another 23.3% of mothers wanted information from public health workers and only 4.7% preferred this information from a general physician.

During the qualitative interview, it was seen that 3 out of 10 mothers had heard about Human Papilloma Virus and knew it was the reason for cervical cancer. However, none of the mothers knew about HPV, they learned about HIV through television.

"I do not about HPV…something like this I heard on TV... maybe the name was HIV…it is a dangerous disease" (mother of an adolescent, Mohakhali Slum)

Most of the mothers (9 out of 10) knew that cervical cancer is a communicable disease. Among 10 mothers, 3 stated that it spreads from one person to another through physical relations as well as by using clothes or other things.

"This can be spread in many ways…. like when one has physical relation with many people or use the things of people who have the disease" (mother of an adolescent, Kamlapur TT para slum).

Out of 10 mothers interviewed only 2 of them stated that bleeding from the uterus, itching, unusual vaginal discharge and uterus coming down were the symptom of cervical cancer. Three out of 10 mothers did not have any knowledge about the prevention of HPV infection. Two out of 10 mothers stated that cervical cancer is preventable through vaccination and proper treatment. Two mothers said if they get suggestions from doctors then they can help their daughters to prevent cervical cancer from a young age. One mother stated that if married females are aware and use condoms during physical relations with their husbands then infection can be preventable and another mother said, they have to be more careful during normal delivery so that the uterus may not become injured and use a new blade to prevent disease.

"If doctors suggest us vaccine it would help us understand why it is important and also if they give it for free…we are poor people" (mother of an adolescent, Rayer Bazar slum)

Knowledge of service providers during the survey:

All service providers had heard about HPV. Almost 98% of them knew that HPV produces diseases; they specifically mentioned it produces cervical cancer. Around 30% of the service providers said that the virus was transmissible, the majority (60%) said that HPV was not transmissible and another 10% of them said they did not know if HPV was transmissible or not. Of those who said the virus was transmissible the majority of them (30%) said it was through unprotected sexual intercourse. Almost all service providers (97%) said the transmission of HPV could be halted and the majority of them said (90%) through vaccination.

During the qualitative interview, it was seen that nine out of 10 service providers have heard about HPV but 5 out of 9 service providers did not give any information about the source where they learnt. One service provider learned about HPV from training, one service provider learned during her diploma course, one service provider learned from his workplace and one service provider does not know about HPV.

"I was taught about HPV during my medical diploma course…we were taught in detail about this" (Service provider, Kamlapur TT Para-Slum).

"We are trained by our supervisors regarding HPV…that how I come to know about HPV" (Service provider, Rayer Bazar Slum).

Seven out of 10 service providers think that HPV is the cause of cervical cancer and the rest 3 service providers do not know anything about the cause of cervical cancer. However, all (10) service providers think that cervical cancer might be transmitted in the human body but they each gave a different opinion about the reason for infection like early marriage and genetics, unsafe normal delivery, unsafe physical relation, tumour, cyst, using the common bathroom.

3.3 Perception of HPV Vaccination among mothers of adolescents

It was found in a survey that 29% of mothers knew that HPV infection is a fatal disease however 72% did not know that HPV infection was life-threatening. Around 24% of mothers believed HPV vaccines completely protect against cervical cancer and 75.3% believed their daughters can easily get affected by HPV. Only 7.3% of urban slum mothers knew the government would provide free vaccination to their daughters. Around 77% of these mothers said that decision of a doctor would influence their decision to vaccinate their daughters. According to these mothers, the hindering factors to vaccinating their daughters were due to the uncertainty of the effectiveness of the vaccine (52%) followed by the side effect of the vaccine (47%). The enabling factor that would influence them to vaccinate their daughters will be free vaccination (96.7%). Almost 99% of the mothers in these slums wanted their daughters to be vaccinated against HPV.

Table 1: Perception of mothers of adolescents towards HPV vaccination (N=150)

Variables	Response Category	Frequency (percentage) n (%)
HPV infection is fatal	Yes	42 (28.9)
	No	0 (0.0)
	Don't Know	108 (72.0)
HPV vaccines protect against cervical cancer	Yes	36 (24.0)
	No	0 (0.0)
	Don't Know	114 (76.0)
The government provides vaccines to girls from 9 years onwards	Yes	11 (7.3)
	No	2 (1.3)
	Don't Know	137 (91.3)
Person influencing the decision for vaccination	Doctor	125 (83.3)
	Family members	12 (8.0)
	Mass Media	5 (3.3)
	Personal Opinion	8 (5.4)
Hindering factors of HPV vaccination	High Dose	2 (1.0)
	Side Effects	70 (47.0)
	Uncertain effectiveness	78 (52.0)
Enabling factors for HPV vaccination	Free vaccination	145 (96.7)
	Information	14 (9.3)
	Physician's recommendation	7 (4.7)
	Method other than vaccination	8 (5.3)
	Others	4 (2.7)
Your daughter can easily get affected by HPV	Yes	113 (75.3)
	No	5 (3.3)
	Don't Know	32 (21.3)
Want to vaccinate your daughter	Yes	148 (98.7)
	No	2 (1.3)

During the qualitative interview, it was seen that all the mothers were interested to vaccinate their daughters against HPV. Three mothers did not feel any barrier towards vaccination but they have fear about side effects like fever, pain, and infection. Three mothers were worried about the cost of the vaccine. They expected free vaccination from the government. One mother did not have any idea about the prevention of vaccination.

"I want to vaccinate my daughter, but I do not know what are the side effects of this vaccine…I am scared about the side effects of this vaccine" (Mother, Rayer Bazar slum)

3.4 Knowledge of service providers on cervical cancer

During the survey, it was found that all service providers thought cervical cancer was a complex disease. Around 90% of service providers said cervical cancer was the leading cause of death among all gynaecological cancers. Among the risk factors for cervical cancers, the service providers thought sexual intercourse at an early age is a common risk factor (86.7%), followed by delivering more children (73%) and having more than one sexual partner (67%). As for the clinical features of cervical cancer, the service providers mentioned lower abdominal pain as a primary clinical feature (80%), followed by bleeding during sexual intercourse and massive bleeding through the genitals (60%).

Table 2: Knowledge of service providers on cervical cancer (N=30)

Variables	Response Category	Frequency (percentage) n (%)
Cervical cancer in females is a complex disease	Yes	30 (100.0)
	No	0 (0.0)
Cervical cancer death is the highest among the gynaecological cancers	Yes	27 (90.0)
	Don't Know	3 (10.0)
Risk factors of the Cervical cancer *(Multiple choice)*	Uterus Infection	8 (26.7)
	Family history	3 (10.0)
	Sexual intercourse at an early age	28 (93.3)
	Long-time uses of the contraceptive pill	4 (13.3)
	More than one sexual partner	20 (66.7)
	Less education	4 (13.3)
	More childbirth	22 (73.3)
	Others	4 (13.3)
Clinical features of Cervical cancer	Massive bleeding through genitals	18 (60.0)
	Bad smell	19 (63.3)
	Lower abdominal pain	24 (80.0)
	Rapid weight loss	8 (26.7)
	Pain during sexual intercourse	19 (63.3)
	Bleeding during sexual intercourse	21 (70.0)
	Others	8 (26.7)

During the qualitative interviews, 7 out of 10 service providers stated that uterine cancer and cervical cancer are not the same. Two out of 10 service providers do not know the symptoms of cervical cancer. The rest of the 8 service providers have mentioned different types of symptoms of cervical cancer.

"Symptoms are bleeding through the vagina, pain in the lower abdomen and sometimes uterus comes out" (service provider, Kamplapur TT para slum).

"I do not know if these two cancers are the same…I do not know much about all these" (service provider, Mohakhali Slum).

3.5 Perception of HPV Vaccine among service providers

In the survey questionnaire, we have included the knowledge question about 3 doses of the HPV vaccine. It was seen through the survey that 83% of service providers knew that the 3 doses of the HPV vaccine. Around 73.3% of service providers knew that the vaccine dosage needs to be completed by 6 months and 20% did not know this period of completion. The majority of them (70 %) thought the age range of HPV vaccination was 15 years and above and 23.3% said that the age range for vaccination was from 9 to 14 years. As for the attitude it was seen that around 80% of service providers were worried about the safety of HPV vaccination although all of them said that people should be assured of the effectiveness of the vaccine.

Table 3: Perception of HPV vaccine among service providers (N=30)

Variables	Response Category	Frequency (percentage) n (%)
Doses of HPV vaccination	3 Doses of HPV	25 (83.3)
	2 Doses of HPV	5 (16.7)
	Don't Know	3 (10.0)
Time for completion of vaccine dose	6 Months	22 (73.3)
	3 Months	2 (6.7)
	Don't Know	6 (20.0)
The age range for vaccination	9-14 years	7 (23.3)
	15 years and above	21 (70.0)
	Don't know	2 (6.7)
Do you think you have enough information about HPV	Yes	4 (13.3)
	No	26 (86.7)
People worried about the safety of vaccination	Yes	24 (80.0)
	No	6 (20.0)
People should be assured of vaccine effectiveness	Yes	30 (100.0)
	No	0 (0.0)

During the qualitative interview, it was seen that all service providers stated that, cervical cancer is preventable and 8 out of 10 service providers mentioned that cervical cancer is preventable through the HPV vaccine. Additionally, 2 service providers stated that by stopping early marriage cervical cancer can be prevented, 1 service provider mentioned that cervical cancer could be prevented through institutional delivery and 3 service providers mentioned that cervical cancer can be prevented through treatment.

All service providers stated that they do not have enough information on HPV, cervical cancer HPV vaccination. They all feel the need for a structured training program including a leaflet, and flipchart on HPV and related issues for the people who live in slum settings. They want to enrich themselves so that they counsel the clients (Adolescents and their mothers) successfully for prevention, vaccination and treatment. They all expect at least 2-3 days of training on HPV and cervical cancer.

"If there is regular training for us, we can aware people in this slum more about HPV, now we serve them with the limited knowledge we have" (Service provider, Mohakhali slum).

4. Discussion

Our findings regarding the knowledge of the mother regarding HPV is similar to a study conducted in the slums of Hubli in Karnataka, India where it was seen that only 7.5% of the mother had heard that HPV can cause cervical cancer (Bathija et al., 2016). In 2019 a study conducted in the urban slums of Nigeria found that only 12.8% of the mothers had heard about cervical cancer. Knowledge of cervical cancer, screening and HPV)immunization was poor among these mothers (Olubodun et al., 2019). Another study conducted in the "*Sat Tola'* slum of

Mohakhali, Dhaka among mothers of daughters aged 10 and below found that 55% of mothers had poor knowledge of cervical cancer transmission and prevention (Khan et al.,2019). Our study revealed that around 96% of the mothers never heard about HPV. Only 4% of the mothers thought this virus produced diseases like cervical cancer.

A 2018 study in Bangladesh revealed that one in five urban women and one in twenty rural women heard about a vaccine that can prevent cervical cancer (Islam et al., 2018). Another study conducted in the '*Sat Tola*' slum of Mohakhali Dhaka revealed that 18% of mothers had heard about the HPV vaccine but nobody knew the age at which the vaccines must be administered (Khan et al.,2019). Likewise in our study Around 24% of mothers who heard about the HPV vaccine believed HPV vaccines completely protect against cervical cancer.

A study conducted in Kenya among the hard-to-reach population in 2015 found that despite little prior knowledge of cervical cancer and HPV, communities were interested in receiving HPV vaccination for themselves as well as their daughters (Watson-Jones et al., 2015). In another study conducted in the slums of Odisha, 75% of the mothers said they wanted to vaccinate their daughters against the HPV virus. Another study conducted in 2014 in Karnataka found that mothers wanted vaccination for their daughters through government-subsidized programs (Montgomery et al., 2014). Over 60% of the mothers in a study conducted in Hong Kong in 2017 agreed that the HPV vaccine costs more than they can afford. The majority of mothers (81.8%) agreed that the government should subsidize the full cost of the vaccine. Only about one-third of the mothers (35.3%) indicated that they would be "very likely" to accept HPV vaccination for their daughters if the vaccines were available for the free vaccine (Loke et al., 2017). In another study conducted in Bangladesh in 2018, it was seen that 92% of urban mothers and 99% of rural mothers wanted HPV vaccination for their daughters (Islam et al., 2018). Indistinguishably in our quantitative survey as well as in qualitative interviews, it was seen that the majority of the mothers in slums were keen to vaccinate their daughters against HPV although they had limited knowledge. These mothers also said during the IDI that they wanted free vaccination from the government. In our survey also 99% of the mothers wanted HPV vaccinations for their daughters.

The majority (76%) of the mothers in a study in Hong Kong stated that doctors' recommendations would influence them to vaccinate their daughters Also 65% of mothers were worried about the side effects of the vaccine (Loke et al., 2017). Similarly, in our study, only 7.3% of urban slum mothers knew the Ministry of Health and Family Welfare (MoH&FW) provides free vaccination to girls 10 years old and above. Around 77% of these mothers said that decision of a doctor influenced their decision to vaccinate their daughter. According to these mothers, the hindering factors to vaccinating their daughters were due to the uncertainty of the effectiveness of the vaccine (52%) followed by the side effect of the vaccine (47%). The enabling factor that would influence them to vaccinate their daughters were free vaccination (96.7%). Almost 99% of the mothers in these slums wanted their daughters to be vaccinated against HPV

In a study conducted in India in 2016, it was seen that 84% of service providers agreed that cervical cancer was the most commonly occurring cancer among all the gynaecological cancers in Indian women (Chawla et al., 2016). A study conducted in China in 2020, found that in general, service providers had satisfactory baseline knowledge regarding HPV and its vaccines compared with other populations (Chen et al., 2020). Analogously in our survey, we found that almost 98% of service providers knew that HPV produces diseases; they specifically mentioned it produces cervical cancer and its transmission can be prevented. Correspondingly in our survey around 90% of service providers knew cervical cancer was the leading cause of death among all gynaecological cancers.

5. Conclusion

The Government of Bangladesh is going to introduce the HPV vaccine for adolescent girls in school and out of school, soon. The results of this study offer the nation-specific substantiation required for the creation of this program. These results highlight the necessity for culturally relevant and focused educational programs to increase understanding of the fundamental causes of cervical cancer and its primary prevention through the HPV vaccine. Despite low knowledge about the disease and its prevention, there was a high level of willingness to receive a vaccine to prevent cervical cancer. As a result, our study implies that adding the HPV vaccine to Bangladesh's regular vaccination schedule would be well-received with well-planned advocacy plan specially with vulnerable segment of the community. The results of this study have significant ramifications for the planning and execution of HPV vaccine programs across the nation.

References

Adams, A. M., Islam, R., & Ahmed, T. (2015). Who serves the urban poor? A geospatial and descriptive analysis of health services in slum settlements in Dhaka, Bangladesh. *Health Policy and Planning*, *30*(suppl 1), i32–i45. https://doi.org/10.1093/heapol/czu094

Bangladesh. (2020). https://gco.iarc.fr/today/data/factsheets/populations/50-bangladesh-fact-sheets.pdf

Bathija, G., Mallesh, S., & Gajula, M. (2016). A study on awareness of cervical cancer among women of reproductive age group in urban slums of old Hubli, Karnataka, India. *International Journal of Community Medicine and Public Health*, 2579–2583. https://doi.org/10.18203/2394-6040.ijcmph20163076

Braun, V., & Clarke, V. (2006). Using thematic Analysis in Psychology. *Qualitative Research in Psychology*, *3*(2), 77–101. https://doi.org/10.1191/1478088706qp063oa

Chawla, Pc., Chawla, A., & Chaudhary, S. (2016). Knowledge, attitude & practice on human papillomavirus vaccination: A cross-sectional study among healthcare providers. *Indian Journal of Medical Research*, *144*(5), 741. https://doi.org/10.4103/ijmr.ijmr_1106_14

Chen, H., Zhang, X., Wang, W., Zhang, R., Du, M., Shan, L., Li, Y., Wang, X., Liu, Y., Zhang, W., Li, X., Qiao, Y., Ma, J., Zhou, J., & Li, J. (2020). Effect of an educational intervention on human papillomavirus (HPV) knowledge and attitudes towards HPV vaccines among healthcare workers (HCWs) in Western China. *Human Vaccines & Immunotherapeutics*, *17*(2), 443–450

Directorate General of Health Services, Ministry of Health and Family Welfare. (2017). *National Strategy for Cervical Cancer Prevention and Control Bangladesh 2017-2022*

Ebu, N. I., Abotsi-Foli, G. E., & Gakpo, D. F. (2021). Nurses' and midwives' knowledge, attitudes, and acceptance regarding human papillomavirus vaccination in Ghana: a cross-sectional study. *BMC Nursing*, *20*(1). https://doi.org/10.1186/s12912-020-00530-x

Ezenwa, B., Balogun, & Okafor. (2013). Mothers' human papillomavirus knowledge and willingness to vaccinate their adolescent daughters in Lagos, Nigeria. *International Journal of Women's Health*, 371. https://doi.org/10.2147/ijwh.s44483

Global strategy to accelerate the elimination of cervical cancer as a public health problem. (2020). www.who.int. Retrieved August 28, 2022, from Cervical Cancer Elimination Initiative (who. int)

Haseen, F., & Sony, S. A. (2017). Cervical Cancer and Ethical issues in HPV Vaccination. *Bangladesh Journal of Bioethics*, *8*(2), 31–37. https://doi.org/10.3329/bioethics.v8i2.35364

Haseen, F., Chowdhury, S., Ferdous, J., Sharmin, S., Hassan, M., Akter. N., Akhter, S., Worthy, R, T., Islam, S.S. (2020). Prevention and Management of Cervical Cancer; A Gender-Lens Review of Programmatic and Sociocultural Dimensions. Protocol of Cervical Cancer (portal.gov.bd)

Haseen, F., Sony, S, A., Basak, D, K. (2017). Knowledge and attitude towards HPV among School-going female adolescents in selected communities of Bangladesh

Hridi, H., Haseen, F., Sharmin, T., Bristy, S., Akter, N., Haney, U., Biswas, B., Ali, M., Rahman, Z., & Islam, S. S. (2022). Assessment of Reproductive Health Status and Quality of Life of Female Adolescents Living in the Slums of Dhaka, Bangladesh During COVID-19 Pandemic Situation: A Mixed-Method Study. *Journal of Health and Medical Sciences*, *5*(3). https://doi.org/10.31014/aior.1994.05.03.224

Islam, J. Y., Khatun, F., Alam, A., Sultana, F., Bhuiyan, A., Alam, N., Reichenbach, L., Marions, L., Rahman, M., & Nahar, Q. (2018). Knowledge of cervical cancer and HPV vaccine in Bangladeshi women: a population-based, cross-sectional study. *BMC Women's Health*, *18*(1). https://doi.org/10.1186/s12905-018-0510-7

Khan, S, Z., & Haseen, F. (2019). Assessment of Knowledge of Cervical Cancer Transmission and Prevention among the mothers of Daughters Aged Below 10 Years. *Journal of Pulmonology Research & Reports*, 1–6. https://doi.org/10.47363/jprr/2019(1)101

Madhivanan, P., Li, T., Srinivas, V., Marlow, L., Mukherjee, S., & Krupp, K. (2014). Human papillomavirus vaccine acceptability among parents of adolescent girls: Obstacles and challenges in Mysore, India. *Preventive Medicine*, *64*, 69–74. https://doi.org/10.1016/j.ypmed.2014.04.002

Markowitz, L. E., Hariri, S., Lin, C., Dunne, E. F., Steinau, M., McQuillan, G., & Unger, E. R. (2013). Reduction in Human Papillomavirus (HPV) Prevalence Among Young Women Following HPV Vaccine Introduction in the United States, National Health and Nutrition Examination Surveys, 2003–2010. *The Journal of Infectious Diseases*, *208*(3), 385–393. https://doi.org/10.1093/infdis/jit192

Montgomery, M. P., Dune, T., Shetty, P. K., & Shetty, A. K. (2014). Knowledge and Acceptability of Human Papillomavirus Vaccination and Cervical Cancer Screening among Women in Karnataka, India. *Journal of Cancer Education*, *30*(1), 130–137. https://doi.org/10.1007/s13187-014-0745-4

Olubodun, T., Odukoya, O. O., & Balogun, M. R. (2019). Knowledge, attitude and practice of cervical cancer prevention, among women residing in an urban slum in Lagos, South West, Nigeria. *Pan African Medical Journal*, *32*. https://doi.org/10.11604/pamj.2019.32.130.14432

Salwa, M., & Abdullah Al-Munim, T. (2018). Ethical issues related to human papillomavirus vaccination programs: an example from Bangladesh. *BMC Medical Ethics*, *19*(S1). https://doi.org/10.1186/s12910-018-0287-0

Singh, S., Sahu, D., Agrawal, A., & Vashi, M. D. (2018). Ensuring childhood vaccination among slums dwellers under the National Immunization Program in India - Challenges and opportunities. *Preventive Medicine*, *112*, 54–60. https://doi.org/10.1016/j.ypmed.2018.04.002

Strengthening vaccination coverage. (2018). www.who.int. Retrieved August 25, 2022, from https://www.who.int/bangladesh/activities/strengthening-vaccination-coverage/strengthening-vaccination-coverage

Strengthening vaccination coverage. (2022). www.who.int. Retrieved August 25, 2022, from https://www.who.int/bangladesh/activities/strengthening-vaccination-coverage/strengthening-vaccination-coverage

Tsu, V. D., Cernuschi, T., & LaMontagne, D. S. (2014). Lessons Learned from HPV Vaccine Delivery in Low-Resource Settings and Opportunities for HIV Prevention, Treatment, and Care Among Adolescents. *JAIDS Journal of Acquired Immune Deficiency Syndromes*, *66*(Supplement 2), S209–S216.

Watson-Jones, D., Mugo, N., Lees, S., Mathai, M., Vusha, S., Ndirangu, G., & Ross, D. A. (2015). Access and Attitudes to HPV Vaccination amongst Hard-To-Reach Populations in Kenya. *PLOS ONE*, *10*(6), e0123701. https://doi.org/10.1371/journal.pone.0123701

Modelling an Extraterrestrial Epidemic

Raywat Deonandan[1], Stefan Litvinjenko[2]

[1,2] Interdisciplinary School of Health Sciences, University of Ottawa

Correspondence: Raywat Deonandan. Email: rdeonand@uottawa.ca

Abstract

Panspermia is the theory that life has been transported between bodies in the solar system by means of asteroid or cometary impact. Assuming that panspermia is true, and that genetically related microbial life exists outside of our planet, then it is possible that such life could pose an infectious threat to the terrestrial biosphere. We offer several assumptions of the characteristics that such life might possess and extrapolate the likely epidemiological compartment approach to be applied when attempting to model the impact of an Earthly epidemic originating from an extraterrestrial pathogen.

Keywords: Panspermia, Epidemiology, Disease Modelling, Space, Exobiology, Astrobiology

1. Panspermia and the Cosmic Transit System

It is now an undeniable fact that terrestrial organisms can exist in both the lower and upper stratosphere (Griffin, 2004, Griffin, 2008, Shivaji et al., 2009, Smith et al., 2010, Yang et al., 2008, Yang et al., 2009). Strong evidence further supports the conclusion that multicellular organisms, like the tardigrade, can persist alive in the vacuum of interplanetary space (Rebecchi et al., 2009). In other words, the assumption that the existence of life is dependent upon conditions found on the habitable portions of Earth has been rendered incorrect by the identification of organisms capable of persisting in hostile, un-Earthlike environments. We call such organisms "extremophiles."

The existence of such extremophiles has brought back to mainstream discussion the fringe hypothesis of *panspermia*, which is the theory that life on this planet originated from microorganisms or chemical precursors of life present in outer space., While it is an idea originating in ancient times, panspermia has only known modern consideration since 1903, when Nobel prizewinning chemist Svante Arrhenius (Arrhenius, 1908) suggested that life on Earth might have originated from extraterrestrial sources. The original underlying thought was that interstellar material might have some organic component, which could have helped to seed life on this planet. The robustness of multicellular extremophiles has given some credence to the idea that the complexity of such cosmic organic material could be something grander than simple molecules, perhaps advancing to something resembling a single-celled organism.

Outer space is not the static, serene environment that many Earth-bound observers imagine it to be. Space is violent and full of collisions. Cometary and meteor impacts on one planet can rain down debris onto another planet (Donn,

1982). Indeed, much of the water in the inner solar system, including the Earth's oceans, might have resulted from repeated impacts with icy comets streaming in from the Oort cloud, or from impacts with ice meteors from the asteroid belt (Billings, 2014). Complex organic molecules aggregate on comets (Chang, 2015) and thus may also travel through the solar system on the cometary transit system. Cometary *panspermia* argues that comets are the carriers and distributors of cosmic life as well as the sites of replication of cosmic bacteria (Wickramasinghe, 2011).

The general *panspermia* theory came to global public prominence when the so-called "Allen Hills meteorite" (ALH84001), which was known from chemical analysis to have originated on Mars, and which likely was transferred to Earth via a violent meteor impact on Mars, showed signs of containing what some believed was a bacterial fossil (Thomas-Keprta et al., 2002). The rock was likely formed on the Martian surface some 4 billion years ago, and was ejected to Earth about 16 million years ago (Lapen et al., 2010). The ancientness of ALH84001 suggested that it would have left Mars when that planet was warmer and wetter, and therefore more welcoming to terrestrial norms of life. It also suggested that any Martian organisms alive on that rock might have either entered the terrestrial ecology or, more intriguing, might have ignited genesis on Earth.

Of the many arguments against the possibility of terrestrial life having originated off-world, one of the most compelling is that of Massimo Di Giulio (Di Giulio, 2010), who argued that since life on Earth went through many evolutionary stages, commencing with a protocellular stage, the initial off-world infection must have been protocellular, as well. A protocell is a collection of self-organized molecules, often lipids, proposed as a stepping stone to the origin of life. Yet experience with protocells suggests that they have extremely limited, if not null, infective power. A non-infective cell could not have triggered our Earthly genesis, as its ability to replicate, or to inspire the replication of others, is limited.

Despite such a rational argument to the contrary, mainstream acceptance of the panspermia hypothesis is growing. It is the core premise for several mass entertainment products, such as the 2000 motion picture, *Mission To Mars*. To some, the growing acceptance of panspermia represents a genuine research paradigm shift (Wickramasinghe and Trevors, 2013). It is nevertheless a dangerous idea, at least to the careers of its proponents. Its most vocal current champion, Sri Lankan astrobiologist Chandra Wickramasinghe, has provocatively suggested that common terrestrial lifeforms, such as the SARS virus and the alga spores present in the "red rain" of Kerala, India, are in fact alien species (Wickramasinghe et al., 2013), and has been derided for his beliefs by more traditional scientists (Lovgren, 2003).

Massimo Di Giulio's argument against panspermia assumes that in order for the panspermia theory to be valid, the organisms that would have traveled to Earth would have had to be complex in nature in order to survive, presumably because less complex progenotes (a hypothetical pre-life stage) would have likely liked the self-reparatory abilities necessary to endure the assaults of radiation and vacuum. While the extremophiles thus far identified that are able to persist in outer space are indeed complex, Di Giulio fails to consider the possibility of non-living genetic materials, and not organisms, traversing interplanetary space, perhaps in plain molecular form or wrapped in a very simple living organic package, such as a virus. In such a scenario, elements of extraterrestrial life could have contributed material to a nascent terrestrial ecology, rather than being its overt and sole source.

2. Panspermia and Disease

All proposed models of panspermia, from those positing off-world sources as the sole origin of Earthbound life to those allowing for a hybridization of geneses, necessarily suggest one implication, that life beyond Earth will be, in some ways at least, biologically similar to familiar terrestrial life. Therefore any alien lifeform arising from the same panspermic source will, to some degree, find purchase within our biosphere. And, conversely, a terrestrial organism would be able to interact with an alien ecology, perhaps even the digestion of alien foods or, in the case of single cell organisms, the incorporation of alien genetic material.

An obvious corollary to this realization is that biospheres originating from the same panspermic cosmic seed can not only exchange genetic material, but can be literally infected by each other's agents. Panspermia allows for the

existence of diseases from outer space, as Wickramasinghe creatively argued was the case for the SARS virus, and as aerospace student Ashley Dale suggested was the origins of Ebola:

> "There is always a chance the Ebola virus could have come from outside this planet at some point during the evolutionary process. We have meteorites from Mars landing on our planet every year, bacteria can survive this journey, we have already seen this in laboratory experiments simulating the extreme environment. Virus particles can also make it through undamaged so there is definitely a possibility something could have arrived back in the evolution of the planet that we are seeing now." (Young, 2014)

Similarly, astronomer Fred Hoyle had suggested that the 1918 Spanish influenza outbreak was the result of a virus that had fallen from space (Millar, 2000). Assuming that Wickramasinghe, Hoyle, and Dale are incorrect, and that all known diseases have banal terrestrial origins, then we have yet to experience a genuine alien epidemic. Should such a pathogen enter our biosphere, how would such an outbreak be modeled epidemiologically? How could we predict its spread and thus manage the outbreak from a public health standpoint?

We propose two possible types of alien infections: toxic and infectious. The former type can deleteriously affect a terrestrial lifeform upon contact. The latter can be transmitted between terrestrial lifeforms, thus creating an outbreak, a possible epidemic, or a possible pandemic. If infection by alien pathogens seems unlikely, given the vast evolutionary distance between organisms from different planets, consider the bacterium *Serratia marcescens*, which can pass from human beings to coral, despite the evolutionary distance between those two organisms. Infectious diseases are diabolical and adaptive monsters, often with a resourcefulness that stymies their multicellular victims and hosts.

The possibility of an infectious agent jumping from alien soil samples to the human biosphere has raised alarms in some sectors of the space science community. The International Committee Against Mars Sample Return (ICAMSR) has, since 2000, argued against any mission to the Red Planet which seeks to bring Martian material back to Earth, precisely to avoid the possibility of an alien epidemic.

ICAMSR's website implores us to consider the following passage from page 114 of Carl Sagan's 1973 book, *Carl Sagan's Cosmic Connection: An Extraterrestrial Perspective* (Sagan, 1973):

> "Precisely because Mars is an environment of great potential biological interest, it is possible that on Mars there are pathogens, organisms which, if transported to the terrestrial environment, might do enormous biological damage - a Martian plague, the twist in the plot of H. G. Wells' War of the Worlds, but in reverse. This is an extremely grave point. On the one hand, we can argue that Martian organisms cannot cause any serious problems to terrestrial organisms, because there has been no biological contact for 4.5 billion years between Martian and terrestrial organisms. On the other hand, we can argue equally well that terrestrial organisms have evolved no defenses against potential Martian pathogens, precisely because there has been no such contact for 4.5 billion years. The chance of such an infection may be very small, but the hazards, if it occurs, are certainly very high."

This is, of course, essentially the plot of the 1969 novel and 1971 film, *The Andromeda Strain*, in which a crashed satellite delivers to Earth micrometeoroid material that contains an alien pathogen, resulting in a fast spreading deadly epidemic.

Discussion of epidemics of alien diseases on Earth is, of course, the domain of extreme speculation and imagination. But it may not be the domain purely of science fiction, as it is seated in the facts of known science and delineated by the acknowledged limitations of life as we know it. Willerslev et al (Willerslev et al., 2003) argued that if an alien pathogen could enter our biosphere, it would imply three things. First, any extraterrestrial source of DNA must arise from ecological conditions similar to Earth. Second, that specialized pathogens must have extraterrestrial hosts similar to those of Earth. And third, that the extraterrestrial source must be close to Earth, to allow for minimal exposure of the genetic material to the hostile and denaturing forces of interplanetary space. Since we know of no planet, beyond the Earth itself, harbouring these conditions, the authors suggest that an alien disease is unlikely.

The arguments of Willerslev et al are diminished by at least two inconvenient truths. First, everything known about life is derived from a sample size of one: the Earth's biosphere. It may be foolhardy to impute universal rules about

cosmic organisms, such as their environmental limits, dimensions, robustness, and life cycles, from observing only the end product of billions of years of evolution on a single planet. Second, it must be acknowledged that organisms are not the only source of infections. We also must contend with strange infectious agents at the far horizon of what is considered life; things like prions.

Prions are small proteinaceous infectious disease-causing agents that are believed to be the smallest infectious particle They are neither bacterial nor fungal nor viral and contain no genetic material (Institute of Medicine Forum on Emerging, 2002). They can fold in multiple ways and can transmit their folding pattern to other proteins. Often, this infective behavior results in extreme fatality when the affected protein is in a living organism. Bovine Spongiform Encephalopathy (BSE), or "mad cow disease," and its human correlate, Creutzfeld-Jakob Disease (CJD) are terrifying incurable diseases caused by prions. Such proteins are technically not alive (though this depends upon one's definition of life), but they do evolve (Li et al., 2010). And, it should be noted, amino acids, which are the building blocks of proteins, and thus prions, have been found on comets (Atkinson, 2009). The possible arrival of an alien prion would violate no laws of biology or physics, nor would it conflict with anything that is known of terrestrial biology or organic chemistry.

Whether that epidemic is caused by a prion, a virus, a bacterium, or something more exotic, the increasing likelihood of a panspermic reality suggests that an Earthbound epidemic caused by an alien pathogen is worthy of epidemiologic and public health attention. Responding to such an epidemic requires epidemiologic modeling. But an alien disease poses some challenges to traditional modeling approaches. If such an epidemic were to befall us, it is advisable to know which of its characteristics are most critical to be studied, in order that useful modeling can be performed.

3. The Epidemiology of Aliens

The underlying assumption of our analysis is that the style of panspermia that would allow for alien diseases on Earth is that sibling biospheres would share a common genetic philosophy, meaning that an alien organism would also have at its cellular core a molecule coding for genetic information, an analogy for our DNA, if not actual DNA. Thus, the pathogen's mutation, like in Earthly cells, would be the reorganization of that genetic material in response to some environmental assault, most commonly solar or cosmic radiation.

3.1. Epidemiologic Modeling

Epidemiologists predict, manage, and help to control epidemics of terrestrial diseases by modeling their spread, thus enabling the marshalling of resources and the appropriate preparation of vulnerable populations. All models rely upon basic assumptions to define baseline parameters that allow for the projection of disease prevalence, incidence, and rate of spread. The utility of such models is obvious. They allow for such critical public health interventions as mass vaccination programs, or even help to determine whether extreme measures, such as mass quarantine, need to be implemented.

A variety of modeling approaches can be applied to infectious disease management, though we only consider the most basic examples for this analysis. For all models explored herein, we feel that four parameters are of particular relevance, and must be estimated: the basic reproductive number, which is the average number of cases that one case generates over the course of its infectious period; the proportion of the population who are susceptible to the disease; the average age at which the disease is contracted; and the average life expectancy of the population. Clearly, only the last parameter can be estimated or computed in absence of any knowledge of the disease. And none of these factors can be surmised about an alien infection without direct examination of a sample or of its observed effects on humans.

An additional assumption in all models considered in this paper is that the population's age distribution is stationary. In other words, in the absence of the disease, most people would live to that population's computed life expectancy, which is a valid assumption for most developed countries with low infant mortality. We also assume that the population mixes in a homogenous manner, with minimal clustering. Obviously, these two assumptions in no way reflect the reality of any known human population. In fact, as an epidemic progresses, the core

assumptions accelerate in their inapplicability as population age distributions become skewed, and as people change their travel and habitation behaviours in response to the threat of infection. So it must be remembered that disease models do not represent reality in all its nuances, but only to the extent that the models' behaviours provide useful insights for policy directives.

Stochastic epidemiologic models seek to estimate the probability distributions of selected disease outcomes, such as death, impairment, or recovery, as functions of various randomly (or pseudorandomly) fluctuating characteristics. A deterministic model, on the other hand, seeks to determine how portions of the population transition from one stage of the disease to the next. The most common of the deterministic models is the SIR model, which uses three compartments or stages: S ("susceptible") is the compartment of people not yet infected with the disease, or, more accurately, those capable of contracting the infection; I ("infected") is the compartment of individuals who have been infected and are capable of spreading it to others; and R ("recovered/removed") is the compartment of those who have been infected and then rendered unable to infect others or to become re-infected, either because of their deaths or immunization. In other words, S→ I → R.

The SIR model, then, uses a fixed population, wherein N = S(t)+I(t)+R(t). Derivatives of each function relative to time provide estimates of the change in the numbers in each compartment, and thus give us a fluid model of the flow of the epidemic from one compartment to the next.

A modification is the SIS model (S → I → S) in which those who recover from the disease are rendered susceptible yet again, as there is no acquired immunity. Another possibility for seriously infectious pathogens is the simple S → I model, in which susceptible individuals become both infected and infectious and remain so.

Some models include a fourth potential latency compartment, E, which describes those individuals who have been exposed to the disease, but are not yet ill, nor are they infectious. In other words, S → E → I → R. The E compartment does not include those that are asymptomatically infected. In reality, all infectious diseases have a latency period. But for some, its length is small enough to be mathematically negligible, at least to the extent that it has any meaningful effect on the larger model.

The utility of each model to an instance of an extraterrestrial infection depends upon the nature of that infection. The question now becomes, what are the critical characteristics of an unearthly pathogen that are essential to allow effective modeling?

3.2. Modeling an Alien Bug

In the event of an alien infection, the major mechanism of pathogenesis must be considered. Pathogenesis is distinct from infectivity inasmuch as the latter describes an agent's ability to infect, whereas the former describes its ability to cause disease. There are three possibilities: direct tissue invasion (much like many earthly parasites or fungi), immunologic enhancement or suppression (much like an allergy or even HIV), or toxin production (much like many bacterial diseases, such as botulism).

A handful of considerations must be acknowledged when embarking on a thought experiment to describe alien disease. First, it may be true that fundamental genetic incompatibility between Earthly and alien life might mean that our bodies would not recognize alien life as living, and vice versa; thus, an alien virus analog would be unable to use our DNA for self-replication. Second, due to such genetic incompatibility, it is possible that an Earthly host would not respond at all to an alien "infection." And third, a truly alien organism might be so physically incompatible with our bodies as to prevent it invading and infecting a human host. Despite these possibilities, we proceed under the assumption that *panspermia* implies a common biological heritage between terrestrial and alien life, thus allowing for physical and genetic compatibility necessary for infection.

To develop a model of an alien epidemic, the mode of disease transmission must be determined. On Earth, we often acquire infections through contact with an infectious person. Contact can be direct or indirect. HIV is transmitted through the most intimate of direct contact. Some infections can be acquired by touching a surface that was touched by a carrier. Or one can imbibe a droplet of fluid exhaled by a carrier, perhaps by inhalation or contact

with one's mucous membranes, which is how the common cold is spread. Non-contact methods of transmission include the vector-borne pathway, like that used by malaria, which uses the bite of a mosquito to spread itself.

In brief, modes of transmission can be either via contact or not requiring contact. Contact-based transmission is either by three avenues: direct physical contact, i.e. body surface to body surface, like that experienced in influenza or chlamydia infection; indirect (also called "fomite") contact, wherein contaminated articles are the medium by which infection is spread to susceptible persons, as in the spread of meningococcal meningitis by contact with contaminated utensils; and droplet contact, wherein relatively large (typically greater than 5 micrometers) droplets of respiratory fluid are exchanged via sneezing and coughing, as in the spread of the common cold.

Non-contact, or indirect, transmission can be subdivided into three types: "airborne", in which droplets of respiratory fluids less than 5 micrometers in size are spread by ventilation systems, as in the spread of Tuberculosis; "vehicle" transmission, in which a single contaminated source spreads the infection, as in a sick chef who spreads his illness via his food preparations; and "vector" transmission, which relies upon another organism, such as a mosquito, to spread the disease.

Each of these scenarios is nightmarish in the context of an extraterrestrial pathogen. If a prion is the expected culprit, then ingestion of some kind would be required, as the affected protein must be in close proximity with the proteins of the affected person. While terrifying, a prion epidemic might just be the most easily controlled, since the most important behavior for public health to control is ingestion.

Prions can enter a host's body mainly through ingestion, not just by eating, but also by the receipt of injections of protein-containing compounds. In theory, the receipt of any blood products represents an avenue for prion entry. Additionally, spontaneous mutations of previously normal, endogenous proteins could result in a prion disease. How an extraterrestrial prion could encourage mutation of terrestrial protein is, of course, unknown, but its possibility should not be easily ignored.

Further characteristics to consider are the disease's incubation period, virulence, and whether there is a limited period of communicability. A high degree of pathogenicity –the degree to which a disease kills its host-- seems likely for an alien menace, since it would not have evolved alongside human beings, and thus would not be able to enact the nuance of preserving a human host while also preserving its lethal qualities. Another interpretation is that there would not have been enough time for the pathogen and human host to have co-evolved alongside one another, thus lessening the ability of the host to defend him or herself from infection for an appreciable amount of time.

So, given what we know of extremophile behavior in vacuum, and applying assumptions about the evolutionary experiences of pathogens that had to endure the harshness of outer space, it seems that an extraterrestrial infection would likely have some predictable characteristics. First, any pathogen that is comet- or meteor-bonded would not require a natural reservoir to sustain itself. This suggests a high pathogenicity, since it would not have evolved an overwhelming necessity to sustain its host.

Second, basic genetic incompatibilities between biospheres suggest a less than optimal ability of a pathogen to act virally to hijack a host's cellular mechanism to mass produce itself. One result might be a very lengthy latency period. Admittedly, this reasoning falters if in fact the confounding factor is simply insufficient time for the alien pathogen to co-evolve alongside its new human host.

Third, given that an alien pathogen would have evolved in an unearthly environment with strange atmosphere, gravity, temperature, and surface materials composition, its ability to sustain itself on Earth outside of a host might be limited. On the other hand, the fact that it survived for a journey of millions of kilometers while embedded in rock or ice suggests that its ability to thrive outside a host might be extraordinary, at least for those pathogens resembling viruses that require a host environment. A cometary pathogen is likely to be more water-reliant, whereas a meteoric pathogen would have been embedded in rock, perhaps in a pocket of gas or fluid. In the final analysis, it seems likely then that such pathogens could be transmitted indirectly, meaning that they would not require direct contact between the carrier and a susceptible person to enact an infection.

The mechanism of infectivity is difficult to surmise. Direct tissue invasion seems unlikely, given that such an attack is possible by many earthly pathogens in part because of millions of years of co-evolution. The release of a toxin would also seem unlikely, given that toxin effectiveness is often a function of genetic fit, thus also requiring millions of years of co-evolution. Therefore, it seems most likely that an immunogenic response would be our undoing. While not a strict certainty, our immune systems might respond to an alien germ as it would a strange inorganic interloper: an allergic reaction, possibly fatal.

Guessing the re-infectivity ability of an alien disease is difficult indeed. Earthly diseases with high re-infectivity potential are ones that mutate quickly or that are difficult for human immune systems to identify. If we assume that physical structures on the surface of the alien pathogen are sufficiently disease-like to resemble Earthly antigens, and thus can trigger an immune response, then re-infectivity is dependent upon the disease's rate of mutation, such that the immune system would be fooled upon its second exposure to the disease. So, will an alien disease be able to mutate quickly? Or at all?

Consider that an organism that survived the harsh vacuum of space would have been exposed to more mutagenic radiation than most creatures on Earth could survive. It would therefore have to be extremely robust to mutation. Thus, it is unlikely to mutate on Earth, and would therefore have very poor re-infectivity potential.

Given these assumptions, the most appropriate deterministic epidemiologic model is, in our opinion, S → E → I → S, with the greatest unknown being the duration of the "E" latency compartment. Mind you, this analysis only applies if the immediate host is a human being. Should an alien pathogen find more comfortable residence within a non-human host, then the effects might be ecological, with selected species detrimentally affected, or, worse, zoonotic. In a zoonosis scenario, the alien pathogen could find a terrestrial non-human genome and physiology more attuned to its needs, then slowly acquire terrestrial genetic information, much like how an avian influenza virus can acquire genetic content from a human host. The result would be a pathogen better attuned to our biosphere, and thus much more likely to eventually infect humans, with a much higher probability of high infectivity, high re-infectivity, and high lethality.

4. Conclusion

There is some evidence that genesis on Earth may have been initiated off-world, suggesting that our biosphere shares characteristics with supposed biospheres on other planets. Via the interplanetary transit system of meteoric and cometary impact, it would then be highly likely that incredibly robust alien microscopic extremophiles are arriving on our planet. The extent to which those organisms could infiltrate our ecology is, of course, uncertain. But those that do have the potential to trigger disease epidemics with unknown parameters.

However, given some reasonable assumptions about such selective extremophilic pathogens, existing epidemiologic models can be used to better understand how such a disease would spread through human populations. The S → E → I → S deterministic model seems the best candidate for understanding and predicting an alien epidemic, with particular emphasis on what we expect to be a lengthy latency period.

Glossary

Basic reproductive number: the average number of secondary infections given the introduction of a single infectious case in a completely susceptible population.
Extremophiles: a microorganism adapted to sustain life and thrive in conditions of extreme temperature, acidity, alkalinity, or chemical concentration.
Incubation period: time interval between the exposure to infectious agent and the first appearance of symptoms
Infectious period: time interval during which the infected host can transmit the infectious agent.
Latency period: time interval between the exposure to an infectious agent and its detection in the host.
Oort cloud: an immense spherical cloud of icy objects that surrounds our solar system
Panspermia: the theory that life is distributed throughout the universe in the form of mediums which harbor microorganisms, of which may propagate under suitable environmental conditions.
Pathogenicity: the ability of an infectious agent to cause pathology or disease

Prions: A proteinaceous infectious agent that is neither bacterial, nor fungal, nor viral and contains no genetic material.

Robustness: organisms exhibiting adaptations to tolerate large changes in variables such as temperature, water availability, salinity or food availability etc.

Tardigrade: commonly referred to as 'water-bear', a water-dwelling, eight-legged, micro-animal capable to withstand tremendous temperatures, radiation, pressure, and food/water scarcity.

Virulence: the degree of pathogenicity of an infectious agent. In other words, a pathogen's ability to invade the tissue of a host. An organism is defined as being pathogenic or not, and, depending upon conditions, may exhibit differing levels of virulence.

Zoonotic/zoonosis: any disease of animals communicable to humans under natural conditions.

References

ARRHENIUS, S. 1908. *Worlds in the making : the evolution of the universe / by Svante Arrhenius ; translated by H. Borns,* London, Harper & Brothers.

ATKINSON, N. 2009. Amino acid found in Stardust comet sample. *The Universe Today*.

BILLINGS, L. 2014. *Rosetta Pours Cold Water on Cometary Origins of Earth's Oceans.* Scientific American.

CHANG, K. 2015. Rosetta's Philae Lander Discovers a Comet's Organic Molecules.

DI GIULIO, M. 2010. Biological evidence against the panspermia theory. *J Theor Biol,* 266, 569-72.

DONN, B. 1982. Comets: chemistry and chemical evolution. *J Mol Evol,* 18, 157-60.

GRIFFIN, D. W. 2004. Terrestrial microorganisms at an altitude of 20,000m in Earth's atmosphere. *Aerobiologia,* 20, 135-140.

GRIFFIN, D. W. 2008. None-spore forming eubacteria isolated at an altitude of 200,000m in Earth's atmosphere: extended incubation periods needed for culture based assays. *Aerobiologia,* 24, 1573-3025.

INSTITUTE OF MEDICINE FORUM ON EMERGING, I. 2002. The National Academies Collection: Reports funded by National Institutes of Health. *In:* KNOBLER, S., LEDERBERG, J. & PRAY, L. A. (eds.) *Considerations for Viral Disease Eradication: Lessons Learned and Future Strategies: Workshop Summary.* Washington (DC): National Academies Press (US)

Copyright © 2002, National Academy of Sciences.

LAPEN, T. J., RIGHTER, M., BRANDON, A. D., DEBAILLE, V., BEARD, B. L., SHAFER, J. T. & PESLIER, A. H. 2010. A younger age for ALH84001 and its geochemical link to shergottite sources in Mars. *Science,* 328, 347-51.

LI, J., BROWNING, S., MAHAL, S. P., OELSCHLEGEL, A. M. & WEISSMANN, C. 2010. Darwinian evolution of prions in cell culture. *Science,* 327, 869-72.

LOVGREN, S. 2003. Far-Out Theory Ties SARS Origins to Comet. National Geographic. *National Geographic News*.

MILLAR, S. 2000. Flu comes from outer space, claim scientists. *The Guardian*.

REBECCHI, L., ALTIERO, T., GUIDETTI, R., CESARI, M., BERTOLANI, R., NEGRONI, M. & RIZZO, A. M. 2009. Tardigrade Resistance to Space Effects: first results of experiments on the LIFE-TARSE mission on FOTON-M3 (September 2007). *Astrobiology,* 9, 581-91.

SAGAN, C. 1973. *The Cosmic Connection: An Extraterrestrial Perspective*, Anchor Press.

SHIVAJI, S., CHATURVEDI, P., BEGUM, Z., PINDI, P. K., MANORAMA, R., PADMANABAN, D. A., SHOUCHE, Y. S., PAWAR, S., VAISHAMPAYAN, P., DUTT, C. B., DATTA, G. N., MANCHANDA, R. K., RAO, U. R., BHARGAVA, P. M. & NARLIKAR, J. V. 2009. Janibacter hoylei sp. nov., Bacillus isronensis sp. nov. and Bacillus aryabhattai sp. nov., isolated from cryotubes used for collecting air from the upper atmosphere. *Int J Syst Evol Microbiol,* 59, 2977-86.

SMITH, D. J., GRIFFIN, D. W. & SCHUERGER, A. C. 2010. Stratospheric microbiology at 20 km over the Pacific Ocean. *Aerobiologia,* 26, 35-46.

THOMAS-KEPRTA, K. L., CLEMETT, S. J., BAZYLINSKI, D. A., KIRSCHVINK, J. L., MCKAY, D. S., WENTWORTH, S. J., VALI, H., GIBSON, E. K., JR. & ROMANEK, C. S. 2002. Magnetofossils from ancient Mars: a robust biosignature in the martian meteorite ALH84001. *Appl Environ Microbiol,* 68, 3663-72.

WICKRAMASINGHE, C. 2011. Bacterial morphologies supporting cometary panspermia: a reappraisal. *International Journal of Astrobiology,* 10, 25-30.

WICKRAMASINGHE, C., WALLIS, J., WALLIS, D. H. & SAMARANAYAKE, A. 2013. Fossil Diatoms in a New Carbonaceous Meteorite. *Journal of Cosmology,* 21, 9560–9571.

WICKRAMASINGHE, N. C. & TREVORS, J. T. 2013. Non-terrestrial origin of life: a transformative research paradigm shift. *Theory Biosci,* 132, 133-7.

WILLERSLEV, E., HANSEN, A. J., RØNN, R. & NIELSEN, O. J. 2003. Panspermia—true or false? *The Lancet,* 362, P406.

YANG, Y., ITAHASHI, S., YOKOBORI, S.-I. & YAMAGISHI, A. 2008. UV-resistant bacteria isolated from upper troposphere and lower stratosphere. *Biological Sciences in Space,* 22**,** 18-25.
YANG, Y., YOKOBORI, S.-I. & YAMAGISHI, A. 2009. Assessing Panspermia Hypothesis by Microorganisms Collected from The High Altitude Atmosphere. *Biological Sciences in Space,* 23**,** 151-163.
YOUNG, M. 2014. Ebola... The deadly virus from outer space causing misery on Earth. *The Daily Star*.

Uses of Artificial Intelligence in Psychology

Seema Irshad[1], Shabana Azmi[2], Nurjahan Begum[3]

[1] Assistant Professor, College of Medicine, King Faisal University, Al-Hasa, KSA
[2] Assistant Professor, Department of Psychology, Sindho-Kanho-Birsha University, West Bengal, India
[3] Assistant Professor, College of Medicine, King Faisal University, Al-Hasa, KSA

Correspondence: Seema Irshad, College of Medicine, King Faisal University, Al-Hasa, KSA, 31982.
Email: seemairshad81@gmail.com

Abstract
Machine learning has a new landscape for humanity in the area of artificial intelligence (AI). Artificial intelligence (AI) approaches have recently been developed to support mental health professionals, primarily psychiatrists, psychologists, and clinicians, with decision-making based on patients' historical data (e.g., clinical history, behavioral data, social media use, etc.). This article reviews developments in artificial intelligence (AI) technologies and their current and potential applications in clinical psychological practice. Issues associated with AI in the context of clinical practice, the potential risk for job loss among mental health professionals, and other ramifications associated with the advancement of AI technology are discussed. The advancement of AI technologies and their application in psychological practice have important implications that can be expected to transform the mental health care field. Psychologists and other mental health care professionals have an essential part to play in the development, evaluation, and ethical use of AI technologies.

Keywords: Artificial Intelligence, Mental Health, Expert Systems, Virtual Reality

1. Introduction

The science of psychology should not only help us to understand our human nature, but it should also help us in our practical affairs. Given the breadth of environments we design for ourselves, there is no limit to the number of domains where we might expect scientific knowledge of human nature to be of use.

Recent developments in cognitive psychology and associated sciences lead us to the conclusion that knowledge and information about human cognitive behavior are adequately advanced to enable its application in computer science and other practical domains. After World War II a wartime collaboration between natural scientists, engineers, and psychologists came major advances, not only with respect to the man-machine systems being designed but also concerning the psychological theory itself. Examples of the latter include the theory of signal detection, manual control theory, and a methodology for the design of cockpit instrument displays. In the last decade or so, these understandings and techniques have engulfed the main areas of human experimental psychology: perception, performance, memory, learning, problem-solving, and psycholinguistics.

Presently, people have gained incredible headway in different fields like neuroscience, quantum physical science, and cerebrum science with man-made reasoning continuing to arise. Numerous approaches to problem-solving have been studied and proposed in psychology, cognitive informatics, and computational intelligence (Matlin, 1998; Ormord, 1999; Rubinsyein and Firstenberg, 1995; Wang et al., 2006 Wang and Ruhe, 2007) as follows,: *Direct facts*, *Heuristic*, *Analogy*, *Hill climbing*, *Algorithmic deduction*, *Exhaustive search*, *Divide-and-conquer*, *Analysis, and synthesis*.)

The concept of "man-made consciousness" was first utilized by John McCarthy at Dartmouth Meeting in 1956. From that point forward, man-made consciousness (computer-based intelligence) has gone through three blasts during many years of the logical and innovative turn of events. As an essential enhancement to human insight, computer-based intelligence successfully expands the human cerebrum and augments its knowledge. Artificial intelligence and the human cerebrum corresponded and have been supporting each other forward.

The role of AI in psychological science is still underestimated by psychological science specialists. Sometimes psychologists reject the use of specialist structures in their fields of endeavor because they worry that the laptop will replace them. The AI has now not reached yet that stage of performance success in emulating simultaneously all pieces of human behavior, but researchers are on the right track to getting there (Klein, 1999).

The psychology of the human-computer interface is generally individual psychology: the study of a human behaving within a nonhuman environment (though, interestingly, interacting with another active agent). The focus of this article is therefore to review the uses of AI technologies that are applicable to activities in psychological practice and research. It is not feasible to present an exhaustive review of all AI technologies or applications in this article, however illustrative examples of AI technology applications that are currently being used or evaluated are described.

2. Preliminaries

Recent years have been marked by many developments in the field of psychology including developments in the field of artificial intelligence (AI). These developments have highlighted serious limitations in human rationality and shown that computers can be highly creative. With this development in the field of computers, we can witness negative effects in the field of psychology. But there are also some positive outcomes for psychologists who want to study creativity. Thus, AI opens up entirely new avenues for studying human creativity in the field of psychology.

Psychology is the science of <u>mind</u> and <u>behavior</u>. Psychology includes the study of <u>conscious</u> and unconscious phenomena, as well as feeling and <u>thought</u>. Psychologists seek an understanding of the emergent properties of brains, linking the discipline to <u>neuroscience</u>. As a social science, psychologists aim to understand the behavior of individuals and groups (Fernald, 2008; Hockenbury & Hockenbury, 2010). In 1890, William James defined psychology as "the science of mental life, both of its phenomena and their conditions." The American Psychological Association (APA) adds that it "embraces all aspects of the human experience, from the functions of the brain to the action of nations, from child development to care for the aged."

Cognitive psychology is the main branch of psychology that deals with machine learning and AI directly. Within this domain, applicability involves simulation-based environment learning, computer-based emotion recognition, intra-group social interaction simulations, cognitive behavioral therapies, computer-based psychiatric therapy, electronic inquiries as well as automatic output generation, and so on.

Figure 1: Shows branches of cognitive psychology and what are there different uses. From the figure, we can understand that cognitive psychology mainly has three branches i.e., (1) human experimental psychology (memory, attention, problem-solving, and language), (2) computer analogies information processing approach (Artificial Intelligence and computer simulation), (3) cognitive neuroscience (brain damage and effect on cognition)
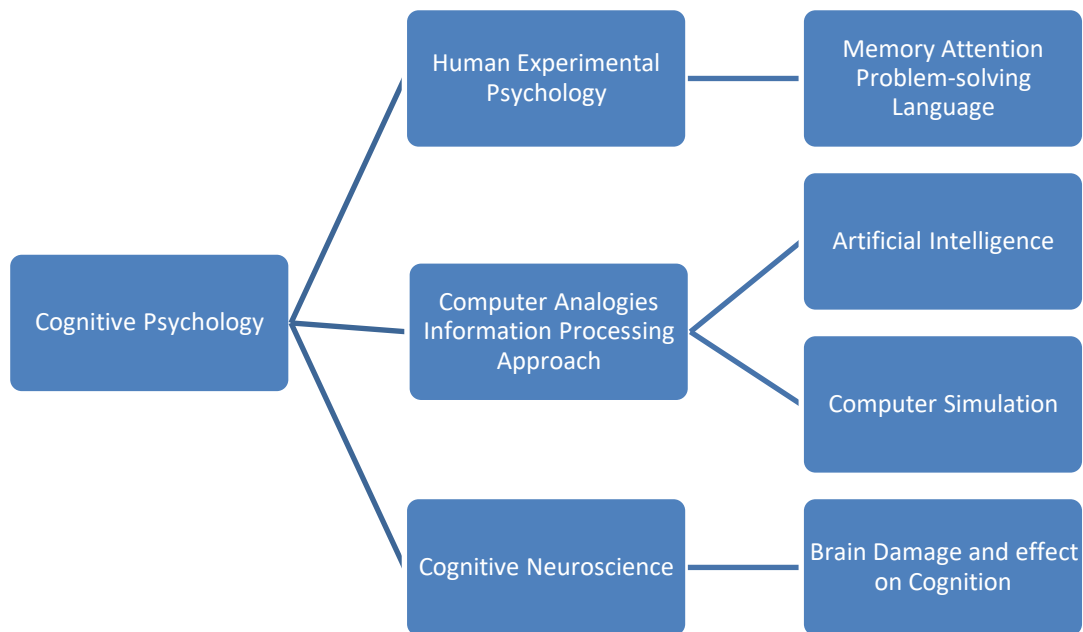
Figure 1: Branches of cognitive psychology and different uses

Cognitive psychology observes the individual as a processor of information, in much the same way that a computer takes in information and follows a program to produce an output. Cognitive function plays a very important role in daily life. Thus, cognitive deficits affect a wide range of areas such as daily life, and academic, vocational, and interpersonal areas (Goldberg & Chengappa, 2009; Green, Kern & Heaton, 2004). Impairment in cognitive function is known to be a pervasive feature of various mental disorders (Kurtz, 2016). Cognitive impairment manifests in various psychiatric disorders such as schizophrenia, bipolar disorder, depressive disorder, attention-deficit/hyperactivity disorder (ADHD), post-traumatic stress disorder (PTSD), and obsessive-compulsive disorder (OCD) (Millan, Agid, Brüne, Bullmore, Carte, Clayton et al. 2012).

The term Artificial Intelligence was developed by John McCarthy to explain a machine's ability to perform those functions that, if a human being will perform, would be considered intelligent, such as reasoning, learning, decision-making, adaptation, control, and perception. This definition of intelligence for a machine is highly challenged by many scientists because of its pyrotechnic and commercial appeal and use.

Russell and Norvig (2009) postulate the most accepted definition for AI today, which is, "the designing and building of agents that receive percepts from the environment and take actions that affect that environment." Moreover, the attention AI is currently receiving is very different from the one in the 1990s. At that time, the focus of the scientist was on logic-based AI, usually under the heading of knowledge representation (KR), whereas today's focus is on machine learning (ML) and statistical algorithms. Recently, it's impossible to find any other emerging technology which has attracted as much attention and gained similar significance in recent years as artificial intelligence (Fast & Horvitz, 2017). There are already numerous applications for AI in the fields of business analytics, medicine, commerce, administration, and education, as well as in the work- and everyday life of most people. But still, unlike any other technology, AI seems to elicit ambiguous and mixed feelings in users (Lichtenthaler, 2020). People are worried about a loss of control, have ethical concerns, and fear the negative impact of AI on work, i.e., the feeling of being redundant. However, they also have high hopes for AI in healthcare and education (Fast & Horvitz, 2017; Cave & Dihal, 2019).

Figure 2: Showing trends of research in psychology related to Artificial Intelligence (AI). From the figure, we can find out that from the 90s till today AI has been a fast-growing area of interest in the field of psychology.
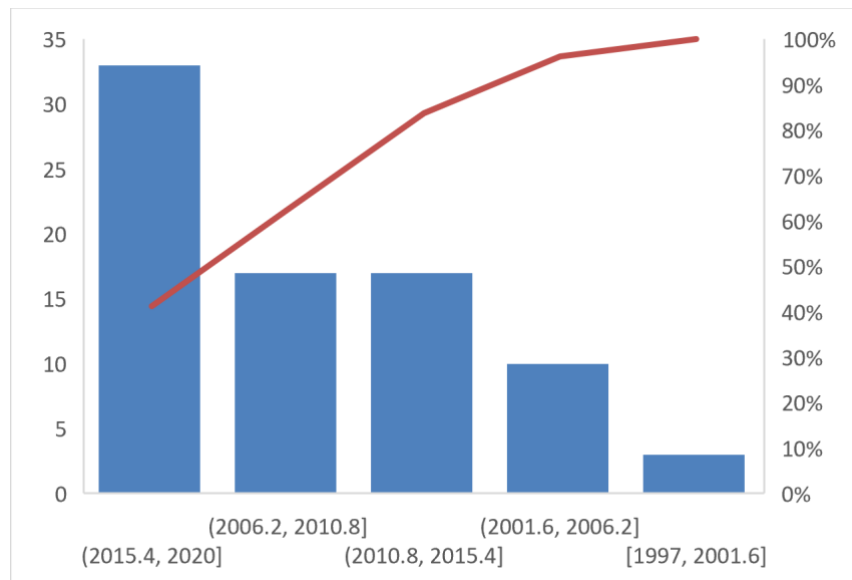
Figure 2: Trends of research in psychology related to Artificial Intelligence (AI)

The coupling of AI technology directly to the human brain has already emerged in the medical field as a way to repair and assist human cognitive or sensory-motor functions. For example, direct brain implants have already been used to control prosthetic limbs (Wolpaw, Birbaumer, McFarland, Pfurtscheller, & Vaughan,2002), and treat non-congenital (acquired) blindness (Naam, 2010). Brain-Computer Interfaces (BCIs) have also been used for nonmedical purposes to communicate with and control devices (Wolpaw, Birbaumer, Mc-Farland, Pfurtscheller, Vaughan, 2002)

Our smartphone has tons of AI-powered capabilities. These include facial recognition that unlocks your phone with your face (AI that sees). They also include voice assistants (AI that hears and speaks in natural language). And, don't forget, predictive text (AI that writes in natural language).

Psychology, particularly mental health, is one of the most recent areas of focus for AI. As AI extends its range, it is becoming increasingly crucial for psychologists, therapists, and counselors to understand the existing capacity and future potential for the technology to transform mental healthcare. Now the question arises, *how can AI help mental health professionals?* In this context, Luxton (2014) states that AI can simulate a practitioner, with capabilities beyond its human counterpart.

While AI can conduct therapy sessions, e-therapy sessions, and assessments autonomously, it can also assist human practitioners before, during, or after sessions. Physical assessments such as increased heart rate or temperature changes in response to challenging questions can provide valuable and insightful additional data for the clinician. Not only that, recording data, managing records, and triggering automatic follow-up actions would free up valuable time for the human professional. There are many examples where AI can be used in the field of psychology:

2.1. Detection and Computational Analysis of Psychological Signal

The *Detection and Computational Analysis of Psychological Signal* project use machine learning, computer vision, and natural language processing to analyze language, physical gestures, and social signals to identify cues for human distress.

2.2. Computer Science and Artificial Intelligence Laboratory

The *Computer Science and Artificial Intelligence Laboratory* at the Massachusetts Institute of Technology has successfully used AI to analyze digital video and identify nonverbal cues, it can also monitor trauma patients' breathing or young babies in distress in hospitals (Hardesty, 2012).

2.3. Watson Health

Watson Health, IBM's AI-enabled analysis tool aim is to bring together data, technology, and expertise to stand in for or supplement professional physical and mental healthcare, performing diagnoses and suggesting treatments (IBM, 2020).

2.4. RP-VITA

The *RP-VITA* robot monitors patients' well-being remotely while accessing their medical records. The multidisciplinary system provides support for psychological, neurological, cardiovascular, and critical care assessments and examinations (InTouch Health, 2020).

2.5. Mental Health Diagnostic Expert System

Mental Health Diagnostic Expert System uses advanced AI technology to encode expert knowledge of mental health disorders, which is then used for diagnoses and proposing treatments (Masri & Mat Jani, 2012).

3. Clinical Diagnostics and Decision Making

Recently to treat psychological problems various computer-assisted therapies where computers are used to deliver some aspects of psychotherapy or behavioral treatment directly to patients via interaction with a computer program, or delivered via the Internet, address at least some of the multiple challenges faced by psychologists and psychiatrists. Luxton (2014) introduces a computational clinician system concept, which is quite complete. Moreover, there are some initiatives devoted to special issues, such as the one from Morales et al. (2017) who use data mining techniques to distinguish between groups with and without suicide risk. Further, Fitzpatrick et al. (2017) present a fully automated conversational agent to deliver a self-help program for college students who identify themselves as having symptoms of anxiety and depression. Gloman et al. in 2019 describe an application that acts as a constant companion for clinically diagnosed patients who suffer psychological illnesses, supporting them during or after an ambulatory treatment. Besides, there are proposals concerning a wider range of issues. Kravets et al. (2017) present full-scale automation of establishing the diagnosis using fuzzy logic for modeling psychiatrist reasoning. D'Alfonso et al. (2017) discuss the development of the moderated online social therapy web application, which provides an interactive social media-based platform for recovery in mental health. To date, more than 100 different computer-assisted therapy programs have been developed for a range of mental disorders and behavioral health problems (Marks, Cavanagh & Gega, 2007). The complexity of content can range from very minimal, text-based formats (much like reading a brochure) to highly sophisticated, interactive, virtual reality formats (Rothbaum, Hodges, Anderson, 2002; Rothbaum, 2009).

Cognitive Remediation (CR) is one of the emerging computer-based therapy. CR has been defined and updated by the Cognitive Remediation Expert Working Group (CREW) in 2005 and 2012: "Cognitive remediation is an intervention targeting cognitive deficit (attention, memory, executive function, social cognition, or metacognition) using scientific principles of learning with the ultimate goal of improving functional outcomes." Early CR programs used paper and pencil for training, but recently, computer-assisted cognitive training programs have been developed and utilized: PSSCogRehab2012, Cogpack, Cogmed, Lumosity, and so on.

A therapist can structure CR in a way that focuses on a specific cognitive domain or encompasses multiple cognitive domains according to treatment goals. For example, among the various cognitive domains, the visuospatial function can be trained alone for 18 sessions (Kim&Kim, 2016) or comprehensive cognitive functions including not only neurocognitive but also social cognitive functions can be trained (Hogarty, Flesher, Ulrich, Carter, Greenwald, Pogue-Geile, et al. 2004). In addition, treatment effects were reported to be greater when CR was provided with other psychosocial rehabilitation programs (Wykes, Huddy, Cellard, McGurk & Czobor, 2011). CR is provided on a one-to-one or group basis, and the number of training sessions varies from program to program. In a study by Jang and Kim (2011), a CR program was provided for 18 sessions, and in other studies, training continued for 28 sessions (Eack, Greenwald, Hogarty, Cooley, DiBarry, Montrose, et al. 2009) or more

than 1 year (Choi & Medalia, 2005). According to a meta-analysis on the effectiveness of CR in patients with schizophrenia, training was carried out for an average of 12.8 weeks (McGurk, Twamley, Sitzer, McHugo & Mueser, 2007).

Attention bias modification (ABM) is a cognitive retraining program of the implicit attention biases that are known to be a causal information processing factor resulting in anxiety symptoms. Individuals in ABM are repetitively trained to shift their attention from negative to either neutral or positive stimuli (e.g., disgusted face to happy face) on a computer screen delivered either in the clinic or online at home. This intends to implicitly change negatively biased to more positively biased thought and habits, thereby reducing anxiety symptoms. Since the first study of ABM (MacLeod, Rutherford, Campbell, Ebsworthy & Holker, 2002), a Meta-analysis by Heeren, Mogoașe, Philippot & McNally (2015) found that ABM delivered in the clinic or laboratory-produced larger effect sizes than those delivered online. Following these meta-analyses, another RCT on ABM in those diagnosed with social anxiety disorder showed medium to large effects on both clinician ratings and self-reports of social anxiety symptoms (Naim, Kivity, Bar-Haim & Huppert, 2018).

Afonso, Rosa, Pereira, Weber, Hook, Albuquerque, and Papa in 2019 conducted a study to find out recurrence plot-based approach for Parkinson's disease (PD) identification. Their work proposes the application of recurrence plots to map the signals onto the image domain, which are further used to feed a Convolutional Neural Network for learning proper information that can help the automatic identification of PD. They have observed an improvement in accuracy concerning the classification of patients (i.e., mean recognition rates above 90%). The promising results showed the potential of the proposed approach toward the automatic identification of Parkinson's disease (Choi, Ha, I'm, Paek, and Lee, 2017).

In another approach to evaluating the efficacy and durability of a therapist-supported method for computer-assisted cognitive-behavioral therapy (CCBT) in comparison to standard cognitive-behavioral therapy (CBT), scientists assigned 154 medication-free patients with a major depressive disorder to either 16 weeks of standard CBT (up to 20 sessions of 50 minutes each) or CCBT using the "Good Days Ahead" program. The study findings indicate that a method of CCBT that blends Internet-delivered skill-building modules with about 5 hours of therapeutic contact was non-inferior to a conventional course of CBT that provided over 8 additional hours of therapist contact (Thase, Wright, Eells, Barrett, Wisniewski, and Balasubramani, 2018; Andrews, Cuijpers, Craske, McEvoy and Titov, 2010). A similar result has been found in another study where scientists have solid evidence for the efficacy of CCBT when the use of a therapeutic computer program is supported by a clinician or other helping professionals. Lower levels of efficacy or ineffectiveness typically have been found when computer programs are used as stand-alone treatments (Wright, Mishkind, Eells, and Chan 2019). Others have argued, that internet-delivered Cognitive Behavior Therapy (iCBT) produced a greater decline in the mean PHQ-9 score. There were also larger improvements in adherence, and a greater proportion engaging in beneficial physical activity. For people with mild to moderate depression and high levels of CVD risk factors, a freely accessible iCBT program (http://www.ecouch.anu.edu.au) produced a small, but robust, improvement in depressive symptoms, adherence, and some health behaviors (Glozier, Christensen, Naismith, Cockayne, Donkin, Neal, Mackinon, and Hickie, 2013).

Table 1 Presented the techniques and methods mostly used in conjunction with a computer (Frost. 2008).

Table 1: computer-based hypnotherapy usage

Problem	Recommended techniques	Used Methods
Stress	Self-hypnosis	Interactive web application
Anxiety	Hypnotherapy	Interactive web application
Depression	Relaxation therapy	Stand-alone application
Phobias in various forms	Meditation	Multimedia support
Cognitive issues (e.g. Positive thinking)	Stress management	Mini mixing desk

The use of expert systems in the mental health field has lagged behind application in the medical field, however, the applicability of AI-enhanced systems is being realized. For example, Masri and Mat Jani (2012) proposed an

AI-based Mental Health Diagnostic Expert System (MeHDES) that would encode human expert knowledge of mental health disorders into a knowledge base using rule-based reasoning techniques. Other practical applications of AI-enabled expert systems include assistance with the review of medication use, monitoring, and identification of contraindications (Bindoff, Stafford, Peterson, Kang, & Tenni, 2012). Moreover, the concept of artificial intelligent multiagent could also be used to have artificial "minds" work collectively to make decisions and provide solutions to problems in clinical practice or research.

The benefit of AI-based clinical decision support systems is that they can deal with high levels of complexity in data and can therefore assist practitioners with extracting relevant information and making optimal decisions. These systems can also help practitioners deal with uncertainty and help speed up decision-making. The application of AI-enabled clinical decision support systems can reduce demands on staff time and it can help reduce barriers to limited practitioner competence in particular areas. Moreover, as humans are susceptible to making mistakes as a result of cognitive errors and fatigue, AI technology has the potential to enhance capabilities and reduce human errors in clinical decision-making in all healthcare fields.

4. Therapeutic Computer Games

Computer games can be used for mental health care purposes such as skills training, behavior modeling, therapeutic distraction, and other therapeutic purposes. Some of the therapeutic benefits of computer games include increased engagement of patients, improved adherence to treatments, and reduced stigma associated with psychological treatment (Matthews & Coyle, 2010). Therapeutic computer games have also been shown to help adolescents improve self-confidence and problem-solving skills (Coyle, Mathews, Sharry, Nisbet, & Doherty, 2005). AI technology is already present in many commercial computer games and has more recently been applied to Internet-based online and social network games (Fujita & Wu, 2012). Machine learning concepts also help make the games customizable to the patient's needs. That is, AI technology can be used to direct gameplay so that the patient practices skills in needed areas, or patients can be coached by virtual intelligence agents within games or other virtual environments such as Second Life (Linden Research, Inc., 2013).

Some authors argued that games have the potential to increase the impact of Internet-based interventions by improving their reach and engagement potential (Zanetta, Zermatten, Billieux, Thorens, Bondolfi, Zullino, et al. 2011; Billieux, Linden, Achab, Khazaal, Paraskevopoulos, Zullino, et al. 2013). They make the point that the ubiquity and variability of the possible game designs (exergame biofeedback, cognitive training, etc.) would help to train or foster specific change mechanisms adapted from traditional evidence-based interventions. According to these authors, the number of trials in the field is still limited. In particular, only a few trials included comparisons between game-based and non-game-based interventions (Khazaal, Chatton, Prezzemolo, Zebouni, Edel, Jacquet, et al., 2013).

While the use of AI in psychology remains a relatively new field, the ubiquity of smartphone technology means that many of us have hardware within easy reach to run the increasing number of AI-inspired psychology apps e.g. woebot, biobase, youper, replica, and tess.

5. Conclusion

The presence of AI technology can already be found all around us. It is used in logistics planning, finance (to monitor and trade stocks and to conduct other banking functions), data analysis, manufacturing, internet search engines, automobiles, mobile device applications (e.g., Apple's Siri speech recognition software), aircraft guidance systems, and in a plethora of other applications. The present article addresses the feasibility of combining psychology and; in other words, how psychology can find support for specific tasks in computation. Approaches to artificial intelligence do not make the computational support more or less useful, and the limits of such an approach as a method for solving a given problem must be understood. From this perspective, AI can play a role as an add-on resource for therapeutic work, in addition to those that already exist.

The entire "cognitive revolution" in psychology during the 1960s led to an interest in computer models of human cognition. The further contributions of psychologists and other health care professionals in the study, development, and implementation of AI technology can be expected. Some of the areas to which psychologists and others in the mental health care field may contribute include research toward the development of new and creative approaches to designing AI technologies, laboratory and field evaluation of AI systems, and the study of how humans and AI interact with each other.

As discussed in this article, there are many practical applications of AI technology that may serve to benefit patients, health care providers, and society by enhancing care, increasing efficiency, and improving access to quality services. There is, nonetheless, the risk of this technology having negative implications as well. In the near term, specific applied use and collaboration with AI-enabled systems that serve to assist mental health care professionals can be expected. In the not-so-distant future, the widespread use of the AI technologies discussed in this article may be commonplace. Psychologists and all mental health care professionals must therefore be prepared to embrace and guide the use and study of AI technologies for the benefit of patients, the profession, and society as a whole.

References:

Afonso, L. C. S., Rosa, G. H., Pereira, C. R., Weber, S. A. T., Hook, C., Albuquerque, V. H. C., Papa, J. P. (2019). "A recurrence plot-based approach for Parkinson's disease identification." *Future Generation Computer Systems*, 94:282-292.

Andrews G., Cuijpers P., Craske M.G., McEvoy P., Titov N. (2010). Computer therapy for anxiety and depressive disorders is effective, acceptable, and practical health care: a meta-analysis. *PLoS One.* 13;5(10):e13196. DOI: 10.1371/journal.pone.0013196. PMID: 20967242; PMCID: PMC2954140.

Billieux, J., Van der Linden, M., Achab, S., Khazaal, Y., Paraskevopoulos, L. Zullino, D. et al. (2013). "Why do you play World of Warcraft? An in-depth exploration of self-reported motivations to play online and in-game behaviors in the virtual world of Azeroth." *Comput Hum Behav.* **29**:103–9. doi: 10.1016/j.chb.2012.07.021

Bindoff, I., Stafford, A., Peterson, G., Kang, B. H., & Tenni, P. (2012). The potential for intelligent decision support systems to improve the quality and consistency of medication reviews. *Journal of Clinical Pharmacy and Therapeutics,* 37, 452– 458. doi:10.1111/j.1365-2710.2011. 01327.x

Cave, S., Dihal, K. (2019). Hopes and fears for intelligent machines in fiction and reality. *Nature Machine Intelligence*. 1, 74–78.

Choi, J. Medalia, A. (2005). "Factors associated with a positive response to cognitive remediation in a community psychiatric sample." *Psychiatr Serv.* 56:602–4.10.1176/appi.ps.56.5.602

Coyle, D., Matthews, M., Sharry, J., Nisbet, A., & Doherty, G. (2005). Personal investigator: A therapeutic 3D game for adolescent psychotherapy. *Interactive Technology and Smart Education*, 2, 73– 88. doi:10.1108/17415650580000034

Eack, S. M., Greenwald, D. P., Hogarty, S. S., Cooley, S. J., DiBarry, A. L., Montrose D. M. et al. (2009). Cognitive enhancement therapy for early-course schizophrenia: effects of a two-year randomized controlled trial. *Psychiatr Serv.* 60:1468–76. 10.1176/ps.2009.60.11.1468

Fast, E., Horvitz, E. (2017). Long-term trends in the public perception of artificial intelligence. *Proceedings of the AAAI Conference on Artificial Intelligence*, 31, 963–969. https://ojs.aaai.org/index.php/AAAI/article/view/10635

Fernald, L. D. (2008). *"Psychology: Six perspectives" (pp.12–15). Thousand Oaks, CA: Sage Publications.*

Fujita, H., & Wu, I. C. (2012). A special issue on artificial intelligence in computer games: AICG. *Knowledge-Based Systems*, 34, 1–2. DOI: 10.1016/j.knosys.2012.05.014

Glozier, N., Christensen, H., Naismith, S., Cockayne, N., Donkin, L., Neal, B. et al. (2019). "Internet-Delivered Cognitive Behavioural Therapy for Adults with Mild to Moderate Depression and High Cardiovascular Disease Risks: A Randomised Attention-Controlled Trial." *PLoS ONE* 8(3): e59139. https://doi.org/10.1371/journal.pone.0059139

Goldberg, J. F., Roy Chengappa, K. N. (2009). "Identifying and treating cognitive impairment in bipolar disorder," *Bipolar Disord*,11:123–37. 10.1111/j.1399-5618.2009. 00716.x

Green, M. F., Kern, R. S., Heaton, R. K. (2004). "Longitudinal studies of cognition and functional outcome in schizophrenia: Implications for MATRICS," *Schizophr Res,* 72:41–51.

Hakamata, Y., Lissek, S., Bar-Haim, Y., Britton, J. C., Fox, N. A., Leibenluft, E. et.al. (2010). Attention bias modification treatment: a meta-analysis toward the establishment of novel treatment for anxiety. *Biol Psychiatr.* 68:982–90. 10.1016/j.biopsych.2010.07.021

Heeren, A., Mogoașe, C., Philippot, P., McNally, R. J. (2015). "Attention bias modification for social anxiety: a systematic review and meta-analysis." *Clinical Psychol Rev.* 40:76–90. 10.1016/j.cpr.2015.06.001

Hockenbury & Hockenbury (2010). Psychology. Worth Publishers.

Hogarty, G. E., Flesher, S., Ulrich, R., Carter, M., Greenwald, D., Pogue-Geile M. et al. (2004). Cognitive enhancement therapy for schizophrenia: effects of a 2-year randomized trial on cognition and behavior. *Arch Gen Psychiatr,* 61:866–76.

Jang, H. J., Kim, M. S. (2011). The effect of computerized attention training on the improvement of cognitive functions in patients with schizophrenia. *Korean J Clin Psychol.* 30:803–23. 10.15842/kjcp.2011.30.3.010

Khazaal, Y., Chatton, A., Prezzemolo, R., Zebouni, F., Edel, Y., Jacquet, J. et al. (2013). Impact of a board-game approach on current smokers: a randomized controlled trial. *Subst Abuse Treat Prev Policy.* **8**:3. doi: 10.1186/1747-597X-8-31747-597X-8-3

Kim, J. H., Kim, M. S. (2016). The effect of visuospatial rehabilitation on the visuospatial function and attention in patients with schizophrenia. *Korean J Clin Psychol.* 35:843–57. 10.15842/kjcp.2016.35.4.012

Kurtz, M. M. (2016). Cognitive remediation for psychological disorders. *Cogn Remediat Improv Funct Outcomes.* 1–12.

Lichtenthaler, U. (2020). Extremes of acceptance: Employee attitudes toward artificial intelligence. *Journal of Business Strategy*, 41, 39–45.

Linden Research, Inc. (2013). Second Life (Version 1.3.2). Retrieved fromhttp://secondlife.com/

Luxton, D. D. (2014). Artificial intelligence in psychological practice: Current and future applications and implications. *Professional Psychology: Research and Practice, 45*(5), 332–339.

MacLeod C, Rutherford E, Campbell L, Ebsworthy G, Holker L. (2002). Selective attention and emotional vulnerability: assessing the causal basis of their association through the experimental manipulation of attentional bias. *J Abnorm Psychol*.111(1):107-23. PMID: 11866165.

Masri R. Y., Mat Jani H. (2012). Employing artificial intelligence techniques in Mental Health Diagnostic Expert System. *In ICCIS: International Conference on Computer & Information Science* (Vol. 1, pp. 495– 499). New York, NY: IEEE.

Matlin, M.W. (1999). *Cognition (4th ed.), Harcourt Brace College Publishers, NY, USA.*

Matthews, M., & Coyle, D. (2010). *The role of gaming in mental health. The use of technology in mental health: Applications, ethics and practice (Vol. 40, pp. 134 –142).*

McGurk, S. R., Twamley, E. W., Sitzer, D. I., McHugo, G. J., Mueser, K. T. (2007). A meta-analysis of cognitive remediation in schizophrenia. *Am J Psychiatr.* 164:1791–802. 10.1176/appi.ajp.2007.07060906

Millan, M. J., Agid, Y., Brüne, M., Bullmore, E. T., Carter, C. S., Clayton N. S. et al. (2012). "Cognitive dysfunction in psychiatric disorders: characteristics, causes and the quest for improved therapy." *Nat Rev Drug Discov*.11:141. 10.1038/nrd3628

Naam, R. (2010). More than human: Embracing the promise of biological enhancement. New York, NY: Broadway Books.

Naim, R., Kivity, Y. Bar-Haim, Y., Huppert, J. D. (2018). Attention and interpretation bias modification treatment for social anxiety disorder: A randomized clinical trial of efficacy and synergy. *J Behav Ther Exp Psychiatry.* 59:19–30. 10.1016/j.jbtep.2017.10.006

Ormrod, J.E. (1998). *Human learning, (3rd ed.), Prentice-Hall Inc.*

Rothbaum B. O., Hodges L., Anderson P. L., Price L., Smith S. (2002). Twelve-month follow-up of virtual reality and standard exposure therapies for the fear of flying. *J Consult Clin Psychol.* 70(2):428-32. doi: 10.1037//0022-006x.70.2.428. PMID: 11952201.

Rothbaum, B. O. (2009). Using virtual reality to help our patients in the real world. *Depression and Anxiety, 26* (3), 209–211. https://doi.org/10.1002/da.20556

Rubinstein, M. F. Firstenberg, I. R. (1995). *Patterns of problem-solving, Prentice Hall, Englewood, NJ, USA.*

Russell, S., Norvig, P. (2009). Artificial Intelligence: *A Modern Approach*, 3rd Edn. Saddle River, *NJ: Prentice Hall*

Thase, M. E., Wright, J. H., Eells, T. D., Barrett, M. S., Wisniewski, S. R., Balasubramani, G. K. et al. (2018). Improving the efficiency of psychotherapy for depression: computer-assisted versus standard cbt. *Am J Psychiatry*. 175(3):242–250. https://doi.org/10.1176/appi.ajp.2017.17010089

Wang, Y. (2002). The real-time process algebra (RTPA). *Annals of Software Engineering: An International Journal,* 14 (2002), pp. 235-274.

Wang, Y., Ruhe, G. (2007). The cognitive process of decision making. *International Journal of Cognitive Informatics and Natural Intelligence,* 1 (2), pp. 73-85.

Wolpaw, J. R., Birbaumer, N., McFarland, D. J., Pfurtscheller, G., &Vaughan, T. M. (2002). Brain-computer interfaces for communication and control. *Clinical Neurophysiology*, 113, 767–791. doi:10.1016/S1388-2457(02)00057-3.

Wright J. H., Mishkind M., Eells T. D., Chan S. R. (2019). Computer-Assisted Cognitive-Behavior Therapy and Mobile Apps for Depression and Anxiety. Curr Psychiatry Rep. 27;21(7):62. DOI: 10.1007/s11920-019-1031-2. PMID: 31250242.

Wykes, T., Huddy, V., Cellard, C., McGurk, S. R., Czobor, P. (2011). A meta-analysis of cognitive remediation for schizophrenia: methodology and effect sizes. *Am J Psychiatr.* 168:472–85. 10.1176/appi.ajp.2010.10060855

Zanetta Dauriat, F., Zermatten, A., Billieux, J., Thorens, G., Bondolfi, G., Zullino, D. et al. (2011). "Motivations to play specifically predict excessive involvement in massively multiplayer online role-playing games: evidence from an online survey." *Eur Addict Res.*, **17**:185–9. doi: 10.1159/000326070000326070

Anesthesia Management of Sectio Caesarian Patients with Eisenmenger Syndrome and Fetal Distress

Indriasari[1], Iwan Fuadi[1], Reza W. Sudjud[1], Irvan[1]

[1] Department of Anesthesiology and Intensive Therapy, Faculty of Medicine, University of Padjadjaran, General Hospital Hasan Sadikin Bandung

Abstract

Brief overview: 27 year old woman, G2P1A0 gravida 35-36 weeks with congenital heart disease (ventricular septal defect) that progresses to Eisenmenger syndrome, respiratory failure and fetal distress underwent an emergency caesarean section. Management: Anesthesia management was performed under general anesthesia with post-operative care in ICU. Prior to induction, pre-oxygenated with 100% O2 was performed, followed by Rapid Sequence Induction with Ketamine 70 mg, and Rocuronium 50 mg. After the patient had fallen asleep the Sellick maneuver was performed, intubated with ETT no. 6.5. Anesthesia maintenance with Sevoflurane 1 vol%, and 100% oxygen. Fentanyl 50 μg was given after the baby was born. Outcome: In this patient, general anesthetic technique was preferred over regional anesthetic technique for better maternal and fetal outcomes because this patient had already experienced respiratory failure and fetal distress, so a caesarean section was decided as soon as possible. The operation lasted for two hours, with SpO2 during the operation reaching 85% and a live baby boy was born with APGAR scores at the 1st ,3rd and 5th minute 6. Postoperatively, the patient remained intubated and was transferred to the intensive care unit with vital signs blood pressure 122/80 mmHg, pulse 96 beats per minute, SpO2 82-85%.

Keywords: Congenital Heart Disease, Cesarean Section, Eisenmenger Syndrome, General Anesthesia, Pregnant Women

1. Introduction

Eisenmenger syndrome (SE) is a heart disease disorder with pulmonary hypertension and bidirectional blood flow. This case was first reported by Victor Eisenmenger in 1897 in a 32-year-old male patient with a ventricular septal defect and in 1958 by Paul Wood in a larger sample of a population of patients with congenital heart disease with increased vascular resistance. Congenital heart diseases that can cause Eisenmenger syndrome include ventricular septal defect, atrial septal defect, atrioventricular septal defect, persistent ductus arteriosus, transposition of the great vessels. (Duan et al., 2016; Yuan,2016)

With this structural defect, pulmonary blood flow will increase in the early phase, which will then cause increased shear stress on pulmonary blood flow resulting in an increase in pulmonary blood pressure and fibrosis. This situation will cause changes in deoxygenated blood flow from the right side of the heart to systemic blood flow

which will cause cyanosis and decreased pulmonary blood flow. The final phase of this condition is called Eisenmenger syndrome (Lopez et al., 2020; Yentis & Steer, 1998).

Obstetric patients with Eisenmenger syndrome have a mortality rate of 30-70%. Eighty percent of deaths occur on the second and thirtieth day after parturition (Cole, Cross, & Dresner, 2001; Dasgupta, Das, Majumdar, & Basu, 2016; Yuan, 2016). In pregnant women with Eisenmenger syndrome, a decrease in systemic vascular resistance that occurs according to the physiological changes of pregnant women will be followed by an increase in vascular vascular resistance which will cause an increase in pressure on the right side of the heart and the occurrence of shunts and hypoxemia (Lopez et al., 2020). This will increase the mortality rate in patients with Eisenmenger syndrome. Eisenmenger syndrome is included in category IV in the WHO pregnancy risk criteria and is a contraindication to pregnancy (Duan et al., 2016; Suk-Young et al., 2007). Where the cause of death can be caused by hypovolemia, arrhythmia, myocardial infarction, and thromboembolism. Therefore, prevention and termination of pregnancy are recommended for pregnant women with Eisenmenger syndrome (Duan et al., 2016; Lopez et al., 2020; Popat & Russell, 2001; Yuan, 2016).

The goal of anesthetic management is to prevent hemodynamic changes and decrease systemic vascular resistance to prevent shunting of blood flow from the right heart to the left (Cole et al., 2001; Dasgupta et al., 2016). Eisenmenger syndrome patients with advanced pregnancy require multidisciplinary coordination involving the anesthesiology, obstetrics, pulmonology, cardiology, neonatology and intensivist departments to improve the prognosis for both mother and baby where hypoxaemia that occurs will cause stunted fetal growth and premature delivery which will increase the rate of morbidity and mortality in infants (Duan et al., 2016; Lopez et al., 2020; Popat & Russell, 2001).

2. Cases

The patient was identified as a 27-year-old woman with gestational status G2P1A0 gravida 34-35 weeks. The patient came with complaints of shortness of breath since 3 days of SMRS which was felt to be getting heavier on 1 day before hospital admission. Complaints of shortness of breath felt continuously, did not decrease with rest, improved with a semi-sitting position. Complaints of shortness of breath did not decrease with the right and left side position. Complaints of shortness of breath accompanied by cough but not accompanied by fever.

History of shortness of breath during strenuous activity that improved with rest was felt since 2 years before hospital admission. History of frequent awakening at night 2-3 hours after falling asleep due to shortness of breath where this complaint improved with a sitting position since 1 week of before hospital admission. The patient is more comfortable sleeping using 2 pillows since 3 days of before hospital admission. The patient has a history of swelling in both legs that comes and goes since 1 month before hospital admission.

The patient has a history of bluish coloration of the lips and fingertips when crying or doing activities. The patient's history of growth and development is known to be smaller than his age. The patient is known to have congenital heart defects since childhood. The patient is not routinely checked for treatment for heart disorders. History of intermittently stopping breastfeeding when the patient still in childhood is unknown. The patient's parental pregnancy history is also unknown. In her first pregnancy, the patient was admitted to the RSHS 3 years ago and underwent Sectio Caesarea surgery, echocardiography examination and was advised to do right heart catheterization but the patient never came back for control. The patient does not routinely take medication to treat his complaints. The patient also never went to the doctor for control during his second pregnancy, only checked twice with the midwife. The history of the patient's first child, a woman with a birth weight of 1900 grams, born prematurely, was born by caesarean section.

The patient came to the hospital with somnolence, blood pressure at 100/70 mmHg, with a pulse rate of 96 beats per minute. The patient experienced respiratory distress with an increase in respiratory rate of 40-42 breaths per minute and a decrease in SpO2 to 70% with a non-rebreathing mask of 15 lpm. Based on physical examination, the patient's anthropometric status was weight 40 kg, height 155 cm and an additional heart sound was found with a grade 3/6 systolic murmur at the lower left border of the sternal line.

Upon admission, the patient underwent laboratory examinations, chest X-rays, and COVID-19 PCR swabs. In the patient's laboratory results, a decrease in Hb was found at 11.0 and other laboratory results were within normal limits. The chest X-ray shows bilateral pneumonia and cardiomegaly without engorgement. The patient had an echocardiographic examination in 2018 with the results: Site solitus, Multiple VSD, perimembranous diameter 9-11 mm, Bidirectional shunt dominant R to L shunt, PDA (-), Dilated RA, RV, Normal LV systolic function with global normokinetic at rest, High probability of PH, Suspect ASD secundum, LVEF : 61%

Based on preoperative examination, patient was diagnosed with G2P1A0 gravida 35-36 weeks + Maternal Congenital Heart Disease + Eisenmenger Syndrome + Respiratory Failure + Former Cesarean Section + Fetal Distress with physical status ASA IV E.

Upon arrival in the operating room, the patient's clinical condition deteriorated. Standard monitoring equipment was installed, namely oxygen saturation, electrocardiography, blood pressure, temperature and vital signs were assessed. Patients with somnolence consciousness, blood pressure 97/68 mmHg, pulse rate 102 beats per minute, respiratory rate 45 breaths per minute, SpO2 60% with non-rebreathing mask oxygen 15 liters per minute. The fetal heart rate was examined with the results of 120-80-100 beats per minute, irregular.

Anesthesia management in our patients was planned under general anesthesia and in the postoperative cardiovascular intensive care room. Pre-oxygenated with 100% O2, and Rapid Sequence Induction with Ketamine 70 mg, Rocuronium 50 mg, Sellick maneuver, intubation with ETT no. 6.5. Anesthesia maintenance with Sevoflurane 1 vol%, given oxygen: air with FiO2 100%. After the baby was born, Fentanyl was given 50 μg.

The operation lasted for two hours, the hemodynamic duration of surgery SpO2 reached 85% (Figure 2). The baby boy was born alive with APGAR scores in the 1st minute 3 and 5th minute 6 and the birth weight was 2200 grams. Oxytocin was given 20 IU in RL 500 ml 20 drops per minute after the baby was born. Intraoperative bleeding 400 ml with a urine output of 50 ml. The patient received 500 ml of crystalloid fluid intraoperatively.

Postoperatively, the patient remained intubated with sedative and was transferred to the cardiovascular intensive care unit with vital signs, blood pressure 122/80 mmHg, pulse 96 beats per minute, SpO2 82-85% with Jackson Reese 10 liters per minute. The patient received the analgesic fentanyl 25 μg/hour IV and was transferred to the cardiovascular intensive care unit. The patient is then treated in the intensive care unit with close monitoring of hemodynamic conditions, respiratory conditions and complications that can occur. During treatment in the cardiovascular intensive care unit, the patient experienced complications of Hospital Acquired Pneumonia and a pulmonary hypertensive crisis occurred. On the 11th day the patient worsened and died in the cardiovascular intensive care unit.

3. Discussion

Pregnancy is a condition that causes hemodynamic changes in the body to meet the increased metabolic needs of the mother and fetus. Changes in cardiovascular physiology that occur during pregnancy will affect the morbidity and mortality rate that occurs in pregnant women with Eisenmenger syndrome such as heart failure, syncope, and death (Duan et al., 2016; Lopez et al., 2020). In the cardiovascular system, there will be an increase in intravascular volume, an increase in cardiac output, a decrease in systemic vascular resistance and hypotension due to the aortic caval syndrome (Arif, Wahab, & Tofani, 2019).

In the first trimester there is a 40-70% decrease in systemic vascular resistance resulting in an increase in stroke volume and cardiac output. This increase in cardiac output reaches its peak in the second trimester, reaching 25-50% and is followed by an increase in pulse rate. Blood volume will increase by 30-50% until the end of the trimester (Gehlot, Verma, & Raiger, 2021). The progressive increase in plasma volume will increase the burden on the right ventricle so that right heart failure can occur (K. W. Arendt & Lindley, 2019; Arif et al., 2019). In the third trimester, the supine position will reduce cardiac output due to compression of the inferior vena cava due to the enlarged uterus (Gehlot et al., 2021).

During labor, uterine contractions will increase stroke volume, cardiac output up to 30-50% higher before the onset of labor. This condition of hemodynamic changes cannot be tolerated by patients with congenital heart disease conditionsl (Canobbio et al., 2017; Rao & Ginns, 2014). Where 80% of deaths occur between the second and thirtieth day after delivery (Cole et al., 2001).

Table 1: Physiological changes in pregnancy (Arif et al., 2019)

Parameter	Changes
Neurologiy	
MAC	-40%
Respiratory	
Oxygen consumption	+20-50%
Airway obstruction	-35%
FRC	-20%
Minute Ventilation	+50%
Tidal Volume	+40%
Respiratory Rate	+15%
PaO2	+10%
PaCO2	-15%
HCO3	-15%
Cardiovascular	
Blood Volume	+35%
Plasma Volume	+45%
Cardiac Output	+40%
Stroke Volume	+30%
Heart Rate	+20%
Sistolic Blood Pressure	-5%
Diastolic Pressure	-15%
Peripheral Vascular Resistance	-15%
Pulmonary Vascular Resistance	-30%
Hematology	
Hemoglobin	-20%
Thrombosit	-10%
Clotting Factor	+30%-50%

The main principle of the anesthetic technique used is to prevent hemodynamic changes that increase the right-to-left shunt and cause hypoxaemia (Cole et al., 2001). This can be done by preventing a decrease in systemic vascular resistance, venous return and cardiovascular depression (Gehlot et al., 2021). If there is a decrease in systemic vascular resistance, the right-to-left shunt will get worse which will trigger hypoxia and aggravate pulmonary hypertension where in pregnant women there has been an increase in cardiac output and pulmonary blood flow (Gurumurthy, Hegde, & Mohandas, 2012). Decreased functional residual capacity and increased oxygen demand due to pregnancy also predispose to maternal hypoxia (K. W. Arendt & Lindley, 2019; Arif et al., 2019).

Both general and regional anesthesia techniques have advantages and disadvantages, and both techniques carry the risk of increasing right-to-left shunts (Gehlot et al., 2021). The anesthetic technique chosen, both general and regional anesthesia, has the same principle, which is to maintain the flow of cardiac output and prevent a decrease in systemic vascular resistance (Arif et al., 2019; Gurumurthy et al., 2012). If regional anesthetic techniques are used, the advantage is that cardiovascular system depression can be avoided, but sympathetic nervous system blockade can occur which will cause a decrease in systemic vascular resistance which will increase the occurrence

of right-to-left shunts (Soefviana & Zulfariansyah, n.d.). In this case, the general anesthetic technique was chosen with the consideration that general anesthetic technique can provide better oxygenation than regional anesthesia technique because this patient has respiratory failure (K. W. Arendt & Lindley, 2019; Gehlot et al., 2021). The thing that must be considered is the use of anesthetic drugs that can reduce systemic vascular resistance such as volatile anesthetics, propofol, barbiturates. In this case, we used ketamine because ketamine does not reduce systemic vascular resistance so it is safe and effective in patients. Ketamine is also considered safe because it keeps spontaneous respiration and laryngopharyngeal reflex intact so that the patient can maintain his or her airway (Arif et al., 2019). The relaxant agent used is rocuronium at a dose of 0.9 -1.2 mcg/kgbw, due to its rapid onset of 60 seconds (Fawcett, 2019). Lipophilic opioids such as fentanyl are components of general anesthetics that can be used because they suppress the neuroendocrine stress response to surgery (Arif et al., 2019). The use of N2O gas should also be avoided because it can increase pulmonary vascular resistance (Gurumurthy et al., 2012; Yen, 2015).

After delivery, the filling volume of the heart increases significantly because of the loss of compression of the inferior vena cava by the enlarging uterus. This will cause an increase in stroke volume, pulse rate, cardiac output which will increase the risk of heart failure (Katherine W. Arendt, Muehlschlegel, & Tsen, 2012). In general, pregnant women with unstable hemodynamic conditions before delivery will experience a worsening in the early postpartum period, namely in the first 24-48 hours, therefore an intensive monitoring room is needed where these patients receive treatment in the cardiac intensive care room (K. W. Arendt & Lindley, 2019; Canobbio et al., 2017).

4. Conclusion

Anesthesia in pregnant patients with Eisenmenger syndrome requires appropriate perioperative anesthetic management. An anesthesiologist must prioritize maternal and fetal outcomes. Regional and general anesthetic techniques have advantages and disadvantages. In this patient, general anesthesia is preferred over regional anesthesia because of the better maternal and fetal outcomes because these patients already have respiratory failure and require anesthetic techniques that further reduce the decrease in systemic vascular resistance.

References

Arendt, K. W., & Lindley, K. J. (2019). Obstetric anesthesia management of the patient with cardiac disease. *International Journal of Obstetric Anesthesia*, *37*, 73–85. https://doi.org/10.1016/j.ijoa.2018.09.011

Arendt, K. W., Muehlschlegel, J. D., & Tsen, L. C. (2012). Cardiovascular alterations in the parturient undergoing cesarean delivery with neuraxial anesthesia. *Expert Review of Obstetrics & Gynecology*, *7*(1), 59–75. https://doi.org/10.1586/eog.11.79

Arif, S. K., Wahab, A., & Tofani, R. M. (2017). Manajemen Anestesia pada Kehamilan dengan Sindrom Eisenmenger. *JAI (Jurnal Anestesiologi Indonesia)*, *9*(1), 19. https://doi.org/10.14710/jai.v9i1.19821

Canobbio, M. M., Warnes, C. A., Aboulhosn, J., Connolly, H. M., Khanna, A., Koos, B. J., Mital, S., Rose, C., Silversides, C., & Stout, K. (2017). Management of Pregnancy in Patients With Complex Congenital Heart Disease: A Scientific Statement for Healthcare Professionals From the American Heart Association. *Circulation*, *135*(8). https://doi.org/10.1161/CIR.0000000000000458

Cole, P. J., Cross, M. H., & Dresner, M. (2001). Incremental spinal anaesthesia for elective Caesarean section in a patient with Eisenmenger's syndrome. *British Journal of Anaesthesia*, *86*(5), 723–726. https://doi.org/10.1093/bja/86.5.723

Dasgupta, S., Das, S., Majumdar, B., & Basu, S. (2016). Caesarean section in Eisenmenger's syndrome: anaesthetic management with titrated epidural and nebulised alprostadil. *Southern African Journal of Anaesthesia and Analgesia*, *22*(2), 65–67. https://doi.org/10.1080/22201181.2016.1145432

Duan, R., Xu, X., Wang, X., Yu, H., You, Y., Liu, X., Xing, A., Zhou, R., & Xi, M. (2016). Pregnancy outcome in women with Eisenmenger's syndrome: a case series from west China. *BMC Pregnancy and Childbirth*, *16*(1), 356. https://doi.org/10.1186/s12884-016-1153-z

Fawcett, W. J. (2019). Suxamethonium or rocuronium for rapid sequence induction of anaesthesia? *BJA Education*, *19*(12), 380–382. https://doi.org/10.1016/j.bjae.2019.09.001

Gehlot, R. Kr., Verma, D., & Raiger, L. K. (2021). A challenging case of a successful outcome of cesarean section with combined spinal–epidural technique in a parturient with Eisenmenger syndrome. *Ain-Shams Journal of Anesthesiology*, *13*(1), 6. https://doi.org/10.1186/s42077-021-00127-9

Gurumurthy, T., Hegde, R., & Mohandas, B. (2012). Anaesthesia for a patient with Eisenmenger′s syndrome undergoing caesarean section. *Indian Journal of Anaesthesia*, *56*(3), 291. https://doi.org/10.4103/0019-5049.98780

Lopez, B. M., Malhamé, I., Davies, L. K., Gonzalez Velez, J. M., Marelli, A., & Rabai, F. (2020). Eisenmenger Syndrome in Pregnancy: A Management Conundrum. *Journal of Cardiothoracic and Vascular Anesthesia*, *34*(10), 2813–2822. https://doi.org/10.1053/j.jvca.2020.02.053

Popat, M., & Russell, R. (2001). CORRESPONDENCE. *International Journal of Obstetric Anesthesia*, *10*(4), 332–333. https://doi.org/10.1054/ijoa.2001.0889

Rao, S., & Ginns, J. N. (2014). Adult congenital heart disease and pregnancy. *Seminars in Perinatology*, *38*(5), 260–272. https://doi.org/10.1053/j.semperi.2014.04.015

Soefviana, S., & Zulfariansyah, A. (2021). Anesthesic Management in Pregnant Woman with Eisenmenger Syndrome. *Jurnal Anestesi Obstetri Indonesia*, *4*(1), 26–34. https://doi.org/10.47507/obstetri.v4i1.51

Lee, S. Y. , Ko, J. S. , Jung, J. W. , Lee, S. M. , Kang, I. S. , & Park, S. W. , et al. (2007). Perioperative management of a parturient with eisenmenger's syndrome undergoing cesarean section :a case report.

Yen, P. (2015). ASD and VSD Flow Dynamics and Anesthetic Management. *Anesthesia Progress*, *62*(3), 125–130. https://doi.org/10.2344/0003-3006-62.3.125

Yentis, S. M., Steer, P. J., & Plaat, F. (1998). Eisenmenger's syndrome in pregnancy: maternal and fetal mortality in the 1990s. *BJOG: An International Journal of Obstetrics and Gynaecology*, *105*(8), 921–922. https://doi.org/10.1111/j.1471-0528.1998.tb10240.x

Yuan, S.-M. (2016). Eisenmenger Syndrome in Pregnancy. *Brazilian Journal of Cardiovascular Surgery*. https://doi.org/10.5935/1678-9741.20160062

Pictures

Day-1	**Day -3**	**Day -6**
Day -7	**Day -9**	**Day -11**
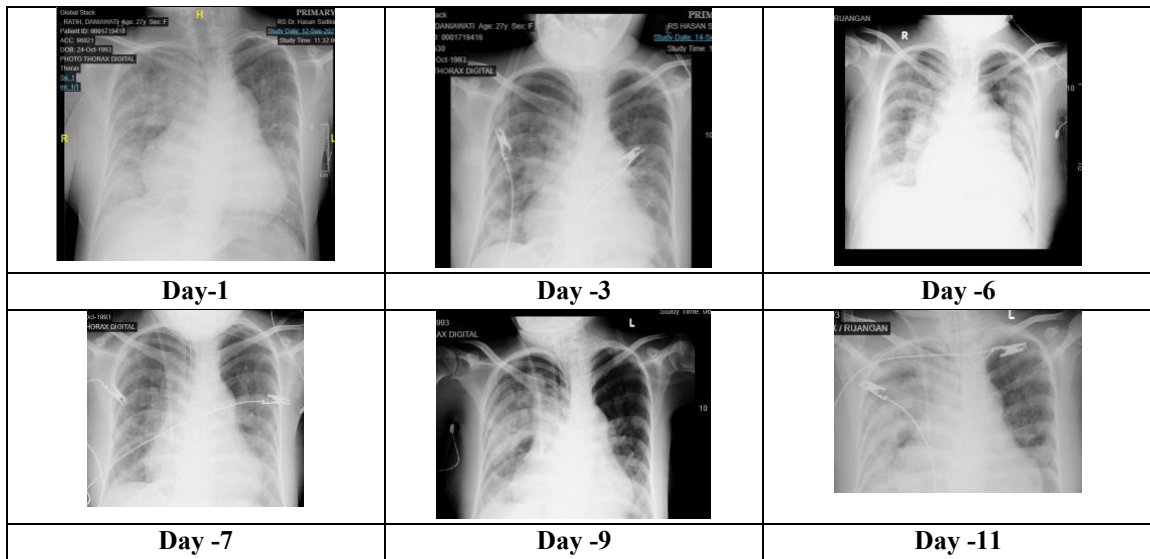
Picture 1: Thorax X-ray
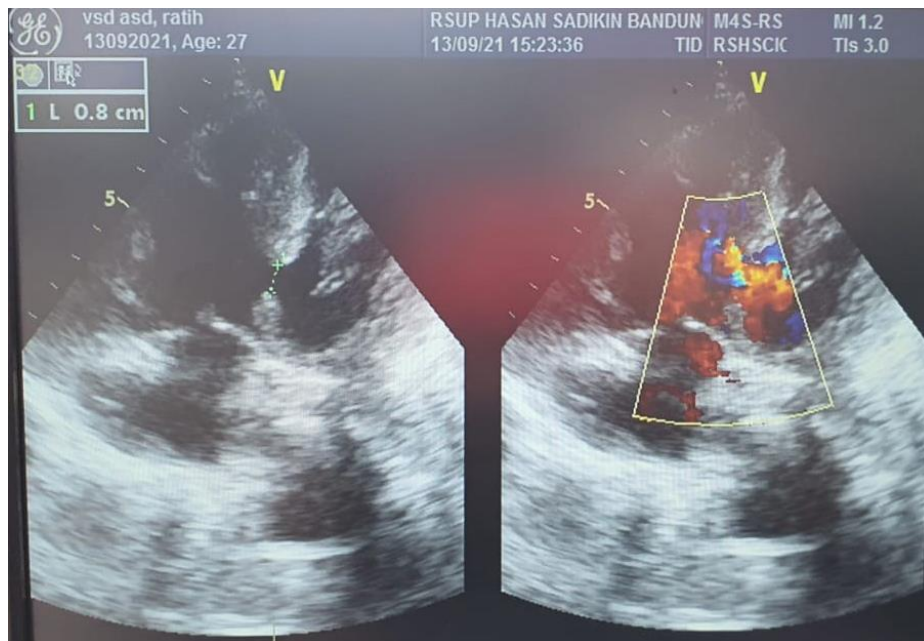
Picture 2: Patient`s Echocardiography

Islamic Perspective on Organ Donation and Brain Death

Ahmad Khan[1], Melanie M. Tidman[2]

[1] A T Still Health Sciences University. ORCID iD: https://orcid.org/0000-0003-4850-9466
Email: sa205310@atsu.edu
[2] Adjunct Professor A. T. Still Health Sciences University, Doctorate of Health Science Program.

Abstract
Worldwide and in the countries, Islamic scholars do not have a consensus on the criteria and definition of brain death. This lack of consensus on the definition of brain death and its legal status has resulted in delays in withdrawal of care and futile care to the brain-dead patient population that negatively strains the limited resources for human organs in the Islamic community. Also, Islamic countries with organ transplantation resources lack legislation on endorsing brain death and its legal status as death which creates delays in harvesting viable organs from eligible donors. These delays can negatively impact the life quality of patients with end-organ failure waiting for an organ and make organs non-viable for transplantation, adding to the already existing shortages in Islamic countries. This brief review aims to clarify some of the barriers in the determination of brain death and organ donation in Islamic countries and address religious and ethical issues that exist that affect issues of access.

Keywords: Brain Death, Islamic Countries, Organ Donation

1. Organ Transplantation and Brain Death: Islamic Perspective

Organ transplantation is not a new term in medicine. The practice of donating organs has been noted in various ancient Greek, Rome, Chinese, and Indian mythology (Bergan, 1997). Advancements in surgical procedures and immunosuppressive drugs have improved the outcome of organ transplant procedures in the last two decades (Grinyo, 2013). In modern medicine, organ transplant has revolutionized the care for the patient populations with end-organ failure. Organ transplantation is a valuable procedure that promotes quality of life and decreases the patient's financial burden caused by the management of end-organ failure. For example, studies indicate that kidney transplantation outperforms dialysis for patients with chronic kidney disease, regarding improved quality of life, and increased survival rates (Tonelli et al., 2011).

Some of the social life implications of organ donation include improving the life quality of the patient population with end-organ failure, and enhancing not only the life quality of the recipient, but also families, friends, spouses, colleagues, and others in the community. Multiple stories are available concerning lives that were changed by organ donation.

Even though organ transplantation has improved the survival rate and quality of life of the patients with end-organ failure, the shortage of organs available for donation remains a significant problem in many countries. In many

countries, supply and demand are not balanced. Many patient populations are waiting for donated organs. According to Global Observatory on Donation and Transplantation (2020), nearly 129,681 organs were transplanted in 2020 worldwide. It is estimated that the reported number of organ transplants represents less than 10% of the need worldwide (World Health Organization, 2022). Hesitancy toward organ donation stems from social, cultural, educational, and religious factors (Da Silva & Frontera, 2015).

2. Organ Donation and Islamic Doctrine

Islamic scholars have highlighted that Islamic scriptures Holy Book of Quran, and Hadith do not have specific verses and Hadith related to organ donation and transplantation (Ali, 2019). However, the Holy Book of the Quran has verses on the importance of saving a life "Whosoever saves the life of one person it would be as if he saved the life of all mankind" (Ali, 1975, p. 70), and the act of charity (Fiqh Council of North America, 2021). Therefore, fatwa (Islamic ethical-legal verdict) abounds that support organ donation and transplantation in light of the importance of life-saving for the good deed. The Fiqh Council supports many fatwa councils that allow organ donation and transplantation in Islam and consider it charity. However, the fatwa councils prohibit selling organs, when it harms and risk the health of the donor and prohibit donating reproductive organs. (Fiqh Council of North America, 2021).

Some Islamic scholars are advocating for cadaver organ donation and using verses of Islamic doctrine that value prolonging human life and helping others. The lack of cadaver organ donation has created opportunities for live donors, such as kidney donors. However, this process of live donation is poorly regulated in many countries, and many organizations have a hand in brokering the donations which creates ethical issues. Some of these ethical issues a lack of appropriate compensation for the donor, the recipient being misled or not given information about the donor's health status, and the organizations involved not using medically appropriate criteria for donor selection (Broumand & Saidi, 2017). These issues can interfere with organ availability and increase the burden of the management of chronic diseases in the community. Research in underserved countries where the population is primarily Muslim is needed to increase people's awareness of the advantages of donating organs to people who need them, and enable Islamic scholars to come to a consensus on allowing cadaver or living donors organs.

Alternatively, some Islamic scholars using limited medical evidence in their argument, oppose organ transplantation from brain-dead patient populations. The determination and definitions of brain death can lead to barriers preventing organ donation in some Islamic countries which be explored next in this review.

3. Major Barrier of Organ Donation in Islamic Countries

3.1. Brain Death Definitions

Even though the concept of brain death is accepted in legislation in several countries worldwide (Greer et al., 2020), determining guidelines for the diagnosis of brain death varies from country to country. One of the basic common concepts among guidelines is that brain death is determined clinically (see Table 1). In addition, ancillary tests are used as supportive or mandatory for confirmation of brain death(Lewis et al., 2020).

Table 1: Clinical Examination Determining Brain Death

Test	Regions of the Brain Tested	Brain Death Indicator
Consciousness	Rostral brainstem, thalamus, bilateral cerebral hemispheres	Absence of response to auditory, visual, or tactile stimulus
Papillary reflux	Upper brainstem	Absence of response to bright light

Corneal Reflex	Middle-to-upper brainstem	Absence of eyelid response when pressure is applied at border of iris with a cotton swab on a stick
Oculocephalic reflex	Middle brainstem	Absence of eye movement with head turning
Oculovestibular reflex	Middle brainstem	Absence of eye movement within 60 seconds of instillation of ice water
Gag reflex	Lower brainstem	Absence of gag reflex in response to bilateral stimulation of posterior pharynx
Couch Reflex	Lower brain stem	Absence of cough in response to deep bronchial suctioning
Motor responses	Brainstem, cerebral hemispheres	Absence of cerebrally mediated response to deep nail bed pressure or proximal stimulation of trunk, arms, and legs

Source: Greer, D. M. (2021). Determination of brain death. New England Journal of Medicine, 385(27), 2554-2561.

One of the critical challenges for organ donation is the definition of brain death. The American Academy of Neurology (AAN) suggested an algorithmic approach and details for clinical diagnosis of brain death, apnea testing, ancillary testing, and the exclusion of confounding factors (AAN, 1995). The AAN (1995) guidelines suggest two neurological exams to confirm the presence of Brain Death with a separation of 6 hours between exams for adults. No source has reported brain function recovery even after a single brain death examination that adhered to AAN guidelines (Da Silva & Frontera, 2015).

Lustbader et al. (2011) suggest that a second neurological exam can decrease organ donation consent rates and organ viability. Lustbader et al. (2011) found that a second neurological confirmatory exam does not add anything to the sensitivity and specificity of brain death diagnosis (Lustbader et al., 2011). The time between when the patient is diagnosed with brain death and the ultimate retrieval of organs is highly sensitive. The longer the time to retrieve organs after the diagnosis of brain death the chance the graft dysfunction and graft rejection increases (Oto et al., 2008).

One of the significant issues that can delay the viable retrieval of accessible organs is the availability of different guidelines for clinical diagnosis of brain death, and lack of standardization for brain death guidelines. This lack of consistency leads to various delays and issues with both legal and religious interpretations. For example, in a study in Saudi, 35.6% of participants did not know whether brain death was a curable condition, and 34.6% of participants responded that they were not sure if brain death is a reliable diagnosis (Alamri et al., 2019). Alamri et al. (2019) indicated that 21% of participants believed brain death is a curable condition (Alamri et al., 2019). Moreover, Al Bshabshe et al. (2016) performed a survey at King Khalid University, Abha, Saudi Arabia, on college students from the college of medicine, dentistry, pharmacy, and applied medical science, and 22.5% of participants believed that brain death is a curable condition (Al Bshabshe et al., 2016). Also, Al Bshabshe et al. (2016) indicated that 92.4% of participants did not know the Islamic perspective on brain death and were unaware of the existence of a fatwa in Saudi (Al Bshabshe et al., 2016). In Islamic communities, a limited understanding of the notion of brain death has led to a reduced rate of organ donation and increased the use of limited intensive care resources (Al-Hashim & Al-Busaidi, 2015).

Wood et al. (2004) suggest that the progression of brain death to somatic death can lead to 10% to 20% loss of viable donors' tissue (Wood et al., 2004). Therefore, preventing delays and improving the timely treatment of donors is critical for organ viability and the long-term outcome of transplanted organs (Anwar & Lee, 2019; Stallone et al., 2020).

In Islamic countries, families are unwilling to discuss or withdraw care from terminally ill patients.. Families will often be unwilling to accept a fatal diagnosis and request aggressive treatment which can then cause challenges for hospitals with limited resources (Pasha & Albar, 2017). These delays can then decrease the viable organ donation rate for people with terminal diseases waiting for organs. In Islamic countries, some religious scholars raise the question about the definition of brain death and clarification as to if brain death is the as cardiopulmonary death and clarification of the state between death and life (Padela et al., 2013).

Even though Islamic scholars have different interpretations of brain death, many Islamic scholars interpret brain death as cardiopulmonary arrest death and consider it death according to Islamic laws (Padela et al., 2013). Also, multiple Muslim organizations acknowledge the clinical diagnosis of brain death as a type of actual death such as the Islamic Figh Academies (IFAs) of the Organization of the Islamic Countries (IOCs), the Islamic Medical Association of North America (Miller et al., 2014).

At the Third International Conference of Islamic Jurist in Amman, Jordan, in 1986, the IFA of the OICs homogenized the concept of brain death into the legal definition of death. According to Albar (1996) and Padela et al. (2011), the legal definition in the Third International Conference of Islamic Jurist found that a person is legally pronounced dead when a doctor declares that total cardiac and pulmonary functions arrest is not reversible or a competent, specialized, and experienced doctor declare total brain functions are not reversible (Pasha & Albar, 2017). Under these conditions, the legal definition reveals that physicians are permitted to discontinue life-supporting measures according to Islamic law (Albar, 1996; Padela et al., 2011).

Moreover, according to Grundman (2005), the Islamic Figh Majma of the Muslim World League in the Kingdom of Saudi Arabia in 1987 issued the criteria for the definition of brain death similar to IFA of the OICs but required confirmation of the requirement by three specialized and competent physicians instead of one specialized and competent physician. According to Jan et al. (2201) Specialized and Competent terminology is defined as physicians who have skills in neurological examination (Jan, 2001). The three physicians can then agree to withdraw life-support despite the presence of respiration and cardiac function under life-support (Pasha & Albar, 2017). Brain Death confirmation tests vary from country to country. In some countries, for example, Saudi Arabia, additional tests are required to confirm the diagnosis of brain death. Further tests include a 30-minute electroencephalography evaluation showing the absence of neural activity and blood flow to the brain by doppler or other diagnostic imaging (Pasha & Albar, 2017).

3.2. Brain Death, Organ Donation and Religious Controversies

Thirteen Islamic countries in South Asia and the Near and Middle East were surveyed, and 12 countries had laws endorsing brain death as legal death, see **Table 2** (Miller, 2016). On the other hand, some Islamic scholars have shown opposition to the conception that brain death is equivalent to complete death (Bedir & Aksoy, 2011). These scholars oppose the American Academy Neurology 2010 updated guidelines. They argue that the guideline does not entail the onset of brain disintegration and irreversible cessation of total brain functions (Rady et al., 2011).

Table 2: Islamic Countries and Organization Endorsed Brain Death

Year	Legal/Judicial Body	Endorsed Brain Death	Classification	Purpose	Criteria Used
1964	**Iran: Ayatollah Khomeini**	Yes	Legal Death	Organ Donation	Not specified
1982	**Saudi Arabia: Senior Religious Scholars Commission**	Yes	Legal Death	Organ Donation	Not specified
1982	**Libya: Law No. 4/1982**	Yes	Legal Death	Organ Donation	Not specified
1983	**Lebanon: Decree Law No. 109**	yes	Legal Death	Organ Donation	Not specified
1985	**IFA-OIC**	Yes	Legal Death	Not Specified	Not specified

				Organ	
1994	**Oman: Ministerial Decision No. 8**	Yes	Legal Death	Donation	Brain Stem
1995	**United Kingdom: Muslim Law Council**	Yes	Legal Death	Organ Donation	Brain Stem
1996	**Indonesia: Council of Ulama**	Yes	Not Specified	Not Specified	Brain Stem
1998	**Morocco: Law No. 16-98**	Yes	Legal Death	Organ Donation	Not specified
1999/2000	**Iran: Act H/24804-T/9929**	Yes	Legal Death	Organ Donation	Brain Stem
2000	**Turkey: Act No. 21674**	Yes	Legal Death	Organ Donation	Brain Stem
2003	**Islamic Medical Association of North America**	Yes	Legal Death	Not Specified	Not specified
2003	**Syria: Law No. 30/2003**	Yes	Legal Death	Organ Donation	Not specified
2010	**Qatar: Doha Donation Accord and Law No. 21**	Yes	Legal Death	Organ Donation	Brain Stem

Source: Miller, A. C., Ziad-Miller, A., & Elamin, E. M. (2014). Brain death and Islam: the interface of religion, culture, history, law, and modern medicine. Chest, 146(4), 1092-1101.AA

Moreover, some scholars have opposed the concept of brain death as it can be abused for organ donation (Al Sayyari, 2008). For example, according to Al Sayyari (2008), Egyptians raised ethical concerns over the procurement of organs from executed prisoners, and these ethical concerns and objections have further boosted the debate by the allegation of the removal of organs from the Muslim political Chinese government oppositions (Gutman, 2012).

4. Summary

In summary, guidelines are available on the criteria of brain death in many countries that lack consistency, and universally to put an end to the inconsistency and controversies among scholars and the lay population, it is critical to develop an international consensus on the criteria for brain death and enhance the culture of organ donation thus saving thousands of lives that are waiting for an organ. Also, an international consensus on brain death will pave the way for the growth of organ transplantation worldwide and assist in increasing people's confidence that, according to religious doctrine and ethical values, it is acceptable to withdraw care from patients with brain death and donate their organs. Furthermore, at a regional level, it is essential to improve organizational and political environments to create national strategies and infrastructures for transplantation. The lack of comprehensive strategies and policies can create illegal and unethical practices as a major barrier to meeting the needs of the patient population with end organ failure. These barriers include, but are not limited to, organ trafficking and commercialization of donated organs. Specific international policies must be put in place to address the issue of illegal trafficking of donated organs to improve the quality of access to these needed resources.

5. Conclusion

Islamic institutions need to consider the current medical evidence in the literature and develop a universal consensus and fatwa on the criteria of the brain death that is medically supported to open the doors of organ donation for Muslim patient populations with end-organ failure. These guidelines that consider religious beliefs can clarify the issues of organ donation for those that live with poor quality of life in the community and spend most of their financial resources on their treatment. Islamic scholars' consensus and fatwa can boost the lay people's awareness of available programs and increase the incidence of consent to organ donation. Furthermore, withdrawal of care and initiation of organ donation will be enhanced by appropriate education of healthcare providers to address lay people's religious concerns. The lack of consensus and unclear definitions of brain death will leave Muslim laypeople and clinicians with uncertainty, and decisions on care withdrawal and organ donation unanswered. Clarification is needed to present guidelines for medical providers to the assure their Muslim patients

and families about the benefits of organ donation and allay fears of conflict of conscience and faith to make informed decisions for themselves and their loved ones.

References

Alamri, M. S., Waked, I. S., Amin, F. M., Al-Quliti, K. W., & Manzar, M. D. (2019). Effectiveness of an early mobility protocol for stroke patients in Intensive Care Unit. *Neurosciences Journal*, *24*(2), 81-88.

Albar, M. A. (1996). Islamic ethics of organ transplantation and brain death. *Saudi Journal of Kidney Diseases and Transplantation*, *7*(2), 109.

Al Bshabshe, A. A., Wani, J. I., Rangreze, I., Asiry, M. A. M., Mansour, H., Ahmed, A. G. N., & Assiri, J. M. (2016). Orientation of university students about brain-death and organ donation: A cross-sectional study. *Saudi Journal of Kidney Diseases and Transplantation*, *27*(5), 966.

Al-Hashim, A. H., & Al-Busaidi, M. (2015). Understanding the concept of brain death in the Middle East. *Oman Medical Journal*, *30*(2), 75-76.

Ali, M. (2019). Our bodies belong to God, so what? God's ownership vs. human rights in the Muslim organ transplantation debate. *Journal of Arabic and Islamic Studies*, *19*, 57-80.

Ali, A. Y. (1975). *The Glorious Quran: Translation and commentary*. eduright4all.

Al Sayyari, A. A. (2008). The history of renal transplantation in the Arab world: a view from Saudi Arabia. *American Journal of Kidney Diseases*, *51*(6), 1033-1046.

Anwar, T. & Lee, J. (2019). Medical management of brain-dead organ donors. Acute Critical Care 34(1), 14-29.

Bedir, A., & Aksoy, Ş. (2011). Brain death revisited: it is not 'complete death according to Islamic sources. *Journal of Medical Ethics*, *37*(5), 290-294.

Bergan, A. (1997). Ancient myth, modern reality: a brief history of transplantation. *The Journal of Biocommunication*, *24*(4), 2-9.

Broumand, B., & Saidi, R. F. (2017). New definition of transplant tourism. *International Journal of Organ Transplantation Medicine*, *8*(1), 49.

Da Silva, I. R. F., & Frontera, J. A. (2015). Worldwide barriers to organ donation. *JAMA Neurology*, *72*(1), 112-118.

Global Observatory on Donation and Transplantation (2020). WHO-ONT. http://www.transplant-observatory.org.

Greer, D. M. (2021). Determination of brain death. *New England Journal of Medicine*, *385*(27), 2554-2561.

Greer, D. M., Shemie, S. D., Lewis, A., Torrance, S., Varelas, P., Goldenberg, F. D., Bernat, J. L., Soucer, M., Topcuouglu, M. A., Alexandrov, A. W., Baldeiserri, M., Bleck T., Citerio, G., Dawson, R., Hoppe, A., Jacobe, S., Manara, A., Nakagawa, T. A., Pope, T. M., ... & Sung, G. (2020). Determination of brain death/death by neurologic criteria: the world brain death project. *JAMA*, *324*(11), 1078-1097.

Grinyó, J. M. (2013). Why is organ transplantation clinically important? *Cold Spring Harbor Perspectives in Medicine*, *3*(6), a014985.

Grundmann, J. (2005). Shariah, Brain Death, and Organ Transplantation: The Context and Effect of Two Islamic Legal Decisions in the Near and Middle East. *American Journal of Islamic Social Sciences*, *22*(4), 1.

Gutmann, E. (2012). Bitter harvest: China's organ donation'nightmare. *World Affairs*, 49-56.

Jan, M. S., Al-Buhairi, A. R., & Baeesa, S. S. (2001). Concise outline of the nervous system examination for the generalist. *Neurosciences Journal*, *6*(1), 16-22.

Lewis, A., Bakkar, A., Kreiger-Benson, E., Kumpfbeck, A., Liebman, J., Shemie, S. D., Sung, G., Torrance, S., & Greer, D. (2020). Determination of death by neurologic criteria around the world. *Neurology*, *95*(3), e299-e309.

Lustbader, D., O'Hara, D., Wijdicks, E. F. M., MacLean, L., Tajik, W., Ying, A., Berg, E., & Goldstein, M. (2011). Second brain death examination may negatively affect organ donation. *Neurology*, *76*(2), 119-124.

Miller, A. C. (2016). Opinions on the legitimacy of brain death among Sunni and Shi'a scholars. *Journal of Religion and Health*, *55*(2), 394-402.

Miller, A. C., Ziad-Miller, A., & Elamin, E. M. (2014). Brain death and Islam: the interface of religion, culture, history, law, and modern medicine. *Chest*, *146*(4), 1092-1101.

Moritsugu, K. P. (2013). The power of organ donation to save lives through transplantation. *Public Health Reports*, *128*(4), 245-246.

Oto, T., Excell, L., Griffiths, A. P., Levvey, B. J., Bailey, M., Marasco, S., & Snell, G. I. M. (2008). Association between primary graft dysfunction among lung, kidney and heart recipients from the same multiorgan donor. *American Journal of Transplantation*, *8*(10), 2132-2139.

Padela, A. I., Arozullah, A., & Moosa, E. (2013). Brain Death in Islamic Ethico-Legal Deliberation: Challenges for Applied Islamic Bioethics. *Bioethics*, *27*(3), 132-139.

Padela, A. I., Shanawani, H., & Arozullah, A. (2011). Medical experts & Islamic scholars deliberating over brain death: Gaps in the applied Islamic bioethics discourse. *The Muslim World*, *101*(1), 53-72.

Pasha, H. C., & Albar, M. A. (2017). Do not resuscitate, brain death, and organ transplantation: Islamic perspective. *Avicenna Journal of Medicine*, *7*(02), 35-45.

Quality Standards Subcommittee of the American Academy of Neurology. (1995). Practice parameters for determining brain death in adults (summary statement). *Neurology*, *45*, 1012-1014.

Rady, M. Y., Verheijde, J. L., & Ali, M. S. (2009, June). Islam and end-of-life practices in organ donation for transplantation: new questions and serious sociocultural consequences. In *HEC forum* (Vol. 21, No. 2, pp. 175-205). Springer Netherlands.

Stallone, G., Pontrelli, P., Rascio, F., Castellano, G., Gesualdo, L., & Grandaliano, G. (2020). Coagulation and fibrinolysis in kidney graft rejection. *Frontiers in Immunology*, *11*, 1807.

Tonelli, M., Wiebe, N., Knoll, G., Bello, A., Browne, S., Jadhav, D., Klarenbach, S., & Gill, J. (2011). Systematic review: kidney transplantation compared with dialysis in clinically relevant outcomes. *American Journal of Transplantation*, *11*(10), 2093-2109.

Wood, K. E., Becker, B. N., McCartney, J. G., D'Alessandro, A. M., & Coursin, D. B. (2004). Care of the potential organ donor. *New England Journal of Medicine*, *351*(26), 2730-2739.

World Health Organization (2022). Human organ and tissue transplantation. https://apps.who.int/gb/ebwha/pdf_files/WHA75/A75_41-en.pdf.

Characteristics of Therapeutic Plasma Exchange Procedures in Patients with Myasthenia Gravis and Guillain Barre Syndrome and their Outcomes during Hospitalization in General Intensive Care Unit Hasan Sadikin General Hospital Bandung in January 2017 to December 2020

Tinni T. Maskoen[1], Aditiya Amini Inggriani[1], M. Erias Erlangga[1]

[1] Department of Anesthesiology and Intensive Care, Faculty of Medicine, Padjadjaran University, Bandung, Indonesia

Correspondence: Aditiya Amini Anggraini, Department of Anesthesiology and Intensive Care, Faculty of Medicine, Padjadjaran University. E-mail: aditiyaamini@gmail.com

Abstract
Background: Myasthenia Gravis and Guillain-Barré syndrome are two of the most common autoimmune diseases affecting the peripheral nervous system in the world. Both of the diseases manifested as progressive muscle weakness, areflexia, and inspiratory muscle weakness which leads to mechanical ventilation support. Therapeutic Plasma Exchange is the first line of treatment according to the American Society for Apheresis (AFSA), which is a relatively safe and often performed procedure In the Intensive Care Unit (ICU), including in Hasan Sadikin Hospital Bandung (RSHS). Purpose: The goal of this study is to obtain the background characteristics of MG and GBS patients and to obtain the outcome of TPE in these patients. Methods: The study was a descriptive study performed on 30 MG and GBS patients who received TPE in the Intensive care unit, RSHS from January 2017 to December 2020. Data for the study was obtained retrospectively from the patient medical record. Results: The result showed that the most common side effect during TPE was electrolyte imbalance. There was no reported morbidity and mortality in MG patients, in contrast to two mortality cases in GBS patients. Length of stay in the intensive care unit was influenced by several factors including age, comorbidities, the severity of MG, and morbidities that occurred during the hospital stay. Conclusion: Outcome of MG and GBS patients with TPE procedure is good in relation with low TPE-unrelated morbidity and mortality.

Keywords: Guillain Barre Syndrome, Length of Stay, Myasthenia Gravis, Morbidity, Mortality, Therapeutic Plasma Exchange

1. Introduction

Myasthenia Gravis (MG) and Guillain-Barré syndrome (GBS) are the most common autoimmune diseases affecting the peripheral nervous system. The incidence of MG in Europe is estimated at 30 from 1 million people per year with male-female ratio of 1:3 (Aydin et al., 2017). The worldwide incidence of GBS is 1.3–4 from 100.000 cases annually and is more common in young adults and older adults (>50 years) with male-female ratio of 3:1.[3–5] Currently, there is no particular registered data regarding MG and GBS in Indonesia (Murthy et al., 2020; Biswas et al., 2020; Ortiz-Salas et al., 2016).

Myasthenia gravis is an autoimmune disease characterized by the presence of antibodies to the acetylcholine nicotinic postsynaptic receptor accompanied by fluctuating muscle weakness. MG is a progressive disease with a high mortality, estimated to be around 5% to 9%. Approximately, 3-8% of patients who experience a *Myasthenia gravis crisis* will die from this condition (Westerberg et al., 2020). The other disease investigated in this studi study was Guillain-Barré syndrome (GBS). GBS is an autoimmune disease of the peripheral nervous system that causes progressive muscle weakness and areflexia The disease is characterized by acute neuromuscular paralysis that ends in respiratory failure and approximately 25% of patients require mechanical ventilation (Nguyen et al., 2012).

Diseases of MG and GBS are the most often conditions indicated to receive TPE therapy in the GICU RSUP Dr. Hasan Sadikin Bandung. Following the guidelines recommended by the American Society for Apheresis (ASFA), the first-line treatment of MG, especially acute phase MG, and GBS crisis is the administration of TPE (McCullough et al., 2019; Li et al., 2018). Therapeutic Plasma Exchange (TPE) procedure uses an extracorporeal technique in which blood plasma is separated from other blood components and exchanged with fluids replacement.[9] The purpose of TPE is removal of toxins present in patient's plasma. Based on research in the United States, TPE has performed as many as 1200 procedures per year and another study reported TPE procedures accounted for 76.8% of the total *therapeutic apheresis*. Regardless, Indonesia has not done a specific study that describes the number of TPE procedures carried out each year (Pham et al., 2019).

Procedure of TPE is generally safe and well-tolerated, though, complications are not evitable. Complications include hemodynamic instability, coagulation disorders, electrolyte disturbances, allergic reactions (pruritus, urticaria and anaphylactic reactions), hematomas at the catheter insertion site, and acute myocardial infarction (Daga Ruiz et al., 2017). Complications, along with the onset of TPE implementation, frequency, and type of fluid replacement are considered to affect the outcomes of patient (Calca et al., 2020).

Several factors that can also contribute to the patient's outcome are the severity of the disease, comorbidities, and precipitating factors. Assessment of patient outcomes was described on the duration of ventilator usage, morbidity, mortality, and length of stay in the GICU as well as the total length of stay in the hospital. Eventhough TPE is a routine procedure that has long been carried out in the GICU Dr. Hasan Sadikin Bandung, there is no data regarding the implementation of TPE and its outcomes for patients. Therefore, this study aims to obtain an overview of the characteristics of MG and GBS patients and to find out the outcomes of implementing the TPE procedure for the diseases.

2. Method

This study used a descriptive method with retrospective data collection. The research subjects were medical records of patients of MG and GBS who had underwent TPE at GICU Dr. Hasan Sadikin Bandung from January 2017 to December 2020. Inclusion criteria were medical records of patients aged 18 years and over, were intubated and using a ventilator while undergoing TPE in the GICU. The exclusion criteria were incomplete patient medical records. The sample size was determined based on the data availability (*purposive sampling*). This research was conducted at RSUP Dr. Hasan Sadikin Bandung in November – December 2021 after obtaining approval from the Research Ethics Committee.

The variables in this study include patient characteristics, characteristics of TPE procedures, complications of TPE procedures, and patient outcomes. Patient characteristics include gender, age, body mass index, comorbidities,

precipitating factors, APACHE II, and MG class. The characteristics of the TPE procedure include the onset, frequency, and type of fluid replacement. Complications of the TPE procedure include hemodynamic disturbances, electrolyte disturbances, impaired coagulation factors, allergic reactions, paraesthesia, hematomas in venous access, and *myocardial infarction*. Patient outcomes included length of use of a ventilator, morbidity, mortality, length of stay in the GICU, and length of stay in hospital.

The collected data were then analyzed using descriptive statistics. The data processing was done using statistical software (Microsoft® Excel 2019 and IBM SPSS 25.0) and displayed in tables. For categorical data (nominal) would be presented in frequency and percentage statistics, while for numerical data (ordinal, interval) would be presented in the average value, standard deviation, median value, minimum value and maximum value.

3. Results

3.1 Data Normality Test

During the study period, there were 48 MG and GBS patients who were treated at the GICU Hasan Sadikin Hospital. Twenty one patients belonged to the MG group with only 19 patients met the criteria of inclusion and exclusion and 19 patients belonged to the GBS with only 11 patients met the criteria of inclusion and exclusion.

The data in this study underwent normality test. Numerical data was tested with Shapiro Wilks because the number of data is less than 50. Table 4.1 describes the results of the normality test for the distribution of this research data. The results of the normality test showed normal distribution of data when the p value in the *Shapiro Wilk test* was more than 0.05.

Table 1: Result of data normality test

Variable	MG (n = 19)		GBS (n = 11)	
	P value	Data distribution	P value	Data distribution
Age	0,225	Normal	0,361	Normal
Body mass index	0,019	Odd	0,001	Odd
APACHE II	0,006	Odd	0,083	Normal
Onset (days)	0,000	Odd	0,164	Normal
TPE frequency	0,000	Odd	0,000	Odd
Duration of Ventilator use	0,017	Odd	0,143	Normal
Length of stay GICU	0,003	Odd	0,011	Odd
Length of stay RSHS	0,016	Odd	0,009	Odd

Normality test using *Shapiro Wilk* (n<50) method, data were declared normally distributed if p-value > 0.05

3.2 Characteristics of Patients

Characteristics of MG and GBS patients in this study included mean age, number of women and men, median body mass index, number of patients with comorbidities, number of patients with comorbid factors precipitating factors, and median and mean APACHE II scores. MG patients were classified according to the MG class.

Table 2: Characteristics of research subjects (n=30)

Characteristics of patients	MG (n = 19)	GBS (n = 11)
a. Age		
Mean (SD)	43,47 (13,94)	34,09 (10,51)
b. Gender		
Male	7 (36,8%)	6 (54,5%)

	Female	12 (63,2%)	5 (45,5%)
c.	Body mass index		
	Median (Q1 - Q3)	20,81 (18,73 - 23,44)	22,89 (22,04 - 24,22)
d.	Comorbid		
	Yes	12 (63,2%)	7 (63,6%)
	No	7 (36,8%)	4 (36,4%)
e.	Precipitating factos		
	Yes	4 (21,1%)	6 (54,5%)
	No	15 (78,9%)	5 (45,5%)
f.	APACHE II		
	Mean (SD)		14,18 (7,39)
	Median (Q1 - Q3)	9 (5 - 16)	
g.	*Myasthenia Gravis* class		
	II	8 (42,1%)	0 (0%)
	IIIb	11 (57,9%)	0(0%)

3.3 Characteristics of TPE Procedure

This study obtained a description of TPE procedure characteristics which included median onset in MG subjects and mean onset in GBS subjects, and data on the number of TPE procedures on subjects and the median. As additional data, was discovered that days of improvement in ventilator mode were found in the median of third cycle in both groups of subjects.

Table 3: Characteristics of TPE procedure

TPE Procedure		MG (n = 19)	GBS (n = 11)
a.	Onset (days)		
	Mean (SD)	-	5,05 (1,43)
	Median (Min - Max)	6 (1 - 29)	-
b.	Frecuency		
	Number of actions (times)	96	58
	Median (Min - Max)	6 (2 - 6)	6 (1 - 6)
c.	Improvement of the ventilator mode (cycle)		
	Median (Min-Max)	3 (1 – 4)	3 (2 – 4)

Furthermore, this study describes the type of fluid replacement in the implementation of TPE. Plasmanate, Nacl 0.9%, Ringer's Lactate, Gelofusine, Fresh Frozen Plasma (FFP) and albumin 4-5% are the types of fluids used in this study. Plasmanate consists of albumin and globulin so that albumin is then included in the plasmanate group.

Table 4: Overview and comparison of the use of replacement fluid

Fluids		MG (n = 19)	GBS (n = 11)
a.	Plasmanat/Albumin 5%	96 (100%)	58 (100%)
b.	NaCl 0,9%	63 (65,6%)	53 (91,4%)
c.	Ringer Laktat	5 (5,2%)	3 (5,2%)
d.	Gelofusine	96 (100%)	58 (100%)
e.	FFP	0 (0%)	0 (0%)

3.4 Complications of TPE Procedure

Complications that occurred during the TPE procedure in the MG group were mostly hypocalcemia and the least was hemodynamic disturbances, namely hypotension. Overall, the total complications in the MG group were 56 events. Total complications in the GBS group occurred in 33 events.

Table 5: Overview and comparison of complications during TPE

Complications		MG (n = 19)	GBS (n = 11)
a.	Hemodynamic disturbances Hypotension	1 (1%)	2 (3,4%)
b.	Electrolyte imbalances		
	Hiponatremia	20 (20,8%)	16 (27,6%)
	Hipokalemia	12 (12,5%)	13 (22,4%)
	Hipocalcemia	32 (33,3%)	12 (20,7%)
c.	Coagulation disorders	6 (6,3%)	5 (8,6%)
d.	Etc	0 (0%)	0 (0%)
e.	Total complications	56 (58,3%)	33 (56,9%)

3.5 Overview of Patients Outcomes

This study obtained a description of the outcome of patients undergoing TPE in each group. The outcome domains studied in this study were length of ventilator use, morbidity; associated and unrelated TPE, mortality; related and unrelated to TPE, length of stay in GICU, and the length of hospital stay.

Table 6: Overview and comparison of patients outcomes

Patients outcomes		MG (n = 19)	GBS (n = 11)
a.	Length of ventilator use		
	Mean (SD)		10,18 (7,72)
	Median (Min-Max)	7 (1 - 23)	
b.	Morbidity		
	TPE associated	0 (0%)	0 (0%)
	TPE unrelated	10 (52,6%)	6 (54,5%)
c.	Mortality		
	TPE associated	0 (0%)	2 (18,2%)
	TPE unrelated	1 (5,3%)	0 (0%)
d.	Length of stay		
	GICU		
	Mean (SD)	13,26 (8,94)	14,64 (11,21)
	Median (Min-Max)	11 (4 - 42)	12 (2 - 41)
	Hospital		
	Mean (SD)	24,74 (13,02)	27,73 (21,66)
	Median (Min-Max)	21 (7 - 62)	21 (5 - 74)

4. Discussion

The patients of MG and GBS has mean age of 43.5 years old and 34.1 years old. Previous research stated that MG is a disease that affects all ages (Bubuioc et al., 2021). Another study reported that the incidence of GBS increases with age but it may be due to the difficulty of diagnosing GBS at a younger age (Sejvar et al., 2011).

Epidemiological reports for the Chinese region stated the proportion of women more than men by 3:1 in MG patients. MG is an autoimmune disease and the disease has been associated to be more common in women. The effect of the hormone estrogen is considered as one of the mediators causing differences in autoimmune women and men. A study conducted on the epidemiology of GBS stated that GBS occurs more often in men than women. The male predominance in GBS differs from most other autoimmune diseases such as multiple sclerosis and systemic lupus erythematosus, which often show higher rates in women (Dong et al., 2020).

Among the patients of MG, 2 of them had BMI of 30 kg/m^2. Obesity in MG patients were assessed as being directly proportional to the presence of comorbidities and the incidence of complications during the TPE procedure. Hypoxia and systemic inflammation that occur in high BMI patients have poor effect on patients' outcomes and could trigger MG crisis (Liu et al., 2017). In the GBS group, there were 2 patients with BMI > 30kg/m2 (obese) and 1 patient with BMI >25kg/m2 (overweight). A cohort study investigating the relationship between BMI and hip circumference with the incidence of GBS revealed positive result. However, another cohort study in Denmark found that BMI was not associated with the risk of developing GBS. This is similar to our study where the mean BMI was normal in GBS subjects but this may be due to the limited number of subjects, making it difficult to describe the overall incidence rate (Winer et al., 2014).

This study found that the most comorbid in MG patients were pulmonary TB in as many as 5 people. A study in Taipei, Taiwan stated that the incidence of pulmonary TB was significantly higher in MG patients in association to immunosuppressant therapy which made them susceptible to exposures of active pulmonary TB infection, and most pulmonary TB infections triggered exacerbations in MG cases. Comorbidity in GBS patients was found in 7 people, of which 3 patients suffered from hypertension, 3 patients from obesity, and 1 patient with *Chronic Inflammatory Demyelinating Polyneuropathy* (CIDP). The presence of comorbidities in the patient affects the outcome and length of treatment (Ou et al., 2013).

Precipitating factors for MG in this study were found in 3 of 19 patients with upper respiratory tract infections. The unknown precipitating factors of the other patients was possibly due to incomplete anamnesis in the medical record. The precipitating factors in the GBS group consisted of 5 GBS patients triggered by upper respiratory tract infections and 1 patient triggered by enteritis et causa suspect dysentery. Infection with C. jejuni is known to most often trigger GBS because the bacteria has a ganglioside-like structure in its lipopolysaccharide layer (Sejvar et al., 2011).

In the MG group, patients were in APACHE II median 9 (5-16). In the GBS subject group, the APACHE II score averaged 14.18 ± 7.39 SD. The APACHE II assessment in this study is only to describe in general the severity and mortality rate when patients enter the GICU which is influenced by the conditions and comorbidities suffered by the patient.

The MG patients in this study was found the most in Myasthenia Gravis class IIIb, as much as 57.9% of the total patients. This is because this study focuses on MG patients who are treated in the ICU and receive TPE therapy during their treatment so that most of the patients enter with symptoms of respiratory problems that require mechanical ventilation assistance.

We found that in the MG group, the TPE procedure onset was at a median of 6 days. In the GBS group, onset was at a mean of 5.05 days. Until present, there has been no study that states the optimal onset of TPE procedures in MG and GBS crisis patients, but a study conducted in Florida stated that after a person has diagnosed with acute phase MG or GBS crisis, immediate treatment is needed in the intensive care room.

The administration of TPE with a median frequency of 6 times in this study was carried out based on recommendations from the ASFA which stated that patients with severe MG could receive TPE 5 to 7 times, while GBS patients could receive TPE up to five times or more. This administration is carried out according to the clinical condition of the patient and must be evaluated after the first and second TPE administration (Pham et al., 2019).

The replacement fluids mostly used in the 96 performed TPE procedures were mostly plasmanate/albumin 5%, gelofusine 100%, and NaCl 0.9% in both MG and GBS groups. Plasmanate is used concurrently with gelofusine. The MG management guidelines used in Indonesia (PERDOSSI 2018) state that the most commonly used replacement fluid is 4%-5% human albumin in physiological saline. One cycle of TPE in adults will remove 150 grams of plasma protein containing 110 grams of albumin and 24 grams of globulins to eliminate 1-2 grams of pathogenic substances. This is the reason for prefering plasmanate as a replacement fluid in TPE because plasmanate contains albumin as well as globulins (Hakim et al., 2019).

Of the 96 TPE procedures performed, it was found that at the beginning of TPE procedure, there were about 52 cases (54.3%) of hypotension, but after fluid management was given, hypotension could be managed in less than 15 minutes and there was only 1 incident (1%) of untreated hypotension complications. The patient with the hypotension had BMI value of 32 kg/m^2 that according to a previous study in America in 2021, there were difficulties in calculating replacement fluids for obese patients so they conduct a greater risk of hypotension (Babariya et al., 2021). In the GBS group, most complications were of electrolyte disturbances. These complications are relatively minor and can be overcome during or after TPE is performed. A study stated that the most common complications of TPE were hypocalcemia and hypomagnesemia due to side effects of using citrate in anticoagulants followed by hypothermia, transfusion reactions, fluid disturbances, electrolyte disturbances, bleeding due to hypofibrinogenemia and thrombocytopenia, hypotension, and gastrointestinal symptoms such as nausea and vomiting (Sergent et al., 2022).

We describe the outcome of MG and GBS patients who received the TPE procedure at several points, namely: duration of ventilator use, morbidity, mortality and length of stay in the GICU, and length of stay in the hospital. We divide the morbidity and mortality in 2 aspects, TPE-associated and TPE-unrelated.

The duration of ventilator use in MG patients had a median value of 7 days. Five patients were on *prolonged ventilator* with the longest duration of 23 days. A study conducted in Germany in 2020 stated that the median use of a ventilator was 12 days and *prolonged ventilation* (>15 days) were affected by age, MG onset, MG grade, and the patient's comorbidities before the onset of MG crisis (Neumann et al., 2020). In GBS subjects, the duration of ventilator use had a mean value of 10.18 days. According to a study conducted in Pakistan, the frequency of need for ventilators ranges from 19% to 43% accompanied by *prolonged* ventilators in cases of severe GBS. The need for ventilators is reported to be very high, reaching 81% in patients with poor prognoses (Siddiqui et al., 2019).

There was no TPE-associated morbidity within the procedure in the MG and GBS subject groups. In the MG group, 4 patients had morbidity due to HAP, 4 patients were due to CAP, and 2 patients had sepsis. A previous retrospective study conducted over 10 years in India stated that 50% of patients experienced some morbidity during the crisis phase of MG (Lal et al., 2013). In the GBS group, 6 patients had *Hospital-Acquired Pneumonia* (HAP). No morbidity caused by the TPE procedure was found in this study, indicating that the TPE procedure is a relatively safe procedure to perform.

The mortality in the MG group was found to be TPE-unrelated in a 69-year-old woman with comorbid DM and hypertension and APACHE II with MG class IIIB. The mortality rate was not as poor as a study conducted in 2013 in India with the mortality rate of 30%.[24] Mortality in the GBS group occurred in two patients with HAP. Both subjects were hypotensive and were given fluids and vasopressors but the hypotension was not treated so the patient fell into *cardiac arrest*. A study conducted in Australia stated that the mortality of GBS patients was greater in patients who used mechanical ventilation and had a high APACHE score (Portugal Rodríguez et al., 2015). TPE itself is a relatively safe procedure with minimal complications so it rarely causes life-threatening conditions.

This research has found that the length of stay in GICU and hospital is influenced by the condition of the patient at the time of initial admission to the hospital. It divides the explanation of treatment on the grounds that the treatment in the GICU focuses on respiratory problems while the total length of hospital stay may be due to other factors.

In this study, we found that overall patients' quality of life in GBS group were lower than MG group. This can be seen from the large comorbidities suffered by the patient (MG 63,2% / GBS 63,6%) , precipitating factors (MG 21,1% / GBS 54,5%), APACHE II scoring (MG 12 / GBS 14,18), duration of ventilator use (MG 7 / GBS 10), TPE unrelated morbidity (MG 52,6% / GBS 54,5%), TPE-associated mortality (MG 0% / GBS 54,5%), length of stay in GICU (MG 11 / GBS 12), and length of stay in hospital (MG 21 / GBS 21). There has been no previous study that examined the quality of life comparison of MG and GBS patients, so further research is needed on this matter.

Limitations in this study were incomplete data sources from patient medical records such as myasthenia gravis class and complaints of complications that occurred during the TPE procedure which was not included and were not asked. Another limitation is that this study has a small sample size so that it cannot cover the whole data.

5. Conclusions

The group of MG patients who were given the TPE procedure at the GICU RSHS had the average characteristics of being of productive age, female sex, and normal BMI. The outcome of the TPE procedure in MG patients in the GICU RSHS is favorable, indicated by the absence of morbidity and mortality associated with the TPE procedure.

The dominance characteristics of GBS patients was male in the productive age range. The outcome of the TPE procedure in GBS patients in the GICU RSHS is good. Cases of mortality during the TPE procedure occurred in 2 patients, but this was related to the patient's unprime condition when the TPE procedure performed. TPE is a relatively safe procedure and is the most recommended treatment for MG and GBS treated in the GICU RSHS, especially in patients with severe clinical symptoms or exacerbating conditions.

Suggestions for RSHS are to carry out routine check-ups before and after TPE procedure to evaluate the magnitude of the complication rate, give a higher albumin concentration at the beginning of the TPE procedure to avoid high incidence of hypotension, complete the recording of data on precipitating factors during history taking and myasthenia gravis class on the medical record, and revise and add details of complications in the TPE report form. A study with a larger number of subjects is needed to obtain a more representative picture regarding the management of TPE for MG and GBS patients in RSHS.

References

Aydin, Y., Ulas, A. B., Mutlu, V., Colak, A., & Eroglu, A. (2017). Thymectomy in myasthenia gravis. *The Eurasian Journal of Medicine,* 49(1), 48-52. https://doi.org/10.5152/eurasianjmed.2017.17009.

Murthy, J. M. K. (2020). Myasthenia gravis: do the subtypes matter? *Ann Indian Acad Neurol,* 23(1), 2. https://doi.org/10.4103%2Faian.AIAN_595_19.

Biswas, A., Singh, H., Philip, J., Pawar, A., & Joshi, R. (2020). A retrospective study on patients of guillain-barre syndrome treated with therapeutic plasma exchange at a tertiary care hospital in western Maharashtra. *Global Journal of Transfusion Medicine.* 5(2), 173-177. https://doi.org/10.4103/GJTM.GJTM_90_20.

Ortiz-Salas, P., Velez-Van-Meerbeke, A., Galvis-Gomez, C. A., & Rodriguez, Q. (2016). Human immunoglobulin versus plasmapheresis in guillain-barre syndrome and myasthenia gravis: a meta-analysis. *Journal of Clinical Neuromuscular Disease.* 18(1), 1-11. https://doi.org/10.1097/cnd.0000000000000119.

Westerberg, E. & Punga, A. R. (2020). Epidemiology of myasthenia gravis in sweden 2006-2016. *Brain and Behavior.* 10(11), e01819. https://doi.org/10.1002%2Fbrb3.1819.

Nguyen, T. C., Kiss, J. E., Goldman, J., & Carcillo, J. A. (2012). The role of plasmapheresis in critical illness. *Crit Care Clin,* 28(3). 453-468. https://doi.org/10.1016%2Fj.ccc.2012.04.009.

McCullough, P. (2019). Contrast induced acute kidney injury. *Critical Care Nephrology.*

Li, L., Xiong, W. C., & Mei, L. Neuromuscular junction formation, aging, and disorders. *Annual Review of Physiology.* 2018. 80(1), 159-188. https://doi.org/10.1146/annurev-physiol-022516-034255.

Pham, H. P., Staley, E. M., & Schwartz, J. (2019). Therapeutic plasma exchange – a brief review of indications, urgency, schedule, and technical aspects. *Transfusion and Apheresis Science.* 58(3), 237-246. https://doi.org/10.1016/j.transci.2019.04.006

Daga Ruiz, D., Fonseca San Miguel, F., González de Molina, F. J., Úbeda-Iglesias, A., Navas Perez, A., & Jannone Fores, R. (2017). Plasmapheresis and other extracorporeal filtration techniques in critical patients. Medicina Intensiva, 41(3), 174-187. https://doi.org/10.1016/j.medin.2016.10.005.

Calca, R., Gaspar, A., Santos, A., Aufico, A., Freitas, P., & Coelho, S. (2020). Therapeutic plasma exchange in patients in a portuguese ICU. *Portuguese Journal of Nephrology & Hypertension,* 34(1): 21-25. http://dx.doi.org/10.32932/pjnh.2020.04.058.

Bubuioc, A. M., Kudebayeva, A., Turuspekova, S., Lisnic, V., & Leone, M. A. (2021). The epidemiology of myasthenia gravis. *Journal of Medicine and Life,* 14(1), 7-16. https://doi.org/10.25122/jml-2020-0145.

Sejva r, J. J., Baughman, A. L., Wise, M., & Morgan, O. W. (2011). Population incidence of guillain-barré syndrome: a systematic review and meta-analysis. *Neuroepidemiology,* 36(2), 123-133. https://doi.org/10.1159/000324710.

Dong, D., Chong, M., Wu, Y., Kaminski, H., Cutter, G., & Xu, X. (2020). Gender differences in quality of life among patients with myasthenia gravis in china. *Health Qual Life Outcomes*, 18(1), 1–13. https://doi.org/10.1186/s12955-020-01549-z.

Liu, X. D., Shao, M. R., Sun, L., Zhang, L., Jia, X. S., & Li, W. Y. (2017). Influence of body mass index on postoperative complications after thymectomy in myasthenia gravis patients. *Oncotarget*, 8(55), 94944–94950. https://doi.org/10.18632%2Foncotarget.19189.

Winer, J. B. (2014). An update in guillain-barré syndrome. *Autoimmune Diseases*, 2014, 1-6. https://doi.org/10.1155/2014/793024.

Ou, S. M., Liu, C. J., Chang, Y. S., Hu, Y. W., Chao, P. W., & Chen, T. J. (2013). Tuberculosis in myasthenia gravis. *The International Journal of Tuberculosis and Lung Disease,* 17(1), 79-84. https://doi.org/10.5588/ijtld.12.0260.

Hakim, M., Gunadharma, S., & Basuki, M. (2019). Pedoman Tatalaksana GBS, CIDP, MG, Imunoterapi [Instructions for the conduct of GBS, CIDP, MG, immunotherapy]. *Perhimpunan Dokter Spesialis Saraf Indonesia,* 75-76.

Babariya, S. P., Vivero, A., Peedin, A., & Karp, J. K. (2021). Therapeutic plasma exchange in patients with severe obesity: A survey of practices in the United States. *Journal of Clinical Apheresis*, 36(6), 802-807. https://doi.org/10.1002/jca.21931.

Sergent, S. R. & Ashurst, J. V. (2022) Plasmapheresis. *Treasure Island (FL): StatPearls Publishing.*

Neumann, B., Angstwurm, K., Mergenthaler, P., Kohler, S., Schonenberger, S., & Bosel, J. (2020). Myasthenic crisis demanding mechanical ventilation. *Neruology,* 94(3), e299-313. https://doi.org/10.1212/wnl.0000000000008688.

Siddiqui, S. H., Siddiqui, T., H., Babar M., Khoja A., & Khan, S. (2019). Outcomes of patients with guillain barre syndrome – experience from a tertiary care hospital of a developing Asian country and review of regional literature. *Journal of Clinical Neuroscience,* 36(6), 802-807. https://doi.org/10.1016/j.jocn.2018.11.031.

Lal, V., Prabhakar, S., Agarwal, R., & Sharma, S. (2013). Clinical profile and outcome of myasthenic crisis in a tertiary care hospital: a prospective study. *Ann Indian Acad Neurol,* 16(2), 203. https://doi.org/10.4103/0972-2327.112466.

Portugal Rodríguez, E., Berrazueta Sánchez de Vega, A., Vara Arlanzón, R., Martínez Barrio, E., del Valle Ortiz, M., & Fernández Ratero, J. (2015). Predisposing factors, neurological complications and sequels of Guillain Barre Syndrome at discharge: experience in an ICU of a third level hospital. *Intensive Care Medicine Experimental,* 3(Suppl 1), A993. https://doi.org/10.1186%2F2197-425X-3-S1-A993.

Bullous Pemphigoid in a 37-Year Old Female: A Case Report and Literature Review

Stefon Monique D. Oxley[1], Brian M. Denney[2]

[1] Chong Hua Hospital Department of Internal Medicine, Cebu City, Philippines
[2] Cebu Velez General Hospital, Cebu City, Philippines

Corresponding author: Dr. Brian M. Denney, RMT, MSMT, Cebu Velez General Hospital, Cebu City, Philippines. Email: bmd1333@yahoo.com

Abstract

Bullous pemphigoid is a blistering disorder which mainly affects the geriatric population predominantly older than 70 years. It is caused by an autoimmune reaction to the hemidesmosomal proteins in basal keratinocytes, causing an inflammatory cascade and subsequent bullae formation. It is rarely encountered in infants, children, and middle-aged adults. Herein, a case of Bullous pemphigoid in a 37-year old female patient is reported. The patient presented with a three-month history of multiple serous fluid-filled tense blisters on the face, neck, trunk, flexor and extensor surfaces of the extremities up to the lower thigh, with areas of excoriation, peeling, erosion and crusting. No involvement of the mucous membranes noted. The lesions were associated with intense pruritus and pain upon rupture. Patient had no other subjective complaints and had an unremarkable past medical history. Patient was initially treated with antibiotics but noted no improvement in her condition. Histologic evaluation of the skin was done and revealed a subepidermal vesicular dermatitis with prominent neutrophilic infiltrates. No hyphae or spores were seen. With these findings, patient was admitted and treated with systemic steroids, antibiotics, and antipruritic medications. Direct Immunofluorescence was done and yielded findings consistent with the diagnosis of Bullous Pemphigoid. The overall response of the patient to therapy was satisfactory. The differentiation of Bullous pemphigoid from other subepidermal bullous diseases is important due to the potential of systemic manifestations and complications of the other diseases. The importance of clinical, histopathologic and immunologic findings in confirming the diagnosis of Bullous Pemphigoid is highlighted in this case report.

Keywords: Bullous Pemphigoid, Female, Case Report

1. Introduction

Bullous pemphigoid (BP), an autoimmune subepidermal dermatosis, predominantly affects people older than 60 years of age, with a peak incidence in the 70s (Kang et al., 2019; Kridin & Ludwig, 2018; Miyamoto et al., 2019; Rawson et al., 2018; Zanella et al., 2011). There is no known ethnic, racial or gender predilection (Miyamoto et al., 2019; Sravyasruthi et al., 2020; Zanella, 2011). The estimated annual incidence in the general population is between 2.4 and 23 cases per million (Bourdon-Lanoy et al., 2005). Reported cases of BP in individuals younger

than 50 years are rarely encountered with incidence rates usually lower than 0.5 cases per million population (Kridin & Ludwig, 2018).

BP is mediated by autoantibodies against the dermo-epidermal junction of the skin and adjacent mucous membrane. Deposition of these antibodies initiate an immunologic response by activation of an inflammatory process which subsequently activates the complement system, releasing products that cause degradation of the extracellular membrane ultimately leading to blister formation. The classic form manifests with large, tense blisters arising on normal skin or on an erythematous or urticarial base on the trunk and extremities accompanied by intense pruritus (Kang et al., 2019). Diagnosis relies on clinical assessment of the characteristic lesion described above, histologic demonstration of subepidermal blister, immunologic detection of IgG and/or C3 deposition at the basement membrane zone of the skin, and quantification of circulating autoantibodies against hemidesmosomal proteins (Miyamoto et al., 2019).

This report emphasizes the importance of considering the possibility of a diagnosis of BP in adults younger than 50 years of old. Furthermore, discussion of the clinical characteristics of the disease in a younger patient is highlighted in this report, comparing it with the usual manifestations seen in geriatric patients. Differentiaton from other subepidermal bullous disorders which closely mimics BP in clinical presentation is also highlighted.

2. Case Report

A 37-year-old Filipino female presented with a three-month history of vesicular lesions and tense blisters associated with severe pruritus and pain upon rupture of the lesions. The lesions were noted initially on the face and neck but gradually spread to the trunk and extremities, up to the lower thigh. There was no history of insect bites, trauma, fever, cough, coryza, myalgias or arthralgias. She previously sought consult and was prescribed with Mupirocin 2% ointment, however lesions persisted. Skin punch biopsy on the abdominal area was done as out-patient and revealed whole epidermal necrosis in the center of the specimen with subepidermal split infiltrated with numerous neutrophils and nuclear dust. In the dermis were superficial perivascular infiltrates of lymphohistiocytes, neutrophils and few eosinophils. No hyphae or spores seen. Patient was prescribed with oral methylprednisolone and Clindamycin but advised admission for further work-up.

She is a known hypertensive maintained on Amlodipine 5mg tablet once daily. No past history suggestive of diabetes, asthma, seizure or any other illnesses. Patient is a non-smoker and non-alcoholic beverage drinker with no history of illicit drug use. Heredofamilial diseases include hypertension on the maternal side and an uncharacterized skin blistering disorder on the paternal side as claimed.

On physical examination, vital signs were within the normal limits. Inspection of the skin revealed multiple serous fluid-filled tense blisters on the face, neck, trunk, flexor and extensor surfaces of the extremities up to the lower thigh, with areas of excoriation, peeling, erosion and crusting (Figures 1a, 1b and 1c). No involvement of the mucous membranes was noted. The rest of the physical examination findings were unremarkable.

A provisional diagnosis of Bullous Pemphigoid was considered. Laboratory work up revealed increased C-reactive protein (18.06, NV: 0-5 mg/L), decreased total protein (5.5, NV: 6.0-8.4 g/dL), decreased A/G ratio (0.7, NV: 1.3-3.0), increased WBC count (11.4, NV: 4.8-10.8 10^3/uL), eosinophilia (10%, NV: 0-7%), increased SGPT (137, NV: 5-50 U/L), normal C3 and C4 levels, negative Anti-nuclear antibody (IF), negative Rheumatoid Factor and clear lung fields with minimal left lower pleural thickening on chest x-ray.

Figures 1a (left), 1b (middle) and 1c (right) show the characteristic lesion of BP described as tense blister arising on an erythematous base. These lesions were located in the lower extremities (1a and 1b) and hands (1c)

As presented by the patient clinically, the lesions of Linear IgA Dermatosis can resemble those of BP, consisting of papulovesicles or larger bullae that are symmetrically distributed on extensor surfaces also associated with moderate to severe pruritus. Histologically, the distinction is made from Direct Immunofluorescence (DIF) microscopy of perilesional skin. Mucosal involvement, however is an important clinical manifestation of Linear IgA dermatosis and was absent in the patient. Dermatitis Herpetiformis (DH) is a papulovesicular skin disease characterized by lesions spread symmetrically over extensor surfaces of the body and is associated with intense pruritus. Histologic examination reveals a neutrophil-rich infiltrate within the dermal papillae. As with Linear IgA Dermatosis, DIF is required to confirm the diagnosis. Bullous Systemic Lupus Erythematosus (BSLE) is a distinctive clinical presentation of SLE that affects young adult females and involves both sun-exposed and non-exposed skin. Lesions may be similar to BP, consisting of blisters appearing on an erythematous base with a predilection for the face, upper trunk and proximal extremities. Skin biopsy findings of subepidermal neutrophilic infiltrates also support the diagnosis. The absence of a history of other systemic symptoms commonly associated with SLE flares, along with a negative ANA result and normal C3 and C4 levels makes the diagnosis of BSLE less likely.

In view of clinical and histologic criteria, the patient was managed as a case of Bullous Pemphigoid and was started on Hydrocortisone 100mg IV every six hours to decrease the inflammatory response and control active blister formation.   She was also given antibiotic prophylaxis of Amoxicillin-clavulanic acid 1.2g IV every eight hours and Cetirizine 10mg tablet, one tablet orally twice a day for relief of pruritus. A sterile gauze dressing soaked in PNSS was applied on affected areas twice a day.

On the first to fourth hospital day, patient noted less pruritus in the affected areas. No subjective complaints of pain, fever or dyspnea. Vital signs remained stable. A 4mm punch biopsy of perilesional skin was taken on the abdominal area and sent for DIF studies in another institution.

On the fifth to ninth hospital day, patient noted relief of pruritus and gradual diminution and flattening of bullae. Patient had no subjective complaints and vital signs remained stable. Complete blood count showed leukocytosis (15.59, NV: 4.8-0.8 10^3/uL) with neutrophilia (78%, NV: 40-74%). An increase from baseline was noted in the patient's SGPT value (126, NV: 5-50 U/L). Patient was started on Dapsone 100mg tablet, one tablet orally once a day, Azathioprine 50mg tablet, one tablet orally once a day and L-carnitine capsule, one capsule orally thrice a day. Intravenous Hydrocortisone was gradually tapered and eventually shifted to Methylprednisolone 16mg tablet,

one tablet orally twice a day. The seven-day course of Amoxicillin-clavulanic acid was completed and patient was eventually discharged with pending DIF results. Patient was advised to continue Azathioprine, Methylprednisolone, Cetirizine, L-carnitine and Mupirocin ointment as take home medications.

Patient returned for follow-up one week after discharge and reported flattening of blisters associated with relief of pruritus. Results of DIF studies revealed linear deposition of fibrinogen, IgA, IgM, and IgG along the basement membrane zone. The strongest fluorescence was seen with C3 and IgG, findings consistent with the diagnosis of Bullous Pemphigoid. Methylprednisolone was tapered to one 16mg tablet once a day and the rest of the take home medications were continued.

3. Discussion

BP is the most common subepidermal immunobullous disease chiefly affecting adults older than 60 years of age rarely in individuals younger than 50 years of age (Baroero et al., 2017; Kang et al., 2019; Kridin & Ludwig, 2018, Rawson et al., 2018; Zanella et al., 2011). Two key hemidesmosomal proteins strongly linked to BP have been identified namely BPAg1, also called BP230, and BPAg2, otherwise known as BP180 (Lee et al., 2014; Parellada et al., 2018; Sravyasruthi et al., 2020; Zanella et al., 2011). Autoantibodies (i.e anti-BP 180) directed to these antigens causes subsequent activation of the classical complement pathway, recruitment of inflammatory cells (mainly eosinophils and neutrophils) and formation of subepidermal bulla (Kang et al., 2019).

Classic forms typically start as pruritic, erythematous lesions and progress into the formation of large tense blisters where intact epidermis forms the roof (Lee et al., 2014). These lesions may occur anywhere but most frequently seen on flexural surfaces, the lower abdomen, and the thighs. Bullae are filled with serous or hemorrhagic fluid and typically, Nikolsky and Asboe-Hansen signs are negative (Kang et al., 2019). The disease is usually widespread, however, localized forms presenting as tense blister to localized areas of involvement have been reported.

The diagnosis of BP fulfills at least 3 of these criteria: (1) clinical findings consistent with BP that is, tense blisters arising from normal, erythematous or urticarial lesional skin affecting the trunk and extremities, (2) histologic evaluation findings suggestive of subepidermal blister with a superficial dermal infiltrate consisting of neutrophils, eosinophils, lymphocytes, and monocytes and macrophages, (3) DIF studies revealing linear deposition of IgG and or complement on the dermo-epidermal junction, and (4) positive anti-BP180NC16AIg antibodies on ELISA determination (Tan & Tay, 2018). These criteria may be used to rule out other subepidermal dermatoses, such as linear IgA dermatosis, dermatitis herpetiformis, inflammatory epidermolysis bullosa acquisita and bullous systemic lupus erythematosus.

In this case, the patient's clinical course was consistent with BP, presenting with tense blisters arising from an erythematous base which initially started on the face and neck progressing to the trunk and limbs. Skin punch biopsy showing a subepidermal vesicular dermatitis and DIF studies revealing IgG and C3 deposition on the skin epithelial basement membrane confirm the diagnosis of BP. Detection of characteristic antibodies by ELISA determination was not done.

The risk of BP increases with advanced age, certain HLA associations, exposure to some drugs (captopril, enalapril, furosemide, spironolactone, amiodarone, losartan, beta-blocker, ibuprofen, fluoxetine, sulfasalazine, chloroquine, D-penicillamine, ampicillin, cephalexin, ciprofloxacin, nalidixic acid, gabapentin and PUVA), and comorbidities such as neurological disease (eg, stroke, dementia, Parkinson's disease), psoriasis, cancer, and skin infection (Kridin & Ludwig, 2018; Lee et al., 2014; Miyamoto et al., 2019). Moreover, the viruses (CMV, EBV, HHV-6, HHV-8, HBV, and HCV), Helicobacter pylori and Toxoplasma gondii, and stress may also induce BP (Sravyasruthi et al., 2020). However, there were no identified triggers nor risk factors associated with the patient in this case.

Treatment is tailored according to the patient comorbidities and disease severity. Current mainstay of therapy includes high potency topical steroids and systemic steroids (Kang et al., 2019). Localized disease may be treated with topical corticosteroids such as clobetasol. In more extensive disease, patients usually respond favorably to

prednisone (0.75-1 mg/kg per day). Immunosuppressive agents, such as azathioprine or mycophenolate, are often used as an adjunct for their potential steroid-sparing effects. Poor prognostic factors include age, comorbidities, low albumin, and high doses of steroids (Bourdon-Lanoy et al., 2005; Lee et al., 2014). Treatment options should halt new blister formation, promote healing of existing lesions, and improve quality of life.

The disease may have peculiarities in the population under the age of 70 years. Studies show an increased expression of anti-BP 180 autoantibodies in younger age groups. Cases in which BP is more widespread are common, with involvement of the head and neck as seen in the index case. Treatment resistance is also commonly encountered, with varying responses to systemic steroids, dapsone or intravenous immunoglobulin in severe cases (Zanella et al., 2011). These are factors that must be considered in the diagnosis and treatment of adolescents and middle-aged adults presenting with blistering diseases.

3. Conclusion

Bullous Pemphigoid, although a disease that primarily affects the elderly, can also manifest in younger patients. A high index of suspicion must be maintained and BP should be included in the differential diagnosis of blistering diseases that present in adolescents and middle-aged adults. The distinction of BP from other subepidermal blistering diseases should be done by DIF studies of perilesional skin, and possibly antibody determination, due to differences in management and response to treatment modalities. The response of BP to steroids is often satisfactory, however the route of administration must be tailored to disease extent, severity and variation especially in younger patients. Adjuncts may be considered if treatment goals are not met.

Acknowledgments

References

Baroero, L., Coppo, P., Bertolino, L., Maccario, S., & Savino, F. (2017). Three case reports of post immunization and post viral Bullous Pemphigoid: looking for the right trigger. *BMC pediatrics*, *17*(1), 60. https://doi.org/10.1186/s12887-017-0813-0

Bourdon-Lanoy, E., Roujeau, J. C., Joly, P., Guillaume, J. C., Bernard, P., Prost, C., Tancrède-Bohin, E., Delaporte, E., Picard-Dahan, C., Albes, B., Bedane, C., Doutre, M. S., Chosidow, O., Lok, C., Pauwels, C., Chevrand-Breton, J., Sassolas, B., & Richard, M. A. (2005). Pemphigoïde du sujet jeune [Bullous pemphigoid in young patients: a retrospective study of 74 cases]. *Annales de dermatologie et de venereologie*, *132*(2), 115–122. https://doi.org/10.1016/s0151-9638(05)79220-6

Kang, S., Amagai, M., Bruckner, A.L., Enk, A.H., Margalis, D.J., McMichael, A.J., & Orringer, J.S. (2019). *Fitzpatrick dermatology*. New York, NY: McGraw-Hill Education.

Kridin, K., & Ludwig, R. J. (2018). The Growing Incidence of Bullous Pemphigoid: Overview and Potential Explanations. *Frontiers in medicine*, *5*, 220. https://doi.org/10.3389/fmed.2018.00220

Lee, C. M., Leadbetter, H. K., & Fishman, J. M. (2015). A case of oropharyngeal bullous pemphigoid presenting with haemoptysis. *Case reports in otolaryngology*, *2015*, 631098. https://doi.org/10.1155/2015/631098

Miyamoto, D., Santi, C. G., Aoki, V., & Maruta, C. W. (2019). Bullous pemphigoid. *Anais brasileiros de dermatologia*, *94*(2), 133–146. https://doi.org/10.1590/abd1806-4841.20199007

Parellada, J., Olivera Arencibia, Y., Watson, H., Parellada, N., Saikaly, L. E., & Saikaly, S. K. (2018). A Case of Bullous Pemphigoid: A Prevalent and Potentially Fatal Condition. *Cureus*, *10*(4), e2533. https://doi.org/10.7759/cureus.2533

Rawson, K., Vinod, S., Sreenivasan, B., & Roy, G. (2018). Drug-induced bullous pemphigod – a case report with review. *Journal of Indian Academy of Oral and Medicine Radiology, 30*(4), 427-431. doi: 10.4103/jiaomr.jiaomr_126_18

Sravyasruthi, P., Swetha, K.R., Saranya, P.V., Pranusha, M., Madhavi, V., Ranganayakulu, D. (2018). A case report on bullous pemphigoid. *EC Pharmacology and Toxicology, 6*(6), 411-413. Retrieved February 23, 2020 from https://www.ecronicon.com/ecpt/pdf/ECPT-06-00178.pdf

Tan, S.K. & Tay, Y.K. (2018). Bullous pemphigoid: profile and outcome in a series of 100 cases in singapore. *Journal of Dermatology and Dermatologic Surgery, 22,* 12-15. doi: 10.4103/jdds.jdds_1_18

Zanella, RR., Xavier, T.A., Tebcherani, A.J., & Sanchez, A.P.G. (2011). Bullous pemphigoid in younger adults: three case reports. *Anais Brasileiros de Dermatologia*, *86*(2). https://doi.org/10.1590/S0365-05962011000200023

Assessment of Smile Dimensions in an Adult Moroccan Population

Moufide Ilham[1], Simour Anas[2], Zineb Serhier[3], Mohamed Bennani Othmani[4], Farid Bourzgui[5]

[1] Dr. Moufid Ilham: Doctor of Dental Medicine, University Hassan II, Faculty of dentistry, Casablanca, Morocco. Present Address: Riad Essalam, Bloc D, num 15, Mohammedia, Morocco. Email: dr.ilhammoufid@gmail.com ORCID: https://orcid.org/0000-0002-3288-0693
[2] Dr. Simour Anass: Doctor of Dental Medicine, University Hassan II, Faculty of dentistry, Casablanca, Morocco. Present Address: 234, Rue Abouzaid Dadoussi, Maârif, Casablanca, Morocco. Email: anasssimour@gmail.com ORCID: https://orcid.org/0000-0002-3289-5713
[3] Prof. Zineb SERHIER Professor, Laboratory of medical informatics, University Hassan II, Faculty of medicine& Pharmacy, Casablanca, Morocco. Email: zserhier@gmail.com https://orcid.org/0000-0003-0419-8133
[4] Prof. Mohamed BENNANI Othmani Professor, Laboratory of medical informatics, University Hassan II, Faculty of medicine& Pharmacy, Casablanca, Morocco. Email: bennanim2000@gmail.com https://orcid.org/0000-0001-7828-8831
[5] Pr. Farid BOURZGUI: Professor and Head of Orthodontics Department, University Hassan II, Faculty of dentistry, Casablanca, Morocco. Corresponding author: Rue Abou Al Alaâ zahar (ex Vésal) - B.P : 9157 Mers Sultan Casablanca. Maroc. Tel. 0021264904702; Email: faridbourzgui@gmail.com . https://orcid.org/0000-0002-0527-9421

Abstract
Background: This study aimed to assess the smile dimensions according to gender, age, and the perception of the overall quality and attractiveness of the smile. Methods: A cross-sectional study including 204 Moroccan men and women distributed over five age categories was conducted between January and September 2021. Gender, age, satisfaction and auto-evaluation of the smile were collected using questionnaire. Then, two images of each participant, one at rest and one upon the largest smile were taken. The following distances were measured on the images: length of the lips and width of the mouth at rest and upon smile, gingival and maxillary central incisor displayed upon smile. Results: Dimensions were significantly more important in men. Women displayed significantly more gingiva. With age, the length of the upper lip at rest increased significantly until the age of 50 and the width of the mouth upon smile continued increasing significantly. 74% of the participants were satisfied with their smile. Participants' satisfaction with their smile was not associated with the degree of gingival display. Conclusion: Males have more important dimensions of the lips and the mouth. Females display more gum than males. Age influences the upper lip length at rest which increases up to the age of 50, and the mouth width upon smile which continues to increase with age. Practical Implications: The definition of specific facial norms for each ethnic group considering gender and age groups is essential to establish diagnoses and orthodontic treatment plans.

Keywords: Facial Expression, Smiling, Tooth Components, Periodontium, Lip, Morocco

1. Introduction

The diagnosis and treatment in modern orthodontics are no longer limited to the evaluation of the skeletal framework of the face and the dental occlusion. Nowadays, they give a capital importance to the smile appearance and the facial aesthetics (Sarver DM, 2015). Moreover, the classic Angle paradigm which considered dental occlusion to be the key word for successful orthodontic treatment has been replaced by the "soft tissue paradigm" aimed at restoring both facial aesthetics and the functions of the manducatory system (Dickens ST et al., 2002). Thus, the aesthetic outcome represents the main motivation of patients seeking an orthodontic treatment (Gazit-Rappaport T et al., 2010).

The major issue of modern orthodontics is to re-establish facial aesthetics that respect the beauty canons of different ethnical groups (Blatz MB et al., 2019). Malocclusion and the need for orthodontic treatment have been associated with oral health-related quality of life and thus with the impact on the patient's overall quality of life (Liu Z et al. 2009).

The soft tissues of the face and perioral region influence therapeutic decision making in orthodontics (Sarver DM, 2015). Adult patients present more challenges to the therapeutic choice process than adolescents and pre-adolescents (Dickens ST et al., 2002). The soft tissue profile that should be obtained after treatment must be adapted to the age and/or gender of the patients (Sarver DM, 2015).

With age, there is an increase in the length of the upper lip and a decrease in the exposure of the maxillary incisors, especially in men (Drummond S & Capelli J, 2016). Studies have shown that with ageing, there is a redistribution without total loss of volume of the upper lip, by decreasing its thickness and increasing its length (Iblher N et al., 2012). While, histomorphometric analysis revealed thinning of the upper lip with evidence of atrophy of the orbicularis muscle (Penna V et al., 2009).

The "normal" values in orthodontics, known as norms, are generally derived from populations of Caucasian origin. These norms cannot be extrapolated to other ethnic groups without proper validation. Johnson's studies (Johnson PF, 1992) showed the existence of ethnic variations, hence the need to establish aesthetic standards for each ethnically diverse population in order to guide treatment plans and optimize outcomes.

The objective of this study was to evaluate the dimensions of the smile in an adult Moroccan population taking into account gender and different age categories.

2. Materials and Methods

We carried out a cross-sectional study to assess the smiling dimensions in a Moroccan adult population according to age and gender. The study was conducted between January and September 2021 and the sample was made up of 204 people. The inclusion criteria were as follows: Moroccan men and women, over 20 years old, who presented at least 4 anterior teeth including the maxillary central incisors. Patients with craniofacial syndrome and a history of craniofacial trauma, patients who received facial fillers, injections, plastic or orthognathic surgery, were excluded. An anonymous questionnaire collecting the following items was submitted for each participant. Which were classified according to the following five age ranges: less than 20 years, between 20 and 30 years, between 30 and 40 years, between 40 and 50 years, between 50 and 60 years and over 60 years. The participants' satisfaction or not with their own smile, as well as the evaluation they gave to their smile according to the Likert scale: Bad - Not bad - Good - Very good. Two full face photos of each participant, one at rest and one with the widest smile, were taken using a Canon EOS Kiss x4 camera. In order to obtain reproducible data, the same parameters were respected when taking all the images: an automatic "portrait" mode, a focal length of 55mm and a distance of 1.5m between the participant and the operator. The head was positioned so as to have a Frankfurt plane parallel to the ground. A ruler held between the fingers and under the chin was used as a reference for magnification measurement. On each snapshot at rest and when smiling, we measured the following variables in centimeters (Figure 1):

- The length of the upper lip (from the sub-nasal point to the lowest point of the upper lip),

- The width of the mouth (from commissure to commissure)
- The length of the lower lip (from the highest point of the lower lip to the sub-labial point).
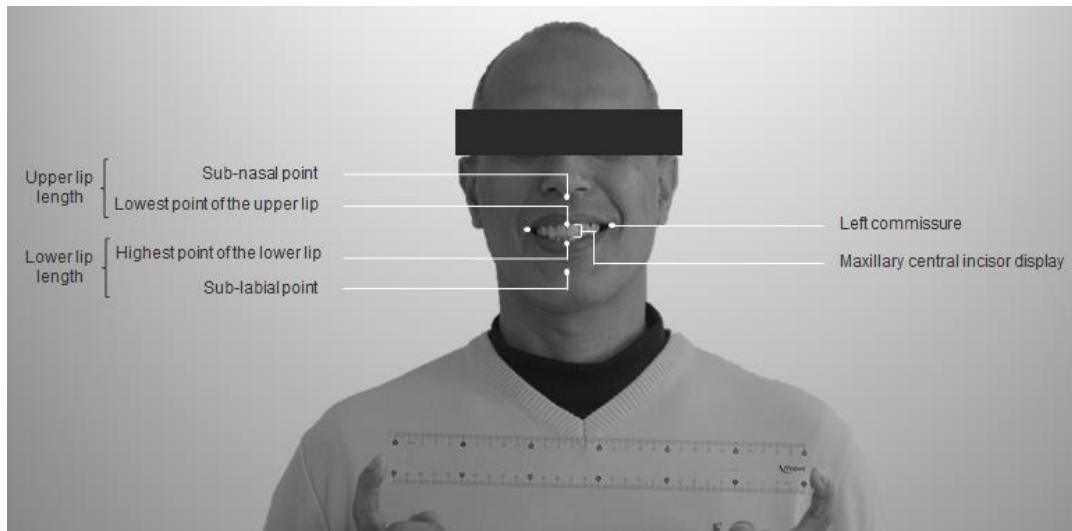

Figure 1: Plot of landmarks on a photo with the widest smile with no gingival display. The same marks were applied to the photos at rest with the exception of the gingival and the maxillary central incisor displays.

On the smiling images, we also measured the gingival and the maxillary central incisor displays. The measurements were carried out using the "ImageJ" software. The statistical analysis was carried out using the software jamovi project (2021) (version 2.0). We used the student's t test to compare the dimensions of the smile according to gender. Mann-Whitney U test was used when Student's t test was not applicable. To compare the dimensions of the smile according to age, we used the ANOVA test. When this was not applicable, we used the Kruskal-Wallis test. We used the Mann-Whitney U test to analyze the relationship between gingival display and the participants' satisfaction. A p-value of 0.05 was defined for the significance of the statistical results. Ethical clearance was obtained from the Ethics Committee (Number 09/21). All participants gave their free and informed consent to participate in this study, after explaining and discussing the objectives of the study and the anonymous and confidential nature as to the use of patients' personal data.

3. Results

204 people participated in this study with 22.5% (46) in each following age groups: >20-30, >30-40, >40-50, >50-60 and 9.8% (20) in the age group >60. Both genders were evenly split with a proportion of 50%. (Table 1) The majority of the participants were satisfied with their smile with a proportion of 74% (Figure 2). 41.2% of the participants attributed the evaluation "not bad" to their smile, followed respectively by the evaluations "good" (32.4%), "very good" (18.1%) and "bad" (5.9%). A minority of 2.9% was not concerned by this evaluation (Figure 3). At rest, the average values of the upper lip length, the mouth width and the lower lip length in centimeters were respectively: 2.09 +/- 0.29, 4.83 +/- 0.38 et 1.67 +/- 0.32. Upon smile, these average values were respectively: 1.60 +/- 0.29, 5.89 +/- 0.51 et 1.67 +/- 0.29. The average value of the maxillary central incisor's display was 0,81 +/- 0,19cm. The gingival display varied from 0 to 0.55cm (Table 2). Gender distribution showed a significant difference for all the smiling and non-smiling dimensions except the crown display. Males presented longer and wider lips than females. The maximal gingival display value was more important in females (Table 3). The distribution by age groups showed a significant difference for the upper lip length at rest that increased with age then decreased after the age of 50. Mouth width upon smile increased significantly with age. All other dimensions did not significantly change with age (Table 4). Every increase of 1cm of the gingival display resulted in a significant average increase of 0.4 cm of the maxillary central incisor display (Table 5). Comparison of satisfaction in relation with gingival display did not show significant results: the gingival display did not significantly influence participants' satisfaction with their smile (Table 6).

Table 1: Sample characteristics

	Number	Percentage (%)
Age group		
>20-30	46	22,5
>30-40	46	22,5
>40-50	46	22,5
>50-60	46	22,5
>60	20	9,8
Females	102	50,0

Satisfaction with smile

26%

74%

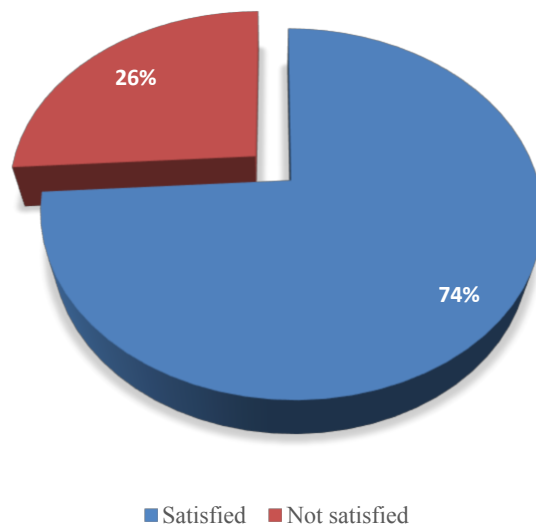■ Satisfied   ■ Not satisfied

Figure 1: Distribution of participants according to their satisfaction with their smile
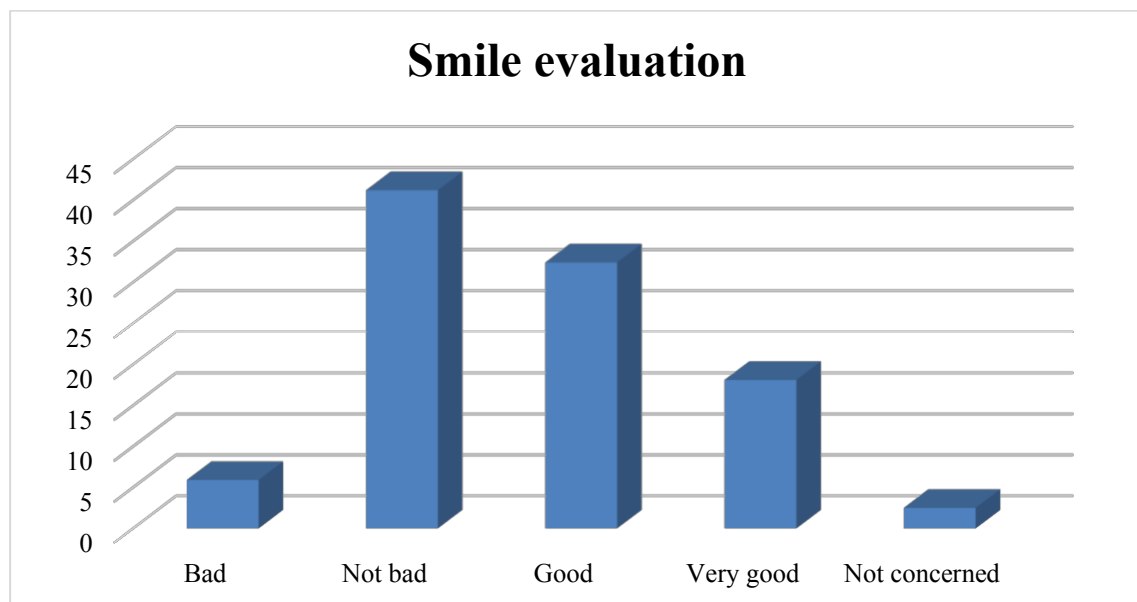
Smile evaluation

Figure 2 : Distribution of participants according to their smile evaluation

Table 2: Average smile dimensions

	Mean (SD) Median (min - max)*
Non-smiling	
Upper lip length (cm)	2,09 (0,29)
Mouth width (cm)	4,83 (0,38)
Lower lip length (cm)	1,67 (0,32)
Smiling	
Upper lip length (cm)	1,60 (0,29)
Mouth width (cm)	5,89 (0,51)
Lower lip length (cm)	1,67 (0,29)
MCI display (cm)	0,81 (0,19)
Gingival display (cm)*	0,00 (0,00 – 0,55)

MCI, maxillary central incisor

Table 3: Comparison of smile dimensions by gender

	Males Mean (SD) Median* (min – max)	Females Mean (SD) Median* (min – max)	*p*-value
Non-smiling			
Upper lip length (cm)	2,18	2,01	<0,001
Mouth width (cm)	4,92	4,74	<0,001
Lower lip length (cm)	1,73	1,62	0.019
Smiling			
Upper lip length (cm)	1,68	1,51	<0,001
Mouth width (cm)	5,98	5,81	0.021
Lower lip length (cm)	1,76	1,58	<0,001
MCI display (cm)*	0,84 (0,00 – 1,10)	0,86 (0,27 – 1,21)	0.463
Gingival display (cm)*	0,00 (0,00 – 0,45)	0,00 (0,00 – 0,55)	0.005

MCI, maxillary central incisor

Table 4: Comparison of smile dimensions by age groups

	>20-30 Mean (SD) Median* (min – max)	>30-40 Mean (SD) Median* (min – max)	>40-50 Mean (SD) Median* (min – max)	>50-60 Mean (SD) Median* (min – max)	>60 Mean (SD) Median* (min – max)	*p*-value
Non-smiling						
Upper lip length (cm)	2,01 (0,21)	2,05 (0,30)	2,16 (0,32)	2,15 (0,28)	2,12 (0,31)	0,036
Mouth width (cm)	4,88 (0,36)	4,80 (0,35)	4,86 (0,37)	4,90 (0,33)	4,58 (0,53)	0,120
Lower lip length (cm)	1,66 (0,21)	1,62 (0,24)	1,73 (0,30)	1,67 (0,26)	1,73 (0,66)	0,437
Smiling						
Upper lip length (cm)	1,59 (0,24)	1,54 (0,30)	1,61 (0,34)	1,65 (0,31)	1,58 (0,23)	0,522
Mouth width (cm)	6,28 (0,43)	5,85 (0,45)	5,84 (0,46)	5,78 (0,47)	5,50 (0,47)	<0,001

Lower lip length (cm)	1,64 (0,27)	1,63 (0,27)	1,75(0,33)	1,67 (0,27)	1,68 (0,33)	0,379
MCI display (cm)*	0,87 (0,58-1,16)	0,86 (0,27-1,21)	0,84 (0,00-1,07)	0,83 (0,13-1,12)	0,86 (0,23-1,05)	0,071
Gingival display (cm)*	0,00 (0,00-0,28)	0,00 (0,00-0,45)	0,00 (0,00-0,36)	0,00 (0,00-0,38)	0,00 (0,00-0,55)	0,144

MCI, maxillary central incisor

Table 5: Results of the linear regression of the maxillary central incisor display according to the gingival display

	B	**p-value**
Gingival display	0,401	<0,001
Constant	0,790	<0,001

Table 6: Comparison of participants' satisfaction with their smile according to the gingival display

	Satisfied **Median (min – max)**	**Not satisfied** **Median (min – max)**	**p-value**
Gingival display (cm)	0,00 (0,00-0,55)	0,00 (0,00-0,45)	0,117

4. Discussion

The aim of this study was to evaluate the dimensions of the smile in an adult Moroccan population according to gender and age, as well as the participants' satisfaction and perception of their smile. The results showed that gender influenced smile measurements: men had larger lip and mouth dimensions. Women in this study displayed more gum tissue than men. The degree of visibility of the maxillary central incisor during smiling, however, was not affected by gender. Age influenced the upper lip length at rest, which increased up to age 50, as well as the mouth width upon the largest smile, which continued to increase with age. The other dimensions were not affected by age.

We distributed the sample of our study according to the overall demographic distribution of the Moroccan population published by the High Commission for Planning. This distribution shows a sex ratio of around 1: 1, hence the parity between men and women in our sample. The first four age groups have an equal distribution of around 22.5% each, unlike the last age group which represents around 10% of the total population.

The results of our study showed a significant difference between both genders for the lips and mouth dimensions ($p \leq 0.05$): men have higher values than women both at rest and when smiling. These results agree with those found in the literature. (Souccar N et al., 2019; Sforza C et al., 2010; Gibelli D et al., 2015); Dickens ST et al., 2002; Drummond S & Capelli J, 2016) On the other hand, the results of our study were significant for the gingival display ($p = 0.005$) but not significant for the maxillary central incisor display ($p = 0.463$). The study conducted by Souccar N et al., 2019 on an African American and Caucasian population showed that the length of the lips and the width of the mouth were greater in males at rest and upon smile. A difference in certain landmarks and in the methods used in this study is to be noted: the calculation of the lengths was based on the upper stomion and the lower stomion instead of the lowest point of the upper lip and the highest point of the lower lip; the study of Souccar N et al., 2019 was performed through three-dimensional surface images instead of two-dimensional images as in our study. On the other hand, our study revealed a significant difference ($p = 0.005$) for the gingival display between the two genders, contrary to the results obtained by Souccar N et al., 2019

A study carried out by Sforza C et al., 2010 from the three-dimensional coordinates of facial landmarks on an Italian population also showed a significant sexual dimorphism for the total height of the lips and the width of the mouth: men had higher values than women.

Regarding gingival display, the results of our study are in agreement with those of studies carried out by Al-Habahbeh R & Al-Shammout R, 2009 and Al-Jabrah et al., 2010 on a Jordanian population which revealed that women displayed significantly more gum when smiling than men. In addition, the study of Al-Habahbeh R & Al-Shammout R, 2009 revealed that the anterosuperior teeth display when smiling was significantly greater in women, unlike our study.In disagreement with our study, Kapagiannidis D et al., 2005 found a significant difference between the two genders for the central incisor display, with higher values in women. In line with our results, (Drummond & Capelli, 2016) showed that gingival display was a female trait. The same authors also found that the maxillary incisor display upon smile characterized women, which disagrees with our results. A full explanation of the sexual dimorphism in the gingival smile line's frequency has yet not been determined (Peck S et al., 1992). Previous data confirms the need to establish gender-specific standards in order to individualize orthodontic treatment while respecting female and male characteristics. On the other hand, the absence of significant results for the maxillary incisor display upon smile, according to our study, suggests that it can be generalized for both genders.

Our study revealed a significant difference between the age groups only for the length of the upper lip at rest, which increased until the age of 50 (p = 0.036), and the width of the mouth upon smile which increased with age (p <0.001). The lower lip, according to our study, did not significantly change in length with age, either when smiling (p = 0.379) or at rest (p = 0.437). Also, the variations in the upper lip length upon smile and the width of the mouth at rest according to age were not significant (p = 0.522 and p = 0.120). These results did not fully correspond to the results found in the literature. (Souccar N et al., 2019; Sforza C et al., 2010; Dickens ST et al., 2002; Drummond & Capelli, 2016; Desai S et al., 2009; Singh B et al., 2013; Dindaroğlu F et al., 2011; Van der Geld P et al., 2008) Our results differed from those of Souccar et; al.'s study 2019 which showed that gingival and maxillary incisor display decreased significantly with age. The same study also found that the upper lip length upon smile and the mouth width at rest significantly increased with age.

The study conducted by Drummond & Capelli, 2016 on four age groups: 19-24, 25-34, 35-44 and 45-60, revealed a significant decrease in the gingival and the maxillary incisor display with age. On the other hand, the same study showed an increase in the upper lip length at rest with age, with larger values in the latter group.ST (Dickens et al., 2002) found that the gingival and the incisor display decreased after the age of 20. Sforza C et al., 2010 reported that mouth width increased significantly with age while the total lip height remained relatively stable in adulthood. (Desai S et al., 2009) showed that the inter-commissural distance at rest differed significantly between age groups. The results of this study for the length of the upper lip were not significant at rest and slightly significant when smiling, which contradicts with our results. According to the same study, a significant difference was noted for the display of the maxillary incisors which decreased from 1.5 to 2mm with age. A study conducted by Singh B et al., 2013 on three age categories: 15-25, 30-40 and 45-55, showed that gingival display did not significantly change with age, which agrees with our results. As for the maxillary incisor display, this study showed a slightly significant decrease in men and no significant result in women. The study also showed that the upper lip length upon smile increased significantly with age for both genders, while at rest it increased significantly for women. Our results agree with those of the study carried out by Dindaroğlu F et al., 2011 on three age groups (17 to 55 years), which showed a significant difference for the upper lip length at rest, with higher values between 38 and 55 years. A significant increase of the inter-commissural width upon smile with age was also reported by this study. In line with our study, Chetan P et al.,2013 found that the upper lip length at rest increased significantly with age. According to their study, this increase also affected the inter-commissural width at rest. It is important to consider the effect of aging on the soft tissues of the perioral region and therefore on the smile. The variations of the upper lip dimensions with age have been histologically explained by the redistribution of its total volume. This redistribution results in the increase of its length and the decrease of its thickness. The aging upper lip also experiences a degeneration of the elastic fibers and collagen fibers which affects its elasticity. (Iblher N et al., 2012; Penna V et al., 2009) In addition, Perenack JD & Biggerstaff T 2006 explained the lengthening of the aging upper lip by a generalized loss of volume following the muscle's atrophy as well as a progressive weakening of the facial attachments suspending the soft tissues of the lip. Chetan P et al.,2013 attributed the increase of the resting upper lip length to the loss of the muscle tonus at rest, the increased flaccidity and the redundancy with aging. They also explained the increase of the inter-commissural width and the commissures' height with age by the sagging of the mouth angles following the increase of muscle length at rest. In our study, these factors

influenced the upper lip length at rest and the mouth width when smiling without noticeable effect on the other parameters. The majority of the participants in our study were satisfied with their smile (74%). The majority of the participants rated their smile as "Not bad" (41.2%) while only 5.9% found their smile to be "bad". These results can be linked to a psychological and socio-cultural component. Van der Geld P et al., 2007 described two dimensions of self-perception of the smile: a social dimension defining the attractiveness of the smile by cultural norms and the judgment of others and an individual dimension related to the satisfaction of the appearance of one's own smile. Other studies have correlated the perception of smile with age, gender, level of education or level of oral hygiene (Strajnic L et al., 2016; Khanna S 2014). The Alkhatib MN et al., 2005's study conducted in the United Kingdom found results consistent with our study. Three-quarters of the participants (76%) were satisfied with their smile and two-thirds (67%) were satisfied with their teeth color. Azodo C & Ogbomo A. 2014 also found that among 399 participants, 79.4% were satisfied with their smile. The study of, Enabulele JE & Omo JO 2017 on a Nigerien population showed that 45.1% were dissatisfied with the general appearance of their smile. Other studies have found opposite results, with higher prevalence of dissatisfaction (Khanna S 2014; (Isiekwe GI & Aikins EA 2019; Hassel AJ et al., 2011). The scientific literature is very rich with studies showing an association between the patients' satisfaction with their smile and the characteristics of the latter, in particular the size, shape, alignment, color and visibility of teeth, the gingival display, the desired treatment etc (Van der Geld P et al., 2007; Alkhatib MN et al., 2005; Azodo C & Ogbomo A. 2014; Enabulele JE & Omo JO 2017; Isiekwe GI & Aikins EA 2019; Tin-Oo MM et al., 2011; Hassel AJ et al., 2011; Al-Zarea BK 2013). However, additional research is needed to assess these factors in the Moroccan population in order to better understand the results of our study. The results we found showed that the maxillary incisor display significantly increased with the increase of the gingival display. Peck S et al., 1992 and Al-Jabrah et; al. 2010, found that participants displaying gingiva in their respective studies had slightly shorter maxillary central incisors, but these results were not significant in both studies. Further studies are necessary to better determine the type of relationship between gingival display and maxillary central incisor display. Our study showed that participants' satisfaction was not significantly correlated with gingival display. Contrary to our results, a study conducted by Antoniazzi et; al. 2017; Antoniazzi RP et al., 2017) showed that the percentage of people who were satisfied with their smile and had excessive gingival display did not exceed 21.1%. Van der Geld et al., 2007 also found that gingival display was a critical factor in people's satisfaction with their smile: a total dental display with a gingival display of 2 to 4mm was considered the most aesthetic according to their study. Other studies in which participants evaluated the smiles presented in images with different gingival display levels showed that the latter significantly influences the perception of the smile attractiveness (Kaya B & Uyar R 2013; Sriphadungporn C & Chamnannidiadha N 2017; Sybaite J et al., 2020; Hunt O 2002; (Tosun H & Kaya B 2020). Excessive gingival display (6 mm) is generally considered the least attractive (Sriphadungporn C & Chamnannidiadha N 2017; Sybaite J et al., 2020).

The results of our study, eliminating gingival display as a factor influencing participants' satisfaction with their smile, suggest the involvement of other factors for the Moroccan population. The literature has studied the association of several dental parameters with smile satisfaction, including the size, shape, display, alignment and color of teeth. The latter is generally the most influencing factor in the self-perception of the smile (Alkhatib MN et al., 2005; Enabulele JE & Omo JO 2017; Isiekwe GI & Aikins EA 2019; Tin-Oo MM et al., 2011; Hassel AJ et al., 2011; Al-Zarea BK 2013). It is therefore necessary to study these parameters and their relation with the satisfaction of the smile among the Moroccan population.

5. Conclusion

Gender influences smile dimensions: males have more important dimensions of the lips and the mouth. Females display more gum than males. The maxillary central incisor display is not affected by gender. Age influence the upper lip length at rest which increases up to the age of 50, and the mouth width upon smile which continues to increase with age. The other dimensions were not affected by age. The majority of the participants were satisfied with their smile. The maxillary central incisor display increased with the gingival display. Participants' satisfaction with their smile is not influenced by gingival display. Further studies are required in order to better study the influence of age on the smile dimensions of the Moroccan population as well as the factors implied in its satisfaction with the smile.

References

Sarver DM. Interactions of hard tissues, soft tissues, and growth over time, and their impact on orthodontic diagnosis and treatment planning. American Journal of Orthodontics and Dentofacial Orthopedics. 2015 Sep;148(3):380–6. DOI: 10.1016/j.ajodo.2015.04.030

Dickens ST, Sarver D, Profitt WR. Changes in frontal soft tissue dimensions of the lower face by age and gender. World J Orthod. 2002 Jan 1;3:313–20. https://web.s.ebscohost.com/abstract?direct=true&profile=ehost&scope=site&authtype=crawler&jrnl=15305678&asa=Y&AN=38012978&h=DDsdSwwIJO9qseB8E9uS2hKFSMqNePJPL6gFqhjcoosF9nRrle71REr3EUvtyqzWz6C%2f1%2bwvdn2RRUTbpZ2hQg%3d%3d&crl=c&resultNs=AdminWebAuth&resultLocal=ErrCrlNotAuth&crlhashurl=login.aspx%3fdirect%3dtrue%26profile%3dehost%26scope%3dsite%26authtype%3dcrawler%26jrnl%3d15305678%26asa%3dY%26AN%3d38012978

Gazit-Rappaport T, Haisraeli-Shalish M, Gazit E. Psychosocial reward of orthodontic treatment in adult patients. Eur J Orthod. 2010 Aug;32(4):441–6. DOI: 10.1093/ejo/cjp144

Blatz MB, Chiche G, Bahat O, Roblee R, Coachman C, Heymann HO. Evolution of Aesthetic Dentistry. Journal of Dental Research. 2019 Nov;98(12):1294-1304. DOI: 10.1177/0022034519875450

Liu Z, McGrath C, Hägg U. The Impact of Malocclusion/Orthodontic Treatment Need on the Quality of Life. The Angle Orthodontist. 2009 May 1;79(3):585–91. DOI: 10.2319/042108-224.1

Drummond S, Capelli J. Incisor display during speech and smile: Age and gender correlations. The Angle Orthodontist. 2016 Jul 1;86(4):631–7. DOI: 10.2319/042515-284.1

Iblher N, Stark G-B, Penna V. The aging perioral region — do we really know what is happening. J Nutr Health Aging. 2012 Jun;16(6):581–5. DOI: 10.1007/s12603-012-0063-7

Penna V, Stark G-B, Eisenhardt SU, Bannasch H, Iblher N. The Aging Lip: A Comparative Histological Analysis of Age-Related Changes in the Upper Lip Complex: Plastic and Reconstructive Surgery. 2009 Aug;124(2):624–8. DOI: 10.1097/PRS.0b013e3181addc06

Johnson PF. Racial norms: Esthetic and prosthodontic implications. The Journal of Prosthetic Dentistry. 1992 Apr;67(4):502–8. DOI: 10.1016/0022-3913(92)90081-k

Souccar N, Bowen D, Syed Z, Swain T, Kau C, Sarver D. Smile dimensions in adult African American and Caucasian females and males. Orthodontics & Craniofacial Research. 2019 May;22:186–191. DOI: 10.1111/ocr.12278

Sforza C, Grandi G, Binelli M, Dolci C, De Menezes M, Ferrario VF. Age- and sex-related changes in three-dimensional lip morphology. Forensic Science International. 2010 Jul;200(1–3):182.e1-182.e7. DOI: 10.1016/j.forsciint.2010.04.050

Gibelli D, Codari M, Rosati R, Dolci C, Tartaglia GM, Cattaneo C, et al. A Quantitative Analysis of Lip Aesthetics: The Influence of Gender and Aging. Aesth Plast Surg. 2015 Oct;39(5):771–6. DOI: 10.1007/s00266-015-0495-7

Al-Habahbeh R, Al-Shammout R. Tooth and Gingival Display in the Anterior Region at Rest and During Smiling. CLINICAL RESEARCH. 2009;4(4):15. DOI:10.12816/0000081

Al-Jabrah O, Al-Shammout R, El-Naji W, Al-Ajarmeh M, Al-Quran A-H. Gender Differences in the Amount of Gingival Display During Smiling Using Two Intraoral Dental Biometric Measurements: Gender Differences in Gingival Display. Journal of Prosthodontics. 2010 Jan 22;19(4):286–93. DOI: 10.1111/j.1532-849X.2009.00562.x

Kapagiannidis D, Kontonasaki E, Bikos P, Koidis P. Teeth and gingival display in the premolar area during smiling in relation to gender and age. J Oral Rehabil. 2005 Nov;32(11):830–7. DOI: 10.1111/j.1365-2842.2005.01517.x

Peck S, Peck L, Kataja M. The gingival smile line. The Angle Orthodontist. 1992 Jun 1;62(2):91–100. DOI: 10.1043/0003-3219(1992)062<0091:TGSL>2.0.CO;2

Desai S, Upadhyay M, Nanda R. Dynamic smile analysis: Changes with age. American Journal of Orthodontics and Dentofacial Orthopedics. 2009 Sep;136(3):310.e1-310.e10. DOI: 10.1016/j.ajodo.2009.01.021

Singh B, Ahluwalia R, Verma D, Grewal SB, Goel R, Kumar PS. Perioral age-related changes in smile dynamics along the vertical plane. The Angle Orthodontist. 2013 May 1;83(3):468–75. DOI: 10.2319/061212-488.1

Dindaroğlu F, Doğan S, Ertan Erdinç A. Smile Esthetics: Age Related Changes, and Objective Differences between Social and Spontaneous Smiles. Journal of Clinical Pediatric Dentistry. 2011 Sep 1;36(1):99–106.

Van der Geld P, Oosterveld P, Kuijpers-Jagtman AM. Age-related changes of the dental aesthetic zone at rest and during spontaneous smiling and speech. The European Journal of Orthodontics. 2008 Aug 1;30(4):366–73. DOI: 10.1093/ejo/cjn009

Chetan P, Tandon P, Singh GK, Nagar A, Prasad V, Chugh VK. Dynamics of a smile in different age groups. The Angle Orthodontist. 2013 Jan 1;83(1):90–6. DOI: 10.2319/040112-268.1

Perenack JD, Biggerstaff T. Lip Modification Procedures as an Adjunct to Improving Smile and Dental Esthetics. Atlas of the Oral and Maxillofacial Surgery Clinics. 2006 Mar;14(1):51–74.

Van der Geld P, Oosterveld P, Van Heck G, Kuijpers-Jagtman AM. Smile Attractiveness. The Angle Orthodontist. 2007 Sep 1;77(5):759–65. DOI: 10.2319/082606-349

Strajnic L, Bulatovic D, Stancic I, Zivkovic R. Self-perception and satisfaction with dental appearance and aesthetics with respect to patients' age, gender, and level of education. Srp Arh Celok Lek. 2016;144(11–12):580–9. https://pubmed.ncbi.nlm.nih.gov/29659216/

Khanna S. Determination of Self Satisfaction with Dental Appearance and Oral Health Status among a Population of Dentate Adults in a Referral Institution. BJMMR. 2014 Jan 10;4(14):2725–35.

Alkhatib MN, Holt R, Bedi R. Age and perception of dental appearance and tooth colour. Gerodontology. 2005 Mar;22(1):32–6. DOI: 10.1111/j.1741-2358.2004.00045.x

Azodo C, Ogbomo A. Self-Evaluated Dental Appearance Satisfaction among Young Adults. Annals of medical and health sciences research. 2014 Jul 1;4:603–7. doi: 10.4103/2141-9248.139339

Enabulele JE, Omo JO. Self perceived satisfaction with dental appearance and desired treatment to improve aesthetics. Afr J Oral Health. 2017 Oct 20;7(1):1-7. DOI: 10.4314/ajoh.v7i1.162230

Isiekwe GI, Aikins EA. Self-perception of dental appearance and aesthetics in a student population. International Orthodontics. 2019 Sep;17(3):506–12. DOI: 10.1016/j.ortho.2019.06.010

Tin-Oo MM, Saddki N, Hassan N. Factors influencing patient satisfaction with dental appearance and treatments they desire to improve aesthetics. BMC Oral Health. 2011 Dec;11(1):6. DOI: 10.1186/1472-6831-11-6

Hassel AJ, Wegener I, Rolko C, Nitschke I. Self-rating of satisfaction with dental appearance in an elderly German population. International Dental Journal. 2008 Apr;58(2):98–102. https://doi.org/10.1111/j.1875-595X.2008.tb00183.x

Al-Zarea BK. Satisfaction with Appearance and the Desired Treatment to Improve Aesthetics. International Journal of Dentistry. 2013;2013:1–7. DOI: 10.1155/2013/912368

Antoniazzi RP, Fischer L de S, Balbinot CEA, Antoniazzi SP, Skupien JA. Impact of excessive gingival display on oral health-related quality of life in a Southern Brazilian young population. J Clin Periodontol. 2017 Oct;44(10):996–1002. DOI: 10.1111/jcpe.12753

Kaya B, Uyar R. Influence on smile attractiveness of the smile arc in conjunction with gingival display. American Journal of Orthodontics and Dentofacial Orthopedics. 2013 Oct;144(4):541–7. DOI: 10.1016/j.ajodo.2013.05.006

Sriphadungporn C, Chamnannidiadha N. Perception of smile esthetics by laypeople of different ages. Prog Orthod. 2017 Dec;18(1):8. DOI: 10.1186/s40510-017-0162-4

Sybaite J, Sharma P, Fine P, Blizard R, Leung A. The Influence of Varying Gingival Display of Maxillary Anterior Teeth on the Perceptions of Smile Aesthetics. J Dent. 2020 Dec;103:103504. doi: 10.1016/j.jdent.2020.103504.

Hunt O. The influence of maxillary gingival exposure on dental attractiveness ratings. The European Journal of Orthodontics. 2002 Apr 1;24(2):199–204. DOI: 10.1093/ejo/24.2.199

Tosun H, Kaya B. Effect of maxillary incisors, lower lip, and gingival display relationship on smile attractiveness. American Journal of Orthodontics and Dentofacial Orthopedics. 2020 Mar;157(3):340–7. DOI: 10.1016/j.ajodo.2019.04.030

Air Chemical Quality and Noise Level in Tourism City Center of Bali 2022

I Nyoman Gede Suyasa[1], Ni Made Marwati[2], Ni Ketut Rusminingsih[3]

[1,2,3] Department of Environmental Health, Poltekkes Kemenkes Denpasar, Bali, Indonesia

Correspondence: I Nyoman Gede Suyasa, School of Management, Department of Environmental Health, Poltekkes Kemenkes Denpasar, Bali, Indonesia. E-mail: suyasanyomangede@gmail.com

Abstract
Tourist destinations activities in Bali, particularly in Tabanan, Badung and Gianyar increased the crowded traffic jam, and impacted to air chemical quality and noise level. This is an observational study in tourist destinations in Tabanan, Badung, Gianyar Regency, totaling 18 sample points. Sampling of air chemistry CO, O3, SO2 and NO2 are measured using an imfinger and analyzed by spectrophotometer, noise level using a sound level meter. The data obtained were analyzed using a free sample t test, both parametric and non-parametric. The results of air chemistry research for CO in Tabanan Regency is 23.33 gr/Nm3, Badung Regency 521, 67 gr/Nm3 and Gianyar Regency 1050.00 gr/Nm3. Meanwhile O3 parameter in Tabanan Regency is 0.17 gr/Nm3, Badung Regency 0, 20 gr/Nm3 and Gianyar Regency 0.12 gr/Nm3. SO2 parameter in Tabanan Regency is 100.00 gr/Nm3, Badung Regency 57.62 gr/Nm3 and Gianyar Regency 41.62 gr/Nm3. NO2 parameter in Tabanan Regency measured 1 ,83 gr/Nm3, Badung Regency 1.83 gr/Nm3 and Gianyar Regency 0.95 gr/Nm3. The concentration is still below the requirements of the Governor of Bali regulation number 16 of 2016 concerning Environmental Quality Standards and Environmental Damage Standard Criteria. While the noise level in Tabanan Regency is 68.55 dB, Badung Regency 70.68 dB and Gianyar Regency 67.85 dB exceeding the maximum noise level for residential area activities of 55 dB. In conclusion, the air chemistry in regencies of Tabanan, Badung, Gianyar are below the standards of local government. Nevertheless, there is an exceeding noise level in those regencies.

Keywords: Air Chemical Quality, Bali, Noise Level, Tourism

1. Introduction

In big cities, motor vehicle exhaust gases contribute as a source of air pollution reaching 60-70%. Important factors that cause the dominant influence of the transportation sector on urban air pollution in Indonesia include rapid (exponential) growth of vehicles, unbalanced transportation infrastructure with the number of existing vehicles, concentration-oriented urban traffic patterns due to the centralization of economic activities and offices in the city center, derivative problems resulting from the implementation of existing urban development policies, such as residential areas moving away from the city center, equality of traffic flow time, type, age and characteristics of vehicles, vehicle maintenance factor; type of fuel used, type of road surface as well as driving cycles and patterns (Nurdjanah, 2015).

Tourist destinations in Tabanan, Badung and Gianyar regencies such as the Tanah Lot area in Tabanan Regency, Kuta in Badung Regency and Ubud in Gianyar Regency have become the attractions for tourist.. These have been the destination visited by many domestic and foreign tourists. Consequently, many vehicles transporting tourists pass the route of the tourist destination and this often cause traffic jams. Crowded traffic jams cause air chemistry quality and noise levels to increase (Rajé et al., 2018).

Air is an important factor in life. However, along with the increase in urban and industrial development as well as the number of vehicles, air quality has changed. This situation will endanger the health of humans, animals and plants, and will change the balance of the environment. The atmosphere around the earth whose function is essential for life is oxygen (O_2) for breathing, carbon dioxide (CO_2) for photosynthesis by leaf chlorophyll, and ozone (O_3) to block ultraviolet rays from the sun (Shykoff & Warkander, 2012).

Fuel containing sulfur will produce pollutant sulfur dioxide (SO_2), fuel containing ash (fly ash) will produce pollutant particles and dust. The process in the industry will affect the quality of pollutant emissions. For example, the wet process in the cement industry will produce less dust than the dry process. The direction and speed of the wind will affect the process of dilution of pollutants in the air and their distribution. The greater the wind speed, the smaller the concentration of pollutants in the air because these pollutants experience dilution. Wind direction determines the direction of the spread of pollutants (Kim et al., 2015).

Each type of engine has its own emission characteristics. Four stroke combustion engines tend to emit CO, HC, and NO_x but are generally low in particulate emissions. The 2 stroke engine has the same emission characteristics but is dirtier because the use of an excessive oil mixture that will result in the emission of unburned oil and the use of oil with a high smoke content. Diesel engines on trucks and buses tend to emit lower CO and HC than gasoline engines, but higher NO_x and particulates (Yasar et al., 2013). The products released from the complete combustion of fuel by vehicles into the atmosphere by mass are carbon dioxide gas and water vapor. However, this condition rarely occurs because some of the carbon dioxide-based fuels become carbon monoxide (CO). The formation of CO is also influenced by the presence of oxygen (O_2) and temperature (Panov et al., 2020).

Preliminary observations in Tabanan, Badung and Gianyar regencies in tourist destinations obtain the information that the traffic jams often occur. This is in accordance with data from the Bali Provincial Transportation Service, the number of vehicle ownership in Bali is 4.1 million, with a ratio of one resident to one vehicle, where the current population of Bali Province is approximately 4.2 million.

This study aims to measure air chemical parameters (CO, O3, SO2 and NO2) and noise levels as well as analyze differences in air chemical parameters and noise levels in the tourism destination areas and city centers of Tabanan, Badung and Gianyar Regencies.

2. Method

This study is observational research with a cross sectional approach. The research locations are tourist destinations and city centers of Tabanan, Badung and Gianyar Regencies; for Tabanan Regency where Tanah Lot is located, Badung Regency with Kuta and Gianyar Regency is with its Ubud. The study was conducted from April to August 2022. The research population is the atmosphere in Tabanan, Badung and Gianyar Regencies. Measurements of air chemistry quality and noise levels were carried out in tourist destinations and the city center of each district. The location of the sample point is shown in Figure 1.
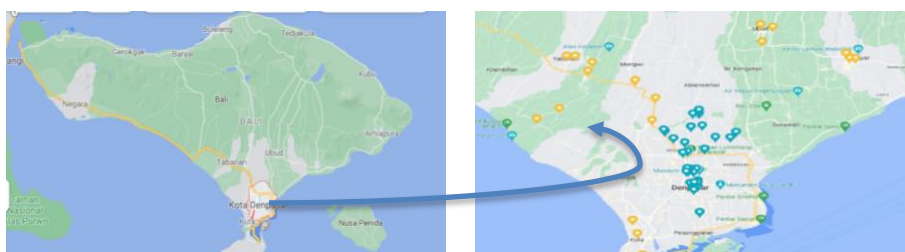

Figure 1: Sampling Location

Figure 1 shows that the location points with the yellow star symbols are chemical sample points and noise levels with a total of 18 points. The sample point for the tourist destination area for Tabanan Regency is in the Tanah Lot, Badung Regency with Kuta and Gianyar Regency is in Ubud.

An air sampling using impinger was applied to get the levels of CO, O_3, SO_2 and NO_2 gases in the atmosphere, with the testing of O_3 parameter with the neutral buffer potassium iodide (NBKI) method using a spectrophotometer (7119-8:2017 SNI 2017), SO_2 parameters using pararosaniline method using a spectrophotometer (7119-7:2017 SNI 2017) and NO_2 parameters using the Griess Zaltzman method using a spectrophotometer (7119-2:2017 SNI 2017). Measurement of the concentration of carbon monoxide (CO) in ambient air uses the direct reading method (real time sampling). This method uses a measuring instrument to directly determine the concentration of carbon monoxide. This tool uses a sensor system based on the chemical and physical properties of the contaminants. The tool used in this study was the Kimo HQ 210 brand CO Analyzer, a handheld portable carbon monoxide (CO) analyzer used to detect and display CO gas concentrations between 0 and 2000 ppm. Measurement of the noise level in the ambient air employed a sound level meter. Differences in air quality in tourist destinations and centers in Tabanan, Badung and Gianyar regencies used free sample t-test analysis at a 95% confidence level.

3. Results
3.1 Weather Condition

Weather conditions at the time of sampling in Badung Regency, Tabanan were quite sunny while in Gianyar Regency the weather was moderately rainy. Weather conditions regarding the average air temperature, humidity, wind speed in tourist destinations and city centers of each district are presented in Table 1.

Table 1: Conditions of average temperature, humidity and wind speed in tourist destination areas and city centers of Tabanan, Badung, Gianyar Regencies

No	Regency	Area	Average Air Temperature (℃)	Average Humidity (%)	Average Wind Speed (km/h)
1	Tabanan	Tanah Lot	28.67±0.58	78.00±1.73	20.60±7.31
		City center	27.33±0.58	78.67±3.21	11.47±0.12
2	Badung	Kuta	29.00±1.00	75.33±3.21	17.20±2.69
		City center	28.67±1.15	74.67±9.02	17.93±2.64
3	Gianyar	Ubud	26.33±0.58	87.67±0.57	11.00±0.70
		City center	26.33±0.58	87.33±1.52	12.37±0.23

Based on Table 1, it shows that for Tabanan Regency there is a difference in the average wind speed in tourist destinations with a speed of 20.60 ± 7.31 km/hour and the city center with a speed of 11.47 ± 0.12 km/hour. This statistics is reinforced by the regional Tanah Lot tourist destination in Tabanan Regency is located in the coastal area.

3.2 Noise Level

Noise measurements using a sound level meter in Tabanan district yielded a noise level of 68.55 ± 3.89 dB, Badung Regency with a noise level of 70.68 dB $\pm$ 4.85 dB and Gianyar Regency with a noise level of 67.85 ± 2.1 dB. These results are compared with the standard regulations of the Governor of Bali Province number 16 of 2016 concerning Environmental Quality Standards and Standard Criteria for Environmental Damage which can be seen in Figure 2.
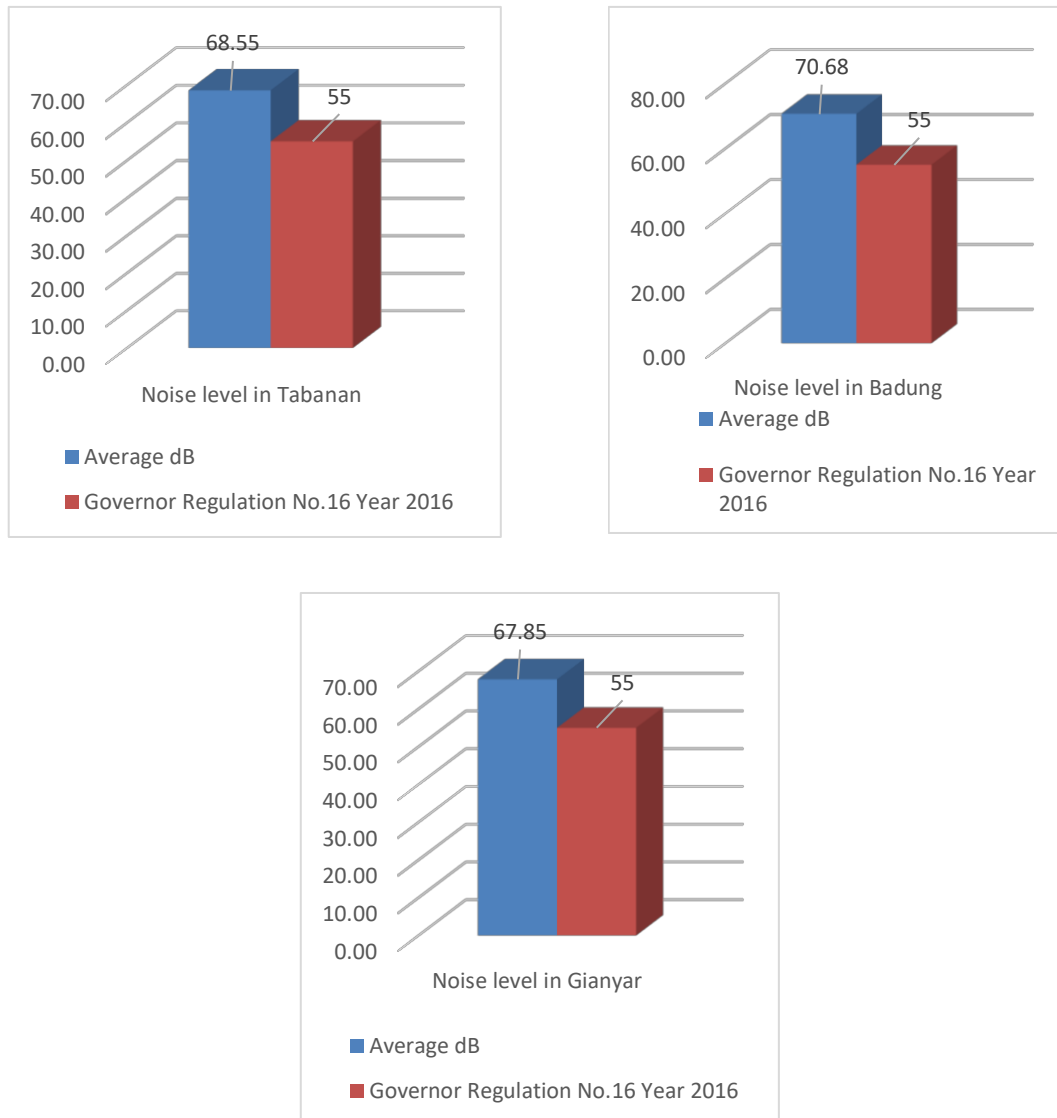
Figure 2: Noise level in Tabanan, Badung and Gianyar regencies in 2022

Figure 2 shows the results of noise levels in Tabanan, Badung and Gianyar regencies that exceed the maximum noise level limit for residential area activities as stated in the Bali Provincial Governor Regulation No. 16 of 2016 of 55 dB. Table 2 shows the comparison of the average noise level between tourist destinations and the city center in each district.

Table 2: Noise level

No.	Regency	Noise Level (dB)	
		Tourism destination	City center
1	Tabanan	67.37±3.51	69.73±4.61
2	Badung	67.16±1.10	74.20±4.52
3	Gianyar	67.10±0.36	68.60±3.08
Total		67.2±1.85	70.84±4.40

Table 2 shows that the average noise level in tourist destinations tends to be lower than the city center in Tabanan, Badung and Gianyar regencies. This shows that the density of transportation in the city center is denser and traffic jam occurs.

3.3 Air Chemical Parameter

Air chemistry measurements for CO, O3, SO2 and NO2 parameters in Tabanan, Badung and Gianyar regencies are presented in Figure 3.

Figure 3: Average air chemistry parameters CO, O_3, SO_3 and NO_2

According to Figure 3, the average results of CO, O_3, SO_3 and NO_2 are still far below the requirements of the Governor of Bali Province regulation number 16 year 2016 concerning Environmental Quality Standards and Standard Criteria for Environmental Damage. Comparison of the average air chemistry of CO, O_3, SO_2 and NO_2 for tourism destination areas and the city center of each district is shown in Table 3.

Table 3: Average air chemistry CO, O3, SO2 and NO2 in tourist destinations and city centers

No.	Regency	Area	Ordinate	Air chemical			
				CO μgr/Nm^3	O$_3$ μgr/Nm^3	SO$_2$ μgr/Nm^3	NO$_2$ μgr/Nm^3
1	Tabanan	Tanah Lot					
		Area 1	-8.554610.115.140410	20.00	0.20	100.00	3.00
		Area 2	-8.593401.115.120338	20.00	0.20	100.00	2.00
		Area 3	-8.604242.115.104324	20.00	0.10	100.00	2.00
		Average		20.00	0.17	100.00	2.33
		City center					
		Area 4	-8.545774.115.143459	30.00	0.30	100.00	2.00
		Area 5	-8.539179.115.131289	30.00	0.10	100.00	1.00
		Area 6	-8.539202.115.125422	20.00	0.10	100.00	1.00
		Average		26.67	0.17	100.00	1.33
2	Badung	Kuta					
		Area 7	-8.708389.115.171894	70.00	0.30	50.00	2.00
		Area 8	-8.722407.115.175430	10.00	0.30	50.00	2.00
		Area 9	-8.744284.115.179000	50.00	0.20	50.00	2.00
		Average		43.33	0.27	50.00	2.00
		City center					
		Area 10	-8.564566.115.173704	1,000.00	0.10	60.00	2.00
		Area 11	-8.582437.115.188133	1,000.00	0.10	50.00	2.00
		Area 12	-8.605417.115.185628	1,000.00	0.20	50.00	1.00
		Average		1.000,00	1.33	53.33	1.67
3	Gianyar	Ubud					
		Area 13	-8.509149.115.271181	900.00	0.10	40.00	2.00
		Area k14	-8.506892.115.262431	900.00	0.20	40.00	1.00
		Area 15	-8.524374.115.263500	900.00	0.10	40.00	0.80
		Average		900.00	0.13	40.00	1.27
		City center					
		Area 16	-8.536417.115.322829	1,200.00	0.10	40.00	0.60
		Area 17	-8.541378.115.325167	1,200.00	0.10	50.00	0.70
		Area 18	-8.541671.115.329146	1,200.00	0.10	40.00	0.60
		Average		1,200	0.10	43.33	0.63

As seen from Table 3, it shows that the average air chemistry parameters CO and SO$_2$ are higher in the city center compared to tourist destinations for Tabanan, Badung and Gianyar Regencies. Carbon monoxide (CO) is a gas that is colorless, odorless, tasteless, and a toxic gas that makes up the atmosphere (Girach & Nair, 2014). (Strode et al., 2015) in his research stated that CO is one of the precursors (formers) of ozone and the main absorber of hydroxyl radicals (OH) in the troposphere. Consequently, CO indirectly impacts the climate by increasing surface ozone where there is sufficient NOx, and increasing the lifetime of methane and other short-term greenhouse gases (GHGs).

3.4 Differences in Chemical and Physical Quality of Air

Based on the results of the independent t test and Mann Whitney for air chemistry parameters CO, O$_3$, SO$_2$, NO$_2$ and noise level, the following results were obtained in Table 4.

Table 4: Independent and Mann Whitney t test results for air chemistry parameters CO, O3, SO2, NO2 and noise level

No	Variable	Average $\mu gr/Nm^3$ in tourist destination	Average $\mu gr/Nm^3$ in city center	e	Sig. independent Mann Whitney	t /
1	CO	321.11	742.22		0.032	
2	O3	0.19	0.13		0.094	
3	SO2	63.33	65.55		0.677	
4	NO2	1.87	1.21		0.046	
5	Noise	67.21 dB	70.84 dB		0.023	

Based on the statistical test results in Table 4, the significance value of the air chemistry parameters CO, NO_2 and noise level is less than 0.05, meaning that there are differences in the results of the average measurement of air chemistry parameters CO, NO_2 and noise levels between tourist destinations and the city center in Tabanan, Badung and Gianyar regencies. Meanwhile, for parameters O_3 and SO_2, a significance value greater than 0.05 indicates that there is no difference in the average values of O_3 and SO_2 parameters between tourist destinations and the city center in Tabanan, Badung and Gianyar regencies.

The results of this study indicate that the level of density or congestion between tourist destinations and the city center in Tabanan, Badung and Gianyar Regencies is different. There are differences in the values of the air chemistry parameters CO, O_3, SO_2, NO_2 and noise levels at each location because there has been an increase of visitors to tourist destination after the global pandemic attack. Meanwhile for the city center there are contributions of vehicles at busy hour and doing office activities. Transportation management is very important to be carried out by the government of Tabanan, Badung and Gianyar Regencies such as car free days, and it is necessary for tourist destinations to add cycling or pedestrian paths as well as do reforestation on the road sides.

4. Discussion

The concentration of pollutants in the air depends on weather conditions. Wind speed and direction, vertical temperature distribution, and humidity are elements that play a role in this weather change. Wind speed affects pollutant distribution. Pollutant concentrations will decrease if the wind is strong and distributes these pollutants horizontally or vertically. The land surface also affects wind speed, whether it is hilly or valleys. Narrow passages for the wind can increase the speed of wind. Temperature change is also a big changing factor. Upward turbulence will bring pollutants to areas with lower temperatures. Pollutants will decrease in concentration and then spreaded by the wind. In addition, the factors influencing air quality and green-housing as a reduction in CO_2 emissions are related to environmental structural elements, such as temperature, wind direction and speed, humidity, rainfall, air pressure, orography and topography which will vary with space and time (Diener & Mudu, 2021).

Traffic noise comes from the sound produced by vehicles, especially from the engines, exhaust, as well as due to the process between the wheels and the road. Heavy vehicles (trucks, buses) and passenger cars are the main noise sources on the highway. In general, controlling noise is divided into three elements, i.e. control of noise sources, control of noise lanes and control of noise receivers (González, 2022). The increase and difference in noise at the location of each atmosphere/ambient air is mostly due to the contribution of the hectic number of vehicles, considering that all sampling locations are located on the edge of the main road in the city center which is often traversed by motorized vehicles, especially large vehicles such as passenger cars, buses, trucks and other heavy vehicles. Noise is caused by the density of traffic flow in each location and busy hours and days for work (Radam & Heriyatna, 2018).

Several studies have shown that CO administration for 1 to 3 weeks at concentrations up to 100 ppm has no significant effect on higher plants. However, the ability to fix nitrogen by free bacteria will be hampered by giving CO for 35 hours at a concentration of 2000 ppm. Likewise, the ability to fix nitrogen by bacteria found in plant roots is also hampered by giving 100 ppm CO for one month (Srikandi, 2008).

Carbon monoxide (CO) is produced by chemical reactions in the atmosphere between hydroxyl radicals (OH) and methane (CH4) and other hydrocarbons, in addition to reactions between alkenes and ozone (O_3), and reactions of isoprene and terpenes with OH and O_3 (Rozante et al., 2017). In addition, other meteorological factors besides air temperature can also affect the concentration of CO in the atmosphere. These meteorological factors include air pressure, and the structure of the boundary layer. Air pressure will affect the diffusion of CO gas in the horizontal and vertical directions in the air, and the boundary layer structure plays an important role in the diffusion of CO gas in the vertical direction (Zeng & Zhang, 2017).

Every human breathes; an average adult inhales more than 3,000 gallons (11.4 m^3) of air each day. The air we breathe, if it is polluted by hazardous and toxic materials, will have a serious impact on human health, especially children who play more in the open air and are more vulnerable to their immune system. Apart from causing cancer and respiratory diseases, air pollutants can also cause smog (pollution), acid rain, reduce the resistance of the ozone layer in the upper atmosphere and have the potential to play a role in global climate change.

Ozone is not a hydrocarbon but the concentration of O_3 in the atmosphere increases as a direct result of the reaction of the hydrocarbons, whereas PAN is a hydrocarbon derivative. The result of the reaction between O and hydrocarbons is a very reactive intermediate product called a hydrocarbon free radical (RO2). Free radicals of this kind can further react with various components including NO, NO2 , O2 , O3 , and other hydrocarbons (Srikandi, 2008)

Sulfur dioxide emissions mainly arise from the burning of fossil fuels containing sulfur, especially coal used for electricity generation or household heating. This sharp-smelling but colorless gas can cause asthma attacks and because this gas stays in the air, it reacts and forms fine particles and acids (Perraud et al., 2015).

References

Diener, A., & Mudu, P. (2021). How can vegetation protect us from air pollution? A critical review on green spaces' mitigation abilities for air-borne particles from a public health perspective - with implications for urban planning. *Science of the Total Environment*, *796*, 148605. https://doi.org/10.1016/j.scitotenv.2021.148605

Girach, I. A., & Nair, P. R. (2014). Carbon monoxide over Indian region as observed by MOPITT. *Atmospheric Environment*, *99*, 599–609. https://doi.org/10.1016/j.atmosenv.2014.10.019

González, A. E. (2022). Overview of Noise Control Techniques and Methods. *IntechOpen*, *32*(tourism), 137–144. https://www.intechopen.com/books/advanced-biometric-technologies/liveness-detection-in-biometrics

Kim, K. H., Lee, S. B., Woo, D., & Bae, G. N. (2015). Influence of wind direction and speed on the transport of particle-bound PAHs in a roadway environment. *Atmospheric Pollution Research*, *6*(6), 1024–1034. https://doi.org/10.1016/j.apr.2015.05.007

Nurdjanah, N. (2015). CO2 Emissions from Vehicle in Denpasar. *Jurnal Penelitian Transportasi Darat*, *17*(1), 1–14.

Panov, Y., Gomelia, N., Ivanenko, O., Vahin, A., & Leleka, S. (2020). Assessment of the effect of oxygen and carbon dioxide concentrations on gas evolution during heat treatment of thermoanthracite carbon material. *Journal of Ecological Engineering*, *21*(2), 139–149. https://doi.org/10.12911/22998993/116326

Perraud, V., Horne, J. R., Martinez, A. S., Kalinowski, J., Meinardi, S., Dawson, M. L., Wingen, L. M., Dabdub, D., Blake, D. R., Gerber, R. B., & Finlayson-Pitts, B. J. (2015). The future of airborne sulfur-containing particles in the absence of fossil fuel sulfur dioxide emissions. *Proceedings of the National Academy of Sciences of the United States of America*, *112*(44), 13514–13519. https://doi.org/10.1073/pnas.1510743112

Radam, I. F., & Heriyatna, E. (2018). A Correlation Analysis of Noise Level and Traffic Flow : Case of One Way Road in Banjarmasin. *Asian Journal of Applied Sciences*, *06*(02), 60–64.

Rajé, F., Tight, M., & Pope, F. D. (2018). Traffic pollution: A search for solutions for a city like Nairobi. *Cities*, *82*(February), 100–107. https://doi.org/10.1016/j.cities.2018.05.008

Rozante, J. R., Rozante, V., Alvim, D. S., Manzi, A. O., Chiquetto, J. B., D'Amelio, M. T. S., & Moreira, D. S. (2017). Variations of Carbon Monoxide Concentrations in the Megacity of São Paulo from 2000 to 2015 in Different Time Scales. *Atmosphere*, *8*(81), 1–17. https://doi.org/10.3390/atmos8050081

Shykoff, B. E., & Warkander, D. E. (2012). Exercise carbon dioxide (CO2) retention with inhaled CO 2 and breathing resistance. *Undersea and Hyperbaric Medicine*, *39*(4), 815–828.

Srikandi, F. (2008). *Polusi Air Dan Udara*. Kanisius.

Strode, S. A., Duncan, B. N., Yegorova, E. A., Kouatchou, J., Ziemke, J. R., & Douglass, A. R. (2015). Implications of carbon monoxide bias for methane lifetime and atmospheric composition in chemistry climate models. *Atmospheric Chemistry and Physics*, *15*(20), 11789–11805. https://doi.org/10.5194/acp-15-11789-2015

Yasar, A., Haider, R., Tabinda, A. B., Kausar, F., & Khan, M. (2013). Comparison of engine emissions from heavy, medium, and light vehicles for CNG, diesel, and gasoline fuels. *Polish Journal of Environmental Studies*, *22*(4), 1277–1281.

Zeng, S., & Zhang, Y. (2017). The Effect of Meteorological Elements on Continuing Heavy Air Pollution : A Case Study in the Chengdu Area during the 2014 Spring Festival. *Atmosphere*, *8*(71), 7–19. https://doi.org/10.3390/atmos8040071

Infection Prevention and Control Practices among Staff Nurses in Hail, KSA: Basis for Improved Patient Safety

Farhan Alshammari[1], Grace Ann Lim-Lagura[2], Romeo Jr P. Mostoles[3], Ferdinand Gonzales[4], Sharifa Alsayed[5], Enrique Mina[6]

[1] College of Nursing, University of Hail, Hail, Saudi Arabia
[2] College of Nursing, University of Hail, Hail, Saudi Arabia
[3] College of Nursing, University of Hail, Hail, Saudi Arabia
[4] College of Nursing, University of Hail, Hail, Saudi Arabia
[5] College of Nursing, King Saud bin Abdulaziz University for Health Sciences, Dammam, Saudi Arabia
[6] College of Nursing, University of Hail, Hail, Saudi Arabia

Correspondence: Grace Ann Lim-Lagura. College of Nursing, Aja Campus, Hail University Complex
Email: graceann1102@gmail.com | Tel: 00966558827916

Abstract
Aim: Hospital acquired infections are preventable with proper healthcare behavior among workers and strict compliance. This study aimed to determine the infection prevention and control practices by staff nurses. Methods: This study utilized the correlational approach in exploring the infection prevention and control practices among nurses in government hospitals in Ha'il region Kingdom of Saudi Arabia. There were 189 respondents resulting from convenience sampling. Descriptive statistics were used to represent the demographic profiles and scores of the participants while Spearman's rho was used to determine the significant relationship between the four (4) dimensions in IPC practice. Data gathering was conducted between November and December 2019. Results: The infection prevention and control guidance (89.96 ± 10.74), healthcare associated infection associated infection (84.92 ± 9.49), and built environment, material and equipment (86.23 ± 12.03) were found to have an advanced level while infection control programme is intermediate in level (29.99 ± 3.99). Meanwhile, a weak positive correlation on ($r=0.191$; $p<.008$) found in infection and control programmed and infection prevention; and IPC programmed level and built materials and equipment ($r = 0.16$; $p<.028$). There is a medium level of correlation between the level of practice in Built materials and equipment ($r = -0.327$). Conclusion: The four dimensions, the level of practice for the Infection Prevention and Control Programme is found to be Intermediate. Whereas, the other three dimensions, Infection Prevention and Control Guidelines, Healthcare-Associated Infections Surveillance, and Built Environment, Materials and Equipment for Infection Prevention and Control at the Hospital Level, showed an Advanced level of practice by the staff nurses. overall, the IPC level of practice among nurses is described to be Advanced. The IPC core components are fully implemented according to the WHO recommendations and appropriate to the needs of the facility.

Keywords: Infection Prevention, Control Practices, Staff Nurses

1. Introduction

Health Associated Infections (HAIs) are infections that become clinically evident after 48 hours of hospitalization and have become a major concern among hospitals around the world. They contribute tremendously to issues surrounding patient safety. HAIs are infections that patients acquire and can be associated with procedures like surgeries and the various devices used in medical procedures, such as catheters or ventilators. Although some HAIs are preventable, they are considered negative indicators of quality of patient care, adverse events, and patient safety issues (Collins, 2008).

All hospitalized patients are susceptible to contracting nosocomial infections. Some patients are at greater risk than others-young children, the elderly, and persons with compromised immune systems are more likely to get an infection. HAIs are known to be due to prolonged hospital stay, long-term disabilities, and increased microbial resistance to drugs. These result in a massive additional financial burden for hospitals, high costs for patients and their families, and unnecessary deaths. Affected patients and healthcare workers suffer from decreased quality of life and sometimes death (Monegro et al., 2021).

Healthcare-associated infections (HAI) in the Kingdom of Saudi Arabia and internationally are associated with increased length of stay, mortality, antibiotics cost, and overall hospital cost. About 250,000 central line-associated bloodstream infections (CLABSI) occur in the US yearly, with a rate of 0.8 per CL-days and attributed mortality of 12%–25%. CLABSI constitutes 14.2%–38.5% of HAIs in the Kingdom, with rates varying from 2.2 to 29.7/1000 CL-days and crude device-associated mortality of 16.8%–41.9%. Similarly, a point prevalence survey was conducted among inpatients in Saudi Arabia, and the findings showed that the most common types of infections were pneumonia (27.2%), urinary tract infections (20.2%), and bloodstream infections (10.5%). Approximately 19.2% of healthcare-associated infections were device associated (Khan et al., 2019).

Literature shows that the incidence of HAIs in hospitals was often not reported. Hence, there were no evident records to suggest the exact number of HAIs, not until 2004, where many hospitals were required to report HAIs (Gastmeier et al., 2005). HAIs are considered an indicator of poor quality of patient care, an adverse event, and a patient safety issue (Collins, 2008).

HAIs are preventable with proper healthcare behavior among workers and strict compliance with evidence-based infection prevention procedures and guidelines (Collins, 2008). The primary concern of every healthcare facility is to control the spread of disease and minimize the incidence of HAIs. It becomes more critical than ever for hospitals to ensure that infectious diseases do not spread. Hence, hospitals developed Infection Prevention and Control programmes and guidelines based on the mandate of WHO to reduce the incidence of HAIs (WHO, 2020). It is therefore, the aim of this study to determine the infection prevention and control practices by staff nurses. The findings of this study will benefit the respondent hospitals to revisit existing protocols. Likewise, the results will aid in strengthening the call for a more heightened patient safety advocacy to counter the increasing incidence of HAIs among hospitals in Saudi Arabia.

2. Theoretical Background

The framework underpinning this study, the Infection Prevention and Control Assessment Framework (IPCAF), by the World Health Organization. The study of Aghdassi et al (2019) was entitled A National Survey on the Implementation of Key Infection Prevention and Control Structures in German Hospitals. The survey was conducted among 736 hospitals using the IPCAF. The results illustrated an overall median score of 690 for all hospitals, which corresponded to an advanced infection prevention and control practice. However, a small percentage of hospitals fell into the category of "Basic," and more hospitals are categorized as "Intermediate" and "Advanced" in infection prevention and control practices. The study reiterated the potentials for improvement, particularly about workload and staffing. The survey represents a successful attempt at promoting IPCAF and encouraging hospitals to utilize WHO tools for hospitals (Aghdassi et al., 2019).

The IPCAF is a tool to support the World Health Organization (WHO) Guidelines on core components of IPC programmes at the acute healthcare facility level. A framework is a systematic tool that provides a baseline

assessment of the infection prevention and control programme and activities of a healthcare facility. Likewise, it provides ongoing evaluations through repeated administration to document the progress of the healthcare facility overtime. The purpose is to continuously improve infection prevention and control measures for excellent patient safety (Aghdassi et al., 2019).

The IPCAF is a structured, close-formatted questionnaire with an associated scoring system. It is a self-assessment tool but can also be used for joint assessments. It is a global tool that is valid for the assessment of IPC standards in any country. The framework's goal is to assess the current IPC situation of the hospital and identify the strengths and gaps that will be useful for plans. It is also considered a diagnostic tool to detect relevant problems that require improvement and identify areas where international standards and requirements can be met (Aghdassi et al., 2019).

Thus, IPCAF gives a score that can be used as an indicator of the level of progress from an improvement perspective. The results can be used to develop an action plan.

3. Methodology

3.1. Research Design

This study utilized the correlational approach in exploring the infection prevention and control practices among nurses in government hospitals in Ha'il, KSA.

3.2. Locale

The four major government hospitals hospitals in Ha'il, Saudi Arabia were chosen and coded as Hospital A, B, C and D. The hospitals are under the jurisdiction of the Ministry of Health (MOH) of KSA. By way of its objectives, policies, and projects, the MOH seeks to accomplish a promising future through its vision to deliver quality integrated and comprehensive healthcare services (MOH, 2019).

3.3. Respondents

The staff nurses from the selected government hospitals of Ha'il, KSA, were formally invited to participate in the study through its Continuing Nursing Education Department. There were a total of 189 respondents as a result from convenience sampling.

3.4. Instrument

The survey questionnaire used in this study was adapted from the Infection Prevention and Control Assessment Framework (IPCAF), which supports the implementation of the WHO Guidelines on core components of IPC programmes at the acute health care facility level. The IPCAF is a systematic tool that can provide a baseline assessment of the IPC programme and activities within the health care facility, and ongoing evaluations through repeated administration to document progress over time and facilitate improvement[7].

Part 1 of the questionnaire is the respondents' demographic profile, which covers the age, gender, nationality, educational attainment, years of service in their respective hospitals, and whether they have attended seminars, training, workshops on IPC, or none at all.

Part II of the questionnaire is divided into four (4) dimensions. Each item in each dimension is appointed with a corresponding point/s based on the IPCAF. Dimension 1 is *Infection Prevention and Control Programme,* which has six items with a total score of 40 points (0 – 10.99 *Inadequate*; 11.00 – 20.99 *Basic*; 21.00 – 30.99 *Intermediate*; 31.00 – 40.00 *Advanced*). Dimension 2 is *Infection Prevention, and Control Guidelines* have 20 items and with a total of 90 points (0 – 22.49 *Inadequate*; 22.50 – 44.99 *Basic*; 45.00 – 67.49 *Intermediate;* and 67.50 – 90.00 *Excellent*). On the other hand, Dimension 3 is *Healthcare-Associated Infections Surveillance* has 24 items with a total score of 95 points (0 – 23.74 *Inadequate*; 23.75 – 47.49 *Basic*; 47.50 – 71.24 *Intermediate*; and 71.25 – 95.00 *Excellent*). Lastly, Dimension 4 *Built Environment, Materials, and Equipment for Infection Prevention and*

Control at the Hospital Level has 16 items and with 110 points (0 – 27.49 *Inadequate;* 27.50 – 54.990 *Basic*; 55.00 – 82.49 *Intermediate;* 82.50 – 110 *Excellent).*

All the scores of the four (4) dimensions are added to determine the overall level of practice. A score of 0 – 83.74 describes the IPC level of practice to be *Inadequate*; a score of 83.75 – 167.49 means the level of practice is *Basic*; a score of 167.50 – 251.24 describes the practice to be *Intermediate*, and finally, a score of 251.25 to 335 is described to be *Advanced* level of practice.

3.5. Statistical Treatment

Descriptive statistics were employed to obtain the mean and standard deviation of each of the four dimensions and the overall mean to describe the level of practice of Infection Prevention and Control. Likewise, Spearman's rho was used to determine the significant relationship between the four (4) dimensions in IPC practice.

3.6. Data Gathering Procedure

The study commenced after clearance was issued from the Institution Review Board of the University of Ha'il. Letters were sent to the respondent hospitals to seek consent for the survey. The survey was done in close coordination with the hospitals' Continuing Nursing Education (CNE) departments. A date was set for the survey questionnaire distribution, and ample time was given for the respondents to answer the questions before the retrieval. Data was encoded and tabulated, and descriptive statistics were employed to treat the data. Data was collected between November of 2019 until January 2020.

3.7. Ethical Consideration

The conduct of the study followed strict compliance to the protocol set by the Ethics Board.   Approval was sought from the hospital directors to conduct the study among its staff nurses. The questionnaires were distributed to the respondents. The respondents were asked to sign informed consent signifying their willingness to participate in the study by answering the survey questions. The informed consent indicated the purpose of the study, their role as participants, and may refuse or withdraw from participating at any point during the data collection. The participants' responses were treated with the utmost confidentiality and were only used solely for the study.

4. Results

4.1. Demographic Profile

Table 1 presents the demographic profile of the respondents. The majority (66.7%) of the respondents are within the 25 to 30 age group, and there are 182 (96.3%) female respondents, as compared to male respondents. Indians, Saudis, and Filipinos comprise the bulk of respondents, and 97.4% of the nurses are with baccalaureate degrees only. Seventy-one or 37.6% are with less than five years of work experience in their respective hospitals. Close to it are 33.3% of the respondents with five to ten years of work experience. Only two or 1.06% of the respondents have more than 25 years of work experience.

Table 1: Demographic profile of the participants. N=189

DEMOGRAPHICS	FREQUENCY	PERCENTAGE (%)
Age:		
25 – 30	120	66.7
31 – 35	44	24.4
36 – 40	18	10.0
41 – 45	2	1.11
46 - 50	5	2.87
Gender		

Male	7	3.7	
Female	182	96.3	
Nationality			
Saudi	67	35.4	
Jordanian	1	0.53	
Egyptian	8	4.23	
Filipino	30	15.9	
Indian	83	43.9	
Educational Attainment			
Baccalaureate	184	97.4	
Masters degree	4	2.12	
Doctorate degree	1	0.53	
Years of Service			
Less than 5 years	71	37.6	
5 – 10 years	63	33.3	
11 – 15 years	31	16.4	
16 – 20 years	17	8.99	
21 – 25 years	5	2.65	
More than 25 years	2	1.06	
Attended Seminars/Trainings Workshops on IPC			
Yes	136	71.96	
No	53	28.04	

In equipping the respondents in infection prevention and control, a big bulk of the respondents (71.96%) have attended seminars or training while employed in the hospitals. Nurses, upon entry to the hospital as employees, are provided with seminars and training on infection prevention and control. These seminars and training are intended to refresh the nurses on their knowledge of infection prevention and control and orient the nurses on hospital protocols.

Table 2: Level of Infection Prevention Control Practices

Dimensions	Mean	Std Dev	Interval		Skewness	Level
Infection Control Programme	29.99	3.99	21.99	37.99	-0.93	Intermediate
Infection Prevention and Control Guidelines	89.96	10.74	60.48	103.43	-1.13	Advanced
Healthcare-Associated Infections Surveillance	84.92	9.49	65.94	103.90	-1.15	Advanced
Built Environment, Materials and Equipment for IPC at the Hospital Level	86.23	12.03	62.16	110.29	-0.27	Advanced
Overall	283.10					Advanced

Total points: 335

Each of the variables is not normally distributed per statistical verification. Hence the amount of skewness was included for extensive description. Thus, by the Chebyshev rule, the total points for the *Infection Control Programme* are 40 points, and the average mean is 29.987. This further emphasizes that the total points generated by at least 75% of the staff nurses fall within 21.99 and 37.99. Moreover, due to the negative skewness (-0.93), it can be noted that at most, 11% of the staff nurses scored less than 18.

The second variable, *Infection Prevention and Control Guidelines*, has a total score of 90 points and has an average mean of 89.96. This explains that the total points generated by at least 75% of the staff nurses fall within 60.48 and 103.43. The negative skewness of -1.13 depicts that at most, 11% of the staff nurses scored less than 50.

Furthermore, the third variable is *Healthcare-Associated Infections Surveillance*, which has a total score of 95 and has an average mean score of 84.92. This signifies that the total points generated by at least 75% of the staff nurses fall within the range of 65.94 to 103.90. Since the amount of skewness is -1.55, at most, 11% of the staff nurses have scored less than 56.

Finally, the fourth variable, *Built Environment, Materials, and Equipment for IPC at the Hospital Level*, is 86.23 on the average. In contrast, the total points generated by at least 75% of the staff nurses range from 62.16 to 110.29. A negative skewness of -0.27 suggests that a total of 11% of the staff nurses score below 50.

Table 3: Correlation of Variables

		IPC Programme	IPC Guidelines	HAI Surveillance	Built environment, materials and equipment
IPC Programme	Corr Coef	1.000	.191	-.063	.160
	Sig. (2-tailed)	.	.008	.389	.028
IPC Guidelines	Corr Coef	.191	1.000	-.009	.327
	Sig. (2-tailed)	.008	.	.904	.000
HAI Surveillance	Corr Coef	-.063	-.009	1.000	-.085
	Sig. (2-tailed)	.389	.904	.	.247
Built environment, materials and equipment	Corr Coef	.160	.327	-.085	1.000
	Sig. (2-tailed)	.028	.000	.247	.

Table 3 demonstrates that *Infection Prevention and Control Programme and Infection Prevention and Control Guidelines* showed a coefficient of r = 0.191 with a p-value of .008, which means that there is a weak positive correlation between the two variables. It further explains that there is a low tendency for the practice of IPC Programme to be increased whenever the practice for IPC Guidelines increases.

Moreover, Table 3 illustrates the weak positive correlation between IPC Programme and Built environment, materials, and equipment, as reflected in the coefficient of r = 0.16 and a p-value of .028. This indicates that whenever the IPC Programme level increases, there is a low tendency for the level of practice in Built materials and equipment to increase.

Finally, the IPC Guidelines and Built materials and equipment with a coefficient of r – 0.327 demonstrate a medium level of correlation between the two variables. This implies a moderate tendency for the level of practice in Built materials and equipment to increase whenever the level of practice in IPC Guidelines increases.

5. Discussion

This study aimed to determine the infection prevention and control practices by staff nurses. In this study, the infection control programmed was found intermediate which means that the healthcare workers and other hospital employees are oriented to the IPC Programme. This can be credited from the fact that the different departments and units of the hospitals are provided with copies of the IPC Programme. Likewise, such programme is included in the hospital information technology system for easier access to employees. According to WHO (2020) because of the growing rate of healthcare-associated infections, there is a worldwide consensus for urgent action for all healthcare facilities to create an infection prevention and control programme. Every infection prevented would mean an antibiotic treatment avoided, and IPC can save millions of lives every year. Further, hospital infection control programmes can help healthcare facilities monitor and improve infection control practices and identify

risks and proactively establish policies to prevent the spread of infections (Rodak, 2012). This result indicates that it is essential for the nurses to feel part and take ownership of the Programmed to facilitate active participation. Likewise, this may mean the need to reorient the nurses on the IPC Programmed of the hospital – including the guidelines, the key individuals involved in the IPC team, the availability of the hospital microbiological laboratory, and budget allocation for the implementation of the IPC Programmed.

The IPC Guidelines was found to have an advanced level of practice, which signifies that the IPC guidelines are fully implemented according to the WHO recommendations and are deemed appropriate to the needs of the hospital. Infection Prevention and Control Guidelines refer to the policies and procedures implemented to control and minimize the dissemination of infections in the hospital and other healthcare facilities. Its purpose is to reduce the rate of infections. Creating policies and procedures in place for infection prevention and control is to ensure patients, employees, and families are protected against infectious diseases and infections by providing guidelines for the investigation, control, and prevention of infections (Habboush et al., 2021). It is important to note that regular lectures and seminars are conducted to keep all nurses updated on trends on infection prevention and control. Each unit in the hospital is also recommended to furnished with the IPC Guidelines for the nurses to review.

The Healthcare-Associated Infection Surveillance was found to have an Advanced level of practice, which means the core components of healthcare-associated infections surveillance are fully implemented according to the guidelines set by WHO, including the recommendations and appropriate needs of the hospitals concerned. The primary goal of any effective infection prevention and control program is to protect patients, healthcare workers, and all others who work in or visit the healthcare care environment. Epidemiologic Principles and methods constitute an essential aspect of infection and outbreak control that hospital IPC teams can use to improve the quality of care. Hence, infection prevention and control surveillance is crucially mandatory and must be strictly implemented to monitor its outcome (Ellis, 2022). Furthermore, infection Surveillance is essential to successful and sustained public health intervention in preventing and controlling infections. Surveillance systems must be tailored to the specific disease or injury that is to be prevented and controlled (Halperin, 2006). Infection prevention and control surveillance data are used to measure the success of infection prevention and control programs, identify areas of concern and improvements, and meet the need of the public reporting mandates and performance goals of the healthcare facility.

The score of nurses on 'Built Environment, Materials and Equipment for IPC at the Hospital Level' in this study signifies the *Advanced* level of practice. This means that this dimension is fully implemented according to the recommendations of the WHO as well as the appropriate needs of the hospitals concerned. For example, Decker and Palmore (2014) described the most waterborne pathogens that cause opportunistic infections in hospital. Some pathogens like Legionella can colonize the deep infrastructure or outlets of hospital water distribution systems. At the same time, other bacteria tend to adhere to biofilms at or near the distal points of use. Moreover, every use of water in all patient care settings must be scrutinized and evaluated for its risk to the harbor and transmit healthcare-associated pathogens (Perkins et al., 2013). Further, published guidelines recommend that each healthcare facility should develop and follow a comprehensive water management program. This includes risk assessment that will identify all water treatment systems at play and all points of water use that pose potential hazards and control strategies to mitigate any hazards (Decker & Palmore, 2014).

There found a significant correlation on the following; infection control programme, infection control guidelines, healthcare-associated infections surveillance, and built environment, materials and equipment for IPC. The results suggest a strong integration of the various components mentioned and essentially embedded in the day-to-day IPC structure and activities of the hospitals. WHO (2018) posits the integrative implementation of the IPC components is not a sole responsibility of the IPC teams, rather, it calls for a broader and continuous development of competencies, collaboration and strong engagement from the different stakeholders. Furthermore, WHO reiterates the relevance of each component to the process of improvement, though the entire process may depend on the local situation. Some hospitals may show full attainment of one or all of the components, while others may need gradual development or may revisit recommendations from previous evaluations. Additionally, the IPC manual proposes a strong collaboration of the various IPC components to strategically build the right system, teach and

check the right things, sell the right messages and ultimately living IPC throughout the entire health system (WHO, 2018).

6. Implication

Overall, the findings of this study appear positive and promising and equally beneficial to everyone desiring optimal patient safety. Infection Prevention and Control, even with all its guidelines, remains a global issue. However, proven strategies to prevent and combat healthcare-associated infections are vital drivers of successful infection control in healthcare facilities. This study recommends that hospitals continue the strict implementation of infection prevention standards and control for improved patient safety. Likewise, this study suggests that a periodic revisit of the GCC Manual based on the World Health Organization Infection Control Guidelines must be done for the hospital staff to update themselves continuously.

This assessment is likewise recommended to be conducted regularly for ongoing evaluation of infection prevention and control practices to determine the current situation and identify strengths, weaknesses, and threats to infection control. The assessment tool gives a score that can be used as an indicator of the level of progress from an improvement perspective. The results can be used to develop an action plan.

7. Conclusion

The four dimensions, the level of practice for the Infection Prevention and Control Programme is found to be *Intermediate*. Whereas, the other three dimensions, *Infection Prevention and Control Guidelines, Healthcare-Associated Infections Surveillance, and Built Environment, Materials and Equipment for Infection Prevention and Control at the Hospital Level,* showed an *Advanced* level of practice by the staff nurses. overall, the IPC level of practice among nurses is described to be *Advanced*. The IPC core components are fully implemented according to the WHO recommendations and appropriate to the needs of the facility.

References

Aghdassi, S. J. S., Hansen, S., Bischoff, P., Behnke, M., & Gastmeier, P. (2019). A National Survey on the Implementation of Key Infection Prevention and Control Structures in German Hospitals: results from 736 Hospitals conducting the WHO Infection Prevention and Control Assessment Framework (IPCAF). *Antimicrobial Resistance And Infection Control,* 2019, 8, 73. https://doi.org/10.1186/s13756-019-0532-4

Collins AS. (2008). *Preventing Health Care–Associated Infections.* In: Hughes RG, editor. Patient Safety and Quality: An Evidence-Based Handbook for Nurse*s.* Rockville (MD): Agency for Healthcare Research and Quality (US), Chapter 41. PMID: 21328782.

Decker BK, Palmore TN. Hospital water and opportunities for infection prevention. Curr Infect Dis Rep. 2014 Oct;16(10):432. doi: 10.1007/s11908-014-0432-y. PMID: 25217106; PMCID: PMC5583638.

Ellis K. (2022, February 19). *Infection Control Today.* https://www.infectioncontroltoday.com/view/surveillance

Gastmeier P, Stamm-Balderjahn S, Hansen S, et al. (2005). How outbreaks can contribute to prevention of nosocomial infection: analysis of 1,022 outbreaks. *Infection Control Hospital Epidemiology*, Volume 4, 357–61. DOI 10.1086/502552.

Khan RM, Subhani J, Arabi YM. (2019). Central line-associated bloodstream infections in the Kingdom of Saudi Arabia. *Saudi Critical Care Journal,* Volume 3, 43-48. https://www.sccj-sa.org/text.asp?2019/3/1/43/259482

Habboush Y, Yarrarapu SNS, Guzman N. (2021, September 13). *Infection Control.* StatPearls. https://www.ncbi.nlm.nih.gov/books/NBK519017/

Halperin, WE. (2006). The role of surveillance in the hierarchy of prevention. *American Journal of Medicine*, 29(4) pp 321-323. doi: 10.1002/(SICI)1097-0274(199604)29:4<321::AID-AJIM8>3.0.CO;2-R.

Monegro AF, Muppidi V, Regunath H. (2021,August 30). *Hospital Acquired Infections*. In: StatPearls. https://www.ncbi.nlm.nih.gov/books/NBK441857/

Perkins, K.M., Reddy, S.C., Fagan, R., Arduino, M.J. and Perz, J.F. (2019). Investigation of healthcare infection risks from water-related organisms: Summary of CDC. *Infection Control & Hospital Epidemiology*, 40(6): 621-626.

Rodak S. (2022, February 19). *8 Steps to Effective Hospital Infection Control Programs*. https://www.beckersasc.com/asc-quality-infection-control/8-steps-to-effective-hospital-infection-control-programs.html

World Health Organization. (2018). *Improving infection prevention and control at the health facility: Interim practical manual supporting implementation of the WHO Guidelines on Core Components of Infection Prevention and Control Programmes.* https://apps.who.int/iris/handle/10665/279788

World Health Organization. (2020, March 19*). Infection prevention and control during health care when novel coronavirus (nCoV) infection is suspected*. https://www.who.int/publications/i/item/10665-331495.

Evaluation of Health Promoting Schools Programme in Saudi Arabia

Saeed G Alzahrani[1]

[1] Department of Public Health, College of Medicine, Imam Mohammad Ibn Saud Islamic University (IMSIU), Riyadh, Saudi Arabia. E-mail: Sgalsaeed@imamu.edu.sa. ORCID: https://orcid.org/0000-0003-0874-4314.

Abstract
Background: The health-promoting school (HPS) is a WHO-sponsored framework. This national study aimed to explore the experiences and progress in implementing the HPS programme in Saudi Arabia (SA). Methods: A self-completed postal questionnaire was sent to all 42 school health departments across SA, and the response rate was 100%. Results: Forty respondents (95%) had implemented the HPS programme. Over 400 schools were involved in the HPS programme of which two-thirds were primary schools. The most common activities addressed were health education activities. Less frequently mentioned were healthy school policies, action on the social environment, and developing links with the community. Evaluation was only through internal processes. The main perceived strengths of the HPS were increasing the awareness of students and school staff and improving the school's physical environment. The main weakness was the lack of legislation and financial support. For further development, the respondents reported the need for financial and human support. Conclusion: This study highlights the growth of the schools participating in the HPS programme. Further research is needed to develop and fully evaluate the effectiveness of the HPS framework in SA.

Keywords: Health Promoting School, Health Promotion, School Health

1. Introduction

Major advances have been made recently in finding the most appropriate and successful solutions for meeting the health needs of populations (Denman 1999). The growth of a new public health movement and the policies of the World Health Organization (WHO) have played a major part in pushing the boundaries of practice (WHO 2001). The WHO European Conference in Scotland in the early 1980s advocated for the health-promoting school (HPS) as an effective approach to health promotion in the school setting (Rogers et al. 1998) . The Ottawa Charter in 1986, the Jakarta Declaration in 1997, and the Recommendations of the WHO Expert Committee on Comprehensive School Health Education and Promotion in 1998 provided the foundation for WHO's Global School Health initiative (WHO 1998). The goal of WHO's Global School Health initiative (1998) is to increase the number of schools that can truly be called "Health Promoting Schools". A health-promoting school (HPS) is defined as a school constantly strengthening its capacity as a healthy setting for living, learning, and working (WHO 1998). The essence of the HPS approach is not blaming the victims for their own health problems. Instead,

it attempts to prevent problems and promote well-being through providing an environment that facilitates health development and influences the vision, perception, and action of all in that particular setting (Dooris 2006; Gray et al. 2006). Furthermore, the health-promoting schools embody a holistic, whole school approach to personal and community health promotion within the school setting (Parsons et al. 1996).

The WHO regional network for the development of health-promoting schools may be the world's most comprehensive and successful international effort to mobilise support for school health promotion. The European Network of Health-Promoting Schools (ENHPS) was the first network launched in 1991 (WHO 1993). It was run and funded by a partnership of the European Commission (EC), the Council of Europe (CE), and the WHO Regional Office for Europe. Other networks such as the Australian Health-Promoting Schools Association was begun in 1992, Western Pacific in 1995, Latin America in 1996, and South Africa in 1996. In both the US and Canada, the Comprehensive School Health Program (CSHP) approach is used more frequently than the HPS concepts (Deschesnes et al. 2003). In many areas "Healthy School Award" schemes have been set up to support the development of health-promoting schools. In the UK, health-promoting schools initiatives have been established by collaboration between local education services, health authorities, and health trusts to encourage schools to become more health-promoting. This initiative recognises schools that are trying to develop in line with the health-promoting school criteria (Lister-Sharp et al. 1999).

Rogers et al. (1998) conducted a national survey aimed at determining the extent and nature of existing Healthy Schools Awards in the UK and how they were being evaluated. They concluded that there has been significant growth in Healthy Schools Award schemes in recent years. This is an indication of a growing consensus amongst professional in education and health sectors about the value of the health-promoting school concept and award scheme as an acceptable method.

Lister-Sharp et al. (1999) conducted a review to evaluate the effectiveness of school-based health promotion interventions. The HPS framework had an impact on the social and physical environment of schools in terms of staff development, school lunch provision, exercise programmes, and social atmosphere. There was evidence that the framework is able to impact positively on aspects of mental and social well-being, dietary intake, and fitness. However, the HPS framework failed to demonstrate effectiveness in all studies included in the review. Lister-Sharp et al. (1999) concluded that the health-promoting school initiative as a new, complex, and optimum method of evaluation is currently under debate.

Stewart-Brown (2006) conducted a systematic review to evaluate the effectiveness of the HPS framework and school health promotion programmes in improving the health and well-being of students. He concluded that school-based programmes promoting mental health were effective in improving young people's health, particularly if developed and implemented using approaches common to the health-promoting schools, such as the involvement of the whole school, changes to the school psychosocial environment, personal skill development, involvement of parents and the wider community. Stewart-Brown (2006) concluded that the effectiveness of different types of programmes varies. School-based programmes that improve conflict resolution and reduce violence and aggression were among the most effective. Suicide-prevention programmes showed evidence of beneficial effects for suicide potential, but the less rigorous studies also identified negative/harmful effects in young males. Moreover, this review confirmed the findings of previous reviews that programmes on preventing substance use are among the least effective of school health promotion programmes. At best, those programmes delay the onset of drug use and reduce the quantity of drugs consumed. In addition, Stewart-Brown also highlighted that the school health promotion programmes that are effective in changing young people's health or health-related behaviour were more likely to be complex, multifactorial, and involve activity in more than one domain (curriculum, school environment, and community). These are features of the health-promoting school framework, and to this extent these finding endorse such approaches.

Lee et al. (2006) assessed the effectiveness of HPS in Hong Kong by comparing schools that had comprehensively implemented the HPS framework with schools that did not reach the standard of HPS. He found that students in healthy schools were better off in terms of self-reported health status and academic achievements. The findings highlighted the importance of healthy policies, empowerment, capacity-building, creating supportive

environments and partnerships to implement the health-promoting schools successfully. In addition, the findings of this study added further evidence to previous studies suggesting that the concept of a whole school approach in tackling health and social issues would improve learning outcomes.

Malikaew et al. (2006) argued that an HPS provides an ideal framework for developing effective oral health promotion through implementation of a range of policies and actions addressing common health risks and conditions. Moreover, Moyses et al. (2003) concluded that children in health-promoting schools had better oral health than children in non-supportive schools.

The HPS programme in Saudi Arabia was adopted in 2002 and passed two stages. In the first stage, the Administration General of School Health (AGSH) introduced the HPS programme to school health departments in the regions through several workshops and meetings (AGSH 2002). The second stage started in 2003, when regional departments of school health implemented the programme in one of their schools as a pilot. The most important achievements from the pilot stage were locating supervisors for the programme in each region and selecting HPS teams in the schools that implemented the programme. The total number of schools involved in the pilot stage was around 72 (AGSH 2006). In addition, the HPS award scheme was set for the regional development of the programme, and it consisted of three stages. In the first stage: preparation for recognition; second stage: evaluation of the activities; and third stage: accreditation and award. This scheme covered eight key areas: school health services; school health education; school health environment (physical, psychosocial); health promotion for school personnel; health promotion for the community; nutrition and food safety; physical education and recreation; mental health, counselling, and social supports.

The experience of Saudi Arabia in this programme is limited; therefore, the need to explore its successes and constraints is important, especially as there were no studies assessing the trend and progress in HPS development. The aim of this study is to explore the experience and progress of the national HPS programme from the perspective of the programme supervisors in school health departments for boys' schools in Saudi Arabia.

2. Methods and Materials

A national cross-sectional observational study was carried out to collect qualitative data. A validated self-completed postal questionnaire was used. The questionnaire consisted of six pages (size A4) with a separate covering letter. The covering letter highlighted the purpose of the study, ethical approval, and the confidentiality of the answers. All of the questions were open-ended. The questionnaire collected information about the extent and nature of the programme, activities being undertaken and how they were evaluated, school management response to HPS initiatives, HPS resources and materials, strengths and weaknesses of the programme activities and tackling problems, the plan to develop the programme, and the support required in the next five years. The questionnaire was sent officially by post to the supervisors of HPS programmes in the 42 educational regions, and they returned it by post or fax to the researcher. The period for collecting data was from April to June 2007.

3.1. Analysis

All the questionnaires were given a number from 1 to 42. The responses were listed, grouped, categorised by theme, and coded according to the guidelines for qualitative researchers (Malterud 1993).

3. The Results

All HPS supervisors in each educational region (n = 42) participated in the study, and all of the questionnaires were returned and filled. The respondents were asked whether the HPS programme existed, and the majority reported yes 95% (n=40), whereas only 5% (n=2) reported no. More than half of the regions 65% (n=26) started the programme in 2003. When asked to explain the reasons for the programme's absence, the following reasons were given: there was no financial support, and shortages of staff and material resources existed. The majority of schools were primary schools 65% (n=306), 21% (n=99) were intermediate, and 14% (n=66) were secondary schools (Table 1).

Table1: Number and types of schools involved in HPS programme.

Type of school	Number involved	Percentage (%)
Primary (6-12 y old)	306	65
Intermediate (12-15 y old)	99	21
Secondary (15-18 y old)	66	14
Total	471	100

The Health Promoting Schools activities

Healthy school policies

With regard to healthy school policies, a minority of respondents mentioned healthy policies in schools. For example, one respondent (no. 11) stated that "there were few health policies related to comprehensive health education programme, safe school environment, strengthening the concepts of HPS and activating the physical activity programme for student." The majority of respondents reported that schools implemented a group of health education programmes such as diet and milk programmes. Furthermore, they stated that schools adopted the Healthy Canteens policy by applying the healthy standards from the Ministry of Education.

School's physical environment

The majority of the respondents stated that the inspection of a school's environment programme was based on observing and monitoring the environment by the HPS programme supervisors (Table 2). They also mentioned periodic visits to check the safety of the school environment such as its drinking water and the cleanliness of the toilets. On the other hand, some respondents mentioned that many of the schools occupied unofficial buildings such as villas, which constrained fulfilment of healthy physical environments.

Table 2: Common weaknesses and problems of the HPS programme.

NO	ITEM
1	Not enough financial support for schools
2	Poor infrastructure for majority of schools
3	Not enough health education messages in curriculum
4	Absence of practical guidance for schools
5	Lack of incentives and rewards for schools and teachers
6	Increasing burden on teachers and schools

School's social environment

The majority of the supervisors mentioned that the health educational programmes were aimed at improving the health and social relationships between students and teachers. The respondents also reported that there were central policies from the Ministry of Education to control the relationships between the students and the teachers in the schools.

Community links

The majority of the supervisors stated that the HPS initiated the periodic meeting with the parents of the students and involved them in decisions related to the development of the education and health of the students. However, three respondents (no. 7, 6, and 38) stated that "the link between the HPSs and the community was neglected."

Links with health care services

The majority reported that the services such as basic vaccinations, inspection of new students, and creating a medical record for each student, in addition to providing curative and emergency services, were provided by school health care units and primary health care centres.

Resources and materials of HPS programme

The majority of respondents reported that the resources and materials available were not sufficient.

Evaluation of HPS activities
The majority of the respondents reported three ways of evaluating the HPS activities:
a. Periodic visits by the school health department supervisors to the participating schools. These visits included inspection of improvements in the physical environment and other activities such as health services and links with the community. The aim of these visits was to evaluate the activities and relevant achievements, as reported by the respondent (33).
b. The school programme teams used pre- and post-questionnaires to assess the improvement in knowledge and attitude of the students. In addition, they observed changes in the social environment, for example, the number of reductions in violence cases between the students.
c. Special reports of the HPS programme covered all activities in each part of the programme. For example, in the physical environment there are indicators such as the presence of enough rubbish baskets and the cleanliness of the classrooms and playgrounds. The programme supervisors completed these forms at the end of each academic semester. For example, one respondent (2) stated that "there were no sufficient number of toilets (8 toilets for 100 students) and sufficient number of fire extinguishers."

However, there was no clear mechanism for evaluation, with several limitations on the evaluation in some areas, such as school social environment, healthy school policy, and links with the community. For example, four respondents (38, 22, 17, and 19) did not complete the questions on how to evaluate the following activities: links with community, school social environment, and links with health services. When was asked how to evaluate school social environment, one respondent (31) stated "giving grade from zero to five." One respondent (24) mentioned only evaluation of the programme action plan. Another respondent argued that there was a need for external assessment to evaluate the activities of the HPS.

Strengths and weaknesses of the HPS activities

Positive strengths
The respondents stated that the HPS improved student and teacher awareness and behaviours. In addition, one respondent (no. 41) reported that the programme helped the constancy of students' healthy behaviours. The majority of respondents reported that the programme improved the schools' physical environment, students' meals, a safe playground, and cleanliness of the buildings. Furthermore, collaborations between school communities and students' families increased in schools that participated in HPS compared with nonparticipants. Some of the respondents reported that the canteens provide healthy meals. Some supervisors stated that there was a reduction in violence and bullying among students. One respondent (no. 40) stated that "schools became more attractive in learning." Moreover, the respondents reported that promoting the health of the school's community became a top priority of the schools' managers, and the collaboration between school health units and schools was improved.

Weaknesses and problems from respondents' perspectives
Table 2 summarises common weaknesses and problems reported by the respondents. The majority of the respondents reported that there was the need for financial support in order to implement the HPS programme. Furthermore, the majority expressed the need for incentives and rewards to encourage schools to participate in the programme.

They mentioned that there was a need for more teacher training and reducing the educational responsibilities of teachers who participated in the programme. The respondents reported that there was a need for more guidelines and reference sources that explained HPS concepts and evaluation processes. In addition, they added that there was a need to increase the participation of local communities and families in planning and evaluating the programme. The majority of respondents also reported the need for sharing experiences among regions through annual meetings. They stated that a clear vision and strategic planning were essential on the national level. They mentioned that there was a need for health personnel (nurses) in the schools,

Future plan and opportunities of the HPS framework
The majority of respondents reported that they planned to provide financial resources through private sector sponsorship, as well as incentives and rewards for schools to participate in the programme. Moreover, some supervisors planned to build a website for HPSs in their region to provide information and share experiences

among schools. In addition, they planned to improve the activity evaluation processes. Some supervisors planned to improve the canteen's health standards in order to improve the students' meals. However, one respondent (no. 3) stated that "we receive guidelines from Administration General of School Health and our role is to implement not to plan."

Types of support

The majority of respondents reported three types of needed support: financial, human, and administrative. Financial support included providing an annual budget for the programme and incentives for teachers. Human support included having health educators (nurses) in each school. Administrative support included rewarding and encouraging supervisors, teachers, and school managers. Finally, the majority of respondents expressed the need to assure a high commitment from all partners in this programme.

4. Discussion

This was a national study covering all school health departments in the 42 educational regions that are responsible for the implementation and development of the HPS programme in Saudi Arabia. It indicated that there had been significant growth in the enrolment of schools in HPS since 2003, with a majority of the regions (95%) implementing the programme. However, there was a disparity in the timing of the HPS implementation among the regions without a clear justification. Over 400 schools are involved in the HPS programme, with the two-thirds (65%) implemented in primary schools. However, there was a wide disparity in the number of HPS schools among the regions.

The study highlighted the extent of HPS activities, although the results do not provide clear evidence that there is considerable investment in this approach. Similar results were found in the study by Rogers et al. (1998), which aimed to determine the extent and existing Healthy School Award in the UK.

There are many dimensions to a health-promoting school, and the main goal is enhancing the health status of the pupils and school staff. This can be achieved by building a healthy school policy, changing the social and physical environment, developing personal skills and involving parents and the wider community. The results indicated that no schools were able to cover all areas of the HPS framework at the same time. This was found in other studies (Deschesnes et al. 2003; Lister-Sharp et al. 1999; Rogers et al. 1998). The HPS framework was built on previous health education programmes that included the provision of health information on specific topics, such as healthy eating and smoking. Moreover, these activities in general are isolated and are not clearly connected in the HPSA scheme. The school physical environment is given high priority in the HPS programme owing to the need for its substantial improvement. This finding was similar to another study in Hong Kong (Lee et al. 2006). However, more than one-third (38 %) of the public schools occupied private buildings that were not a suitable environment for education. Therefore, schools in private buildings constrained the expansion of the HPS programme.

There were limitations in the implementation of some aspects of the HPS programme such as healthy school policy and school social environment. The reason is that these two concepts were not included in the key activities of the HPSA scheme. Other key aspects of the health-promoting school concept that received less attention were developing links with community and health care services. In general, HPS activities have been implemented as a traditional health education model. The health-promoting schools approach needs further attention and development.

Regarding the evaluation of HPS activities there was a clear limitation, as it depended only on the reports and regular monitoring visits of the physical environment of the schools. There was no time scale for the evaluation; the main method was internal assessment by the HPS teams in the schools. The multifaceted, complex nature of the health-promoting school poses a considerable challenge for evaluation. Indicators of achievements in all areas need to be addressed and fully specified in order to derive appropriate measures. In addition, the evaluation is necessary to provide evidence that the HPS framework is implemented as an integrated set of components.

The Health-Promoting Schools Award (HPSA) schemes have been set up to enhance the implementation and the development of the concept of health-promoting schools. In the KSA, the key area of the HPSA scheme was more

likely to be a comprehensive school health programme (CSHP) rather than an HPS framework, and the scheme had no clear effect on the schools.

The lack of administrative, financial, and human support from the upper sectors involved in the HPS was considered the main weakness. These problems were mentioned in another study conducted by Lister-Sharp et al. (1999). The lack of financial and human resources for essential school facilities undermines the whole school approach. In addition, the lack of practical guidance for schools was reported as a common weakness. Practical guidance is an essential resource for schools to implement the programme; for example, in the UK the national healthy school status was a guide for schools which targeted school management. It aimed to outline the National Healthy School Programme, introduce the concepts of national healthy school status, and describe the benefits of becoming a 'Healthy School' (DoH 2005). The political commitment, upstream policies, and support of policy makers are essential for successful implementation of the HPS framework.

There is increasing awareness of students and the need to improve the physical environment of schools. Similar findings are found in other studies (Lister-Sharp et al. 1999; Mitchell et al. 2000; Moon et al. 1999).

This study was the first national survey conducted to assess the health-promoting school framework across the Kingdom of Saudi Arabia. The responses provided recent data on the experience and progress of the health-promoting schools from the perspectives of the programme supervisors in school health departments in the 42 educational regions. Much information was collected on different aspects of the HPS framework that provided a clear view of school experiences in the programme.

The study used a self-completed (postal) questionnaire method for collecting the data. Telephone interviews or follow-ups with the participants were not possible to collect more information on certain questions.

5. Conclusions

The aim of this study was to explore the experience and progress of the national health-promoting schools programme in Saudi Arabia from the perspective of the programme supervisors. Key findings highlighted significant growth in schools participating in the programme. The common theme of the HPS programme was a traditional health education model with fewer health promotion interventions. Healthy school policy was not included in the key components of the Health-Promoting School Award scheme, and the school social environment was rarely involved in the programme. The lack of financial and human support was considered the main weakness of the HPS programme. There were clear limitations in the planning and evaluation of HPS activities. The future of HPS looks promising. Further studies are needed to evaluate the effectiveness of the HPS framework.

References

AGSH. 2002. The health promoting schools programme. Riyadh; Saudi Arabia: Administration General of School Health (AGSH).

AGSH. 2006. The health promoting schools project. Riyadh; Saudi Arabia: Administration General of School Health (AGSH).

Denman S. 1999. Health promoting schools in england-a way forward in development. Journal of Public Health. 21(2):215-220.

Deschesnes M, Martin C, Hill AJ. 2003. Comprehensive approaches to school health promotion: How to achieve broader implementation? Health Promot Int. 18(4):387-396.

DoH. 2005. National healthy school status: A guide for schools. London; UK: Department of Health (DoH).

Dooris M. 2006. Healthy settings: Challenges to generating evidence of effectiveness. Health Promot Int. 21(1):55-65.

Gray G, Barnekow Rasmussen V, Young I, World Health Organization. Regional Office for E, European Network of Health Promoting Schools. International Planning C. 2006. Health-promoting schools : A practical resource for developing effective partnerships in school health, based on the experience of the european network of health promoting schools / by gay gray, ian young and vivian barnekow. Copenhagen : WHO Regional Office for Europe.

Lee A, Cheng FF, Fung Y, St Leger L. 2006. Can health promoting schools contribute to the better health and wellbeing of young people? The hong kong experience. J Epidemiol Community Health. 60(6):530-536.

Lister-Sharp D, Chapman S, Stewart-Brown S, Sowden A. 1999. Health promoting schools and health promotion in schools: Two systematic reviews. Health Technol Assess. 3(22):1-207.

Malikaew P, Watt RG, Sheiham A. 2006. Prevalence and factors associated with traumatic dental injuries (tdi) to anterior teeth of 11-13 year old thai children. Community Dent Health. 23(4):222-227.

Malterud K. 1993. Shared understanding of the qualitative research process. Guidelines for the medical researcher. Family practice. 10(2):201-206.

Mitchell J, Palmer S, Booth M, Davies GP. 2000. A randomised trial of an intervention to develop health promoting schools in australia: The south western sydney study. Australian and New Zealand Journal of Public Health. 24(3):242-246.

Moon A, Mullee MA, Rogers LL, Thompson RL, Speller V, Roderick PJ. 1999. Helping schools to become health-promoting environments—an evaluation of the wessex healthy schools award. Health Promotion International. 14:111-122.

Moysés ST, Moysés SJ, Watt RG, Sheiham A. 2003. Associations between health promoting schools' policies and indicators of oral health in brazil. Health Promot Int. 18(3):209-218.

Parsons C, Stears D, Thomas C. 1996. The health promoting school in europe: Conceptualising and evaluating the change. Health Education Journal. 55(3):311-321.

Rogers E, Moon AM, Mullee MA, Speller VM, Roderick PJ. 1998. Developing the 'health-promoting school'--a national survey of healthy schools awards. Public Health. 112(1):37-40.

Stewart-Brown S. 2006. What is the evidence on school health promotion in improving health or preventing disease and, specifically, what is the effectiveness of the health promoting schools approach? Copenhagen: World Health Organization. Available at: http://www.euro.who.int/document/e88185.pdf. Accessed on 15 March 2007.

WHO. 1993. The european network of health-promoting schools Copenhagen: World Health Organization. Available at: https://www.euro.who.int/__data/assets/pdf_file/0004/252391/E62361.pdf. Accessed at 15 March 2007.

WHO. 1998. Who's global school health initiative: Health promoting schools; a healthy setting for living, learning and working. Geneva: World Health Organization. Available at: https://www.paho.org/hq/dmdocuments/2016/1998-GlobalSchoolHealthInitiative.pdf. Accessed at 15 March 2007.

WHO. 2001. Local action: Creating health promoting schools. Information series on school health. Geneva: World Health Organization. Available at: https://apps.who.int/iris/bitstream/handle/10665/66576/WHO_NMH_HPS_00.3.pdf. Accessed at 15 March 2007.

Anaesthetic Management of Patient with Left Atrial Myxoma, Coronary Artery Disease 3 Vessels Disease, and Parkinson's Disease

Hana Nur Ramila[1], Adwitya Darmesta Gandhi N[1], Reza Widianto Sudjud[1]

[1] Department of Anaesthesiology and Intensive Care, Faculty of Medicine University of Padjadjaran, Hasan Sadikin General Hospital Bandung

Correspondence: Adwitya Darmesta Gandhi N, Department of Anaesthesiology and Intensive Care, Faculty of Medicine University of Padjadjaran, Hasan Sadikin General Hospital Bandung. Tel: +62 812-2145-4104. E-mail: darmesta.gandhi@gmail.com

Abstract

Myxomas are the most common primary benign intracavitatory tumour with the incidence of 0.5 per million populations. Myxomas account for 0.3% of all cardiac surgeries performed. Clinically, they are characterized by a triad of embolisation, obstruction of blood flow, and constitutional symptoms (Goodwin's triad). Meanwhile Parkinson's disease is a degenerative neurologic disorder caused by degeneration of nerve cells in the substantia nigra causing weakness motor coordination. Symptoms include tremor, bradykinesia, rigidity, and postural instability. Achieving a satisfactory hemodynamic performance is the primary objective in the management of cardiac surgery patient. Optimal cardiac function ensures adequate perfusion and oxygenation of other organ systems (in particular vital organs) and improves the chances for an uneventful recovery from surgery. A 61-year old female diagnosed with Coronary Artery Disease 3 Vessel Disease (CAD 3 VD), Parkinson's disease, and left atrial myxoma was brought to the emergency department with dyspnea. The patient has undergone angiography and the echocardiography result was LVEF 59% with global normokinetic, LA myxoma causing non-significant mitral flow. LA myxoma excision under general anaesthesia on CPB was planned. Balanced general anaesthesia on cardiopulmonary bypass forms the basis of Anaesthetic management of Cardiac myxomas. However specific individual considerations will have to be made regarding drugs, doses, regional anaesthetic choices, anticoagulation and post-operative management. There is no simple anesthetic technique for patients with Parkinson'. Therefore, careful preoperative assessment, administration of drugs during and after anesthesia, as well as avoiding agents that are known to trigger Parkinson's symptoms is a major factor in reducing postoperative morbidity and mortality.

Keywords: Anesthetic Management, CAD 3VD, Cardiopulmonary Bypass, Myxoma, Parkinson's Disease

1. Introduction

Myxomas are commonest primary benign intracavitarytumorss with the incidence of 0.5 per million population (MacGowan et al.,1993). Myxomas account for 0.3% of all cardiac surgeries performed (Castells et al.,1993). Myxomas are twice more common in females than in males and the mean year of occurrence is 55 years (Godwin.,1963). Myxomas commonly arisefrom the left atrium but 25% occurs in the right atrium or ventricles. (Godwin.,1963). Clinically, they are characterized by triad of embolisation, obstruction of blood flow, and constitutional symptoms (Goodwin's triad) (Feng et al., 1990). About 17-59% of patients with myxomas present as an embolic event, while cerebral embolisation occurs in up to 45%, and this commonly occurs in the middle cerebral artery territory as in our case (Feng et al., 1990).

Parkinson's disease is a degenerative neurologic disorder caused by degeneration of nerve cells in the substantia nigra causing weakness in motor coordination. These nerve cells die or become damaged because they loose the ability to produce dobutamine. Symptoms include tremor, bradykinesia, rigidity, and postural instability (Feng et al 1990).

Patients undergoing cardiac surgical procedures are extensively monitored. Hemodynamic alterations and myocardial ischemia that occurs during the induction of anesthesia, in the prebypass period, during CPB, and following resumption of cardiac activity can have significant adverse effects on myocardial function and recovery (Feng et al., 1990).

It should be noted that even though both hypertension and tachycardia can increase myocardial oxygen demand, an increase in heart rate results in more myocardial ischemia at an equivalent increase in oxygen demand. Standard monitoring in the operating room consists of a five-lead ECG, central venous catheter (CVC), a radial arterial line, pulse oximetry, an end-tidal CO2 measurement, a Swan-Ganz pulmonary artery (PA) catheter, cerebral oximetry, and a urinary Foley catheter to measure urine output, core body temperature and intraoperative transesophageal echocardiography (TEE) should be obtained (Feng et al.,1990).

Anesthetic management must be individualized, taking into consideration the patient's age, comorbidities, the nature and extent of coronary or valvular disease, the degree of left ventricular dysfunction, and plans for early extubation. These factors will determine which medications should be selected to avoid myocardial depression, tachycardia, or bradycardia, or to counteract changes in vasomotor tone. Generally, a balanced anesthetic technique using a combination of narcotics and potent inhalational agents is used for all open-heart surgery to minimize myocardial depression (Feng et al.,1990).

2. Case

A 61-year old female diagnosed with Coronary Artery Disease 3 Vessel Disease (CAD 3 VD), Parkinson's disease, and left atrial myxoma was brought to the emergency department with dyspnea. She had a past history of hypertension for over 2 years. She was diagnosed with CAD since 2021 and was on medical therapies furosemide 1x40 mg, bisoprolol 1x2,5 mg, candesartan 1x8 mg, nitroglycerin 1x2,5, amlodipine 1x10 mg, allopurinol 1x100 mg, Clobazam 1x10, Clopidogrel 1x75 mg, levodopa 1x125 mg, Trihexylphenidyl 1x1 mg. She weighs 42 kg.

The patient had undergone angiography for preoperative indications. The echocardiography result was global normokinetic with LVEF 59%, LA myxoma causing non-significant mitral flow. The patient has hypertension as coexisting disease. LA myxoma excision under general anaesthesia on CPB was planned.

Angiography results show a codominant system. The left main artery appears fine. The left anterior descending vessel showed moderate stenosis in the mid, severe stenosis in the distal and in the ostial branches of diagonal 1 and diagonal 2. The intermediate ramus showed severe stenosis in the ostial. The left circumflex artery showed severe stenosis distally and ostium OM 1. The right coronary artery showed mild stenosis proximally.

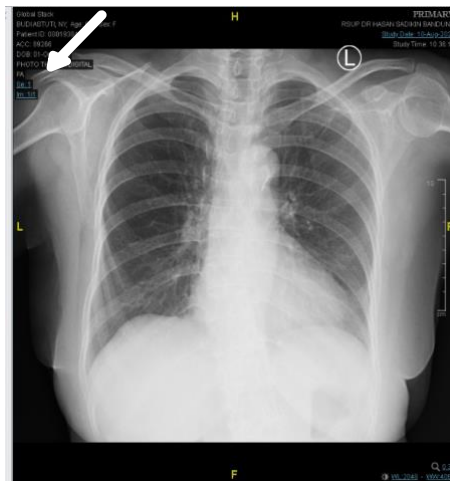Figure 1: Echocardiography showing mass in the Left atrium (arrow)

Figure 2: Photo thorax show cardiomegaly without swelling, atheroclerosis of aorta, scoliosis of the thoracic vertebrae

Figure 3: Angiography show CAD 3 VD

All the routine preoperative investigations were within normal limits. Patient was taken into operating room and arterial line was secured in right radial artery under local anaesthesia. Before the induction of anesthesia, the patient was preoxygenated for 3-5 minutes, then given midazolam 3 mg, fentanyl 150 mcg, propofol 40 mg, and rocuronium 40 mg intravenously. Intubation was done with cuffed endo-tracheal tube size 8. Anaesthesia was maintained with sevoflurane. A 7 Fr triple lumen central venous catheter was inserted through left subclavian vein. Baseline ACT (activated clotting time) was 150sec. Patient was heparinized with 16000 IU of IV Heparin and ACT was maintained > 8 minutes and the patient went into cardiopulmonary bypass. Total Cross clamp time was 40 minutes and total bypass time was 44 minutes. During the bypass period, anesthesia was maintained using continous propofol infusion.

Intraoperative, a LA Myxoma sized 2 x 1,4 cm was excised, with a stalk attached to the interatrial septum (IAS). Excision of LA Myxoma was done including part of the IAS to which the myxoma was attached and the created ASD was closed with pericardial patch.

Intraoperative investigations of arterial blood gas analysis, hemoglobin level, blood sugar, and electrolytes were within normal limits. Intravenous protamine 160 mg was givenfor reversal of heparin effect. ACT was 120 seconds after protamine injection. Total duration of anaesthesia was 4 hours and 25 minutes and total duration of surgery was 4 hours. The patient received 1.5L of Ringers Lactate, 500ml of Gelofusine (Gelatine 3.5%) and two pints (700ml) of packed red cells were also transfused intraoperatively.
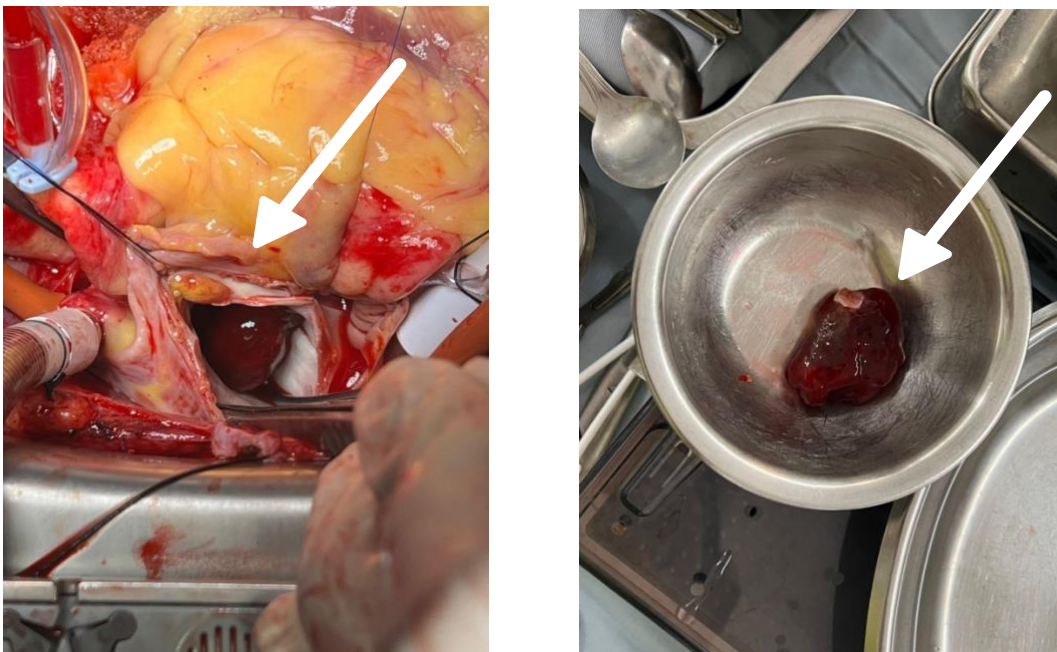

Figure 4: LA myxoma, just after excision (arrow)

The patient was transferred to the ICU, still intubated and sedated with propofol infusion. The patient's heart rate was 90 bpm and BP 118/78 mmHg, on dobutamine infusion 5μg/kg/min. Patient was extubated in the ICU after a few minutes and was kept on non-rebreathing mask with oxygen 15 lpm, RR 20/min and SpO_2 97%. For analgesia, the patient received continuous intravenous morphine 1mg/hour. At the early postoperative period, the chest drain production was about 130ml/hour, intravenous traneksamic acid 1 gram was given. Levodopa as the medication for Parkinson's was continued immediately after surgery through a nasogastric tube. As the blood pressure was maintained, the dobutamine infusion was decreased and stopped at the same day. Postoperative laboratory investigations were within normal limits.

On the third postoperative day, all routine investigations were normal. Urine catheter and central venous catheter were removed. The patient was then shifted to the ward where she was observed for three more days whilst the chest and limb physiotherapy was continued. LMWH was stoppedon seventh post- operative day and t h e

p a t i e n t was discharged. She was then advised to follow up after one week and continue physiotherapy.

3. Discussion

Myxomas are commonest primary benign intracavitatory tumors with the incidence of 0.5 per million populations (Castells et al.,1993). Clinically, they are characterized by triad of embolisation, obstruction of blood flow, and constitutional symptoms (Goodwin's triad) (Feng et al., 1990). A b o u t 17-59% of patient with myxoma present as embolic event, while cerebral embolisation occurs in up to 45%, and this commonly occurs in the middle cerebral artery territory as in our case (Feng et al.,1990).

Three things must be considered when starting the induction are oxygenation, fluid status, and selection of drugs that does not make the heart work harder. Pre-oxygenation is needed to optimize blood oxygen levels. In addition, CVC placement should be done to ensure the patient remains in a normovolemic state. The combination of fentanyl, midazolam, and sevoflurane is the drug of choice used for induction, because it can minimize the cardiac depressant effect. However, the beneficial effects on the heart are still obtained.

Obstruction to blood flow can present with heart failure or syncope in 41 – 79% of cases (Mac Giwan et al., 1993). Left ventricular outflow tract obstruction because of the mass can mimic mitral stenosis and can cause pulmonary hypertension and even congestive heartfailure (Mac Gowan et al.,1993). Right sided myxoma can also be associated with obstruction and can present as cardiovascular collapse during induction of anaesthesia (Mac Gowan et al., 1993).

Fever, malaise, weight loss, fatigue, anemia, andraised erythrocyte sedimentation rate are common constitutional symptoms which occur in around 90% patients with myxomas.(Feng et al.,1990) These features resolve immediately after surgery and are believed to be due to release of inflammatory mediators from tumour cells (Namboodiri et al., 2004).

Structurally, there are two types of myxomas, one withround, non-mobile surface, and another polypoid type with irregular shape, mobile surface and this latter type has the higher incidence of embolism and this is the commonest type to prolapse into the ventricles (Swenson et al., 2005).

Surgical management is the treatment of choice for myxomas but open-heart surgery immediately after cerebral embolisation is considered contraindicateddue to problems of hemorrhagic, infarction or progressive cerebral oedema (Swenson et al., 2005). Another school of thought considers immediate surgery as the treatment, as recurrent embolisation can be fatal (Peters et al., 1974). The recurrence of myxoma has been reported to be less than 2% on most series (Mac Gowan et al., 1993).

Anaesthetic considerations include the consideration for patient undergoing open-heart surgery. A detail history and a meticulous clinical examination is a must. Risk factors for cardiovascular diseases, other comorbid conditions, NYHA classification for functional status of the patient should also be assessed properly (Disesa et al., 1988). Preoperative evidence of heart failure, pulmonary hypertension and evidence of outflow obstruction should be obtained (Moritz et al., 1989). Patient with history of embolism should be properly treated with anticoagulants according to guidelines and then planned for surgery (Bateman et al., 1983). Apart from routine blood and urine investigations, chest roentgenogram,electrocardiography, and echocardiography is essential. Echocardiography not only gives information about the size of the tumour, but can also locate the origin of the myxoma (Knepper et al., 1988). In this regard, trans-esophageal echocardiography (TEE) is superior to transthoracal echocardiography (TTE) (Mac Gowan et al., 1993).

Even though arrhythmias are uncommon, atrialarrhythmias –if present— should be treated either pharmacological or with electric cardioversion as indicated (Knepper et al., 1988). In patients with evidence of embolism, other investigations are required depending on the site of embolism. CT scan and MRI are helpful in embolic stroke while Doppler studies are helpful in cases of peripheral vessel involvement, e.g. carotid or femoralarteries (Moritz et al.,1989).

Adequate premedication helps in allaying anxiety, and avoids detrimental haemodynamic changes due to it (Disesa et al., 1988). Apart from basic monitoring; invasive arterial pressure monitoring and central venous line placement is a must in patient undergoing myxoma excision (Disesa et al., 1988). Pulmonary artery catheterization is not necessary unless there are specific indications for it. The use of TEE has now been considered a useful tool for intraoperative diagnosis, localization of the tumour, and also for confirmation of adequate removal (Mac Gowan et al., 1993). The anaesthetic regimen for conducting anaesthesia for myxoma excision is not different from any other cardiac surgery, but a balanced anaesthetic approach is now the preferred method (Bateman et al., 1983). Opiates, along with volatile anaesthetic agents, which have additional advantage of inducing ischemic preconditioning (in patients likely to have ischemic myocardial insults), and any of the commonly used muscle relaxants can be combined for the balanced approach (Bateman et al., 1983). Benzodiazepines, forms a core component of the balanced approach and midazolam in particular is preferred for minimal effect on coronary blood flow autoregulation. After the aortic cross clamping and the patient on CPB, anaesthesia can be maintained with the volatile agent through the CPB or can be maintained on low dose propofol infusion for sedation (Disesa et al., 1988). However, induction with propofol is not advised because of action causing significant depression of myocardium, and hypotension owing to decrease systemic vascular resistance (Disesa et al., 1988).

After the excision of tumour and repair of the opening site, weaning from CPB and reversal of heparin with protamine, checking regular blood gas parameters and activated clotting time are similar to any other cardiac surgery (Peters et al., 1974). Fast track cardiac anaesthesia or early extubation following surgery is the goal and shall be preferred unless any complications or contraindications occur (Bateman et al., 1983).

Regional anaesthetics, intrathecal or epidural have advantages because of their desirable effects on stress response, haemodynamics, coronary perfusion pressure, myocardial blood flow redistribution and chances of early extubation, but their use is not common, maybe because of concerns for anticoagulation, and potential to cause haematoma and its neurological consequences (Bateman et al., 1983).

Post-operatively, the patient should be monitored in an intensive care unit or other high dependency units, where constant supervision, monitoring and vigilance are available (Peters et al., 1974). Anticoagulation should be resumed postoperatively in patients with history of embolism, and in those who were on anticoagulation preoperatively.(Disesa et al.,1988) High incidence of arrhythmias and conduction disturbances have been reported both in early and late post-operative periods (Knepper et al., 1988).

Myocardial ischemia occurs when the oxygen supply to the heart is insufficient to meet metabolic needs. This mismatch can result from a decrease in oxygen supply, a rise in demand, or both. The most common underlying cause of myocardial ischemia is obstruction of coronary arteries by atherosclerosis. In the presence of such obstruction, transient ischemic episodes are usually precipitated by an increase in oxygen demand as a result of physical exertion. Ventricular hypertrophy due to hypertension can predispose the myocardium to ischemia because of impaired penetration of blood flow from epicardial coronary arteries to the endocardium (Ha J.W et al., 1999).

A low cardiac output state in patients with a history of CAD may result from abnormal preload, contractility, heart rate, or afterload. It may also be noted in patients with satisfactory systolic function but marked left ventricular hypertrophy and diastolic dysfunction. The principal management of this condition are: 1. Ensure satisfactory oxygenation and ventilation; 2. Treat ischemia or coronary spasm if suspected to be present –myocardial ischemia often responds to intravenous nitroglycerin (NTG) but may require further investigation if it persists; 3. Optimize preload by raising filling pressure with volume infusion; 4. Stabilize the heart rate and rhythm; 5. Improve contractility with inotropic agents –this should be based on an understanding of the α, β or nonadrenergic hemodynamic effects of vasoactive medications and their anticipated effects on preload, afterload, heart rate, and contractility; 6. Reduce afterload; 7. Maintain blood pressure (Ha J.W et al., 1999).

The main perioperative concern in our patient was the past history of hypertension for over 2 years, CAD (CTO in LAD and RCA, 89-90% stenosis in LCX), low EF (27%), extensive myocard infarction (from apical to basal) with hypertrophy as well as global function impairment of the left ventricle. Providing safe anesthesia to these

patient who are posted for CABG has always been challenging. Hemodynamic alterations and myocardial ischemia that occur during the induction of anesthesia, in the prebypass period, during CPB, and following resumption of cardiac activity can have significant adverse effects on myocardial function and recovery. It should be noted that even though both hypertension and tachycardia can increase myocardial oxygen demand, an increase in heart rate results in more myocardial ischemia at an equivalent increase in oxygen demand (Ha J.W et al.,1999).

Perioperative management of Parkinson's patients is a challenge for an anesthesiologist. Attention must be focused on three things, the administration of anti-Parkinson's drugs in the perioperative period, the possibility of adverse interactions from anesthetic drugs with antiparkinsonian drugs, as well as physiological disturbances caused by Parkinson's disease.

If it is decided to perform general anesthesia, it needs to be done with anticipation of the possibility of a difficult airway, hyperreactive airway and aspiration due to excessive secretions. The possibility of postoperative mechanical ventilation should also be considered. In patients undergoing general anesthesia, rigidity following high or low doses of fentanyl may be observed in normal patients. However, people with Parkinson's are more likely to have postoperative confusion and hallucinations (Kumar et al., 2004) (Morganet al., 2006).

Furthermore, it is important to ensure that patients receive treatment in the postoperative period. Routine doses of anti-Parkinson's drugs should be continued as soon as possible after surgery to prevent exacerbation symptoms. Stopping levodopa suddenly can cause exacerbations symptoms, especially dysphagia and rigidity of the chest wall skeletal muscles affecting ventilation ability and disturbance of respiration, or neuroleptic malignant syndrome (NMS) may occur (Nicholson et al., 2002).

In the use of inhaled anesthetic agents, one thing that must be avoided is the possibility of tachyarrhythmias due to the use of halothane in Parkinson's patients treated with levodopa, because halothane can sensitize the heart to catecholamines. There have been no reports of adverse effects with isoflurane, sevoflurane, or desflurane in Parkinson's patients. Isoflurane and sevoflurane are the inhaled agents of choice although they may cause hypotension, especially in patients with autonomic neuropathy and in those with autonomic neuropathy (Robert.,2011).

4. **Conclusion**

Achieving a satisfactory hemodynamic performance is the primary objective in the management of cardiac surgical patient. Optimal cardiac function ensures adequate perfusion and oxygenation of other organ systems (in particular vital organs) and improves the chances for an uneventful recovery from surgery. Balanced general anaesthesia on Cardiopulmonary Bypass forms the basis of anaesthetic managementof cardiac myxomas. However specific individual considerations will have to be made regarding drugs, doses, regional anaesthetic choices, anticoagulationand post-operative management. There is no simple anesthetic technique for selecting anesthesia Parkinson's patient. Therefore, careful preoperative assessment, administration of during and after anesthesia, as well as avoiding agents that known to trigger Parkinson's symptoms is a major factor in reduce postoperative morbidity and mortality.

References

MacGowan, S. W., Sidhu, P., Aherne, T., Luke, D., Wood, A. E., Neligan, M. C., & McGovern, E. (1993). Atrial myxoma: national incidence, diagnosis and surgical management. _Irish journal of medical science, 162(6),_ 223–226. https://doi.org/10.1007/BF02945200.
Castells, E., Ferran, V., Octavio de Toledo, M. C., Calbet, J. M., Benito, M., Fontanillas, C., Granados, J., Obi, C. L., & Saura, E. (1993). Cardiac myxomas: surgical treatment, long-term results and recurrence. _The Journal of cardiovascular surgery, 34(1),_ 49–53. https://pubmed.ncbi.nlm.nih.gov/8482704/
Goodwin J. F. (1963). Diagnosis of left atrial myxoma. _Lancet (London, England), 1(7279),_ 464–468. https://doi.org/10.1016/s0140-6736(63)92359-6.

Fang, B. R., Chiang, C. W., Hung, J. S., Lee, Y. S., & Chang, C. S. (1990). Cardiac myxoma—clinical experience in 24 patients. _International journal of cardiology, 29(3),_ 335–341. https://doi.org/10.1016/0167-5273(90)90123-m.

Namboodiri, K. K., Chaliha, M. S., Manoj, R. K., & Grover, A. (2004). Central nervous embolism as an usual presentation of left atrial myxoma. _Journal of postgraduate medicine, 50(2),_ 151. http://www.bioline.org.br/pdf?jp04047

Swenson, J. D., Balley, P. L. (2005). Intraoperataive diagnosis of atrial myxoma by TEE. _Miller's Anaesthesia. Churcill Livingstone._

Disesa, V. J., Collins, J. J., Jr, & Cohn, L. H. (1988). Considerations in the surgical management of left atrial myxoma. _Journal of cardiac surgery, 3(1),_ 15–22. https://doi.org/10.1111/j.1540-8191.1988.tb00213.x.

Peters, M. N., Hall, R. J., Cooley, D. A., Leachman, R. D., & Garcia, E. (1974). The clinical syndrome of atrial myxoma. _JAMA, 230(5),_ 695–701. https://pubmed.ncbi.nlm.nih.gov/4479298/

Moritz, H. A., & Azad, S. S. (1989). Right atrial myxoma: case report and anaesthetic considerations. _Canadian journal of anaesthesia = Journal canadien d'anesthesie, 36(2),_ 212–214. https://doi.org/10.1007/BF03011447.

Bateman, T. M., Gray, R. J., Raymond, M. J., Chaux, A., Czer, L. S., & Matloff, J. M. (1983). Arrhythmias and conduction disturbances following cardiac operation for the removal of left atrial myxomas. _The Journal of thoracic and cardiovascular surgery, 86(4),_ 601–607. https://pubmed.ncbi.nlm.nih.gov/6621088/

Knepper, L. E., Biller, J., Adams, H. P., Jr, & Bruno, A. (1988). Neurologic manifestations of atrial myxoma. A 12-year experience and review. _Stroke, 19(11),_ 1435–1440. https://doi.org/10.1161/01.str.19.11.1435.

Ha, J. W., Kang, W. C., Chung, N., Chang, B. C., Rim, S. J., Kwon, J. W., Jang, Y., Shim, W. H., Cho, S. Y., Kim, S. S., & Cho, S. H. (1999). Echocardiographic and morphologic characteristics of left atrial myxoma and their relation to systemic embolism. _The American journal of cardiology, 83(11),_ 1579–A8. https://doi.org/10.1016/s0002-9149(99)00156-3.

Kumar, T.K.S., Ali, M., & Hirakannawar, A. (2004). Clinical experience and surgical considerations in the management of cardiac myxomas. _Indian Journal Thoracic Cardiovascular Surgery, 20,_ 77–82. https://doi.org/10.1007/s12055-004-0046-3

Morgan, G.E., Mikhail, M.S., & Murray M.J. (2006). _Anesthesia for patients with neurologic & psychiatric disease in Clinical anesthesiology._ Lange Medical Book/McGraw-Hill Medical Publishing Division.

Nicholson, G., Pereira, A. C., & Hall, G. M. (2002). Parkinson's disease and anaesthesia. _British journal of anaesthesia, 89(6),_ 904–916. https://doi.org/10.1093/bja/aef268.

Robert, M.B. (2011). _Cardiovascular management: Manual of perioperative in adult cardiac surgery._ Blackwell's publishing.