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Dynamics of COVID-19 Vaccination Policy in Indonesia: Analysis of Readiness and Implementation

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Abstract
Implementing COVID-19 vaccination in Indonesia, a country with 17,000 islands and 38 provinces presents significant challenges, including reducing transmission risk and promoting economic recovery. This study aims to raise a policy issue perspective on the implementation of COVID-19 vaccination. It begins by exploring the influencing factors using the policy analysis triangle framework, examining the content, context, processes, and actors involved, to understand the dynamics of vaccination policy readiness and implementation. The analysis investigates the current landscape, regulatory framework, and execution, which serve as indicators of Indonesia's readiness for COVID-19 vaccination. Between March 2020 and February 2022, the Indonesian government enacted 16 regulations, including Government Regulations, Ministerial Regulations, and Ministerial Decrees, to facilitate vaccination efforts against the pandemic. Despite these efforts, significant challenges remain, such as limited vaccine availability, distribution logistics, and public acceptance pose significant hurdles to the policy's successful implementation. The study highlights that Indonesia's vaccination strategy is influenced by political, social, and economic factors, along with global pandemic trends. Despite initial unpreparedness, evident in the rapid policy development during the pandemic's early phases, Indonesia's strategic adjustments facilitated a notable vaccination coverage milestone, achieving over 70% for the first dose by 2021 and the second dose by mid-2022. This progression showcases the country's resilience and capacity to navigate the multifaceted obstacles inherent in a large-scale vaccination campaign.

Keywords: Implementation, Readiness, Vaccination Policy, COVID-19 Pandemic, Indonesia

1. Introduction and Standing Position

One of the efforts made by the Indonesian government to overcome the Coronavirus Disease-2019 (COVID-19) pandemic is to follow vaccination developments that various countries have carried out as input for the national vaccination program (Dewi, 2022). The vaccination program aims to reduce the risk of transmission of COVID-19 through the establishment of herd immunity, ultimately achieving group protection.

Implementing vaccination against COVID-19 demands meticulous planning, resource optimization, diligent field

execution, and adherence to scientific advancements for policy formulation. Indonesia, home to 275.7 million people across 17,000 islands and 38 provinces as of mid-2022, faces challenges in resource allocation and mobilization for its vaccination efforts. On August 22, 2022, the national vaccination target was increased to 234.7 million, resulting in adjustments to the target achievement (Aditama, 2021). Coverage rates were 86.6% for the first dose 72.7% for the second dose, and 25.2% for the third dose. However, during this time, first-dose coverage fell below 70% in three provinces, namely Maluku, West Papua, and Papua. Additionally, 18 provinces had second dose rates under 70%, and 22 provinces saw less than 30% achievement for the third dose (Rokom, 2021). This article explores and discusses the existing varied implementation of COVID-19 vaccination across Indonesia from the public's perspective as beneficiaries of the policy. Then, it raises a debate on the pros and cons of implementing the COVID-19 vaccination policy, highlighting various perspectives on its rollout. It starts with providing the exploration of the influencing factors using the policy analysis triangle framework, by examining the content, context, processes, and actors involved, to understand the dynamics of vaccination policy readiness and implementation.

2. Methods

Data for this study, spanning October 2020 to February 2022, was gathered through a literature study (secondary) by examining sources from various literature, such as journals, books, policy documents, websites, online news media, and reports from valid and official sources. The methodology involves synthesizing and analyzing collected data to assess the situation regarding COVID-19 vaccination readiness, policy implementation, and regulatory frameworks in Indonesia. It also examines priorities, achievements, and policy goals, reflecting government efforts toward vaccination implementation. Utilizing the policy analysis triangle, the study analyzed content, context, processes, and actors, including a textual analysis of policies concerning vaccination criteria, community priorities, vaccine types, implementation schedules, and guidelines. The analysis also examined the impact of hoax news, infrastructure availability, vaccine supply constraints, and the need for additional health workers, exploring how these factors influenced the overall vaccination strategy and stakeholder involvement. This comprehensive approach provided a deep understanding of Indonesia's preparedness for implementing COVID-19 vaccination.

3. Results and Discussion

The results of the health policy analysis regarding the dynamics of the government's COVID-19 vaccine implementation reveal insights into governmental readiness for the implementation of COVID-19 vaccination. Based on field realities, these findings clarify the situation's what, why, and how. Consequently, this article integrates results and discussions into a single section, covering an overview of the current state, an analysis of vaccine readiness, regulatory frameworks, priorities, achievements, and policy objectives. This structure reflects the government's readiness efforts in implementing the COVID-19 vaccination.

3.1 Current situation: Analysis of Readiness for Implementation of COVID-19 Vaccination

Declared a global pandemic by the WHO, the COVID-19 virus reached Indonesia in early March 2020, spreading nationwide and profoundly affecting politics, economy, culture, and public health, resulting in fatalities (Presiden RI, 2020). To combat this, the Ministry of Health prioritized vaccination as a critical strategy to curb transmission, reduce morbidity and mortality, achieve herd immunity, and protect society so that it can be socially and economically productive (Farmalkes, 2022). Vaccination priorities were strategically implemented due to early limitations in vaccine availability and types. These constraints were caused by global increases in COVID-19 vaccine demand that exceeded production capacities.

Indonesia's archipelagic structure complicates vaccine distribution and implementation, with further challenges from varying infrastructure, storage facilities, and health personnel needs in its decentralized system (Rahayu, 2021). The strategy for prioritizing vaccine distribution to health facilities and community implementation involves equipping locations with essential refrigeration, personal protective equipment, and health supplies evenly across all regions. This initiative, launched in 2021 with a budget of 50.2 trillion rupiahs, was executed across all Indonesian provinces, coordinated at both the provincial level by governors and the regency/city level

by local government leaders. Fortunately, the expenses were offset through international collaborations, partnerships in vaccine programs, and multilateral agreements, ensuring efficient procurement of the necessary vaccine doses.

During the vaccine implementation, a significant challenge that occurred was the emergence of hoax news in various media regarding the COVID-19 vaccine, falsely claiming it contained harmful substances that could lead to death, infertility, an increase in male vital organ size, and DNA. A late 2020 survey by the World Health Organization (WHO), Technical Advisory Group on Immunization (ITAGI), United Nations International Children's Emergency Fund (UNICEF), and the Ministry of Health involving 115,000 respondents from all 34 provinces revealed that misinformation led to 8% refusal and 27% hesitancy towards vaccination. Aceh Province had the lowest acceptance rate at 46% (K. RI, 2020a). To boost COVID-19 vaccination acceptance, the government implemented a communication strategy involving community and religious leaders, organizations, and health partners to enhance public participation in the vaccination program. Additionally, it ensured that health service facilities, including community health centers, hospitals, and clinics, were prepared to meet vaccination requirements. These requirements included having qualified health professionals (doctors, nurses, or midwives), appropriate cold chain storage for vaccines, and operational permits for health service facilities (Farmalkes, 2022; K. RI, 2021).

Indonesia's first COVID-19 vaccination was administered to President Joko Widodo at the Istana Negara (State Palace) on January 13, 2021, using the Sinovac vaccine, the first to arrive in the country. Initially, the vaccination was prioritized for health workers across all 34 provinces in Indonesia (K. RI, 2022). Early challenges included a limited vaccine variety, inadequate facilities for vaccination and storage, and a shortage of vaccinators. In response, the government improved health facilities, diversified vaccine types, and expanded eligibility to more groups. By early 2022, Indonesia ranked fourth globally in vaccination numbers, following China, India, and the United States in terms of the number of people vaccinated compared to the total number of injections worldwide (Permenkes, 2020). This ranking reflects the dynamic health policies in place to address challenges and adapt quickly during the pandemic.

3.2 The dynamics of changes in policy regarding the implementation of COVID-19 vaccination in Indonesia

The dynamics of changes in policy for implementing COVID-19 vaccination were in response to societal challenges, aiming to speed up vaccination efforts regionally and nationally. The first regulation, Presidential Regulation Number 99 of 2020, on vaccine procurement and Implementation of Vaccinations for the COVID-19 Pandemic, was stipulated on October 6, 2020 (Pemerintah RI, 2020).

The data collection process and setting program vaccination targets were carried out into two categories, namely top-down and bottom-up data collection; then, the validated data were entered into the information system for the COVID-19 vaccination data (Kepmenkes, 2021a). The pandemic heavily impacted tourism-dependent areas and regions crucial for migrant workers, significantly affecting their economies. To rejuvenate tourism, Bali, Batam, and Bintan were prioritized for vaccination, requiring 13.3 million doses in total 4 million for Bali and 9.3 million for Batam and Bintan using Sinovac and AstraZeneca vaccines (Rosylin, Guntur, Khairina, & Yustriani, 2023). By July 2022, Bali exceeded a 50% third-dose vaccination rate, with DKI Jakarta and the Riau Islands above 40%, and Yogyakarta, West Java, and East Kalimantan above 30% (Amalia, 2022). Despite an initial increase in April 2022, the third dose coverage declined after May 2022, reaching only 26.45% by September. The uptake for the third dose was significantly lower compared to the first and second doses, which saw a 60% increase over six months (June-December 2021) (Amalia, 2022). In contrast to just a 20% increase for the third dose of vaccine (January-June 2022). This decrease was attributed to a decline in COVID-19 cases, indicating a need for new strategies to boost third-dose vaccination rates in adapting to the evolving situation. To address the COVID-19 pandemic, the Indonesian government issued 16 vaccination-related policies through Presidential and Minister of Health Regulations and Decrees from March 2020 to February 2022, as shown in Figure 1 below:

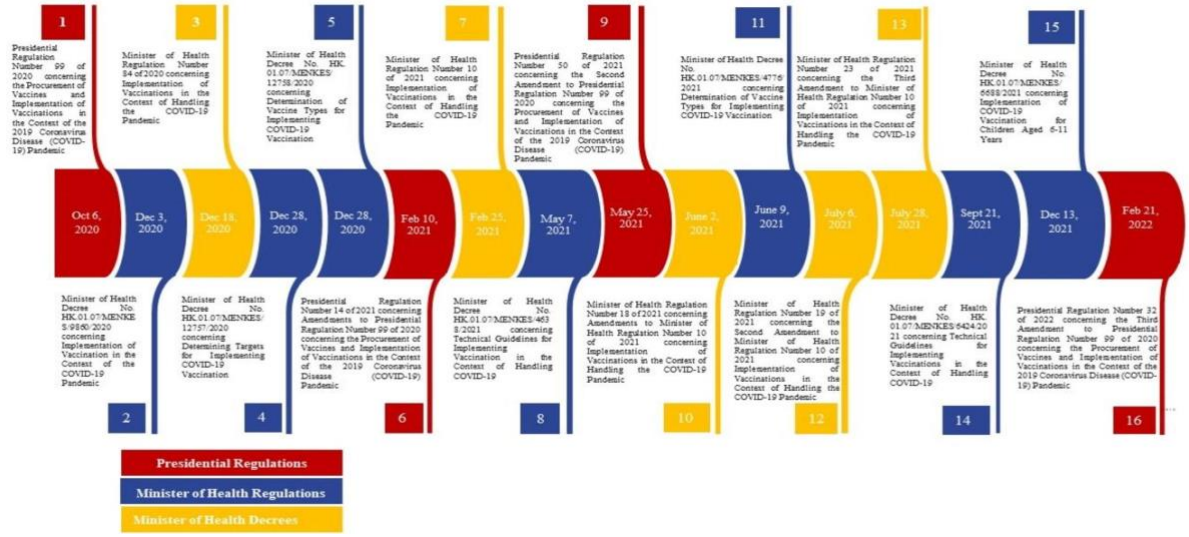

Figure 1: Policies related to the Implementation of COVID-19 Vaccination in Indonesia

The Changes in regulations for COVID-19 vaccination in Indonesia between 2020-2022 are evident in the aspects of vaccination implementation, vaccine types, vaccination targets, and vaccinations sites. Details of this policy can be seen in Table 1.

Table 1: Details of policies related to the implementation of COVID-19 vaccination in Indonesia

No	Type of Regulation	Regulations and Changes
	Implementation of Vaccination	
	Presidential Regulation	The Presidential Regulations issued regarding the implementation of vaccination are: a. Presidential Regulation Number 99 of 2020 b. Presidential Regulation Number 14 of 2021 c. Presidential Regulation Number 50 of 2021 d. Presidential Regulation Number 33 of 2022 - Presidential Regulation Number 99 of 2020 regulates the criteria, priorities, regions, schedules, stages, and standards for implementing vaccination with considerations from the Committee for Handling COVID-19 and National Economic Recovery. The implementation involves collaboration between the Ministry of Health, other ministries, regional governments, State-Owned Enterprises (BUMN), private entities, and various organizations as needed. - Regarding matters regarding the implementation of vaccinations that have been regulated, there have been no changes in Presidential Regulation Numbers 14 of 2021 and 50 of 2021 (Pemerintah RI, 2020; P. RI, 2021a, 2021b) - However, in Presidential Regulation Number 33 of 2022, an additional article elucidates the involvement of legal entities/business entities in organizing vaccination implementation (P. RI, 2022).
	Minister of Health Regulation	The Minister of Health Regulations issued regarding the implementation of vaccination are: a. Minister of Health Regulation Number 84 of 2020 b. Minister of Health Regulation Number 10 of 2021 c. Minister of Health Regulation Number 18 of 2021 d. Minister of Health Regulation Number 19 of 2021 e. Minister of Health Regulation Number 23 of 2021 - In Minister of Health Regulation Number 84 of 2020, it is elucidated that vaccination is free of charge, and implemented in stages according to the COVID-19 vaccine availability, with the Central Government leading, assisted by the Provincial, City/Regency Governments (Permenkes, 2020). Minister of Health Regulation Number 10 of 2021 largely repeats these terms but expands the list of implementers to include legal/business entities. Additionally, it distinguishes between program vaccinations and cooperative vaccinations, both free and dependent on the availability of the COVID-19 vaccine. - In Minister of Health Regulation Number 18 of 2021, the provisions relating to the implementation of vaccination have not changed, and they are still the same as Minister of Health Regulation Number 10 of 2021 (Permenkes, 2021a, 2021b). - Minister of Health Regulation Number 19 of 2021 discusses similar matters. However, there is an additional elucidation regarding cooperation vaccinations carried out by legal/business entities for employees and their

		families or other individuals who are still related to the family, which can be carried out for individuals (Permenkes, 2021c). - Minister of Health Regulation Number 23 of 2021 still contains the things written in the previous Minister of Health but omits the provisions regarding the individual implementation of cooperation vaccinations (Permenkes, 2021d).
	Minister of Health Decree	Minister of Health Decrees issued regarding the implementation of vaccination include: a. No. HK.01.07/MENKES/12757/2020 b. No. HK.01.07/MENKES/6688/2021 c. No. HK.01.07/MENKES/4638/2021 d. No. H.K. 01.07/MENKES/6424/2021 - In Minister of Health Decree No. HK.01.07/MENKES/12757/2020, it is explained how to notify the public who meet the criteria for receiving the COVID-19 vaccine via Short Message Service (SMS) Blast and is required to carry it out unless the SMS recipient does not meet the requirements set for COVID-19 vaccination (Kepmenkes, 2020a). - Minister of Health Decree No. HK.01.07/MENKES/6688/2021 regarding the Implementation of Vaccination for Children Aged 6-11 Years includes the type of vaccine used, namely Biofarma and/or Corona Vac, which is injected intramuscularly twice with an interval of 28 days. This injection must begin with screening first. - The stages of vaccination implementation are stipulated in detail in Minister of Health Decree No. HK.01.07/MENKES/4638/2021 and Minister of Health Decree No. H.K. 01.07/MENKES/6424/2021 (Kepmenkes, 2021a) (Kepmenkes, 2021c). These decrees regulate the implementation of vaccination in stage I (January 2021), stage II (February 2021), and stage III (July 2021).
	Vaccine Type	
	Presidential Regulation	The Presidential Regulations issued regulating the types of vaccines are as follows: a. Presidential Regulation Number 99 of 2020 b. Presidential Regulation Number 14 of 2021 c. Presidential Regulation Number 50 of 2021 d. Presidential Regulation Number 33 of 2022 The type and number of vaccines determined by the Minister of Health are vaccines that meet Distribution Permit Number (NIE) and Emergency Use Authorization (EUA) from the Food and Drug Supervisory Agency (BPOM) and with consideration from the Committee for Handling COVID-19 and National Economic Recovery. The above is regulated in Presidential Regulation Number 99 of 2020 and has not been changed in Presidential Regulation Number 14 of 2021, Presidential Regulation Number 50 of 2021, and Presidential Regulation Number 33 of 2022 (Pemerintah RI, 2020; P. RI, 2021a, 2021b, 2022)
	Minister of Health Regulation	The Minister of Health Regulations issued regulating the types of vaccines are as follows: a. Minister of Health Regulation Number 84 of 2020 b. Minister of Health Regulation Number 10 of 2021 c. Minister of Health Regulation Number 18 of 2021 d. Minister of Health Regulation Number 19 of 2021 e. Minister of Health Regulation Number 23 of 2021 - Minister of Health Regulation Number 84 of 2020 regulates the type of vaccine used, which must obtain approval from BPOM through EUA and NIE and by the recommendations of the National Immunization Expert Advisory Committee and the Committee for Handling COVID-19 and National Economic Recovery (Permenkes, 2020). - In Minister of Health Regulation Number 10 of 2021, additional provisions regarding the type of vaccine used in cooperation vaccination must differ from program vaccination (Permenkes, 2021a; P. RI, 2021b). In Minister of Health Regulation Number 18 of 2021, there are also changes to the provisions, namely (Permenkes, 2021b): ● If, under certain conditions, to meet vaccination needs, the COVID-19 vaccine used for cooperation vaccination can be the same as program vaccination. ● Certain conditions referred to as the type of COVID-19 vaccine can be obtained from grants, donations, or gifts from the community or other countries and cannot be traded. ● The COVID-19 vaccine used for the vaccination program is specially marked so the naked eye can recognize it. - In Minister of Health Regulation Number 19 of 2021 and Minister of Health Regulation Number 23 of 2021, the provisions regarding vaccine types have not changed and are still the same as Minister of Health Regulation Number 18 of 2021 (Permenkes, 2021c, 2021d).
	Minister of Health Decree	The Minister of Health Decrees which regulate the types of vaccines are: a. No.HK.01.07/MENKES/9860/2020 b. No.HK.01.07/MENKES/12758/2020 c. No.HK.01.07/MENKES/4776/2021 d. No.HK.01.07/MENKES/6688/2021 - In Minister of Health Decree No. HK.01.07/MENKES/9860/2020, it is regulated that the type of COVID-19 vaccine used is a vaccine that has completed the third phase of clinical trials and has received NIE and EUA from BPOM. The COVID-19 vaccine used was produced by PT Bio Farma, AstraZeneca, China National Pharmaceutical Group Corporation (Sinopharm), Moderna, Pfizer Inc. and BioNTech, and Sinovac Biotech Ltd. Changes can be made based on recommendations from the National Immunization Expert Advisor and

		taking into account the considerations of the Committee for Handling COVID-19 and National Economic Recovery (Kepmenkes, 2020b). - In Minister of Health Decree No. HK. 01.07/MENKES/12758/2020, there are additional types of COVID-19 vaccines, namely Novavax Inc. and Sinovac Life Sciences Co., Ltd. This vaccine uses the same provisions as the previous Minister of Health Decree(Kepmenkes, 2020c) . - In Minister of Health Decree No. HK.01.07/MENKES/4776/2021, there are several changes to the type of vaccine, namely the addition of the type of COVID-19 vaccine, namely CanSino Biologics Inc, Genexine, Johnson and Johnson. Determining this type of vaccine also uses the same provisions as the previous Minister of Health Decree (Kepmenkes, 2021b). - Minister of Health Decree No. HK.01/07/MENKES/6688/2021 stipulates the type of vaccine for children aged 6-11 years, namely using the Biofarma COVID-19 vaccine and/or Coronavac, which have received EUA and NIE permits from BPOM (Kepmenkes, 2021d).
	Vaccination Targets	
	Presidential Regulation	Three Presidential Regulations were issued which regulate the target recipients of the COVID-19 vaccine, namely: a. Presidential Regulation Number 14 of 2021 b. Presidential Regulation Number 50 of 2021 c. Presidential Regulation Number 33 of 2022 - Vaccination targets are stated in Presidential Regulation Number 14 of 2021 and have not been changed in Presidential Regulation Number 50 of 2021 and Presidential Regulation Number 33 of 2022. The Ministry of Health determines targets for vaccine recipients based on data collection. Target recipients must participate in the vaccination unless they do not meet the criteria for receiving the COVID-19 vaccine. If the designated target recipient does not carry out the COVID-19 vaccination, administrative sanctions will be determined. However, if the refusal causes obstacles to controlling the spread of COVID-19, he can also be subject to witnessing the provisions of the law for infectious disease outbreaks (P. RI, 2021b, 2022) (P. RI, 2021a). - Vaccination targets are no longer regulated in Presidential Regulation 48 of 2023 concerning Ending the Handling of the 2019 Corona Virus Disease (COVID-19) Pandemic.
	Minister of Health Regulation	The criteria for vaccine recipients are as follows: a. Minister of Health Regulation Number 84 of 2020 b. Minister of Health Regulation Number 10 of 2021 - Minister of Health Regulation Number 84/2020 states that the determination of recipients of the COVID-19 vaccine is based on a study by ITAGI and/or the Strategic Advisory Group of Experts on Immunization of the World Health Organization (SAGE WHO). Recipients are categorized into priority groups, each registered in only one group. These groups, which include health personnel, legal and public officers, community leaders, educators, government officials, vulnerable populations, and economic actors, can be adjusted based on ITAGI's recommendations and insights from the COVID-19 and National Economic Recovery Committee (Permenkes, 2020). - In Minister of Health Regulation Number 10 of 2021, there are changes regarding the criteria for vaccine recipients. These are divided into four groups: health workers and health service facility supporters, older and public service workers, vulnerable people, and other communities (Permenkes, 2021a).
	Minister of Health Decree	The vaccination targets are also stated in the Minister of Health Decree: a. No.HK.01.07/MENKES/12757/2020 b. No.HK.01.07/MENKES/6688/2021 c. No.HK.01.07/MENKES/4638/2021 d. No.HK.01.07/MENKES/6424/2021 - In Minister of Health Decree No. HK.01.07/MENKES/12757/2020, setting targets for vaccination implementation uses the One Data Information System for COVID-19 Vaccination (Kepmenkes, 2020a). - Minister of Health Decree No. HK.01.07/MENKES/6688/2021 sets specific vaccination targets for children aged 6-11 (Kepmenkes, 2021d). - Minister of Health Decree No. HK.01.07/MENKES/4638/2021 explains the vaccination targets for each stage in more detail. Priority vaccination targets are divided into three stages; each recipient is detailed thoroughly (Kepmenkes, 2021a). - In Minister of Health Decree No. HK.01.07/MENKES/6424/2021, which was published, made several adjustments regarding vaccination targets, namely that ITAGI provides recommendations for types of vaccines that can be used for ages 12-17 years and pregnant women so that the target in stage 3 is added to the target ages 12- 17 years old and in pregnant women (Kepmenkes, 2021c).
	Vaccination Place	
	Presidential Regulation	The location for vaccination is not explicitly regulated in the Presidential Regulation.
	Minister of Health Regulation	The Minister of Health Regulations that regulate the location of vaccine implementation include the following: a. Minister of Health Regulation Number 84 of 2020 b. Minister of Health Regulation Number 10 of 2021 c. Minister of Health Regulation Number 19 of 2021 - Minister of Health Regulation Number 84 of 2020 regulates places for vaccine implementation in health

		facilities owned by the Central Government, Regional Government, or community/private sector that meet the requirements (Permenkes, 2020). - In Minister of Health Regulation Number 10 of 2021, there are additional provisions regarding additional vaccination implementation, namely (Permenkes, 2021a). 1) Vaccination implementation is added at the COVID-19 vaccination service post in coordination with the Community Health Center, Provincial Health Office, and City/Regency Health Office. 2) Cooperation vaccination is carried out by legal/business entities only with private health facilities or self-owned business health facilities that meet the requirements and coordinate with the regency/city health office. These health facilities are also not places for program vaccination services. - In Minister of Health Regulation Number 19 of 2021, there are additional locations for implementing COVID-19 vaccination as long as they meet the specified requirements (Permenkes, 2021c).
	Minister of Health Decree	Several Minister of Health Decrees regulate vaccination locations as follows: a. No.HK.01.07/MENKES/6688/2021 b. No.HK.01.07/MENKES/4638/2021 c. No.HK.01.07/MENKES/6424/2021 - Minister of Health Decree No. HK.01.07/MENKES/6688/2021 explains that the implementation of COVID-19 vaccination for ages 6-11 years is carried out at designated health facilities. Vaccination services can be carried out at schools, other educational units, or Child Welfare Institutions (LKSA) in collaboration with the Education Service, Regional Offices of the Ministry of Religion, or Social Services (Kepmenkes, 2021d). - In Minister of Health Decree No. HK.01.07/MENKES/4638/2021, there is an additional elucidation that the location for cooperation vaccination can only be carried out in public/private health facilities that meet the requirements and not program vaccination service facilities (Kepmenkes, 2021a). - In the Minister of Health Decree No. HK. 01.07/MENKES/6424/2021, changes include allowing vaccinations for ages 12-17 at schools, madrasas, and Islamic boarding schools, monitored by the Regency/City Health Office or Community Health Center in coordination with the Education Office and the local Regional Office/Ministry of Religion. This regulation also explains that health facilities carrying out cooperation vaccinations must first stop program vaccination services. Once these activities are completed, they must report to the Local Regency/City Health Office before resuming the usual vaccination program (Kepmenkes, 2021c).

3.3 The government's readiness to implement the COVID-19 vaccination.

The Indonesian government aims to achieve herd immunity against COVID-19 by vaccinating 70% of the Indonesian population, or equivalent to 182 million people. Given the global demand for vaccines and limited suppliers meeting the required qualifications, reaching this goal presents a challenge (Aditama, 2021).

To manage the vaccination process, the Decree of the Director General of Disease Prevention and Control No. HK.02.02/4/423/2021 outlines technical instructions, dividing the vaccination into four phases based on the vaccine's availability, arrival time, and safety profile (Farmalkes, 2022). These stages are differentiated based on the implementation time and target groups, prioritizing regions with high numbers of confirmed cases (K. RI, 2020b). Stage 1 targets health workers and support staff, while Stage 2 prioritizes public service workers and those over 60 years. Stage 3 is aimed at vulnerable individuals aged 18 and over, and Stage 4 focuses on the broader community and economic actors using a cluster approach dependent on vaccine availability (Farmalkes, 2022; Kepmenkes, 2021a; Rosylin et al., 2023). Despite challenges, Indonesia accelerated its vaccination efforts, administering 283.6 million of the 439.76 million available doses by December 31, 2021, achieving a 76.8% distribution rate achieving a 76.8% distribution rate (Kepmenkes, 2021a). Figure 2 details the quarterly vaccination progress from 2021 to 2022**.**

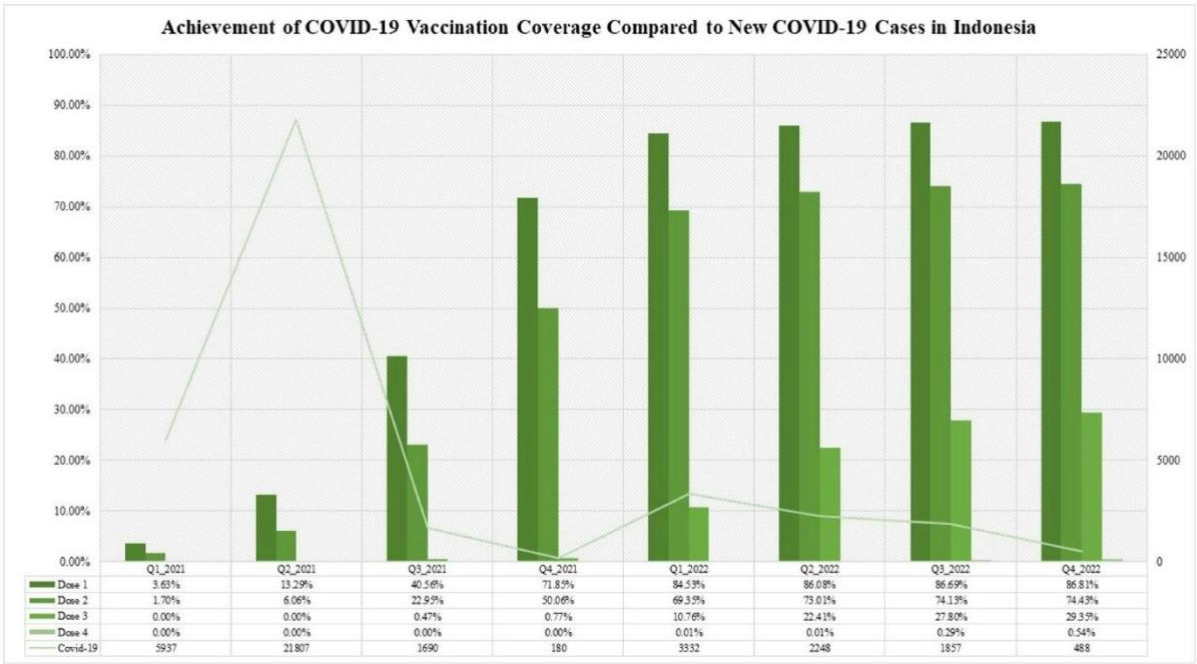

Figure 2: Development of Vaccination Achievement and COVID-19 Cases in Indonesia

Source: covid.go.id, which has been reprocessed

The figure shows that by the fourth quarter of 2021, Indonesia hit its vaccination target with a first dose coverage of 71.85%, and by mid-2022, second dose coverage reached 73.01% (Amalia, 2022). However, as of July 2022, only Bali surpassed a 50% third dose target, with DKI Jakarta and the Riau Islands above 40%, and Yogyakarta, West Java, and East Kalimantan above 30% (Permenkes, 2020). Third dose coverage increased in April 2022 but declined post-May, hitting only 26.45% by September (Rokom., 2022). This decline contrasts with the 60% increase seen in the first and second doses from June to December 2021(Indonesia, 2021; Rokom., 2022), compared to just a 20% increase in the third dose from January to June 2022 (KPCPEN, 2022).

As COVID-19 cases decline, adapting strategies to boost third-dose coverage is essential. The numerous regulations reflect the government's cautious, resource-adjusted approach to the vaccine rollout. Initial challenges included limited vaccine types and quantities, distribution hurdles, and insufficient storage and healthcare facilities, emphasizing the need for preparatory planning. Yet, continuous policy updates in response to global shifts underscore the government's commitment to pandemic management via vaccination efforts.

Despite third dose coverage reaching only 30% in the second quarter of 2022 due to fewer COVID-19 cases, the success of Indonesia's vaccination effort can be seen in the achievement of coverage of the first dose of COVID-19 vaccination in 2021 and the second dose in the second quarter of 2021. By 2022, it will reach above 70% of Indonesian society.

Data-related policies, specifically Presidential Regulation Number 39 of 2019 on One Indonesian Data (*Kebijakan Satu Data)*, streamline data management across central and regional agencies to enhance the planning and implementation of Indonesia's vaccination efforts. This initiative ensures high-quality data generation for policy development. Challenges include integrating numerous standalone applications, sectoral data-sharing hesitations, and inconsistencies in data collection across platforms. To facilitate efficient tracking of COVID-19 cases, the government introduced the PeduliLindungi application. Initially, the PeduliLindungi app helped track COVID-19, evolving to screen individuals in public areas, and manage lab results and vaccine certificates. In July 2022, the Satu Data Indonesia initiative launched the SATUSEHAT platform to manage health data, integrating with health facilities, labs, and pharmacies as well as BPJS Health. On March 1, 2023, PeduliLindungi became SATUSEHAT Mobile, adding features like electronic patient records. This data management enhancement aids Indonesia's crisis readiness and response, especially during health emergencies and threats. The limitation of this article is that the

analysis is from the perspective of writers who come from outside policymakers. Hence, it needs to be enriched with insights from policymakers or the government.

4. Conclusion

From March 2020 to February 2022, the Indonesian government issued 16 Presidential Regulations, Ministerial Regulations, and Ministerial Decrees to facilitate COVID-19 vaccination, focusing on staged implementation, taking into account vaccine availability, which necessitates prioritizing based on recipient's criteria, geographic areas, administration stages, and vaccination type. Initial policies highlighted government readiness amidst limitations in vaccine quantity and type, distribution issues, and resource constraints in healthcare. However, from 2020 to 2022, evolving vaccination policies significantly lowered COVID-19 cases in Indonesia, achieving over 70% coverage for both initial and follow-up doses. Effective vaccination strategy hinges on public education about vaccine safety and robust collaboration between government bodies and stakeholders. There is a critical need to strengthen the One Data Indonesia policy to ensure systematic data integration across central and regional agencies, enhancing data accessibility and usability for quality policy-making during health crises. Additionally, the Ministry of Health must augment human resources to better manage health crises like pandemics. Tailoring policies to regional and cultural specifics is crucial to building community trust and fostering effective health crisis management. Enhancing partnerships with stakeholders and community leaders is also vital for implementing successful health strategies.

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The Association Between Documents and Activities of Hospital Management with Patient Safety Incident Reporting: The 2019 Indonesia Health Facilities Research

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Abstract
Patient safety incident (PSI) reporting is essential to identify underlying problems and improve safety, but PSI reporting in Indonesian hospitals is still low. This study examines factors that contribute to PSI reports. It employed a cross-sectional design and analyzed data from Indonesia's 2019 Health Facilities Research. Methods: According to the criteria, the sample consisted of 462 hospitals. We evaluate the data using the chi-square test. The independent variables were documents, including strategic plans and hospital bylaws; activities included implementing a quality control system, monitoring and evaluation, internal audits, service evaluation and quality control, and periodic meetings. Results: Even though most hospitals already have documents and carry out activities, reports regarding PSI are still lacking in the surveyed hospitals, with half not having any. In Indonesian hospitals, all variables were significantly associated with PSI reports. Hospitals with these documents and management activities, like strategic plans, internal audits, or evaluations, have more PSI reports. Conclusion: The number of PSI reports has increased due to changes in reporting culture, which may indicate a safer culture rather than necessarily an increasing risk. Adopt a comprehensive, data-driven strategy, concentrating on incident reporting and detection. Hospital management must sustainably monitor, assess, and evaluate to encourage PSI reporting.

Keywords: Patient Safety, Near-Miss, Adverse Events, Reporting, Indonesia, Health Facility Research

1. Introduction

Patient safety has become an important issue in healthcare systems worldwide for the last 20 years (Institute of Medicine, 2000). Adverse events (AEs) are one of the leading causes of patient injury (Griffin & Resar, 2009). The AEs rate varies from 7% to 40% (Hibbert et al., 2016). Although some AEs are hard to avoid, studies have shown that 6%–83% of AEs are preventable (Panagioti et al., 2019; Zanetti et al., 2020). Healthcare providers encounter the challenge of enhancing patient safety by AEs detecting and preventing (Hanskamp-Sebregts, Zegers,

Wollersheim, van Gurp, & Westert, 2019). Early detection of AEs is a top concern for patient safety; identifying and analyzing AEs can provide a deeper understanding of healthcare systems' vulnerabilities. When AEs are reported, evaluated, and measured, they can be used as primary data in developing policies and strategies to improve quality and safety and become reliable and achievable (Eggenschwiler et al., 2022; Zanetti et al., 2020; Zhang et al., 2017). However, this is only possible if healthcare providers take this duty (Howell et al., 2017). Experts assume near-misses occur 3 to 300 times more often than AEs (Barach & Small, 2000). However, reporting and analyzing near-miss events should be further utilized as a safety improvement resource. It will help prevent AEs and ultimately improve quality and safety (Harriette Van, Alisha, & Travis, 2015). Patient safety incidents (PSI), including AEs and near-misses, that are not appropriately reported will waste opportunities for quality and safety improvement in healthcare providers (Harriette Van et al., 2015; Heavner & Siner, 2015; Walshe, 2000). Although this is consequential, many obstacles prevent people from reporting (Oweidat, Al-Mugheed, Alsenany, Abdelaliem, & Alzoubi, 2023).

The World Health Organization (WHO) has developed a framework for PSI reporting systems that every country can utilize and adopt (World Health Organization, 2005, 2016). Nevertheless, there is variation in reporting levels between countries, and some countries are less likely to implement the system well (Dhamanti, Leggat, Barraclough, Liao, & Abu Bakar, 2021). Indonesia established a national PSI reporting system in 2005, with two reporting levels: internal and external. Internal reporting at the hospital level instructs written reports regarding all incidents. External reporting at the national level is anonymously reported to the National Patient Safety Committee, including near-misses to sentinel incidents (Hospital Patient Safety Committee, 2015). Even though it has been implemented for more than 15 years, the PSI reporting system in Indonesia still needs to be further improved (Dhamanti, Leggat, Barraclough, & Rachman, 2022).

Recently, healthcare quality has become increasingly critical, sparking interest in monitoring and assessing provider performance. Continuous monitoring system evaluations facilitate the early detection of adverse event trends and changes in healthcare provider performance, which can be used as an effective tool for quality improvement. It will help prevent potentially hazardous situations, expedite corrective action, and improve overall performance (Sibanda et al., 2009; Wang, Wang, Lou, Li, & Zhang, 2013; Zeng, 2016). Healthcare leaders, as critical stakeholders, are primarily responsible for solving this challenge. Interest in effective and sustainable interventions to decrease harm to patients is increasing. Intervening at the organizational level and actively involving staffers in preventing patient safety risks is a promising solution (Hanskamp-Sebregts, Zegers, Boeijen, et al., 2019). Healthcare providers' phases to improve quality are setting priorities, continuous processes, and determining an appropriate framework for implementing initiative programs (Sadeghifar, Jafari, Tofighi, Ravaghi, & Maleki, 2014).

Hospitals should construct adaptable strategic plans, implement them effectively, and establish procedures for handling PSIs to increase patient safety and organizational performance (Mira et al., 2020). One of the most effective strategies for organizational success is carrying out strategic planning well (Sadeghifar et al., 2014). Even though policies governing PSI reporting exist, implementing them is still inappropriate (Dhamanti et al., 2022; Sulahyuningsih, Tamtomo, & Joebagio, 2017; Susrajat & Munir, 2022). The hospital's duties and responsibilities are very important here. Its implementation must be monitored, assessed, and evaluated for maximum results. An effective system for monitoring PSIs is needed to prevent their non-reporting, as monitoring and supervision will increase the willingness to report PSIs (Fathiyani & Ayubi, 2022; Vermeulen, Kleefstra, Zijp, & Kool, 2017). Besides that, audits and feedback are widely used in quality improvement to monitor and change the behavior of health professionals (Hanskamp-Sebregts, Zegers, Boeijen, et al., 2019). Unreported incidents will seriously weaken the capacity of incident reporting systems to encourage understanding and improve quality and patient safety. Understanding the aspects contributing to underreporting is critical to improving PSI reporting systems. However, only a few still highlight this in Indonesia. We examined the factors associated with the availability of PSI data in Indonesian general hospitals using the Health Facilities Research 2019 (RIFASKES) data, which are based on documents and activities related to management factors.

2. Method

This research was cross-sectional and analyzed data from the Indonesia Health Facilities Research 2019 (RIFASKES). The initial survey collected data on hospitals, community health centers, and other facilities. The information collected includes characteristics of facilities, management, organization, planning, implementation, evaluation, supporting facilities, and information systems. Furthermore, hospitals are the emphasis of this study's data. In RIFASKES, the hospital population consists of two groups: referral hospitals and hospitals selected based on sampling, totaling 532. There are two types of hospitals: general and specialized. A general hospital provides health services for all areas and types of diseases. A specialized hospital provides health services primarily for specific types of diseases or in one field only based on organs, scientific disciplines, age, or other aspects. This study excluded specialized hospitals and only included general hospitals, resulting in 462 hospitals. We used the chi-square test to determine the significance.

This research explores the availability of PSI reports and the factors that influence their reporting in Indonesian general hospitals. The PSI for this study focused on both near-miss and adverse events. Near-miss events are events related to medical procedures that almost cause injury or disability to the patient. Adverse events are unforeseen incidents that lead to patient harm, stemming from the execution of a necessary action or the failure to take one rather than the patient's inherent illness or condition. The study's independent variables consisted of documents, including strategic plans and hospital bylaws; activities included implementing a quality control system, monitoring and evaluation, internal audit, service evaluation and quality control, and periodic meetings. The PSI report is declared "yes" if the hospital has data on the number of PSI reports supported by the existence of this document. The analysis focused on hospital management activities, determining "yes" based on the presence of supporting data or documents. Monitoring and evaluation are declared "yes" if the hospital conducts assessments and monitoring procedures to guarantee the efficiency and effectiveness of hospital performance. When implementing a quality control system, the answer is "yes" if the hospital uses the Malcolm Baldrige, EFQM Excellence Model, ISO, or another quality control system and has supporting documentation. Service evaluation and quality control are "yes" if the hospital maintains, monitors, and audits hospital quality through management reviews, internal audits, and implementing safety and infection control procedures with supporting documentation in place. Internal audit is declared "yes" if the hospital carries out activities to assess the conformity of services to standards, including medical audits for cases of death or complex cases, as proven by the existence of audit documents. Periodic meetings are declared "yes" if the hospital holds regular meetings between hospital leadership and staff supported by documents, reports, or notes.

Table 1: Description of the sample (n=462)

Hospital characteristics	n (%)
Accreditation status	
No	49(10.6)
Base	146(31.6)
Middle	33(7.1)
Main	54(11.7)
Plenary	180(39.0)
Ownership	
Private	192(41.6)
Government	270(58.4)
Class	
D	123(26.6)
C	196(42.4)
B	126(27.3)
A	17(3.7)
Size	
<200	303(65.6)
≥200	159(34.4)
Regional category	
Outside Java-Bali	270(58.4)
Java-Bali	192(41.6)

3. Results

3.1 Frequency Distribution

The characteristics of the general hospitals in this research are that most are accredited: 413 (89.4%), with the most prominent accreditation status being plenary (39%). The government owns the most general hospitals, 58.4%, with the majority being in class C (42.4%). Based on the grouping of beds, most hospitals have less than 200 beds, or 65.6%. At 41.6%, most general hospitals are outside Java-Bali (Table 1). The number of general hospitals with no data on near-miss events is 236 (51.1%), while those that have data are 226 hospitals (48.9%). The number of general hospitals with data on adverse events is 233 (50.4%), while 229 hospitals (49.6%) do not. The majority of hospitals have a strategic plan document: 438 hospitals (94.8%); have hospitals bylaw: 416 hospitals (90%); did not implement a quality control system: 238 hospitals (51.5%); have carried out monitoring and evaluation: 318 hospitals (82.5%); have internal audit: 316 hospitals (68.4%); have service evaluation and quality control: 339 hospitals (73.4%); and have periodic meetings between management and staff: 449 hospitals (97.2%) (Table 2).

Table 2: Patient safety incidents and documents and activities of hospital management (n=462)

Variable	n (%)
Data of near miss events	
No	236(51.1)
Yes	226(48.9)
Data of adverse events	
No	229(49.6)
Yes	233(50.4)
Strategic plan documents	
No	24(5.2)
Yes	438(94.8)
Hospital bylaw	
No	46(10)
Yes	416(90)
Implementation of a quality control system	
No	238(51.5)
Yes	224(48.5)
Monitoring and evaluation	
No	81(17.5)
Yes	381(82.5)
Internal audit	
No	146(31.6)
Yes	316(68.4)
Service evaluation and quality control	
No	123(26.6)
Yes	339(73.4)
Periodic meetings	
No	13(2.8)
Yes	449(97.2)

Presents the number of hospitals that have near-misses in Table 3 and adverse events in Table 4 data based on the independent variables in this study: the existence of strategic plan documents, hospital bylaw, implementation of a quality control system, monitoring and evaluation, internal audit, service evaluation and quality control, and periodic meetings. Of the hospitals with strategic plan documents, 51.91% have data on near-miss events, and 52.7% have adverse events. In comparison, most hospitals that do not have a strategic plan document did not have data on the number of near-misses and adverse events, amounting to 91.7%. Based on the existence of the hospital bylaw document, most hospitals with data on near-miss events (51.7%) and adverse events (53.6%) have hospital bylaws. Unlike hospitals that do not have hospital bylaws, most hospitals have no near-miss data (76.1%) and no adverse events data (78.3%). Hospitals that did not implement a quality control system did not have data on near-misses (61.8%) and adverse events (58.8%). Most hospitals that carry out monitoring and evaluation have data on near-miss events (54.1%) and adverse events (55.9%). In contrast, hospitals that do not have monitoring and

evaluation are hospitals where the majority do not have data on near-miss or adverse events. Most hospitals with near-miss and adverse event data carry out service evaluation and quality control activities, have internal audits, and have regular meetings between management and staff.

Table 3: Association between documents and activities of hospital management with near-miss (n=462)

Variable	Data of near-miss events		P-value	OR (95% CI)
	No (%)	Yes (%)		
Strategic plan documents				
No	22 (91.7)	2 (8.3)	0.000	11.514
Yes	214 (48.9)	224 (51.1)		(2.675-49.559)
Hospital bylaw				
No	35 (76.1)	11 (23.9)	0.001	3.403
Yes	201 (48.3)	215 (51.7)		(1.683-6.883)
Implementation of a quality control system				
No	147 (61.8)	91 (38.2)	0.000	2.450
Yes	89 (39.7)	135 (60.3)		(1.686-3.562)
Monitoring and evaluation				
No	61 (75.3)	20 (24.7)	0.000	3.590
Yes	175 (45.9)	206 (54.1)		(2.084-6.184)
Internal audit				
No	118 (80.8)	28 (19.2)	0.000	7.071
Yes	118 (37.3)	198 (62.7)		(4.416-11.324)
Service evaluation and quality control				
No	103 (83.7)	20 (16.3)	0.000	7.977
Yes	133 (39.2)	206 (60.8)		(4.713-13.501)
Periodic meetings				
No	12 (92.3)	1 (7.7)	0.006	12.054
Yes	224 (49.9)	225 (50.1)		(1.554-93.478)

Table 4: Association between documents and activities of hospital management with adverse events (n=462)

Variable	Data of adverse events		P-value	OR (95% CI)
	No (%)	Yes (%)		
Strategic plan documents				
No	22 (91.7)	2 (8.3)	0.000	12.275
Yes	207 (47.3)	231 (52.7)		(2.852-52.838)
Hospital bylaw				
No	36 (78.3)	10 (21.7)	0.000	4.160
Yes	193 (46.4)	223 (53.6)		(2.011-8.602)
Implementation of a quality control system				
No	140 (58.8)	98 (41.2)	0.000	2.167
Yes	89 (39.7)	135 (60.3)		(1.494-3.143)
Monitoring and evaluation				
No	61 (75.3)	20 (24.7)	0.000	3.867
Yes	168 (44.1)	213 (55.9)		(2.244-6.662)
Internal audit				
No	122 (83.6)	24 (16.4)	0.000	9.929
Yes	107 (33.9)	209 (66.1)		(6.048-16.302)
Service evaluation and quality control				
No	103 (83.7)	20 (16.3)	0.000	8.706
Yes	126 (37.2)	213 (62.8)		(5.139-14.749)
Periodic meetings				
No	12 (92.3)	1 (7.7)	0.004	12.829
Yes	217 (48.3)	232 (51.7)		(1.654-99.496)

3.2 Association Between Documents and Activities of Hospital Management with Near-Miss and Adverse Event

The chi-square test results showed that all variables had a significant relationship ($\alpha<0.05$). We found differences between near-miss and adverse event data in Indonesian general hospitals. Strategic plan documents have the highest OR value of 11,514 (2,675-49,559) for near-miss event data and 12,275 (2,852-52.838) for adverse event' data. Hospital bylaw has an OR value of 3.403 (1.683-6.883) for near-miss data and 4.160 (2.011-8.602) for adverse event data. Implementing a quality control system has an OR value of 2.450 (1.686-3.562) for near-miss data and 2.167 (1.494-3.143) for adverse event data. Monitoring and evaluation have an OR value of 3.590 (2.084-6.184) for near-miss data and 3.867 (2.244-6.662) for adverse event data. Internal audit has an OR value of 7.071 (4.416-11.324) for near-miss data and 9.929 (6.048-16.302) for adverse event data. Periodic meetings between management and staff had the largest OR of 12,054 (1,554-93,478) for near-miss, while for adverse events, it was 12,829 (1,654-99,496); see Tables 3 and 4.

4. Discussion

Reporting PSI is critical to improving patient safety. However, reports regarding PSI in the surveyed hospitals are still lacking. More than half of these hospitals do not have near-miss data. Similarly, nearly half of these hospitals lack data on adverse events. Near-miss, also known as close calls, is a safety improvement resource underutilized because of a lack of precise definition and reporting. The systematic reporting and analysis of near-misses is crucial to preventing adverse events and enhancing patient safety (Harriette Van et al., 2015). Experts assume near misses happen three to three hundred times more frequently in healthcare settings than adverse events (Barach & Small, 2000). Healthcare organizations should also consider near misses as opportunities for quality improvement (Harriette Van et al., 2015). Compared to adverse events, reporting near misses offers many benefits, such as fewer barriers to data collection, limited liability, and the ability to capture, study, and use recovery patterns for improvement (Barach & Small, 2000).

Poor reporting of patient safety incidents misses opportunities to enhance safety (Harriette Van et al., 2015). Incident reports are crucial in enhancing quality improvement by providing valuable information for education and modification (Heavner & Siner, 2015; Walshe, 2000). Reports on incidents involving the quality of care can reveal hazards to patient safety (Taylor et al., 2008). Still, certain obstacles prevent people from reporting, like forgetting to report, fear of punishment or blame, and concern about disciplinary action (Oweidat et al., 2023). As a crucial first step toward enhancing patient safety, a study recommends organizational and legal modifications to encourage the normalcy of discussing one's shortcomings and mistakes. A punitive search for responsible parties makes it difficult to prevent new adverse events, as there is a tendency to hide what is happening. It should also foster a culture of fair rewards, which requires increased transparency regarding incidents and steps taken to prevent them in the future (Mira et al., 2020). Organization-level factors present a modifiable target for patient safety improvement initiatives. Still, their association with the hospital adverse event rate needs to be better understood (Sauro, Baker, Tomlinson, & Parshuram, 2021). Limited, mainly low-quality evidence supports healthcare performance associations (Brand et al., 2012).

This research analyzes administrative and management factors in hospital organizations related to the existence of patient safety incident reports. The analysis results show that all variables are significant in the presence of data on near-misses and adverse events in general hospitals. Changes in incident reporting culture have led to an increase in the number of reported incidents. However, more incidents reported are not necessarily a sign of increased risk but can also be considered a sign of a safer culture (Vermeulen et al., 2017). PSI reporting is one of the steps needed to improve patient safety, as it can provide a broad picture of the incident and how it happened. It can be used as basic data for policymaking and making patient safety programs in hospitals (Fathiyani & Ayubi, 2022).

4.1 Existence of Documents: Strategic Plan and Hospital Bylaw

This study's results show that strategic plan documents and hospital bylaws were significantly associated with patient safety incident reports in general hospitals. A strategic plan is formed based on vision, mission, goals,

policies, programs, and activities oriented to what is to be achieved within a certain period, including the main tasks and functions of the hospital. Hospital bylaws or internal hospital regulations are written provisions that regulate the organization, position, roles, duties, and obligations of a hospital's three main elements: the owner, hospital manager, and medical staff. Most Indonesian hospitals surveyed had strategic plans and hospital bylaws, but patient safety incident reporting needed improvement. Nearly half do not have data on near-misses or adverse events.

Research has shown that a comprehensive program, including strategic planning, is associated with reduced adverse events (Álvarez-Maldonado, Reding-Bernal, Hernández-Solís, & Cicero-Sabido, 2019). However, hospitals with a documented strategic plan have yet to implement it efficiently and achieve valid outcome evaluations (Sadeghifar et al., 2014). Hospitals will face challenges in managing adverse events, with many needing more protocols for effective response. Therefore, developing and implementing a strategic action plan is necessary to respond to this challenge. To improve patient safety and organizational performance, hospitals should develop flexible strategic plans, implement them effectively, and establish protocols for managing adverse events (Mira et al., 2020). Therefore, hospital management needs to sustainably monitor, assess, and evaluate the implementation of existing regulations to ensure they run well.

4.2 Management Activities

Prior studies have demonstrated that monitoring, assessing, audit, evaluation, and quality control activities are necessary to maintain and enhance quality and safety. An effective system for monitoring incidents is needed to prevent incidents from going unreported (Fathiyani & Ayubi, 2022). A range of studies have demonstrated the effectiveness of various strategies in increasing incident reporting.

4.2.1 Implementation of a quality control system

Implementation of a quality control system is statistically associated with data on near-miss and adverse events. Its implementation in hospitals can increase incident reporting rates. In this study, most hospitals did not implement a quality control system such as Malcolm Baldrige, ISO, EFQM Excellence Model, or other quality control techniques. Also, most hospitals do not have incident data, especially near-miss. Although near-miss data is also essential for learning, many hospitals do not have this data. Implementing a quality management system (QMS), which involves establishing standard operating procedures, quality control measures, and continuous process monitoring to ensure accuracy and reliability, significantly impacts patient safety. Healthcare providers with a robust QMS have lower medical error rates (AlHarshan et al., 2023). Another similar study found that implementing an ISO-based quality management system can help hospitals improve incident reporting to promote quality and safety. These measures contribute to better medical quality, increased reporting intention, and improved hospital incident management systems (Le Duff, Daniel, Kamendjé, Le Beux, & Duvauferrier, 2005). One effort to improve PSI reporting is by implementing a quality control system. Healthcare providers must continue investing in QMS to ensure the highest quality and safety standards.

4.2.2 Monitoring and evaluation

Hospital monitoring and evaluation is continuously observing and assessing the effectiveness and efficiency of hospital performance based on the Decree of the Minister of Health of the Republic of Indonesia Number 496/Menkes/SK/IV/2005 concerning hospital audit guidelines. The aim is to improve the quality and standardization of hospitals. Recently, there has been much interest in monitoring and evaluating healthcare provider performance because healthcare quality is becoming increasingly important. By enabling the early detection of adverse event trends and changes in healthcare provider performance, continuous monitoring system evaluations help prevent potentially unsafe situations, speed up corrective action, and enhance overall performance, serving as an effective tool for quality improvement (Sibanda et al., 2009; Wang et al., 2013; Zeng, 2016). Evaluating and enhancing individual, unit, and organizational aspects can improve incident reporting (Fathiyani & Ayubi, 2022). Supervision improves the willingness to report patient safety incidents. It reduces risks

associated with medication safety, encouraging a culture of safety and reporting (Vermeulen et al., 2017). This study demonstrates the need for monitoring and evaluation to promote the reporting of patient safety incidents.

4.2.3 Internal audits

Most of the surveyed hospitals had carried out internal audits. The analysis results show that internal audits are significantly associated with data on near-miss and adverse events. The internal audit referred to in this study is an activity to assess whether staff have provided services according to standards, including medical audits for cases of death or complex cases. Internal audits are essential to healthcare quality management because they are a basis for assessing the effectiveness of quality control and surveillance (Morozov et al., 2021). Hospital boards view internal audits as adequate for governing patient safety, helping to identify patient safety issues, and proactively steering improvements (van Gelderen et al., 2017). Therefore, audits are often utilized as interventions to improve the quality of care and patient safety in hospitals, although their effectiveness varies (Hanskamp-Sebregts, Zegers, Wollersheim, et al., 2019; Hanskamp-Sebregts, Zegers, Boeijen, et al., 2019; van Gelderen et al., 2017). However, well-organized investigation and feedback regarding patient safety issues will not be enough to decrease the occurrence of insufficient patient safety outcomes; without focus and organizational support in implementing audit-based corrective efforts, quality improvement through patient safety audits will remain limited (Hanskamp-Sebregts, Zegers, Wollersheim, et al., 2019). The internal audit function is positively and significantly related to sustainability reporting practices in non-healthcare organizations. However, a functioning internal audit can be assessed based on the board audit committee's recommendations and improvement decisions (Tumwebaze, Juma, Twaha Kigongo, Bonareri, & Mutesasira, 2022).

4.2.4 Service evaluation and quality control

Service evaluation and quality control are associated with near-miss and adverse event data in surveyed hospitals. Evaluation activity involves internal audits and management reviews. Meanwhile, quality control involves monitoring, maintaining, and auditing hospital quality to ensure quality, meet established service standards, and satisfy customers through safety. Most hospitals conducting service evaluation and quality control activities have data on adverse events and near-misses. Research has shown a link between service quality and adverse events in healthcare settings. Higher degrees of internal service quality is related to a decline in the frequency of adverse events (Zheng et al., 2018); likewise, reports about service quality weaknesses raise the chance of adverse events (Taylor et al., 2008). Adverse event reports, a vital component of these mechanisms, provide valuable data for quality improvement (Walshe, 2000). Implement practical service evaluation and quality control mechanisms to identify and mitigate potential issues that could lead to adverse events.

4.2.5 Periodic meetings

Patient safety combines people and processes, and both elements depend on leadership. A thoughtful patient safety strategy requires leaders to engage on a personal level (Jarrett, 2017). The results showed that periodic meetings between leaders and staff held regularly within the hospital environment were significantly associated with data on near-misses and adverse events in the surveyed hospitals. They were the variable with the highest OR value in this study. Organizations that provide regular meetings to brief regular reports, connect, and engage staff with leaders to discuss existing or emerging patient safety issues (Chapman et al., 2020). They can have brief conversations with transparent, open, and two-way communication between leaders and staff, increasing situational awareness and improving safety (Aldawood, Kazzaz, AlShehri, Alali, & Al-Surimi, 2020; Chapman et al., 2020; Murray, Clifford, Scott, Kelly, & Hanover, 2024). As critical stakeholders, leaders have the primary responsibility to solve this challenge. Leaders can foster patient safety through personal engagement, such as weekly safety rounds and daily safety calls. This activity not only allows staff to learn about safety concerns with feedback but also demonstrates to staff their commitment to the importance of patient safety (Jarrett, 2017).

5. Conclusion

The study investigates the availability of PSI reports and factors influencing near-misses and adverse events data in Indonesian general hospitals, finding all variables significant. Our research findings support the evidence that

periodic meetings and strategic plan documents have higher OR values and are essential in influencing the availability of PSI reporting data in general hospitals. In addition, hospitals that have implemented monitoring and evaluation, internal audits, service evaluation and quality control, or periodic meetings have more PSI reports. Due to changes in reporting culture, the number of PSI reports has increased. However, more PSI reports may indicate a safer culture rather than increased risk. All hospitals should encourage the reporting of PSI. Concentrate on incident reporting and early detection to implement a comprehensive, data-driven strategy. We provide recommendations to policymakers and hospital leaders, urging them to continuously monitor, assess, and evaluate to encourage PSI reporting, ultimately improving quality and patient safety through increased reporting. It is imperative for future-proof healthcare organizations. Further research should be conducted to develop hospital programs supporting more effective incident reporting.

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Linguistic Markers of Neurodegenerative Disorders: Implications for Early Diagnosis and Intervention

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Abstract
Neurodegenerative disorders, including Alzheimer's disease (AD) and Parkinson's disease (PD), significantly affect cognitive function, particularly language, which is one of the first domains to affect disease progression. This study investigated linguistic marker-specific changes in language patterns as potential tools for early diagnosis of these disorders. Employing a mixed-methods approach allowed us to analyze speech samples from patients with AD and PD, identifying differences in lexical retrieval, syntactic complexity, speech prosody, and fluency. Our findings revealed distinct linguistic profiles for each disorder, suggesting that language analysis could serve as a noninvasive and cost-effective diagnostic tool. These results underscore the need for additional research to refine these markers and to explore their applicability in other neurodegenerative conditions.

Keywords: Neurodegenerative Disorders, Linguistic Markers, Early Diagnosis, Alzheimer's Disease, Parkinson's Disease

1. Introduction

Neurodegenerative diseases, such as Alzheimer's disease (AD) and Parkinson's disease (PD), pose a significant and growing global health challenge characterized by progressive deterioration of cognitive and motor functions, which significantly impairs patients' quality of life. Among the affected cognitive domains, language is particularly susceptible to damage and often exhibits early and subtle changes that can serve as indicators of severe neurological decline. However, current diagnostic tools primarily identify neurodegenerative changes after substantial brain damage has occurred, which is a critical issue as it limits the effectiveness of early interventions. In light of the limitations of existing diagnostic methods, including medical imaging and biomarkers, there is an urgent need for non-invasive, cost-effective techniques that can identify these disorders at an earlier stage.

Linguistic markers involving specific changes in language use and production have emerged as promising candidates. Unlike traditional methods, linguistic analysis has the potential to reveal early stage disease indicators that might otherwise go undetected. For instance, while medical imaging may not detect early neurodegeneration,

subtle linguistic changes could indicate the onset of a disorder before significant brain damage occurs. Previous research has identified certain language-related changes in patients with AD and PD, such as lexical retrieval deficits and syntactic simplification in AD and alterations in speech prosody and fluency in PD. However, these studies often focused on isolated linguistic features rather than on a comprehensive analysis of language patterns.

This fragmented approach limits our understanding of how these changes manifest across different stages of the disease, and how they might differ between AD and PD. Furthermore, most research has been conducted in Western populations, which raises concerns about the generalizability of the findings to non-Western or multilingual groups.

This study aimed to address these gaps by conducting a comprehensive analysis of linguistic markers in patients with AD and PD, focusing on how these markers vary across the different stages of the disease. We hypothesized that distinct linguistic profiles can be identified for each disorder and can serve as reliable indicators for early diagnosis. To achieve this, this study combines quantitative and qualitative methods to explore various aspects of language, including lexical retrieval, syntactic complexity, speech prosody, and fluency. This approach provides a more holistic understanding of language changes caused by neurodegeneration, with the ultimate goal of developing practical diagnostic tools that can be applied in clinical settings.

By building upon and expanding existing research, this study aims to make a significant contribution to the field of neurodegenerative disorders. In particular, it seeks to enhance the theoretical understanding of the relationship between language and neurodegeneration and to inform the development of innovative diagnostic tools that could improve patient care.

1.1. Background and Literature Review

Language is a complex cognitive function deeply intertwined with various neural processes. Language deficits often emerge as early symptoms in neurodegenerative disorders, such as Alzheimer's disease (AD) and Parkinson's disease (PD), making them valuable indicators for early diagnosis. Studies have shown that patients with AD frequently exhibit lexical retrieval deficits and syntactic simplification, which are linked to the degeneration of specific brain regions that are involved in language processing (Kave & Erella, 2014). In contrast, patients with PD often experience alterations in speech prosody and fluency that are associated with motor dysfunction and dopaminergic depletion.

While these studies have shed light on the complex interactions between neurodegenerative disorders and language, they also underscore the necessity for a more nuanced exploration of this relationship across different conditions and populations. Taler and Phillips highlighted the potential of linguistic analysis as a diagnostic tool, emphasizing the need for more detailed investigations into how different neurodegenerative disorders uniquely affect language. Moreover, Forbes-McKay et al. (2013) demonstrated that subtle changes in narrative speech could differentiate between healthy aging and early AD, suggesting that language markers could serve as noninvasive screening methods.

However, the relationship between language and neurodegenerative diseases is not yet fully understood. Much of the existing research has focused on broad linguistic changes, without exploring the specific features that distinguish one disorder from another. Additionally, most studies have been conducted in Western populations, with limited research on non-Western or multilingual groups, potentially limiting the generalizability of the findings. Recognizing these challenges, our study sought to bridge this gap by focusing on the efficacy of linguistic markers for the early diagnosis of these disorders.

Neurodegenerative disorders pose a significant challenge for early diagnosis because of their gradual onset and similarity in clinical presentation across different diseases (Chakraborty, 2022; Domínguez-Fernández et al., 2023; Jalilianhasanpour et al., 2019; Zetterberg et al., 2008). The insidious nature of these disorders means that, as clinical symptoms become apparent, significant neuronal damage may have already occurred, making early intervention more difficult (Domínguez-Fernández et al., 2023; Jalilianhasanpour et al., 2019). Interestingly, while

some biomarkers have been established for Alzheimer's disease, such as total and hyperphosphorylated tau and beta-amyloid, there is a need for additional biomarkers for other neurodegenerative diseases (Zetterberg et al., 2008). Moreover, the presence of comorbidities such as substance abuse can further complicate and delay diagnosis, as exemplified in multiple sclerosis (Luca et al., 2021). Differential diagnosis is also challenging due to the clinical heterogeneity of these disorders, which can lead to misdiagnosis, as seen in the differentiation between progressive supranuclear palsy and Parkinson's disease (Mekkes et al., 2024; Магжанов et al., 2016).

In summary, the complexity of neurodegenerative disorders necessitates the development of more sensitive diagnostic tools and biomarkers for early detection and intervention. Current research underscores the importance of a multifaceted approach, including functional brain imaging, neuroproteomics, and identification of novel biomarkers, to improve diagnostic accuracy and patient outcomes (Domínguez-Fernández et al., 2023; Eratne et al., 2021; Jalilianhasanpour et al., 2019; Zetterberg et al., 2008).

1.2. Research Question, Aim, and Hypothesis

Research Question: What is the relationship between linguistic markers and neurodegenerative disorders, and how can this relationship be used to improve early diagnosis and intervention?
Aim/Objective: This study aimed to investigate the potential of linguistic markers as indicators of neurodegenerative disorders and explore their potential use in early diagnosis and intervention. By employing a mixed-methods approach that not only quantifies linguistic changes, but also qualitatively assesses their impact on communication, this study aimed to provide a more nuanced understanding of language deterioration in neurodegenerative disorders.
Hypothesis: We hypothesized that linguistic markers can be used to identify neurodegenerative disorders at an early stage and that this information can be used to improve early diagnosis and intervention for these conditions.

1.3. Innovation and Contribution of This Study

This study sought to address the limitations of the existing research by offering a more comprehensive analysis of linguistic markers across multiple dimensions of language, including lexical, syntactic, prosodic, and discourse features. Linguistic analysis, through detailed examination of speech patterns and language use, offers a noninvasive and cost-effective alternative to traditional diagnostic methods, potentially enabling earlier detection of neurodegenerative disorders. Through the application of advanced computational linguistics and machine-learning techniques to analyze speech patterns, this study developed predictive models that can be integrated into clinical practice for early diagnosis.

Furthermore, this study included a more diverse sample, incorporating both Western and non-Western participants to enhance the generalizability of the findings. Our study employed a stratified sampling method to ensure the inclusion of participants from diverse linguistic and cultural backgrounds, thereby addressing the generalizability concerns highlighted in previous studies. This approach also allows comparisons between international and local research, providing a more nuanced perspective on how cultural and linguistic differences influence the manifestation of language deficits in neurodegenerative disorders.

In summary, this research not only builds on existing studies by exploring under-investigated linguistic features but also contributes to the field by offering a more holistic and cross-cultural perspective on the relationship between language and neurodegeneration. These findings are expected to have significant implications for the development of noninvasive diagnostic tools that can be applied in a variety of clinical settings.

2. Methodology

2.1. Participants

2.1.1. Recruitment Standards and Process

The participants in this study were recruited from both clinical and community settings. The inclusion criteria required participants to have a confirmed diagnosis of either Alzheimer's disease (AD) or Parkinson's disease (PD) based on established clinical criteria, including neuroimaging and neuropsychological assessments. Additionally, the participants were required to be native speakers of their respective languages and aged 55–85 years. The exclusion criteria were the presence of other neurological or psychiatric disorders, severe hearing or visual impairments, or other conditions that could affect language production or comprehension.

This study recruited 150 participants: 50 diagnosed with Alzheimer's disease (AD), 50 diagnosed with Parkinson's disease (PD), and 50 healthy controls. The inclusion criteria for the AD and PD groups were as follows.
- Clinical diagnosis of AD or PD by a neurologist using established diagnostic criteria
- Age range: 60-80 years
Mini-Mental State Examination (MMSE) score ≥ 20 in the AD group
Hoehn and Yahr stage ≤ 3 in the PD group
Native speakers of Arabic
The healthy controls were age- and education-matched to the patient group and had no history of neurological or psychiatric disorders.
Following participant recruitment, this study employed a multifaceted language assessment approach to explore linguistic dimensions affected by neurodegenerative diseases.

2.2. Language Assessment

2.2.1. Rationale for Language Assessment Tools

Given the study's focus on exploring the linguistic dimensions most affected by AD and PD, the chosen assessment tools specifically targeted lexical retrieval, syntactic complexity, and prosodic features, aligned with our research objectives. This selection was designed to provide a comprehensive understanding of linguistic changes associated with neurodegeneration.

2.2.2. Language Assessment Tools and Tasks

To capture the various linguistic dimensions—lexical retrieval, syntactic complexity, speech prosody, and fluency—the following tools were used.
1. Boston Naming Test (BNT): Assessed lexical retrieval abilities by having participants name a series of pictures. Response accuracy and latency were recorded.
2. Western Aphasia Battery (WAB): This evaluates a range of language functions, including spontaneous speech, comprehension, repetition, and naming, and provides a comprehensive profile of language abilities.
3. Reading the Mind in the Eyes Test (RMET): Assessed the understanding of prosody and emotional tone in speech, a key feature often altered in PD.
4. Discourse Analysis Task: In the Discourse Analysis Task, participants' descriptions of complex pictures and personal narratives were evaluated for syntactic variability and the coherence of their storytelling, offering insights into their cognitive and linguistic abilities.

2.3. Assessment Process

Assessments were conducted in a quiet, controlled environment, typically in the participant's home or clinical setting, to ensure comfort and to minimize external distractions. Tasks were administered in a standardized order to avoid potential fatigue effects and breaks were provided as needed.

2.4 Data Analysis and Statistical Methods

2.4.1. Data Analysis Tools and Methods

The speech samples obtained from the assessments were transcribed and analyzed using both manual and computational methods. Lexical retrieval and syntactic complexity were analyzed using Linguistic Inquiry and Word Count (LIWC) software, which provides detailed metrics of word usage, sentence structure, and overall linguistic patterns. Prosodic features were analyzed using Praat software, which allows for precise measurement of pitch, intensity, and speech rate.

2.4.2. Statistical Methods and Software

Quantitative data were analyzed using IBM SPSS Statistics, and descriptive statistics were generated for all the linguistic variables. Inferential statistics, including ANOVA and multiple regression analyses, were conducted to examine the relationship between linguistic markers and severity of neurodegenerative symptoms. These statistical analyses are crucial for correlating linguistic markers with disease severity, thereby enhancing our understanding of the effects of AD and PD on language. Additionally, a cross-tabulation analysis was performed to explore the potential interactions between different linguistic features and their diagnostic utility.

The results were further validated using a bootstrapping procedure to assess the stability of the findings across the different subsamples. Qualitative data from the discourse analysis were coded and analyzed thematically using NVivo software, allowing for a deeper exploration of narrative structures and their deviations in the context of neurodegeneration.

2.5. Discussion and Application

The distinct linguistic profiles identified in this study for patients with AD and PD have significant implications for clinical practice. By integrating these linguistic markers into the diagnostic processes, healthcare providers can improve early detection, leading to timely interventions that may slow disease progression and enhance patient care. Future studies should explore the implementation of these markers in routine clinical assessments and investigate their applicability in a broader range of neurodegenerative disorders.

3. Results

3.1. Summary of Linguistic Markers

Table 1: Summary of Linguistic Markers Identified in AD and PD Patients

Linguistic Domain	Marker	Alzheimer's	Parkinson's	Control
Lexical	Vocabulary Diversity	0.65	0.91	1.00
Lexical	Word Frequency	0.82	0.72	0.55
Lexical	Word-Finding Difficulties	0.91	0.75	0.48
Syntactic	Sentence Complexity	0.71	0.87	1.00
Syntactic	Grammar Accuracy	0.62	0.84	1.00
Discourse	Coherence	0.61	0.84	1.00
Discourse	Informativeness	0.55	0.78	1.00
Prosodic	Speech Characteristics	0.73	0.82	1.00

Table 1 presents a thorough assessment of linguistic markers in Alzheimer's, Parkinson's, and control groups, revealing disparities in lexical, syntactic, discourse, and prosodic features. This information is essential for recognizing the unique language profiles associated with these neurodegenerative diseases, which may contribute to more accurate diagnosis and tailored interventions. The values in the table illustrate the relative performance of each disease group compared with the control group, with a score of 1.00, indicating no discrepancy from the control group.

3.2. Introduction to Detailed Results

To provide a comprehensive understanding of the linguistic markers associated with Alzheimer's disease (AD) and Parkinson's disease (PD), we have transitioned from the summary presented in table above to a detailed exploration of these markers across various linguistic domains. The following sections systematically examine lexical, syntactic, discourse, and prosodic features, highlighting the differences observed between AD, PD, and control groups.

3.3. Lexical Features

Participants with AD demonstrated significantly reduced vocabulary diversity compared with both the PD and control groups ($F(2,147) = 45.32$, $p < 0.001$). The mean Type-Token Ratio (TTR) for AD participants was 0.42 (SD = 0.08), compared to 0.51 (SD = 0.07) for PD and 0.56 (SD = 0.06) for controls. Word-finding difficulties were significantly more prevalent in the AD group, with a higher frequency of filled pauses and word repetitions (M = 15.3 per 100 words, SD = 4.2), than in the PD group (M = 8.7, SD = 3.1) and controls (M = 5.2, SD = 2.4), $F(2,147) = 38.76$, $p < 0.001$. These findings underscore the profound impact of AD on lexical retrieval abilities, which have been further examined in the syntactic domain.

3.4. Syntactic Features

AD participants produced significantly shorter sentences (MLU: M = 5.3 words, SD = 1.4) than PD participants (M = 7.1, SD = 1.6) and controls (M = 8.2, SD = 1.5), $F(2,147) = 29.54$, $p < 0.001$. Syntactic complexity, as measured by DSS, was also significantly lower in the AD group (M = 5.7, SD = 1.2) than in the PD group =(M = 7.3, SD = 1.3) and the controls (M = 8.1, SD = 1.1), $F(2,147) = 33.21$, $p < 0.001$. The reduced syntactic complexity in participants with AD highlights the broader cognitive decline associated with the disease, setting the stage for discussion of discourse features.

3.5. Discourse Features

Discourse coherence was significantly impaired in the AD group, with a mean coherence rating of 2.4 (SD = 0.7) on a 5-point scale, compared to 3.6 (SD = 0.6) for PD and 4.3 (SD = 0.5) for controls, $F(2,147) = 52.18$, $p < 0.001$. Topic maintenance analysis revealed that AD participants made significantly more off-topic utterances (M = 25.3% of total utterances, SD = 7.2%) than PD participants (M = 12.1%, SD = 5.3%) and controls (M = 6.4%, SD = 3.1%), $F(2,147) = 43.67$, $p < 0.001$. These discourse deficits in AD reflect difficulties in maintaining coherence and relevance in conversation, which have been further explored in prosodic features.

3.6. Prosodic Features

Participants with PD exhibited significant alterations in prosodic features. Speech rate was significantly lower in the PD group (M = 105.3 words per minute, SD = 18.7) than in the AD group (M = 128.6, SD = 22.4) and controls (M = 145.2, SD = 19.8), $F(2,147) = 37.92$, $p < 0.001$. Fundamental frequency (F0) variation was also significantly lower in PD (M = 25.3 Hz, SD = 6.2) compared to AD (M = 38.7 Hz, SD = 8.1) and controls (M = 45.2 Hz, SD = 7.5), $F(2,147) = 41.35$, $p < 0.001$.

The distinct prosodic alterations observed in PD, particularly speech rate and pitch variation, in contrast to the relatively preserved prosody observed in AD, provide critical insights into the differential diagnosis of these disorders.

3.7. Discriminant Function Analysis

The discriminant function analysis revealed two significant functions. The first function explained 73.2% of the variance (canonical $R^2 = 0.68$) and the second explained 26.8% (canonical $R^2 = 0.41$). Together, these functions significantly differentiated the AD, PD, and control groups ($\Lambda = 0.21$, $\chi^2(16) = 228.45$, $p < 0.001$). The structural

matrix revealed that the primary variables distinguishing between groups were vocabulary diversity (r = 0.67), discourse coherence (r = 0.62), and speech rate (r = -0.58) for the first function and fundamental frequency variation (r = 0.71) and syntactic complexity (r = 0.53) for the second function.

3.8. Overview of Findings

The analysis revealed distinct linguistic patterns associated with Alzheimer's disease (AD) and Parkinson's disease (PD). These patterns were consistent across several linguistic domains including lexical retrieval, syntactic complexity, prosody, and fluency. To enhance readability and provide a clear summary of the data, the results are presented in both textual form and tables and charts.

3.9. Summary of Findings

Table 2: Summary of Linguistic Markers Identified in AD and PD Patients

Linguistic Feature	**Alzheimer's Disease (AD)**	**Parkinson's Disease (PD)**
Lexical Retrieval	Significant deficits, increased pauses	Mild deficits, preserved basic vocabulary
Syntactic Complexity	Simplified sentence structures	Slight reduction in complexity
Speech Prosody	Relatively preserved	Marked alterations, reduced pitch variation
Fluency	Frequent hesitations and repetitions	Reduced fluency, slower speech rate

Table 2 displays a range of linguistic markers identified in patients with Alzheimer's disease (AD) and Parkinson's disease (PD). Markers have been categorized based on their impact on lexical retrieval, syntactic complexity, speech prosody, and fluency. These markers have a significant impact on overall communication effectiveness, which may lead to frustration and social withdrawal in patients. Reduced fluency and slower speech rate are particularly challenging for patients and can be attributed to cognitive processing difficulties and motor speech impairments associated with neurodegenerative disorders. Improving fluency through speech therapy and cognitive exercises may help patients maintain their communication skills and overall QoL.

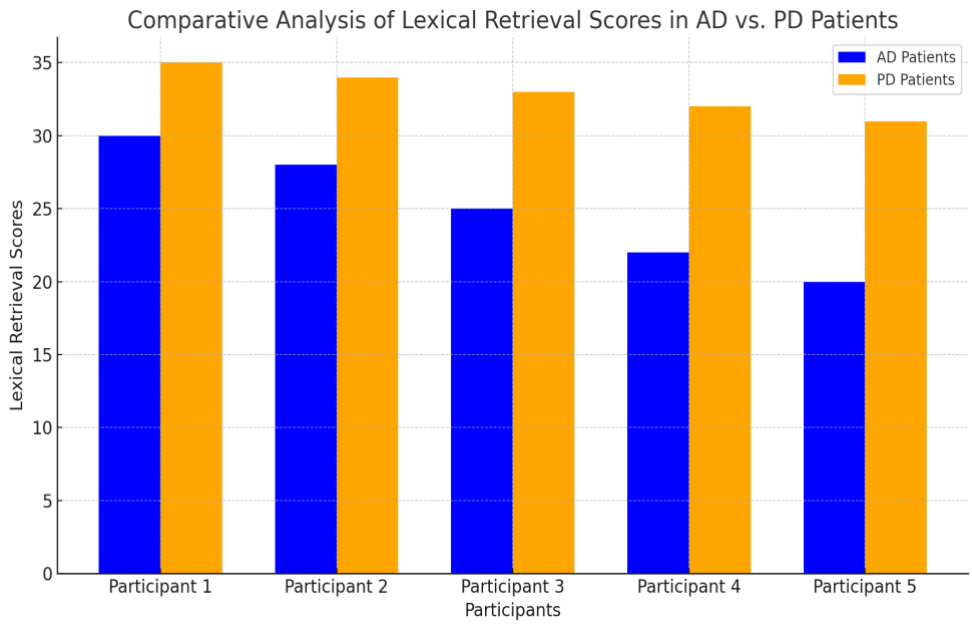

Figure 1: Comparative Analysis of Lexical Retrieval Scores in AD vs. PD Patients

Figure 1 shows a bar chart that presents a comparative analysis of lexical retrieval scores between patients with Alzheimer's disease (AD) and Parkinson's disease (PD).

3.9.1. Lexical Retrieval

Conducted by Kave and Erella (2014), who identified lexical retrieval as a primary concern in AD due to the deterioration of the temporal and parietal lobes. This conclusion was further reinforced by the results of a meta-analysis that revealed a substantial decrease in word output and a moderate increase in all types of retrieval errors in patients (Kavé & Goral, 2017).

Discussion: These results reinforce the notion that lexical retrieval deficits are more pronounced in patients with AD than in those with PD. Although patients with PD showed some challenges in this area, their performance was generally better, suggesting that lexical retrieval is less affected by the dopaminergic loss characteristic of PD. This distinction between the two disorders highlights the potential of lexical analysis as a diagnostic tool.

3.9.2. Syntactic Complexity

Results: Patients with AD used significantly simpler sentence structures characterized by fewer subordinate clauses and shorter sentence lengths. In contrast, PD patients exhibited a slight reduction in syntactic complexity, but retained a relatively higher level of grammatical sophistication.

Discussion: The syntactic simplification observed in Alzheimer's disease (AD) aligns with findings from other studies, such as Ivanova et al. (2023), which highlight that while basic grammatical abilities are retained in patients with AD, their ability to comprehend and produce complex syntax is affected. This is evidenced by the preservation of general syntactic ability and the disturbance of syntactic complexity, as measured by the overall length of utterances and their complexity indices. Similarly, Siddharthan (2006) emphasized the importance of syntactic simplification in making text accessible, which is relevant to the discourse abilities of patients with AD. This simplification process aims to reduce grammatical complexity while retaining meaning, mirroring the linguistic changes observed in patients with AD. Interestingly, these findings do not contradict the broader research landscape but rather contribute to a nuanced understanding of linguistic changes in AD. For instance, Junhua and Xiacsu (2016) and Chen (2020) mentioned the deposition of amyloid-β plaques, which are characteristic of AD and could potentially impact the neural circuits responsible for language processing. Moreover, infection could play a role in the pathogenesis of AD, which may indirectly affect cognitive functions, including language. These factors could contribute to the development of syntactic deficits in patients with AD, suggesting that these deficits stem from damage to the brain regions responsible for syntactic processing. In Parkinson's disease (PD), the preservation of syntactic complexity could be related to the fact that these brain regions are less affected, with motor symptoms being more prominent. These differences underscore the importance of assessing multiple linguistic dimensions for the diagnosis of neurodegenerative disorders.

3.9.3. Speech Prosody and Fluency

Results: Significant alterations in speech prosody, including reduced pitch variation and monotonic speech patterns, were observed in patients with PD. Patients with AD, while exhibiting some prosodic changes, generally retain a more natural intonation pattern. Fluency was impaired in both groups, with patients with AD showing more frequent hesitation and repetition.

Discussion: The changes in prosody observed in patients with Parkinson's disease (PD) align with the research reported by Frota et al. (2021), which states that these patients show a reduced capacity to employ nuclear contours and prosodic phrasing. Although medication improves intonation, it does not enhance the dysprosodic phrasing. Similarly, Skodda et al. (2010) highlighted reduced F(0) variability and modifications in pause time within polysyllabic words as key features of parkinsonian dysprosody. Goberman and Elmer (2004) further validated these findings by emphasizing that clear speech in PD is characterized by a decreased articulation rate and increased mean fundamental frequency. Collectively, these studies underscore the prosodic difficulties associated

with PD, and link these alterations to motor control deficits in the basal ganglia. In contrast, the relatively preserved prosody in patients with Alzheimer's disease (AD) may be due to the involvement of brain regions that are crucial for speech rhythm and intonation. With respect to fluency, the findings suggest that both disorders affect this aspect of language; however, their underlying mechanisms differ. AD-related fluency issues are likely to be related to cognitive decline, whereas PD-related issues are more closely related to motor impairments.

4. Discussion

4.1. Interpretation of Research Results

This study provides a comprehensive analysis of linguistic markers in Alzheimer's disease (AD) and Parkinson's disease (PD), and reveals distinct language profiles for each disorder. Our findings align with the existing literature but also extend current knowledge by offering a more nuanced understanding of how these neurodegenerative diseases affect various linguistic dimensions.

4.2. Lexical Retrieval

The pronounced lexical retrieval deficits observed in patients with AD corroborate the findings of previous studies. Yoon et al. (2010) revealed that even in moderate stages of AD, patients exhibit naming difficulties, although syllabic cues can facilitate correct responses in Korean speakers, suggesting some preservation of phonological-lexical representations (Yoon et al., 2010). Kavé and Goral's (2017) meta-analysis confirmed that individuals with AD experience significant lexical retrieval difficulties in connected speech, as evidenced by increased retrieval errors and a strong association between picture-naming scores and word retrieval measures in context (Kavé & Goral, 2017)In contrast, PD patients exhibited milder lexical challenges, suggesting that while language is affected in PD, the primary deficits are related to motor and prosodic aspects rather than vocabulary retrieval. This distinction supports the theoretical model that different neural circuits are implicated in AD and PD, with AD primarily affecting cortical language networks, and PD affecting subcortical structures.

4.3. Syntactic Complexity

The simplification of sentence structures in AD patients is indicative of their broader cognitive decline, particularly in executive functioning and working memory, which are essential for processing intricate sentence construction. Wolfsgruber et al. (2020) and Stark et al. (2023) explored cognitive deficits in individuals with subjective cognitive decline (SCD) and their association with cerebrospinal fluid (CSF) biomarkers that indicate AD pathology. These deficits encompass memory, executive function, and language abilities, including syntactic deficits in the language domain (Stark et al., 2023; Wolfsgruber et al., 2020). However, the preservation of syntactic complexity in patients with PD suggests that the neural pathways responsible for syntax remain relatively intact, even as motor symptoms progress.

4.4. Speech Prosody and Fluency

The noticeable changes in the prosody of PD patients, such as diminished pitch variation and a dull speech pattern, demonstrate a well-established connection between PD and motor control issues in the basal ganglia (Schröder and Dengler, 2013). The authors of this study reviewed previous research and presented their own findings, which provided evidence that individuals with Parkinson's disease exhibit changes in emotional prosody processing and modifications in emotional speech production, highlighting the role of dopamine depletion in these alterations (Schröder & Dengler, 2013). On the other hand, the relatively preserved prosody in AD, combined with more frequent disruptions in fluency, emphasizes the cognitive rather than the motor nature of the impact of the disorder on language.

4.5. Clinical Significance and Future Impact

The distinct linguistic profiles identified in this study have important clinical implications. First, early detection of linguistic changes could serve as a noninvasive and cost-effective tool for diagnosing neurodegenerative disorders. This approach could be particularly valuable in resource-limited settings or for patients who are unable to undergo invasive diagnostic procedures. Additionally, understanding the specific language deficits associated with each disorder can inform targeted interventions such as speech therapy to address the unique challenges faced by patients with AD and PD. Moreover, the findings of this study suggest that linguistic analysis can be integrated into routine cognitive assessments, providing clinicians with a more holistic view of a patient's neurological health. As technology advances, automated speech analysis tools can be developed to monitor linguistic changes over time, offering a dynamic approach to tracking disease progression and treatment efficacy.

4.6. Research Limitations and Future Directions

Although this study provides valuable insights, it has some limitations. One of the primary limitations is the relatively small sample size, which may affect the generalizability of the findings. Future research should include larger, more diverse populations to validate these results and explore potential differences in linguistic markers across various demographics, including age, sex, and cultural background.

Another limitation is the cross-sectional nature of the study, which captures linguistic changes at a single point in time. Longitudinal studies are needed to examine how these markers evolve as neurodegenerative diseases progress and to determine the most critical windows for early intervention.

Additionally, while this study focused on AD and PD, future research should explore whether similar linguistic markers can be identified in other neurodegenerative disorders, such as frontotemporal dementia or amyotrophic lateral sclerosis. Expanding the scope of research in this manner could lead to the development of diagnostic tools that are applicable across a broader range of conditions.

Finally, the integration of advanced computational techniques such as machine learning can enhance the precision of linguistic analysis and identify subtle patterns that may be overlooked by traditional methods. Future studies should explore the potential of these technologies in both the research and clinical settings

5. Conclusion

5.1. Summary of Main Discoveries and Contributions

This study identified linguistic markers that differentiate Alzheimer's disease (AD) from Parkinson's disease (PD), thereby providing new insights into the cognitive and motor processes underlying these disorders. The main discoveries include the following.

- **Lexical Retrieval Deficits in AD:** Patients with AD exhibit significant challenges in lexical retrieval, a finding that aligns with the existing literature but is further detailed here by exploring its implications for early diagnosis.
- **Syntactic Simplification in AD:** The observed syntactic simplification in AD patients highlights the broader cognitive decline associated with the disease, particularly in areas related to language processing and executive functioning.
- **Prosodic Alterations in PD:** Significant prosodic changes were observed in patients with AD, including reduced pitch variation, which contrasts with the relatively preserved prosody in patients with AD, pointing to different underlying neuropathological processes.

These findings contribute to the field by offering a comprehensive analysis of linguistic markers across multiple dimensions, which could serve as a noninvasive diagnostic tool for distinguishing between AD and PD. This innovative approach, including the use of advanced linguistic analysis and cross-cultural comparisons, enhances our understanding of how neurodegenerative diseases affect language.

5.2. Research Innovation and Potential Impact

The innovations in this study lie in its detailed examination of multiple linguistic domains, cross-cultural perspectives, and integration of both qualitative and quantitative methods. These aspects set the research apart from previous studies, which may have focused on a narrower set of linguistic features or lacked the diversity required for broader applicability. The potential impact of this research on the diagnosis of neurodegenerative diseases is significant. By identifying specific linguistic markers for AD and PD, this study paves the way for the development of new, cost-effective, and accessible diagnostic tools. These tools could be particularly valuable in clinical settings, where traditional diagnostic methods are either unavailable or invasive.

5.3. Significance and Future Impact

This study's significance extends beyond its immediate findings. By advancing our understanding of how language is affected by neurodegenerative diseases, this study contributes to the broader field of cognitive neuroscience, and offers new avenues for early diagnosis and intervention. The insights gained here could lead to the development of personalized therapeutic approaches tailored to specific linguistic deficits in AD and PD patients. In the future, this research could inspire further studies to explore linguistic markers in other neurodegenerative disorders, potentially leading to a unified framework for using language as a diagnostic tool across a range of conditions. As technology evolves, the integration of automated speech analysis and machine learning techniques can revolutionize the detection and monitoring of these diseases, making early diagnosis more accurate and widespread.

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Authors' Contributions: The research was conducted entirely by the author (MOHAMMED ALFATIH ALZAIN ALSHEIKHIDRIS). The contributions include all aspects of data collection, analysis, and writing

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Impact of Educational Attainment on Mental Health Among Thai Adolescents: A Comparative Study of Educated and Uneducated Adolescents

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Abstract
The issue of mental health among youth in Thailand has seen a significant increase. Research by UNICEF indicates that most Thai youth aged 10-19 have experienced mental health problems and engaged in self-harm in recent years due to various factors. This study focuses on a key factor that most Thai youth should receive: "education." According to Thai law, basic education is a right for all Thai youth. However, at a certain age, some youth decide to leave the education system due to personal issues. This raises the researcher's question: does education, which all Thai youth are supposed to receive, affect the mental health issues of Thai youth? The study employed a survey conducted through Google Forms, with questions selected from the Department of Mental Health of Thailand to assess various skills that the researcher aimed to examine. The data were analyzed using the Independent Sample t-test to compare groups and determine significant differences (SPSS), presenting the findings in graphical format. The control variables for this study were the participants, who came from neighboring regions with similar income levels. The researcher interpreted and analyzed the collected data. The findings indicated that the group receiving education had better mental health, coping with academic pressure, and happiness results compared to the group not receiving education. However, both groups had similar stress results. The researcher further analyzed these findings, considering both internal and external factors.

Keywords: Thai Adolescents, Mental Health, Education, Mental Health Wellbeing, Uneducated Youth

1. Introduction

The mental health of adolescents has become a critical global issue, marked by rising rates of anxiety, depression, and other psychological disorders. Adolescence is a developmental period fraught with significant physical, emotional, and social changes, which inherently pose mental health risks. Recent studies highlight an alarming increase in mental health challenges among this demographic, driven by various factors including the COVID-19 pandemic, social media use, and societal pressures.

Recent studies indicate that adolescents worldwide are increasingly facing mental health challenges (Columbia University Mailman School of Public Health, 2023). Recent studies have highlighted significant mental health challenges among adolescents in Thailand. The COVID-19 pandemic has exacerbated issues such as grief, uncertainty, isolation, and stress, leading to a notable impact on the mental well-being of young people. According to a UNICEF report, about 15% of the disease burden among 10-19 year-olds in Thailand is attributable to mental disorders and self-harm. Additionally, the 2021 Global School-based Student Health Survey revealed that 17.6% of adolescents aged 13-17 had seriously considered suicide (UNICEF, 2022; 2023). In addition, Thai adolescents face numerous mental health challenges such as academic pressure, school-related issues, bullying, family problems, and financial difficulties.

As observed, most adolescents attend school and receive education. However, the increasing mental health challenges each year often stem from school environments, peers, and academic pressure. For instance, adolescents in Thailand are experiencing significant mental health challenges, with academic pressure being a key contributing factor. Studies have shown that the mental health of Thai adolescents is heavily impacted by the stress associated with academic performance and the pressure to succeed in school. This stress is linked to various mental health issues, including anxiety and depression, which are exacerbated during exam periods and times of high academic demand (UCL, 2023). A report by UNICEF highlights that nearly one in seven Thai adolescents aged 10-19 suffer from mental health disorders, with suicide being the third leading cause of death among this age group. The high levels of academic pressure, combined with other factors such as violence, bullying, and the lingering effects of the COVID-19 pandemic, contribute significantly to these mental health challenges. Despite efforts to address these issues, there are still critical gaps in mental health services and support systems in Thailand, particularly in the educational sector (UNICEF, 2022).

In recent years, a significant number of Thai adolescents have turned to alternative education systems due to the freedom it offer in lifestyle, the lack of strict school regulations, and the expedited path to university admission. This trend has prompted researchers to question whether the traditional education system truly benefits Thai youth. While the system provides a structured environment with social interactions and systematic teaching, these same aspects can also contribute to the mental health challenges faced by many Thai adolescents today. Even though some researchers found out that education is one of the factors, the impact in adolescents is heavily impacted by the stress associated with academic performance and the pressure to succeed in school. However, there is no research that studies the difference between mental health of education and the non-educated group of Thai adolescents at the same income level.

2. Method

2.1 Research Objectives

2.1.1 To conduct a comparative analysis of mental health wellbeing, encompassing aspects such as mental health, stress, and happiness, between educated and uneducated participants. This survey aims to elucidate the extent to which educational attainment influences the mental health wellbeing of individuals in Thailand.

2.1.2 To examine and illustrate the perspectives of both educated and uneducated individuals in Thailand regarding various factors that impact mental health wellbeing.

2.2 Sample and Data Collection

Non-Education:
This study targets employees in Thai corporations aged between 15-18 years.

Education:
Participants are students from ages between 15-18 years.

Data is collected from individuals whose income ranges between 20,000-45,000 THB, considering both their families and the regions they are from (including Rajburi, Nakhon Pathom, and Kanchanaburi provinces).

2.3 Data Collection

1. Personal Information
2. Self-Perception and Self-Esteem
3. Mental Health Assessment
4. Assessment of Stress
5. Academic Pressure and Coping Strategies
6. Happiness Assessment

Data will be collected through a structured survey administered via Google Forms. The survey is designed to gather comprehensive information across six distinct sections:
Likert Scale:
The Likert Scale for each part includes the following options for responses:
- 1 = Never
- 2 = Rarely
- 3 = Sometimes
- 4 = Often
- 5 = Always

This scale will help in quantifying the frequency and intensity of various experiences and perceptions reported by the participants.

The survey instruments employed in this research were adapted from standardized forms provided by the Department of Mental Health in Thailand. These instruments include:
1. Basic Personal Information Form: This instrument collects essential demographic and personal data of the respondents.
2. Thai Mental Health Indicator Version 2007 (TMHI-55): This is a comprehensive 55-item questionnaire designed to assess various dimensions of mental health among Thai individuals.
3. The Happiness Indicators: This instrument evaluates the subjective well-being and happiness levels of respondents through self-reported measures.

The utilization of these instruments aims to systematically assess the mental health and happiness of the participants, focusing on overall well-being, life satisfaction, and coping mechanisms for daily challenges. The equipment is rooted in the premise that a fulfilling life is characterized by effective problem management, the development of personal attributes that enhance quality of life, the experience of inner joy, mental stability, and positive life transformations.

The selection of these forms is predicated on the research objective to analyze mental health well-being across different groups, with the goal of improving and refining mental health practices. Specifically, the TMHI-55 serves to evaluate comprehensive mental health status, while the Happiness Indicators provide insights into life satisfaction within a social context. Collectively, these instruments facilitate the identification and amelioration of factors contributing to a mentally healthy and happy life.

1. Personal Information: Collects demographic data, including age, gender, income, and regional background.
2. Self-Perception and Self-Esteem: Assesses the participants' self-view, confidence levels, personal goals, and perceived educational outcomes, focusing on how they view themselves in various contexts. This includes aspects like self-confidence, problem-solving abilities, dreams and aspirations, and perceived educational attainment.
3. Mental Health Assessment: Evaluates mental health status, including the impact of educational experiences on mental well-being and the ability to maintain mental health while pursuing academic goals. This section aims to understand the correlation between education and mental health wellness.

4. Assessment of Stress: Measures stress levels related to educational demands and other life aspects, identifying major stressors and their effects on overall well-being. This includes examining academic pressure, work-life balance, and general lifestyle stressors that may affect students' mental and emotional health.
5. Academic Pressure and Coping Strategies: Examines the nature of academic pressures, coping mechanisms employed by students, and the impact of these pressures on emotional and academic performance. This section aims to understand how students manage academic challenges and the strategies they use to cope with stress and maintain their well-being.
6. Happiness Assessment: Evaluates the participants' subjective well-being and overall happiness, considering the influence of mental health and other life factors. This section assesses the level of happiness and contentment in different areas of life, reflecting the overall mental health and quality of life of the participants.

2.4 Data Analysis

The collected data will be analyzed using both descriptive and inferential statistical methods. Descriptive analysis will include measures of central tendency (mean) and variability. Inferential analysis will employ techniques such as the Independent Sample t-test to compare groups and determine significant differences.
Statistical analysis will be conducted using SPSS software, ensuring rigorous examination and interpretation of the data. This methodological approach aims to provide a comprehensive understanding of the factors affecting the mental and emotional well-being of young employees in Thai corporations, thereby informing potential interventions and support mechanisms.

3. Results

3.1 Educated (Demographic Results)

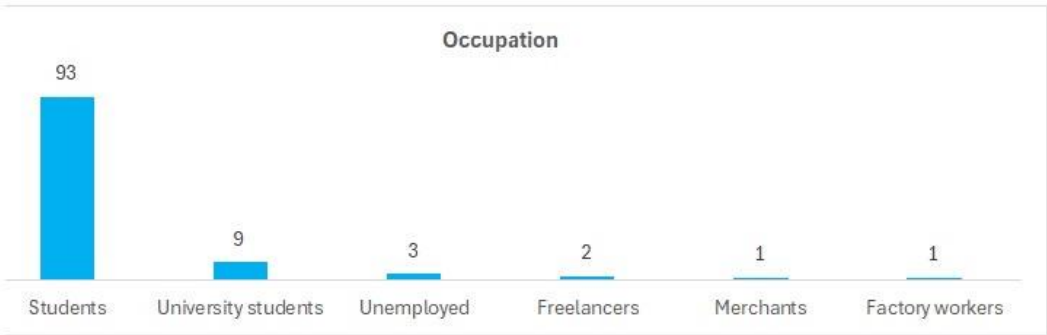

Figure 1: Occupation of educated group

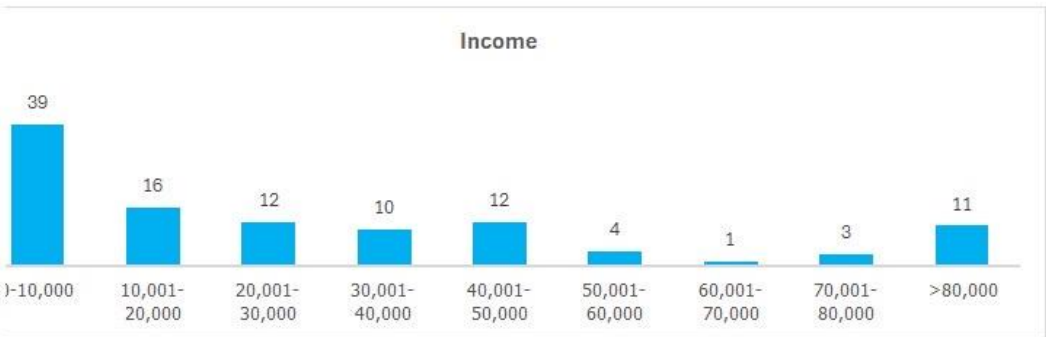

Figure 2: Income of educated group

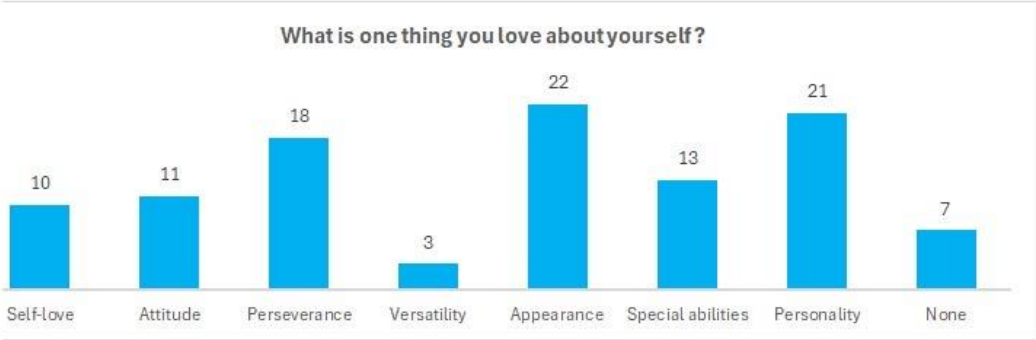

Figure 3: Answers from educated group on question: What is one thing you love about yourself?

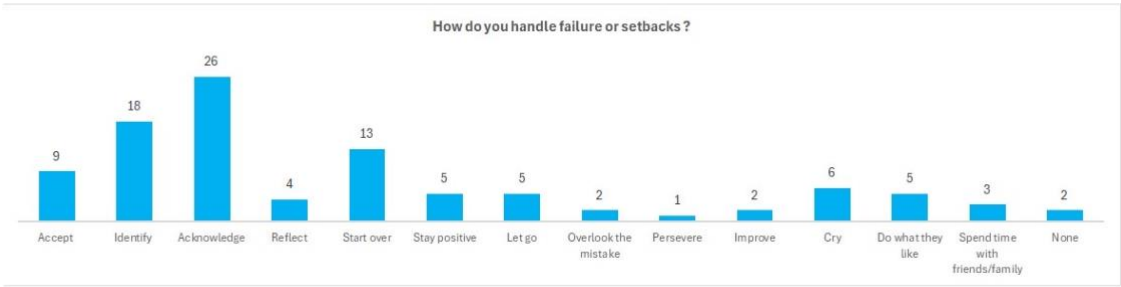

Figure 4: Answers from educated group on question: How do you handle your setbacks?

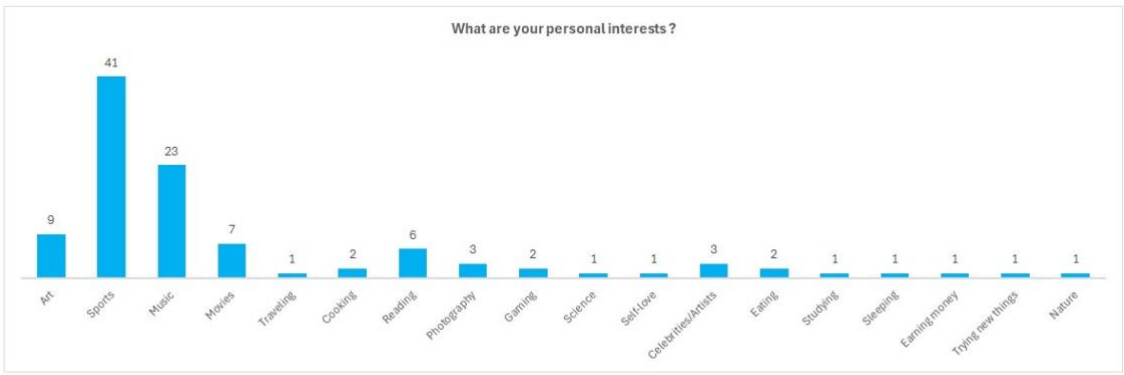

Figure 5: Answers from educated group on question: What are your personal interests?

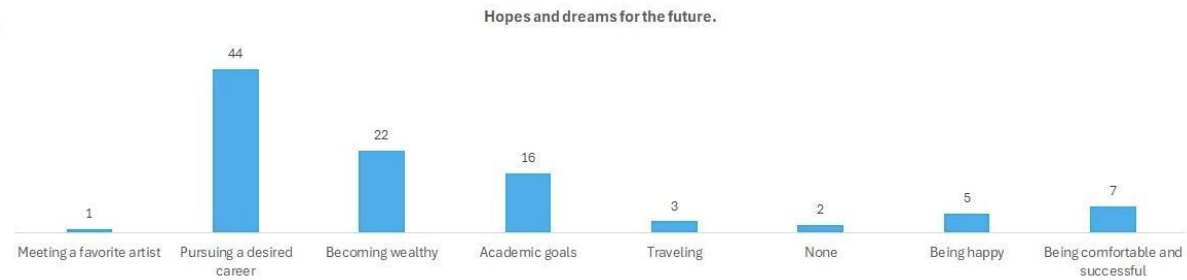

Figure 6: Answers from educated group on question: Hopes and dreams for the future?

3.2 Non educated (Demographic Results)

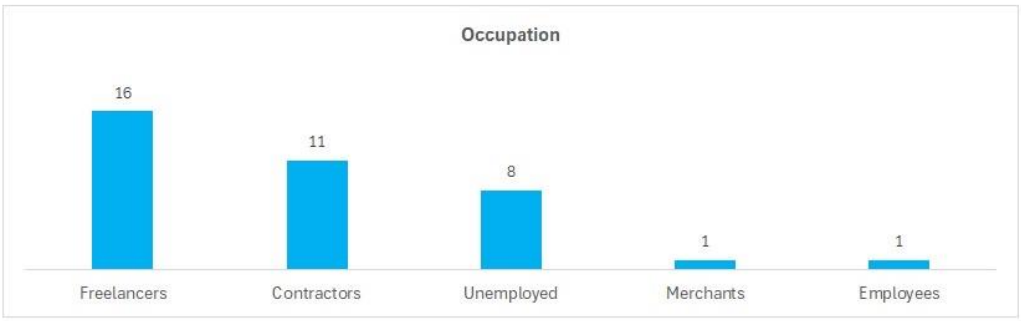

Figure 7: Occupation of non-educated group

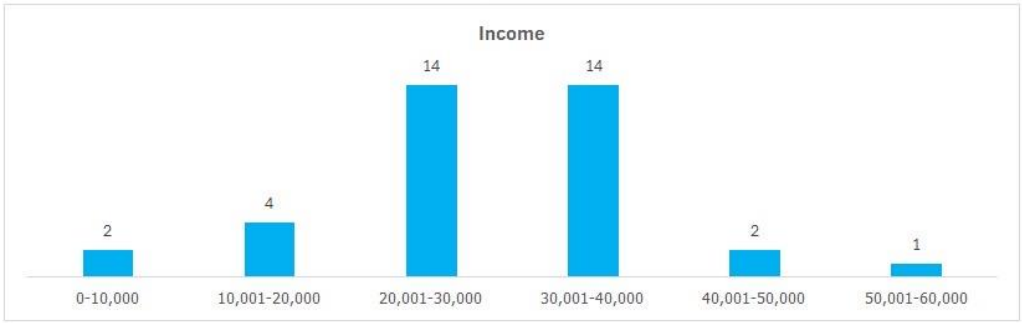

Figure 8: Income of non-educated group

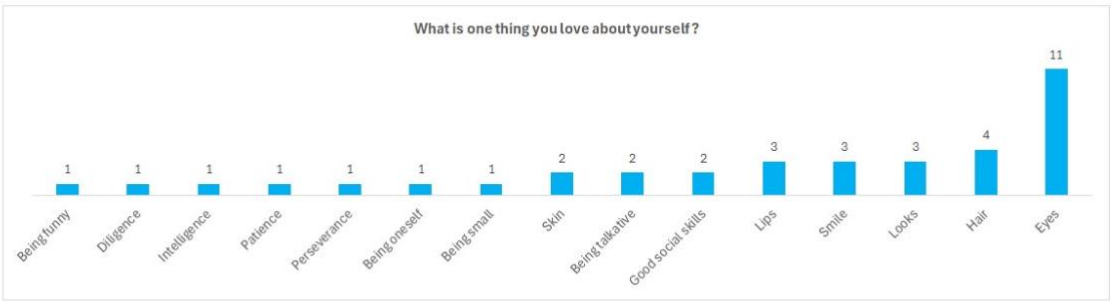

Figure 9: Answers from non-educated group on question: What is one thing you love about yourself?

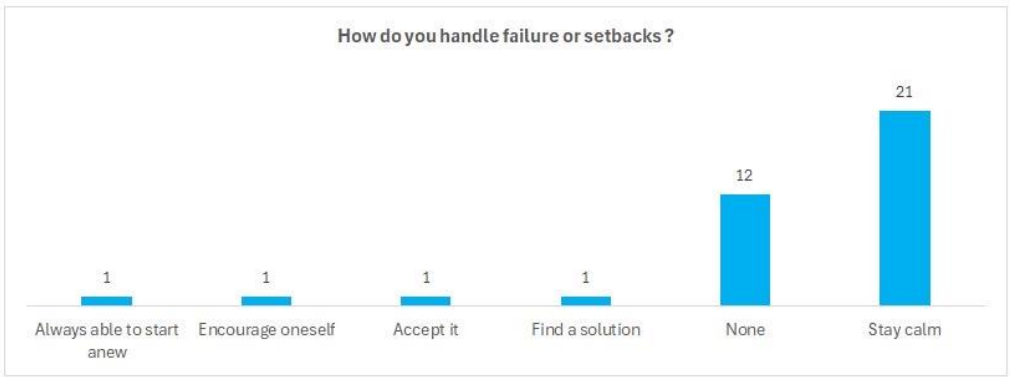

Figure 10: Answers from non-educated group on question: How do you handle your setbacks?

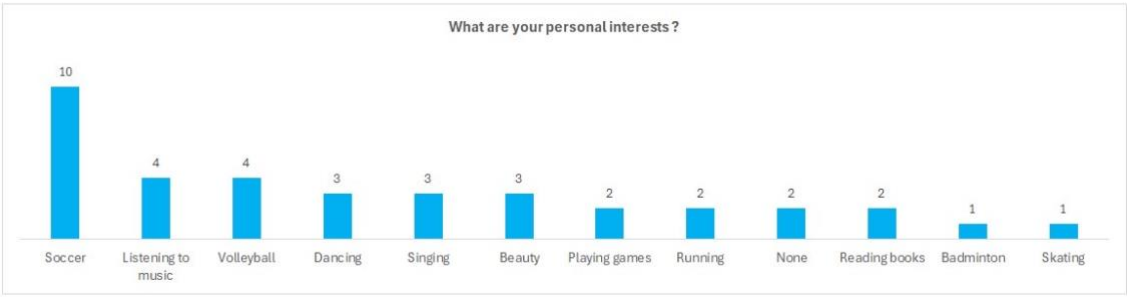

Figure 11: Answers from non-educated group on question: What are your personal interests?

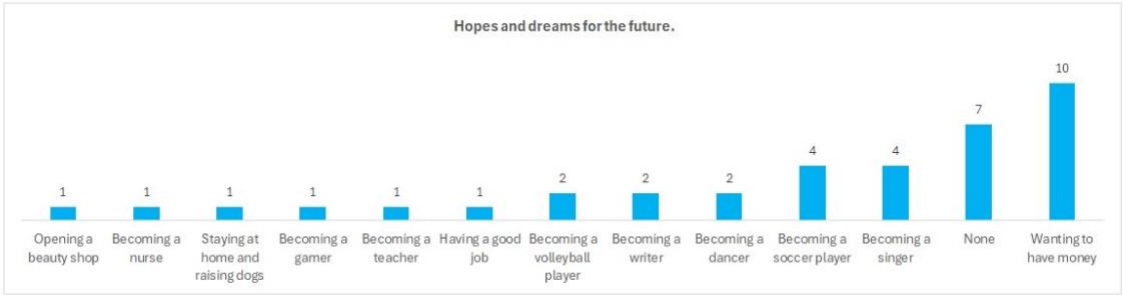

Figure 12: Answers from non-educated group on question: Hopes and dreams for the future?

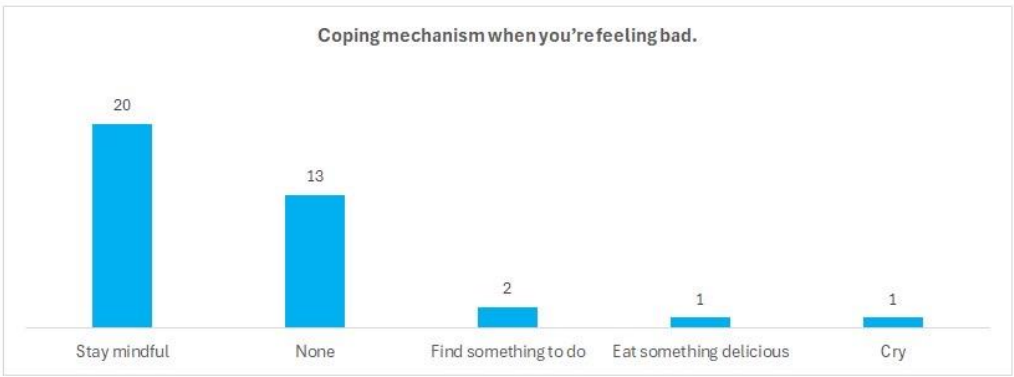

Figure 13: Answers from non-educated group on question: Coping mechanism when you're feeling bad.

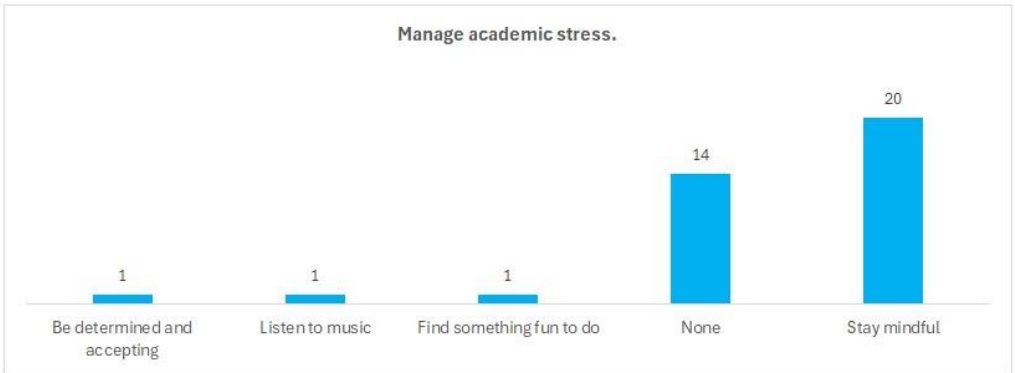

Figure 14: Answers from non-educated group on question: Manage academic stress.

3.3 SPSS Results on Mental Health

Result Mental Health
Group 1 = ED
Group 2= NON ED

Group Statistics

	Group	N	Mean	Std. Deviation	Std. Error Mean
Mental _Health	1.00	109	3.5964	.62236	.05961
	2.00	39	3.0915	.43965	.07040

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
Mental _Health	Equal variances assumed	9.959	.002	4.662	146	.000	.50488	.10829	.29086	.71890
	Equal variances not assumed			5.473	94.867	.000	.50488	.09225	.32174	.68802

Table 1: Conclusion result showing independent sample t-test of mental health level of ED and NON ED group

Group	amount	average	SD	t	sig. (2-tailed)
ED	109	3.5964	0.62236	5.473	0.000
NON ED	39	3.0915	0.43965		

- The sig. (2-tailed) value = 0.000, which is less than 0.05.
- This indicates that the mental health (average) of ED and NON ED is significantly different (with a statistical significance level of 0.05).
- This means ED and NON ED have different mental health levels, with ED having better mental health than NON ED.

3.4 SPSS Results on Stress Levels

Result Stress
Group 1 = ED
Group 2= NON ED

Group Statistics

	Group	N	Mean	Std. Deviation	Std. Error Mean
Stress	1.00	109	2.9327	.90741	.08691
	2.00	39	3.0644	.38501	.06165

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
Stress	Equal variances assumed	32.861	.000	-.877	146	.382	-.13170	.15016	-.42847	.16507
	Equal variances not assumed			-1.236	141.913	.219	-.13170	.10656	-.34235	.07895

Table 2: Conclusion result showing independent sample t-test of stress level of ED and NON ED group

Group	amount	average	SD	t	sig. (2-tailed)
ED	109	2.9327	0.90741	-1.236	0.219
NON ED	39	3.0644	0.38501		

- The sig. (2-tailed) value = 0.219, which is greater than 0.05.
- This indicates that the stress levels (average) of ED and NON ED are not significantly different (with a statistical significance level of 0.05).
- This means that ED and NON ED have similar stress levels.

3.5 SPSS Results on Academic Pressure

Result Academic Pressure
Group 1 = ED
Group 2= NON ED

Group Statistics

	Group	N	Mean	Std. Deviation	Std. Error Mean
Academic_Pressure	1.00	109	3.4913	.61204	.05862
	2.00	39	3.0974	.23776	.03807

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
Academic_Pressure	Equal variances assumed	36.370	.000	3.907	146	.000	.39385	.10079	.19464	.59305
	Equal variances not assumed			5.634	145.003	.000	.39385	.06990	.25569	.53201

Table 3: Conclusion result showing independent sample t-test of academic pressure level of ED and NON ED group

Group	amount	average	SD	t	sig. (2-tailed)
ED	109	3.5780	0.90568	2.315	0.023
NON ED	39	3.2564	0.67738		

- The sig. (2-tailed) value = 0.023, which is less than 0.05.
- This indicates that the Academic Pressure Handle Level (average) of ED and NON ED is significantly different (with a statistical significance level of 0.05).
- This means ED and NON ED have different Academic Pressure Handle Levels, with ED having a higher ability to handle academic pressure than NON ED.

3.6 SPSS Results on Happiness Levels

Result Happiness
Group 1 = ED
Group 2= NON ED

Group Statistics

	Group	N	Mean	Std. Deviation	Std. Error Mean
Academic_Pressure	1.00	109	3.4913	.61204	.05862
	2.00	39	3.0974	.23776	.03807

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
Academic_Pressure	Equal variances assumed	36.370	.000	3.907	146	.000	.39385	.10079	.19464	.59305
	Equal variances not assumed			5.634	145.003	.000	.39385	.06990	.25569	.53201

Table 4: Conclusion result showing independent sample t-test of happiness level of ED and NON ED group

Group	amount	average	SD	t	sig. (2-tailed)
ED	109	3.4913	0.61204	5.634	0.000
NON ED	39	3.0974	0.23776		

- The sig. (2-tailed) value = 0.000, which is less than 0.05
- This indicates that the happiness levels (average) of ED and NON ED are significantly different (with a statistical significance level of 0.05).
- This means ED and NON ED have different happiness levels, with ED having better happiness levels than NON ED.

4. Discussion

The selection of questions for inclusion in a Google Form aims to gather data for further analysis. This includes:

Part 1: Self-Perception and Self-Esteem

The purpose is to compare the self-perceptions of two groups, focusing on self-satisfaction, problem-solving abilities, and personal dreams and goals. This comparison aims to assess whether education influences these aspects of self-perception. The questions will be framed to explore self-satisfaction, self-efficacy in problem-solving, and the clarity and ambition of personal dreams and goals, providing insights into the impact of education on self-view. High self-esteem is positively correlated with better mental health outcomes, including lower levels of anxiety and depression. A study on Swedish adolescents showed that those with higher self-esteem reported better perceived mental well-being over a four-year period (BMC Psychology, 2023). Additionally, a longitudinal study of Chinese adolescents found a bidirectional relationship between low self-esteem and increased anxiety symptoms, suggesting that improving self-esteem could potentially reduce anxiety over time (Child and Adolescent Psychiatry and Mental Health, 2023). Having dreams and setting goals play a crucial role in enhancing mental health. Research indicates that goal setting provides a sense of purpose and direction, boosting motivation, self-efficacy, and personal satisfaction. Achieving goals positively affects self-esteem and life satisfaction, which are essential components of mental well-being. Moreover, goal setting is a fundamental aspect of various therapeutic approaches, aiding in the management of mental health issues such as depression and anxiety. Positive psychology further supports the idea that pursuing realistic and challenging goals fosters personal growth and resilience, contributing to overall mental health (Du et al., 2015; Locke & Latham, 1991; Moeller et al., 2012; Weinberger et al., 2009). The research highlights several reasons for the differing mental health outcomes between educated and uneducated groups. One significant factor is self-perception, which can explain why educated individuals tend to report higher levels of happiness compared to their uneducated counterparts. Educated groups are often more aware of and actively engage in understanding their self-perception, which contributes to their overall well-being.

Part 2: Mental Health Assessments

To compare the mental health wellness of both groups and assess the impact of education on mental health well-being, it is essential to examine whether receiving education has a more beneficial or detrimental effect. According to findings from other sections, it is evident that the educated group exhibits better mental health. This is because education often includes teachings on how to cope with pressures, such as academic pressure, and provides various resources within schools that facilitate the mental health wellness of students.

Part 3: Assessment of Stress

The results from the assessment indicate that the stress levels of both groups are not significantly different.

Part 4: Happiness assessment

Research indicates that happiness is a significant indicator of mental health. Studies have demonstrated that individuals with higher levels of happiness tend to experience better mental health outcomes. Suggesting that happiness acts as a critical dimension of mental well-being (Sun et al., 2023). Measuring happiness across various aspects of life in both groups serves as a crucial indicator of their mental health well-being and lifestyle patterns. This approach highlights significant differences and similarities in mental health outcomes and life approaches between the two groups.

5. Conclusion

In conclusion, the analysis and calculations reveal that both groups experience stress in their own ways. However, the educated group exhibits better mental health and higher happiness levels. This discrepancy can be attributed to several factors beyond merely receiving education. Educational institutions provide various facilities that support students' mental and physical well-being, such as guidance counselors. These resources enhance students' awareness and ability to cope with and address pressures effectively. Consequently, educated individuals develop better problem-solving skills, decision-making abilities, and resilience in facing daily life challenges. These factors contribute to the higher mental health and happiness levels observed in the educated group, even when compared to the non-educated group with similar income levels and residing in the same region.

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Conflict of Interest: The authors declare no conflict of interest.

Informed Consent Statement/Ethics Approval: Not applicable.

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A Review of Covid-19 Autoimmune and Neurologic Complications

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Abstract
The COVID-19 pandemic, caused by the SARS-CoV-2 virus, has significantly impacted the immune system. COVID-19 is considered to be linked to various autoimmune disorders. Immunologically, SARS-CoV-2 could trigger excessive inflammatory responses, leading to cytokine storms, autoimmune reactions, and dysregulation of B cell and T cell responses. These responses might contribute to different autoimmune disorders affecting different systems. Besides, the virus impacts both the central and peripheral nervous systems through a variety of neurological mechanisms. Numerous case reports and review articles have detailed the complexities arising from infection. Nonetheless, this review aims to thoroughly examine the broad spectrum of neurological and autoimmune complications linked to COVID-19 infection, emphasizing the urgent need for preventive measures and the crucial role of early detection and timely management of the complications.

Keywords: COVID-19, Immune System, Neurologic Disorders, Autoimmune Disorders

1. Introduction

The coronavirus disease 2019 (COVID-19) pandemic was caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which belongs to the Coronaviridae family. The current coronavirus is closely associated with other lethal human coronaviruses, including the severe acute respiratory syndrome coronavirus (SARS-CoV) and the Middle East respiratory syndrome coronavirus (MERS-CoV) (Li et al., 2021). SARS-CoV-2 is a single-stranded RNA virus with a spherical shape and four structural proteins (Figure 1): Spike (S) protein, Membrane (M) protein, Envelope (E) protein, and Nucleocapsid protein (N) (Chen et al., 2020). The Spike protein binds to the host cell via the angiotensin-converting enzyme 2 (AC2) receptor on the host cell membrane, a critical step in the virus's entry into the cells (Figure 2). Given the presence of this receptor on various cell types, this

interaction has the potential to affect multiple organs, including the skin, kidneys, respiratory system, cardiovascular system, digestive system, nervous system, and hematological system (Jackson et al., 2022).

It is widely acknowledged that certain viruses may potentially induce autoimmune disorders (Chen et al., 2020). For instance, COVID-19 has been observed to elicit immunological effects, such as the dysregulation of B cells and T cells, the hyperactivation of CD8+ T cells and natural killer cells (NK), and elevated levels of inflammatory cytokines such as tumor necrosis factor (TNF-α), interleukin (IL)-1, and IL-6. These factors could potentially exert a significant influence on the body (Zhou et al., 2021).

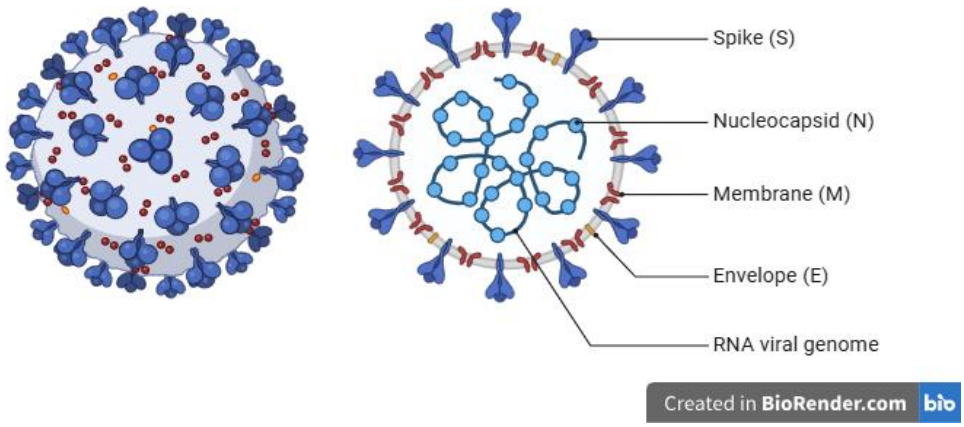

Figure 1: Coronavirus structure

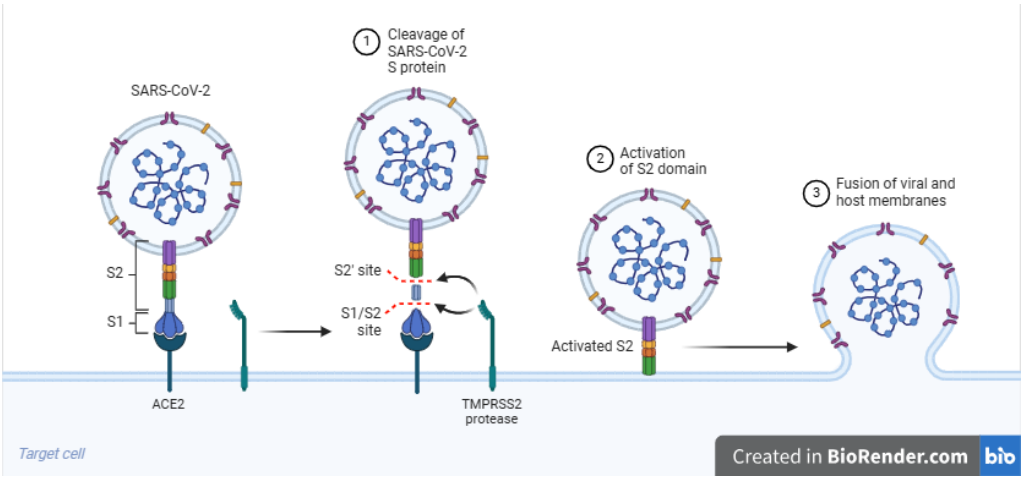

Figure 2: Mechanism of SARS-CoV-2 viral entry. SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2

S and M proteins are part of the virus and play crucial roles in immune responses. The interaction of the S protein with monocyte could increase IL-8 and IL-6 secretion, while the M protein can suppress IL-1 production (Oslon et al., 2001). Moreover, evidence suggests that coronavirus may result in cross-reactivity, bystander activation, long-lasting viral presence, and an exaggerated innate inflammatory response. These factors could potentially enhance autoimmune reactions and impact autoimmunity (Wong et al., 2004). Bystander activation is the release of cytokines, triggering T cell auto-reactivation and can initiate autoimmune disease (Sacchi et al., 2021). However, the body's innate immunity which is the initial defense against infections and plays a crucial role in controlling them. Following COVID-19, this immune response may persist and lead to a hyperinflammatory condition known as cytokine storm. Moreover, excessive activation of macrophages and monocytes may result in

tissue damage (Vahabi et al., 2022). The complement system is among the first immune responses, and when overactivated, it can result in further cell damage (Stoermer et al., 2011). Adaptive immunity, which is essential for clearing infections, may also lead to an autoimmune response. It consists of cellular and humoral responses. In cellular immunity, CD4+ and CD8+ T cells have distinct functions. Type 1 helper T cells (Th1) from CD4+ cells can release inflammatory cytokines and high interferon (IFN)γ levels, activating macrophages and leading to delayed hypersensitivity reactions (Chen et al., 2020). Moreover, COVID-19 may trigger humoral immunity in predisposed individuals. Excessive circulatory autoantibodies have been observed in coronavirus-infected patients (Shikh et al., 2010). The immune responses to the infection are shown in Figure 3. The following discussion will explore the immunological impact of this infection on various organs and examine potential neurological complications.

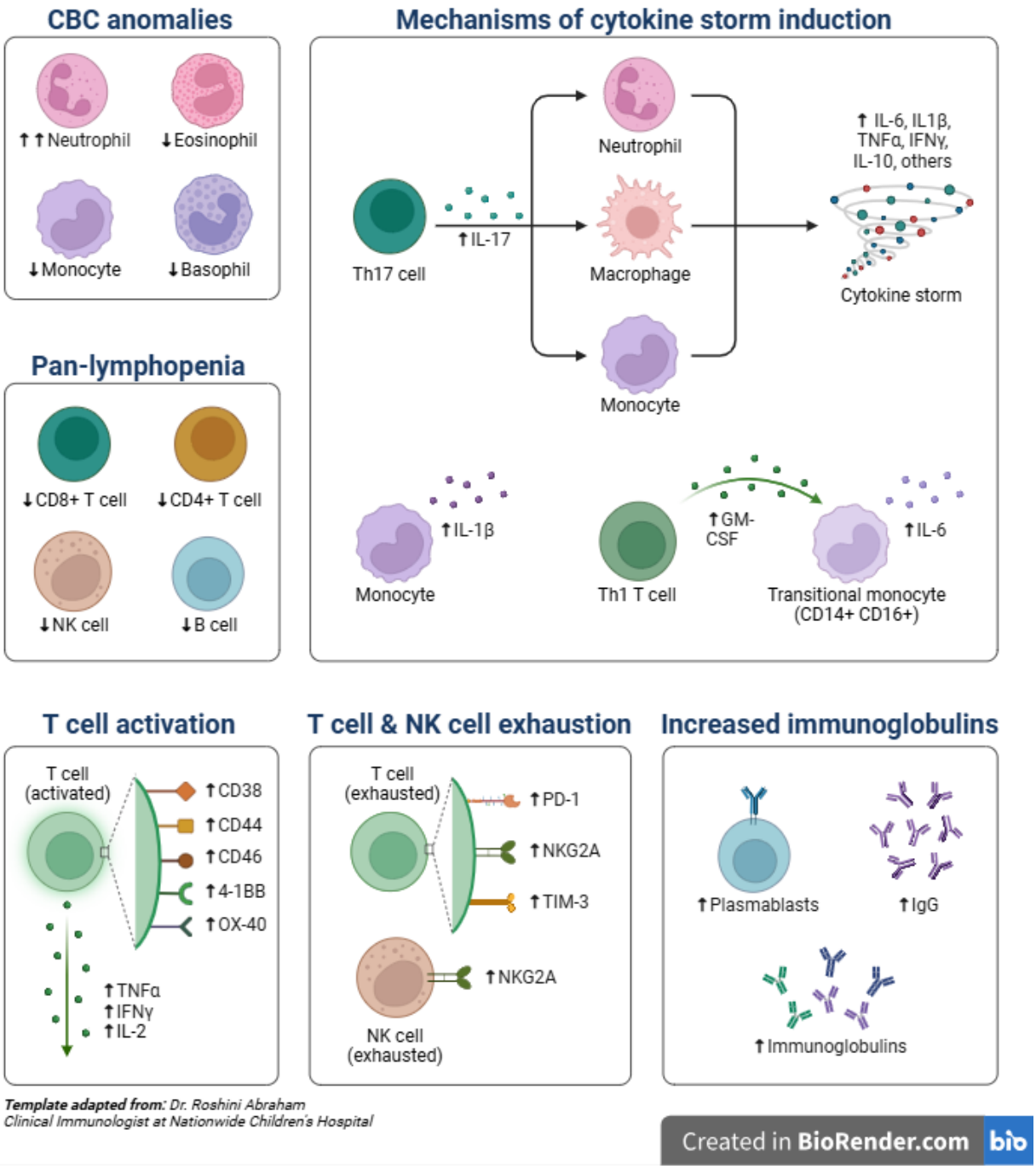

Figure 3: Immune mechanisms affected by coronavirus

2. Endocrine Complications

The overactivity of the immune system, particularly involving Th1/Th17 lymphocytes, may result in the release of pro-inflammatory cytokines (IL1-6, TNFα) and cytokine storms. This could lead to acute and delayed thyroid dysregulation (Caron et al., 2020). There were reports of abnormal thyroid function during the acute and sub-acute phases of COVID-19 infection (Ippolito, 2020). An increase in thyroperoxidase antibodies (TPO Ab) was reported in some studies after infection (Anaya et al., 2021. Lui et al., 2021). In their comprehensive review, Vamshidhar and colleagues (2023) suggested that COVID-19 may have the capacity to trigger Graves' disease in susceptible individuals by affecting the immune system. A systematic review conducted by Tutal et al. (2022) highlighted that COVID-19 might trigger and initiate autoimmune thyroid disease and exacerbate pre-existing thyroid conditions. They demonstrated that both Graves' disease and Hashimoto's thyroiditis could develop as a result of the infection. It has been observed that the likelihood of developing subacute thyroiditis is doubled within the first six months following the onset of COVID-19 (Lee et al., 2023). Additionally, an elevated risk of complications was observed beyond six months from the onset of the infection, with a higher incidence among female individuals. Aref Zade et al. (2024) have indicated that COVID-19 infection may be linked to euthyroid sick syndrome, thyroiditis, as well as clinical and subclinical hypothyroidism and hyperthyroidism. The systematic review by Rehman et al. (2021) identified a correlation between COVID-19 infection and subacute thyroiditis. They found that 71.4% of involved patients were women, and the mean days of thyroiditis symptoms onset after infection was 25.2+/-10.1.

Diabetes mellitus (DM) is recognized as a predisposing factor for severe COVID-19 illness. A potential cause is thought to be the hyperinflammatory response, as diabetic patients continuously have low-grade inflammation. Conversely, this chronic inflammation is magnified with COVID-19 infection (Azar et al., 2020). New onset diabetes cases were reported in those without a history of disease, and it was expressed that cytokine activation provokes insulin resistance and actuates hyperglycemia (Boddu et al., 2020). However, other mechanisms have been suggested, such as oxidative stress and drug side effects (Shrestha et al., 2021). Shrestha et al. (2021) conducted a systematic review to evaluate the correlation between the risk of diabetes mellitus (DM) and COVID-19 infection. Their findings suggest that COVID-19 may be linked to the new-onset DM in adults. In a meta-analysis organized by Rahmati and colleagues (2023), an increased risk of new cases of type-1 DM in children and adults was reported. Recently, Bellia et al. (2023) performed a meta-analysis and found a higher incidence of diabetes mellitus in individuals with a history of COVID-19 infection. They also noted an increased risk in those who needed hospitalization due to illness severity and those older than 60 years old. Stathi et al.'s meta-analysis (2023) announced the increased risk of type-1 DM and diabetic ketoacidosis due to immunity destroying pancreatic beta cells. According to their results, after infection, patients experienced a latency period ranging from 3 to 84 days before the onset of symptoms related to DM.

During the COVID-19 infection, some cases were reported that presented with atypic symptoms of infection; they showed symptoms of adrenal insufficiency and were diagnosed with Addison’s disease (Bhattarai et al., 2021. Beshay et al., 2022). Sanchez et al. (2022) reported a case of Addison’s disease five months after infection and suggested an autoimmune etiology for the disease. However, other mechanisms, such as adrenal hemorrhage and infarction, have been reported as causative factors in some instances of adrenal insufficiency (Elhassan et al., 2023).

3. Connective Tissue Disorders

In 2020, Ciaffi et al. (2020) conducted a comprehensive review and found that rheumatologic symptoms may be the initial sign of COVID-19 or arise during infection. According to Mudge and colleagues (2024), the time from infection diagnosis to inflammatory musculoskeletal presentations could range from 0 to 120 days.

Based on the Migliorine meta-analysis (2023), COVID-19 could provoke reactive arthritis. Chaudhry et al. (2022), reported different types of acute arthritis with a latency period of 4-14 weeks after COVID-19 presentations. Cioffi

et al. meta-analysis (2023) determined that a range of rheumatic musculoskeletal disorders, including joint pain, inflammatory arthritis, and fibromyalgia, have been frequently observed within 1-12 months following COVID-19 infection. Bouden et al. (2024) examined case reports of post-COVID arthritis and showed an incidence of 9.2% for rheumatoid arthritis. However, reactive arthritis was reported to be the most frequent form of articular involvement.

Kouranloo et al. meta-analysis (2023) assessed the relationship between COVID-19 infection and connective tissue disorders. They found that idiopathic inflammatory myositis and systemic lupus erythematosus were the most common disorders following infection, and young women were most affected. Additionally, they suggested a potential association between these two conditions. After the emergence of the coronavirus, there has been a notable increase in dermatomyositis cases. In response, Holzer and colleagues (2022) conducted a review study, revealing that COVID-19 can induce new-onset dermatomyositis by activating the interferon pathway of inflammation.

Different types of vasculitis have been described as complications of COVID-19 infection. Wong et al. (2022), in their systematic review, examined various types of rash and found a man-to-woman ratio of 4:5. Giryes et al. (2022) assessed cases of large vessel vasculitis as well as medium and small vessel vasculitis presenting during or following infection. They stated there is a low risk for these types of complications. Immunoglobulin A vasculitis, a condition more prevalent in pediatric patients, has shown an increased incidence among adults with COVID-19 infection, as indicated by a meta-analysis conducted by Messova and colleagues (2022). The analysis revealed a higher prevalence of renal involvement and a male predominance. Additionally, the time lapse between the onset of infection and vasculitis presentations ranged from 2 to 120 days.

Regarding inflammatory conditions in the pediatric population, Sharma et al. (2022) examined Kawasaki syndrome and multisystem inflammatory syndrome case reports. They estimated a pooled prevalence of 29%. Batu et al. (2022) assessed COVID-19 related vasculitis in children. They found a median age of 13 and a male-female ratio of 2:3, with a latency period of 2-120 days after infection. The IgA vasculitis was shown to be more common, and the skin was the most affected organ. However, the overall risk for vasculitis complications was low. Sachdeva et al. meta-analysis (2022) expressed an incidence of 32% neurological involvement in multisystem inflammatory syndrome in pediatrics.

Respecting systemic lupus erythematosus (SLE), the Kouranloo review (2023) reported a female predominance and found 50% of renal involvement. Based on the data from Assar et al.'s review article (2022), the mean time between lupus presentations and infection was 24.86 (13-60 days). Renal and pulmonary involvement were more common. All cases tested positive for antinuclear antibody (ANA), and the second most common autoantibody reported was anti-double-stranded DNA (anti-ds DNA). In the study conducted by Lupu et al. (2023), cases of SLE in the pediatric population were documented. Most occurrences were observed in children between 11 and 13, and symptoms of SLE typically appeared within two months following infection.

Fineschi et al. (2021), Carroll et al. (2023), and Zou et al. (2024), outlined cases of scleroderma following infection. Zou et al. found a 1:3 male-female ratio after COVID-19 infection. According to the Carroll report, the latency period was about two weeks. In their review article, Aram and colleagues (2021) provided examples of scleroderma flare-ups. Interestingly, Yu et al. (2023) reported a case of a known scleroderma who progressively developed Sjogren's disease following COVID-19 infection.

4. Dermatologic Diseases

Lim et al. (2023) reported that about 60% of the included infected population presented with skin conditions. Regarding evaluating complications of COVID-19, Igbal et al. (2023) conducted a meta-analysis and expressed a prevalence of 25% dermatologic complications. There have been reported cases of new-onset vitiligo following coronavirus infection (Herzum et al., 2022. Kasmikha et al., 2023. Vigilizzo et al., 2023). Symptoms of vitiligo have been noticed to appear 7-10 days following a COVID-19 infection (Kasmikha et al., 2023).

Janodia and colleagues (2022) documented instances of guttate psoriasis emerging for the first time following a COVID-19 infection, and they introduced certain cases of psoriasis flare-up after infection. Additionally, Dadras (2021) reported a case of pustular psoriasis following the infection with a latency period of 26 days. In their systematic review, Aram et al. (2021) examined case reports detailing dermatological complications associated with COVID-19. Their findings indicate that psoriasis and alopecia areata were the most predominant presentations.

Reports of simultaneous COVID-19 infection and dermatomyositis have been documented (Borges et al., 2021). However, Albakri et al. (2022) reported dermatomyositis flare-up symptoms six weeks after the infection. New cases of dermatomyositis following infection were reported by Hadis and colleagues (2022) and Hozler et al (2022). The patient introduced by Hadis had a latent period of two months after infection. Ortega et al. (2021) documented a new case of dermatomyositis in an 11-year-old girl four months following the coronavirus infection.

In their report, Kim et al. (2023) presented a case of pemphigus vulgaris occurring concurrently with infection symptoms. After contracting COVID-19, there have been new instances of pemphigus vulgaris, with a latency period ranging between 14 and 40 days (Medeiros et al. 2021. Zou et al. 2022. Pastukhova et al. 2024). Additionally, Xie et al. (2023) reported a case of pemphigus foliaceus after the infection presentations. In their review article, Aram et al. (2021) presented a case of pemphigus vulgaris, though the patient tested positive during hospitalization for bullous lesions and stated to have simultaneous conditions.

Lim et al. (2023) evaluated 354527 patients with coronavirus infection and found a 1.12% prevalence of alopecia areata and 1.74% for alopecia totalis post-coronavirus infection. They also indicated a correlation between infection severity and the risk of alopecia totalis. Christensen et al. (2022) investigated the association between coronavirus and alopecia areata. They concluded that alopecia could be a dermatologic coronavirus manifestation or appear 1-2 months after the infection. Additionally, Nguyen et al. (2022) mentioned that the common forms of alopecia associated with COVID-19 are androgenic alopecia, telogen effluvium, and alopecia areata.

5. Hematologic Diseases

In their review, Yazdanpanah et al. (2022) reported cases of autoimmune hemolytic anemia and immune thrombocytopenic purpura (ITP) following COVID-19 infection. Alharbi's meta-analysis (2022) found that ITP associated with coronavirus infection was more prevalent among male and older patients (mean: 59.5± 19), and the mean latency period was 18.1± 21.9 and up to 125 days.

A systematic review by Jacobs et al. (2022) on hemolytic complications associated with infection revealed a slight male predominance. The onset of hemolysis occurred within 0-20 days from the initial onset of infection (median time of 7 days).

Taherianfard et al. (2021) reviewed cases of infected patients who have developed hematologic conditions. According to their results, ITP was the most common disorder. Ono et al. (2024) investigated cases of ITP after COVID-19 infection. The findings revealed that the median age of affected individuals was 61 years, with 12% of cases occurring in pediatric patients. Moreover, over half of the patients presented with moderate to severe symptoms. Additionally, thrombotic thrombocytopenic purpura (TTP) patients have been described following COVID-19 infection (Tehrani et al., 2021. Mushtaq et al., 2023). The Chaudhary review (2022) found that 72% of TTP cases were in females. The mean age was 48.2 years. The average time from COVID-19 symptoms to hematologic presentations was ten days, and 27.3% of cases exhibited neurological symptoms.

6. Gastrointestinal and Hepatic Diseases

Cases of ulcerative colitis (UC) have been presented after COVID-19 infection (Aydin et al., 2021. Taxonera et al., 2021. Elbadry et al., 2022. Kartsoli et al., 2022). Senthamizhselvan (2021) and Tursi (2022) reported Crohn's

disease triggered by a coronavirus infection. Additionally, Kim et al. (2023) presented cases of pediatric patients with inflammatory bowel disease (IBD) following infection.

During their cohort investigation, Hileman and colleagues (2024) assessed the risk of new IBD among 3,908,592 individuals after contracting COVID-19. They found an adjusted risk ratio of 0.84 for Crohn's disease and 1.25 for UC. According to the cohort study by Syed et al. (2023), there was evidence to suggest that COVID-19 infection might act as a trigger for the onset of IBD. Inokuchi et al. cohort study (2024) expressed a notable risk for autoimmune diseases, such as IBD conditions, which remained significantly elevated even after 56 weeks from the infection onset.

By running an observational study, Cakir et al. (2022) stated the increased frequency of celiac disease in pediatrics during the pandemic in Turkey. Interestingly, Mostafavi et al. (2023) described a new case of celiac in combination with autoimmune hepatitis three months after COVID-19 presentations in a 13-year-old female individual. However, Lexner et al. (2023) did not find any increase in the prevalence of celiac disease in their retrospective observational study in Sweden.

Cases of autoimmune hepatitis have been outlined following COVID-19 infection (Kabacam et al., 2021. Durazo et al., 2022. Volchkova et al., 2022. Martini et al., 2023). Balraj (2021) and Cunha-Silva (2023) documented instances of overlap syndrome involving autoimmune hepatitis and primary biliary cholangitis in a patient who had previously experienced symptoms of infection. The patient in Balraj's case had a latency period of approximately one month.

7. Neurologic Disorders

It has been proposed that the coronavirus may affect the nervous system through various mechanisms. The virus could enter the brain through the bloodstream and immune cells. Also, it can reach the brain through the olfactory, vagus, and trigeminal nerves. Additionally, it could disrupt the blood-brain barrier (Kempuraj et al., 2024). During the initial stage of an infection, the nervous system can be impacted by a lack of oxygen, inflammatory response, and hypercoagulable state, leading to conditions such as acute encephalopathy, encephalitis, cerebrovascular disease, and Guillain-Barre syndrome (Bridwell et al. 2020. Lodigiani et al., 2020. Poyiadji et al., 2020. Sedaghat et al., 2020). Some authors found that approximately 36% of their infected patients presented with neurological symptoms. These findings were more prevalent in severe cases of infection. They also revealed a potential relationship between anosmia or dysgeusia and neurological findings (Mao et al., 2020). According to Li et al. (2023), encephalopathies and stroke are cited as the most frequent complications of COVID-19. Luo et al. (2022) reported an approximate 2.0% risk of ischemic strokes in infected patients in their meta-analysis. Hippisley et al.'s (2021) examination of 12 million UK patients revealed an elevated susceptibility to arterial and venous thromboembolism, as well as an increased likelihood of stroke and cerebral venous sinus thrombosis.

Delayed complications such as headaches, brain fog, and mood disorders have been diagnosed, and the incidence of these symptoms does not correlate with the severity of the acute infection (Dangayach et al., 2022). Other neurologic issues, like sleep disorders and dizziness, have been reported (Pinzon et al., 2022). Based on the meta-analysis by Yassin et al. (2021), neurological sequelae have been reported at a rate of 2.5%. On the other hand, neurological sequels have been reported in pediatric-infected individuals. Antoon et al. (2022) revealed a frequency of 7.0% of neurological complications in this group. In the upcoming chapters, we will assess the typical neurological complications associated with COVID-19 as well as autoimmune nervous system complications.

7.1. Neuropathic Pain

Burakzagi et al. (2022) reported cases of neuropathic pain as a presentation of long COVID-19. In an observational cohort, Odozor and colleagues (2022) found a higher risk of peripheral neuropathy within three months post-infection. Montes et al. (2022) follow-up of 77 hospitalized patients for a mean of six months after discharge showed a prevalence of 25% neuropathic pain disorders in their study population. Joshi et al. (2022) conducted a

meta-analysis assessing reported cases of neuropathic pain. They discovered that the onset of symptoms could be from 15 days before to 45 days after respiratory symptoms. Stefano and colleagues (2023), in their meta-analysis, reported a frequency of 0.4%-25% with a pooled estimate of 10% for neuropathic pain after COVID-19 infection. Odozor et al. (2022) conducted an observational study to evaluate the sensory complications of infection. The study revealed that these complications manifested in 1-6% of cases subsequent to a COVID-19 infection, exerting a more pronounced effect on the lower extremities.

7.2. Cognitive Impairment

By conducting a systematic review, Fanshawe et al. (2024) assessed articles regarding cognitive issues in recovered COVID-19 individuals. They found an increased risk of moderate impairment in various aspects of cognition from one month to one year after recovery. They suggested that this damage may remain over time and should be considered by healthcare workers. The results of a meta-analysis performed by Perrottelli and colleagues (2022) are surprising. They included 72 studies in their review and found generalized cognitive impairment in 31 works. According to their findings, executive functions and memory were the most affected areas. Regarding memory assessment, working memory and visuospatial were more influenced. In individuals having a single impairment, attention was the prominent affected domain. Speed processing, that is, the ability to concentrate and cognitive speed, was severely affected by coronavirus. The results of the meta-analysis of Tavares et al. (2020) suggested the likelihood of cognitive decline in mildly infected patients even six months after COVID-19. Jaiswal et al. (2019) explored that Parkinson's disease may get worse due to COVID-19 infection.

7.3. Demyelinating Complications

Schulta et al. (2021) conducted a comprehensive review of 20 reported transverse myelitis cases in 2020. They found a mean latency period of 10 days from infection onset, and the majority of cases had mild symptoms of infection. However, transverse myelitis has been reported after COVID-19 infection with different latency periods; as in Adamec et al. systematic review (2022), most cases had an intermediate (8-21 days) latency duration.

Mahmoud and colleagues (2023) evaluated 32 cases of Guillain-Barre syndrome after infection. They reported a median latency period of 11.5 days in patients. Pimentel et al. (2023) included 436 case reports of Guillain-Barre syndrome in their meta-analysis. Their investigation revealed an average latent period of 19 days. Regarding the symptoms, most cases presented with generalized weakness, and both lower and upper limb involvement was common and the facial nerve was the most common cranial nerve affected in these patients. Respecting autonomic manifestations, blood pressure abnormality was more common. Neophytou et al. (2023) performed a meta-analysis of individuals with Miller-fisher syndrome following COVID-19 infection. They found an average latency of 11 days from infection onset and neurologic symptoms, and 95% of patients complained of ophthalmoplegia, while 73% presented with the classic triad of disease.

Zelada-Rios et al. (2021) collected 30 case reports of disseminated encephalomyelitis. They found a latency period of 10-54 days after infection and neurologic presentations. The condition was not associated with the severity of respiratory symptoms, and they stated cases of affected children. Manzano et al.'s systematic review (2021) revealed higher mortality in cases of demyelinating encephalitis after COVID-19 infection. However, two-thirds of the cases in their study had severe respiratory symptoms requiring intensive care unit admission.

In 2021, some systematic reviews investigated the influence of COVID-19 on neuromyelitis optica spectrum disorders and multiple sclerosis (Aghajanian et al., 2024. Seyedmirzaei et al., 2024. No increase in relapse rates or new disease cases was found in their studies. Lotan and colleagues (2022) conducted a comprehensive review of inflammatory demyelinating diseases of the central nervous system, encompassing 67 articles. They discovered an average latency period of 11.5 days (ranging from 6 to 90 days) from the onset of infection to the development of neuromyelitis optica spectrum disorders. Indeed, the researchers identified an average latency period of 13.5 days, with a maximum duration of 180 days after COVID-19 disease. They reported a relatively low rate of demyelinating disorders in relation to the infection rate. Parsonage-Turner syndrome, an inflammatory condition of the brachial plexus, also has been reported following infection (Cornea et al., 2023).

8. Conclusion

COVID-19 has proven to be a complex condition, with acute manifestations and the potential to trigger autoimmune conditions and influence the nervous system through different mechanisms**.** Dysregulation of the immune system can result in early or late complications that impact nearly every system within the body. This might lead to the development of conditions such as diabetes, autoimmune thyroiditis, and different connective tissue disorders. Additionally, it can lead to demyelinating diseases and non-immunologic neurological conditions like neuropathic pain and cognitive decline**.** As we move forward, it is essential to acknowledge the potential for various complications in both immediate and delayed scenarios. Early recognition and timely management of these issues are essential. Further research is needed to fully comprehend the exact mechanisms of these conditions and to develop policies for prevention and treatment in affected individuals.

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Knowledge and Attitude Towards Exclusive Breastfeeding Among Lactating Mothers, Balancing Feeding and their Effect on Children's Health Status in District Area, Western Kordofan: Descriptive Cross-Sectional Study

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Abstract
Breastfeeding is important to infant health and survival in Sudan. Exclusive breastfeeding is considered an important criterion when practicing child nutrition, as infants consume only breast milk deprived of introducing any additional food or drink, not even water, and the child continues in this state for six months after birth. To effectively implement and promote breastfeeding in communities, it is necessary to understand the social and demographic factors relevant to infant feeding choices. This study examined cognitive trends regarding breastfeeding in a sample of mothers from the West Kordofan community. Methodology: About 576 housewives participated in descriptive cross-sectional study of children aged 59-60 months. The chosen structured questionnaire was used as the data collection method. The likelihood ratio with a confidence rate of 95% was also used to measure the strength of the association, and the statistical significance was determined at P-value <0:05. Result: The study showed that most of the responding mothers are aware of absolute breastfeeding. Nearly (80%) of the mothers are aware that breast milk alone is sufficient in the first six months. The research also explained that more than half of the study population (55%) have poor general knowledge, while (45%) of them have good knowledge. The analysis showed that the information of respondents from the study population has a significant relationship with the occurrence of diarrhea cases, vitamin A intake, and low birth weight. The analysis also shows the possibility of lower rates of diarrhea in children whose mothers have excellent knowledge of food and nutritional practices. [(95% CI: 0.492-0.874) p-v=0.004)]. Conclusion: Housewives' knowledge of breastfeeding has a significant relationship with the health status of children. Mothers' prior knowledge of vitamin A and its benefits contributed clearly and logically to eating foods rich in vitamins. p-v=0.000].

Keywords: Exclusive, Breast Feeding, Knowledge, Attitude, Complementary Feeding, Millennium Development

1. Introduction

Breastfeeding represents the most important and cost-effective public health policy and has a significant impact on morbidity and mortality rates in third-world countries (Leshi et al. 2016). The period of absolute breastfeeding is limited to the infant consuming breast milk only without any liquids, including water, or other solid nutrients. With the exception of oral perfusion treatment solutions or instillation, and taking vitamins and tablets (Hassen et al. 2021) According to the World Health Organization, breastfeeding is of great benefit to mothers and children alike (Kedir et al. 2020 and Lauer et al. 2019). International statistics indicate that approximately 44% of infants and newborns are breastfed in the first four months of their lives. (Zakarija-Grković et al. 2020 and Anonymous 2020). The fourth-millennium development goal is worried through reduce child death. (Ogbonna et al. 2000) Researchers believe that the absence of appropriate health facilities outside housing, inconvenience, conflicts at work, family pressure, and poor education negatively affect women's desire and interest in practicing absolute breastfeeding. (Forbes et al. 2003) Research has also shown that one of the most important obstacles to practicing breastfeeding is the professional situation. (Agunbiade and Ogunleye 2012), (Mahgoub et al. 2002) But with urbanization and urbanization, which witnessed remarkable development, in addition to the industrial revolution, more women joined the workforce in their countries. (Mundagowa et al. 2021) The World Health Organization indicated that about 40% of newborn deaths occurred in children under one month old, most of them within seven days of birth. (Osibogun et al. 2018) Sankar et al. They were able to look into a systematic study to determine the association between adequate breastfeeding practice and the mortality of children in infancy. They initiate that the hazard aspects associated with breastfeeding and infant mortality were all higher in infants who were not breastfed compared to infants who practiced exclusive breastfeeding in the first five years of their lives. In addition, the risk of infection-related deaths is twice as high in children who are not breastfed compared to those who are exclusively breastfed. Research directed by Manjapallikkunnel, explained that mothers who are of great age and have a high level of education have a clear association with sufficient knowledge of absolute breastfeeding. However, mothers who have sufficient knowledge, but we find that only approximately half of them practice absolute breastfeeding for six months. Therefore, raising the educational level of mothers and promoting correct behavior regarding exclusive breastfeeding and its benefits among girls will greatly increase its practice. (Manjapallikkunnel et al. 2023). Within the framework of promoting breastfeeding as one of the effective public health measures to reduce infant mortality, the Ascension Ministry of Health has issued measures promoting Practice breastfeeding immediately after birth and continuing it exclusively for a period of six months, then following it with complementary feeding until weaning. (Saudi Ministry of Health 2022) A new reference study in Ethiopia showed that the total practice rate of exclusive breastfeeding during the six-month period was 60.4% (Wake & Mittiku, 2021). All of the above recommendations regarding the practice of breastfeeding are consistent with the recommendations of the World Health Organization and UNICEF regarding the necessity of mothers practicing and changing their concepts regarding exclusively breastfeeding their children during the first half year of his birth and then presenting complementary diets that are appropriate and safe for the children's ages after the first six months. (UNICEF, 2018).

Successful breastfeeding can be achieved by following effective strategies that contribute to behavior change, such as education, communication, and positive communication. The core source of breastfeeding for women is always insufficient due to its dependence on family and friends. Different religious, cultural and social beliefs also have a significant impact on breastfeeding. The main goal of this research is to identify the level of knowledge and attitudes of mothers towards exclusive Brest feeding and complementary feeding, and their effect on children's health status.

2. Method

576 responding mothers who had children of breastfeeding age in the area of Al-Hattah were subjected to a cross-sectional study. This study included mothers of children born within 42 weeks and in good health, free of complications and without major birth defects. Mothers who had no desire to participate in the study were excluded. The sample was selected by calculating the proportionality rate, where 50% was calculated as the prevalence of absolute breastfeeding in previous studies, and an absolute accuracy of 5% was assumed, with a

confidence level. 95%, and the sample size was estimated at 576 after calculating it according to the aforementioned data and applying it to the equation.

The cluster method was used as a multi-stage technique to select participants in the research. It was followed to select the research community in three different stages, which included the research area as a city, then neighborhoods, and finally residential homes. Permits to conduct the research were obtained from the competent authorities represented by the Ministry of Health in the locality, then the approval of the mothers participating in the study. A structured questionnaire was used as a means of collecting data and was administered by pre-trained persons who conducted the direct interview. This questionnaire included socio-demographic characteristics and questions about the knowledge and attitudes of breastfeeding mothers towards exclusive breastfeeding. Total knowledge was calculated by summing the responses of all students in all questions after creating a composite variable. A score of zero represented incorrect answers and a score of one for correct answers. Those whose scores were equal to the average (8.2) or higher than that were considered to have good knowledge. While those whose scores were below average were considered to have poor knowledge regarding exclusive breastfeeding and complementary foods. Regarding questions related to attitudes toward breastfeeding, the Infant Feeding Behavior Scale, which consists of several items, was used as a tool used to evaluate attitudes toward breastfeeding in different cultural settings. The general attitudes of all participants were determined by calculating scores on the attitudes toward breastfeeding questions, which consist of six questions, and their overall score is the same. Participants whose scores were higher than or equal to the average score (3.04) were considered to have positive attitudes, while those who received scores below the average were considered to have negative attitudes toward absolute breastfeeding.

The data was transcribed into Excel, and the Statistical Package for the Social Sciences, version 26.0, was used. Bivariate analysis was used in the statistical analysis, and the Chi-square test was also used, $p<0.05$ was considered significant.

Participants were notified and assured that all data and information collected will be confidential and used for research purposes only, and that the results reached through this research will contribute effectively to health policies and decision-making, which will help improve the implementation of health programs in the region.

3. Results

Table 1: Demographic characteristics

Demographic characteristics	Response category	No	%
Age of mothers	≤ 25	311	40.5
	26-30 years	323	42.1
	31-35 years	67	8.7
	≥36	67	8.7
Social status	Continuous marriage	616	80.2
	separate	95	12.4
	widow	57	7.4
Mothers educational level	Illiterate	122	15.9
	Basic education	251	32.7
	Higher secondary education	246	32.0
	undergraduate	126	16.4
	post graduate	23	3.0
Mothers' occupation	farmer	166	21.6
	laborer	54	7.0
	Employee	157	20.4
	house wives	391	51.0
Monthly income	≤ 2000	474	61.7
	2001-5000 SP	233	30.3
	≥ 5000 SP	61	7.9

The sample of the present study comprised (N=349) fitted to 26-30 years' peer group. Almost semi of the contributors (51.6%) had higher education and postgraduate education. Further than half of the participants (51%) were housewives. 61.7% of participants were low-income, less than 2000 SP. The demographic features are more exposed in the Table 1.

Table 2: Familiarity of mothers towards among exclusive breast-feeding.:

Items	Results	No	%
exclusive breastfeeding	yes	644	83.9
	no	124	16.1
Breastfeeding children is sufficient for 6 months	yes	606	78.9
	no	162	21.1
What is the right time to give babies breast milk?	After taking drinks	116	15.1
	Immediately after birth	390	50.8
	After the first hour of birth	262	34.1
Breastfeeding protects from diarrhoea	yes	642	83.6
	no	35	4.6
	i do not know	91	11.8
Duration of absolute breastfeeding	≤month	106	13.8
	Three months or less	188	24.5
	From 4-6 months	277	36.1
	≥6 months	197	25.7
Knowledge of complementary foods	yes	634	82.6
	no	134	17.4
appropriate age to give complementary foods	Less than 6 months	136	17.7
	6 months	229	29.8
	more than 6 months	403	52.5
What are the benefits of foods rich in Vitamin A	yes	670	87.2
	no	33	4.3
	I do not know	65	8.5
Knowledge of iron-rich foods	yes	662	86.2
	no	106	13.8
benefit of eating foods rich in iron	yes	647	84.2
	no	51	6.6
	do not know	70	9.1

The study indicates that the level of knowledge among breastfeeding mothers is very high, as shown in Table 1, which shows that the majority of mothers (83.9%) have a high degree of knowledge about absolute breastfeeding, and 78.9% of mothers express their opinion that breast milk alone is considered sufficient for children. During the first six months of life, more than three-quarters (82.6%) of the study population of mothers were aware of the practice of complementary feeding for children. Also, most of those studied indicated that they knew the benefit of eating foods rich in vitamin A, as well as foods rich in iron.

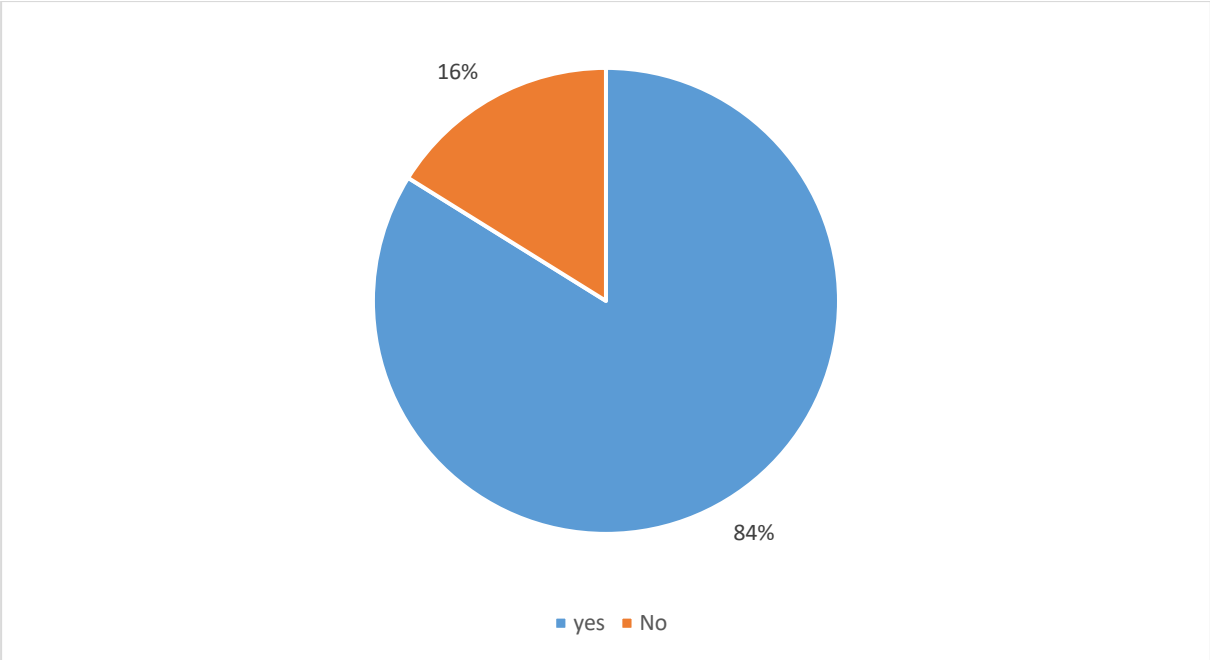

Figure 1: knowledge of mothers among breast-feeding and complementary feeding

The figure above indicates that the general knowledge level of the study participants regarding breastfeeding and complementary feeding was divided into good and poor levels. Therefore, the majority of mothers (83%) have good knowledge, while the remaining mothers (16%) have weak knowledge.

Table 2: The relationship between the level of maternal awareness and the incidence of diarrhea, vitamin intake, or low weight in newborn infants.

Variables	Response category	Knowledge		value	95% Confidence Interval		X^2	p-v
		Poor (No/ %)	Good (No/ %)		Lower	Upper		
diarrhea occurrence	Yes	211	208	.656	.492	.874	8.303	.004
	No	212	137					
vitamin A consumption	Yes	345	238	1.989	1.422	2.781	16.43	.000
	No	78	107					
low birth weight	Yes	136	145	.654	.486	.878	7.991	.005
	No	287	200					

It became clear through the analysis that the level of knowledge of the mothers participating in the study about exclusive breastfeeding has a significant relationship with the occurrence of cases of diarrhea and vitamin A intake, (p-v=0.004)]. in addition to the low weight of newborns. The analysis also explains that the probability of diarrhea occurring in children decreases as mothers' knowledge of good nutritional practices increases. Prior knowledge of vitamin A and its benefits had a clear impact on eating foods rich in vitamins in general, including vitamin A.(p-v=0.000). In addition, this health awareness has greatly contributed to reducing cases of underweight newborns. (p-v=0.005).

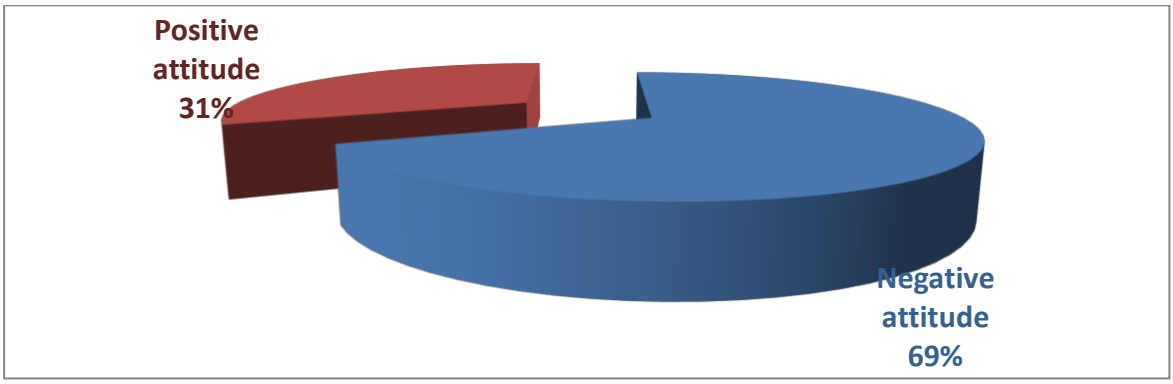

Figure 2: Attitude of mothers among absolute breast-feeding

Figure (2) The figure above explains the general attitudes of the study participants towards exclusive breastfeeding, which were classified as positive attitudes and negative attitudes. As a result, approximately two-thirds of the study population (69%) showed negative attitudes towards exclusive breastfeeding, while the remaining (31%) had positive attitudes towards exclusive breastfeeding and complementary feeding.

Table 3: The relationship between mothers' attitudes toward breastfeeding, nutritional status, level of education, and environmental factors

prevalence of malnutrition	Response category	Attitude		Total	X^2	p-v
		Negative attitude (No/ %)	Positive attitude (No/ %)			
Malnutrition	acute malnutrition	97(12.6)	92(12.0)	189(24.6)	47.82	.000
	moderate malnutrition	332(43.2)	91(11.8)	423(55.1)		
	well nourished	98(12.8)	58(7.6)	156(20.3)		
	Total	**527(68.6)**	**241(31.4)**	**768(100)**		
Maternal education	Illiterate	111(14.5)	11(1.4)	122(15.9)	44.76	.000
	primary school	172(22.4)	79(10.3)	251(32.7)		
	secondary and high school	156(20.3)	90(11.7)	246(32.0)		
	university	69(9.0)	57(7.4)	126(16.4)		
	post graduate	19(2.5)	4(0.5)	23(3.0)		
	Total	**527(68.6)**	**241(31.4)**	**768(100)**		
Hand washing	Before feeding	223(29.0)	91(11.8)	314(40.9)	8.58	.035
	before breast feeding	161(21.0)	73(9.5)	234(30.5)		
	after cleaning baby's bottom	86(11.2)	59(7.7)	145(18.9)		
	before food preparation	57(7.4)	18(2.3)	75(9.8)		
	Total	**527(68.6)**	**241(31.4)**	**768(100)**		
Disposal of human excreta	pit latrine	316(41.1)	163(21.2)	479(62.4)	12.57	.014
	improved pit latrine	173(22.5)	51(6.6)	224(29.2)		
	septic tank	17(2.2)	13(1.7)	30(3.9)		
	No facility	21(2.7)	14(1.8)	35(4.6)		
	Total	**527(68.6)**	**241(31.4)**	**768(100)**		
sources of water	deep well	228(29.7)	50(6.5)	278(36.2)	47.10	.000
	public network	205(26.7)	155(20.2)	360(46.9)		
	Rain water	55(7.2)	19(2.5)	74(9.6)		
	Surface water	39(5.1)	17(2.2)	56(7.3)		
	Total	**527(68.6)**	**241(31.4)**	**768(100)**		

The analysis explains that there is a significant and logical connection between mothers' attitudes toward exclusive breastfeeding, malnutrition, mothers' level of education, and use of clean drinking water sources. It was observed that the participants had negative attitudes about moderate malnutrition and showed a noticeable logical connection. [(p=.000, X2 = 47.82]. Moreover, it turns out that mothers who have a pre-university education level have more negative attitudes towards breastfeeding than mothers who have a university education level or above, as they showed a significant logical connection. [(p=.000, X2 = 44.76]. Mothers who practice personal hygiene, such as washing hands before feeding children and practicing exclusive breastfeeding, are likely to have positive attitudes toward breastfeeding. [(p=.035, X2 = 8.58]. Regarding the process of disposing of human waste, the study showed that there is no significant correlation. [(p=.014, X2 = 12.57]. The study showed that using a pit toilet is more likely than other methods of disposing of human waste. However, it was noted that there are logical correlations between mothers' attitudes and the use of pure drinking water sources. (p=.000, X2 = 44.76). As shown. In the table above.

4. Discussion

This study aims at understanding the level of knowledge and attitude of breastfeeding among mothers and the factors associated with good knowledge about breastfeeding. In this study, majority (84%) of participants had proper knowledge, whereas the residual 16% of them owned poor knowledge. A study directed in a comparable situation in semi-urban Nigeria, North India, likewise displays equal outcomes (71.3%) (Bhutta et al. 2018, WHO 2017 and Nigel et al. 2016) also, study conducted by Fawad in Ghana has disagreed; it shows that mother was well informed and had proper knowledge and positive attitude toward breastfeeding. Other study conducted by Garg, also agrees, which explain that moms had extremely high knowledge and neutral views on breastfeeding. (Verma et al. 2017) fitted to 26-30 years age group. Closely half of the contributors (51.6%) Their education level is higher than secondary school. More than half of the participants (51%) were house wives. 61.7% of participants were low income, less than 2000 SP. These factors are closely related to the mothers' level of knowledge. It became clear from the study that working mothers show a lack of continuity in exclusive breastfeeding compared to housewives, as they tend to continue with exclusive breastfeeding.

A comparable result was described by the result directed in the semi-urban sub-district of Adigrat, Tigrai, Ethiopia (Aude-Hélène et al. 2021) Canada (Mise et al. 2017) Sri Lanka (Anonymous 2013). Bangladesh (Mbada et al. 2013). Taiwan (Tadele et al. 2016). Goba district, Southeast Ethiopia (Jelly et al. 2022), and Northwest Ethiopia (Singh et al. 2018). The maternal employment status also effects the continuation of breastfeeding till optimal age. The results have shown that 51% lactating mothers are housewives and 49% of them are working women. The maternal education of mothers also had a huge impact on the knowledge, attitude and practices of lactating mothers towards exclusive breastfeeding. the illiteracy level of lactating mothers is 42% while 19% of mothers have intermediate level education and 39% are graduated. Similarly, a survey was conducted and published by John Elflein in 2017. (Gonah and Mutambara 2016).

The knowledge about breastfeeding is very important as if a mother has proper knowledge about breastfeeding, it will help her in the process and same goes for the attitude of a mother towards breastfeeding and the health of her child. Improved Knowledge and attitude could contribute to increasing the prevalence of exclusive breastfeeding in both working and non-working mothers (Atchibri and Dako 2017) It became clear through the analysis that the level of knowledge of the mothers participating in the study about exclusive breastfeeding has a significant relationship with the occurrence of cases of diarrhea and vitamin A intake, (p-v=0.004)]. in addition to the low weight of newborns. The analysis also explains that the probability of diarrhea occurring in children decreases as mothers' knowledge of good nutritional practices increases. Prior knowledge of vitamin A and its benefits had a clear impact on eating foods rich in vitamins in general, including vitamin A.(p-v=0.000). In addition, this health awareness has greatly contributed to reducing cases of underweight newborns. (p-v=0.005).

Concerning the attitude of mothers, the average score was 34 which displays an impartial attitude among breastfeeding. About (69%) of mothers had negative attitudes towards exclusive breast-feeding, while the remaining (31%) of the participants owned positive attitudes. This result might be due to the fact that around half of the mothers have professions that may be an obstacle to practicing breastfeeding on a regular basis, in addition

to the fact that around half of the mothers also have a weak educational level. These results agreed by Rinku Rani Das, (Ratnayake and Rowel 2018) and Marjia Sultana, (Akter and Rahman 2010). Other study disagreed with our result conducted by Chekol Abebe, et al, in north Ethiopia (Babakazo et al. 2015). Our research shows that there is a statistically significant relationship amongst the average mothers' attitude scores and malnutrition. (p=.000, X2 = 47.82). On the other hand, the study showed that mothers who had only pre-university education were more affected by negative attitudes towards absolute breastfeeding compared to those who had more than university education, as they showed a logical connection as a result of their awareness of absolute breastfeeding. [(p=.000, X2 = 44.76]. In addition, an important suggestion was detected amongst mothers' attitudes and sources of water (p=.000, X2 = 44.76).

5. Conclusion

Housewives' knowledge of breastfeeding has a significant relationship with the health status of children. Mothers' prior knowledge of vitamin A and its benefits contributed clearly and logically to eating foods rich in vitamins. p-v=0.000]. In addition, mothers' knowledge of good and beneficial nutrition in terms of nutrients, and absolute breastfeeding practices and complementary foods have clearly and effectively helped reduce cases of low birth weight. p-v=0.005].

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Preference of the Mouthwash Ingredients Wild Cosmos Leaf Extract (*Cosmos Caudatus*) among Organoleptic Test Panelists

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Abstract
Kenikir leaves are one of the traditional medicines used in Indonesia, yet only some studies investigate the compounds tested against them. This study aimed to evaluate Kenikir leaves as mouthwash with organoleptic tests and determine the differences in preferences. This type of research is quasi-experimental. The sample size is 32 people as organoleptic test panelists. The parameters were the color, smell, and taste of Kenikir leaf extract mouthwash material with original, mint, and mixed fruit flavors with a hedonic scale with ethnic groups of Jawa, Flores, Lombok, Bali, and Timor. The study results showed that regarding the color, the panelists preferred the mixed fruit color, with a $p = 0.032$ ($p < 0.05$). Regarding the smell, the panelists preferred the mixed fruit with $p = 0.019$ ($p < 0.05$). The panelists preferred the taste of mouthwash ingredients with mint flavor, but the assessment difference was insignificant at $p = 0.276$ ($p > 0.05$). Timor people like the product most. Meanwhile, the Flores ethnic group hardly likes all mouthwash products with Kenikir leaf extract. In conclusion, most preferred organoleptic test panelists of mouthwash ingredients are mouthwash ingredients with mixed fruit aroma/smell, color, and mint flavor.

Keywords: Organoleptic Test, Panelist, Mouthwash, Kenikir (*Cosmos Caudatus*)

1. Introduction

Plaque contains many bacteria, and inflammation can occur in the gingival tissue (Murakami et al., 2018). Gingivitis is caused by deposits of microbial plaque, usually in or near the gingival sulcus. Maintaining oral hygiene is of utmost importance to stop the progression of the disease. Plaque control is one of the most integral methods to control bacterial growth. Mechanical plaque control is the primary method for removing and controlling plaque, and toothbrushing plays a significant role. (Balan et al., 2018; Preethi & Ramamurthy, 2015).

About 80% of people around the globe rely on traditional medicine. As many as 170 of the 194 WHO Member States have reported using conventional medicine. Most Indonesians, especially in rural areas, also use traditional herbal medicines. Kenikir, known as the wild cosmos or *Cosmos caudatus*, is one of the vegetables Indonesians often consume. This is because the kenikir is an herbal plant that benefits human health. Research shows that Kenikir leaves extracted using ethanol and other solvents showed the presence of active compounds flavonoids, saponins, alkaloids, tannins, and polyphenols (Utami et al., 2024). Research also shows that kenikir leaves contain alkaloids, triterpenoids, phenolics, quinones, and flavonoids by phytochemical screening by methanol extract. Meanwhile, the ethanol extract contains flavonoids, saponins, phenolics, alkaloids, and quinones (Masitah et al., 2023; Phong et al., 2022).

Organoleptic testing is an evaluation that relies on the sensory perception process. This sensing process is described as a physio-psychological activity involving the awareness or recognition of an object's characteristics due to sensory stimulation from the object. Measurement of assessment using the five human senses is also called sensory assessment and is subjective. Organoleptic assessment requires a panel of people or groups to assess the quality of the product. The assessment usually takes the subjectivity of impressions (Damaziak et al., 2019; Sipos et al., 2021). People who are panel members are called panelists. Although traditional medicine has been used for a long time, it is not completely safe because it is a strange compound to the body, so it is very important to know its potential toxicity. Toxic effects on living things can be seen and may not be if the dose absorbed is relatively tiny. The damage can be limited to cells only (Aydın et al., 2016; Mihafu et al., 2020; Quintanilla-Casas et al., 2020).

This research aims to investigate the preference of panelists for the organoleptic test towards kenikir extract as a mouthwash.

2. Method

This quasi-experimental study of organoleptic testing was conducted with a post-test-only design without a control group design. The population of panelists are several Indonesian ethnic groups, namely Javanese, Flores, Lombok, Balinese, and Timorese, who lived in Denpasar City and its surroundings and came to fulfill the invitation to get an explanation before being selected as untrained panelists. The sample size in this study was 32 people, with an equal number of men and women. Samples of mouthwash extract from kenikir leaves were provided to panelists randomly, and the panelists' booth was also provided randomly.

The inclusion criteria include male or female adults aged between 20-35 years, 1) Male or female adults aged between 20-35 years, able to read and write, serious, open, and honest, healthy, and not suffering from illnesses that can influence the vision, smell, and taste. Meanwhile, the sample exclusion criteria are those who do not heed the prohibitions required during the study, are absent during the survey, resigning after completing the informed consent.

The data collection was for the color, smell, and taste of the kenikir leaf extract mouthwash using a hedonic scale with five measurement digits, namely: Strongly like (5), Like (4), Neutral/Neither Agree nor Disagree (3), Dislike (2) Strongly Dislike (1). Each panelist was given an assessment sheet in the form of a checklist.

The research was performed first by preparing kenikir leaf extract and producing it as a mouthwash. Later, the researchers looked for volunteers who were willing to be untrained panelists. Once the volunteers or the samples were obtained, an informed consent was signed. An interview was also performed with volunteers with questions and answers to determine their background and health conditions. The panelist selection stage was carried out based on intuition and rationality toward the sensitivity and knowledge of prospective panelists. Besides, the preparation of the tasting room and its completeness were also accomplished.

The collected assessment data were analyzed univariately, namely descriptive tests to determine the frequency and percentage, and then the differences in data between groups were tested using the Kruskal Wallis test.

3. Results

The results of the Kruskal-Wallis test of the panelists' organoleptic assessment of the color, smell, and taste of the mouthwash material made from kenikir leaf extract with various flavors are presented in Table 1.

Table 1: Mouthwash evaluation from the color, smell, and taste

No.	Mouthwash evaluation parameter	Flavor	n	Mean Rank	X^2	df	p-value
1.	Color	Original		42.84			
		Mint	32	44.28	6.883	2	0.032
		Mixed fruit		58.36			
2.	Smell	Original		39.17			
		Mint	32	48.89	7.931	2	0.019
		Mixed fruit		57.44			
3.	Taste	Original		45.06			
		Mint	32	54.70	2.573	2	0.276
		Mixed fruit		45.73			

Table 1 shows that the panelists most liked mixed fruit colors. The result of p-value is 0.032 ($p < 0.05$). The smell parameter got the same result that mixed fruit color dominates with a p-value of 0.019 ($p < 0.05$). Meanwhile, for the taste, the panelists prefer the mint flavor to mixed fruit and original flavors, with a p-value of 0.276 ($p > 0.05$).

Table 2: Assessment based on color with the Kruskal-Wallis test

Parameter	Flavor	Ethnic Group	n	Mean Rank	X^2	df	p-value
Color	*Original*	Jawa	6	12.83			
		Flores	6	15.50			
		Lombok	6	9.42	9.736	4	0.045
		Bali	6	22.50			
		Timor	8	21.81			
	Mint	Jawa	6	15.92			
		Flores	6	15.25			
		Lombok	6	11.33	4.048	4	0.400
		Bali	6	21.00			
		Timor	8	18.38			
	Mixed Fruit	Jawa	6	18.08			
		Flores	6	10.08			
		Lombok	6	16.00	5.696	4	0.223
		Bali	6	16.08			
		Timor	8	20.81			

Table 2 shows that the Balinese liked the original flavor color the most, with a p-value of 0.045. Meanwhile, for mint, the Balinese also liked it the most, with a p-value of 0.400. However, in the mixed fruit, Timorese liked the most compared to other ethnic groups, with a p-value of 0.223.

Table 3: Assessment based on smell with the Kruskal-Wallis test

Parameter	Flavor	Ethnic Group	n	Mean Rank	X^2	df	p-value
Smell	*Original*	Jawa	6	14.83			
		Flores	6	12.33	4.448	4	0.349
		Lombok	6	14.67			
		Bali	6	17.17			
		Timor	8	21.75			
	Mint	Jawa	6	21.00			
		Flores	6	12.50	3.195	4	0.526
		Lombok	6	15.92			
		Bali	6	15.00			
		Timor	8	17.69			
		Jawa	6	20.17			

Mixed Fruit	Flores	6	11.33	6.668	4	0.155
	Lombok	6	18.92			
	Bali	6	12.25			
	Timor	8	19.00			

Table 5 shows no significant difference in preference because the p-value is more than 0.05 i.e. 0.349, 0.526, and 0.155.

Table 4: Assessment based on taste with the Kruskal-Wallis test

Parameter	Flavor	Ethnic Group	n	Mean Rank	X^2	df	p-value
Taste	Original	Jawa	6	16.33			
		Flores	6	13.67	4.776	4	0.311
		Lombok	6	15.17			
		Bali	6	13.67			
		Timor	8	21.88			
	Mint	Jawa	6	18.00			
		Flores	6	12.33	2.376	4	0.667
		Lombok	6	15.00			
		Bali	6	17.00			
		Timor	8	19.25			
	Mixed Fruit	Jawa	6	16.83			
		Flores	6	10.00	10.850	4	0.028
		Lombok	6	14.33			
		Bali	6	13.67			
		Timor	8	24.88			

Table 4 shows no significant difference in preference between ethnic groups regarding the taste of flavored mouthwash ingredients with p-values of 0.311, 0.667, and 0.028 respectively for original, mint, and mixed fruit flavors.

Table 5: Preference of panelists in organoleptic tests of mouthwash products with various flavors

No.	Experiment	n	Mean Rank	X^2	df	p-value
1.	Color in original flavor	32	290.80	98.951	17	0.000
2.	Color in mint flavor		296.17			
3.	Color in mixed fruit flavor		366.34			
4.	Smell in original flavor		318.28			
5.	Smell in mint flavor		383.09			
6.	Smell in mixed fruit flavor		432.02			
7.	Taste in original flavor		275.09			
8.	Taste in mint flavor		334.38			
9.	Taste in mixed fruit flavor		282.11			

Table 5 shows that the most preferred mouthwash product for its smell and color is a mixed fruit and mint flavors. Meanwhile, for the taste, the panelists prefer mint and mixed fruit flavors. The difference in this assessment is significant at $p = 0.000$ ($p < 0.05$).

4. Discussion

Researchers have widely used the hedonic test to measure the product level. Six levels are used in hedonic measurement, i.e., strongly like, like, somewhat like, neutral, dislike, and strongly dislike. This test is also widely used to evaluate final products. A hedonic scale can be used to determine differences in practice. Hedonic tests require a certain number of panelists (Gusti Agung Ayu Hari Triandini & Gde Adi Suryawan Wangiyana, 2023; Zuhdi & Khairi, 2022).

The results of the descriptive test in this study showed that for the mouthwash material of kenikir leaf extract, most panelists, namely 34.4% and 53.1%, stated that they strongly liked the color of the mouthwash material, while

40.6% stated that they neutral about the color of the mouthwash material. The results show that regarding the color, the panelists prefer the mixed fruit to mint and original flavors. The difference in the evaluation indicates significance with a $p = 0.032$ ($p < 0.05$). This shows that the organoleptic test panelists preferred the color of the mouthwash material with mixed fruit flavor over other flavors.

The evaluation of the smell parameter shows that most panelists (34.38%, 46.88%, and 62.5%) said they strongly like mouthwash with original, mint, and mixed fruit flavors. Only a tiny portion, namely 3.13%, 3.13%, and 0% stated they strongly dislike the smell of the kenikir leaf extract mouthwash. The panelists' assessment of the smell of the mouthwash showed that they prefer the smell of the mouthwash with mixed fruit flavor. The difference result is significant at $p = 0.019$ ($p < 0.05$). These results indicate that the panelists preferred the smell of the mouthwash with mixed fruit flavor to the others, and this difference in preference was significant at $p < 0.05$.

A neutral evaluation was obtained when the panelists assessed the taste of the mouthwash, in detail 56.25% of respondents. However, for the mouthwash with mint and mixed fruit flavors, the majority of panelists, namely 34.38% and 31.25%, said they strongly liked the taste. The analysis shows that the organoleptic test panelists preferred the taste of the mouthwash with mint flavor, mixed fruit, and original flavors, respectively. However, the assessment difference is insignificant at $p = 0.276$ ($p > 0.05$). These results indicate that panelists prefer the mouthwash's taste with mint flavor to the others.

The results of the organoleptic assessment based on the ethnic groups' preference for the color of the original mouthwash show that the Balinese prefer the color of the original mouthwash, followed by the Timor, Flores, Java, and Lombok groups. This difference in preference is significant with a $p = 0.045$ ($p < 0.05$). In the assessment of preference for mouthwash with mint and mixed fruit flavors between the ethnic groups, there is no significant difference with a value of $p = 0.400$ and $p = 0.223$ ($p > 0.05$).

The result data on the parameter of smell present no significant difference in preference. The same results were also obtained in the preference for ethnic groups. The Kruskal-Wallis test expresses that the most preferred mouthwash product is a mouthwash with mixed fruit and mint based on smell and color.

The findings of this study indicate that the mouthwash formula made from kenikir leaf extract could serve as a herbal product in the country, aligning with the "back to nature" approach. This method allows for the incorporation of various herbal ingredients as antimicrobial agents in different cosmetic products, including mouthwash. Given that the use of herbal medicines in the world continues to increase, as well as in Indonesia, it is expected that drug manufacturers will be interested in continuing to develop herbal medicines, especially kenikir leaf extract (Ahmed et al., 2023; Chaachouay & Zidane, 2024; Rahayu et al., 2020). The results of this study describe organoleptic test panelists' preference for mouthwash products with kenikir leaf extract. The most preferred mouthwash formula is a formula with mint and mixed fruit flavors so that it can be used as a reference if this formula is to be developed into a product with economic value.

It is recommended for future research to conduct similar research with an interview with panelist regarding their habits of using other brands of mouthwash with similar flavors, such as mint and mixed fruit. This will affect the panelists' assessment of the mouthwash and toothpaste products with kenikir leaf extract because the subjective and psychological reactions of the panelists also influence the organoleptic evaluation. Several of these panelists stated that the mouthwash product, especially with the original flavor, felt sticky on the tongue and tasted bitter, so people rarely prefer it.

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Impact of Physical Activity on Reducing Blood Glucose and Insulin in Gestational Diabetes: A Meta-Analysis

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Abstract
Gestational diabetes mellitus is a pregnancy complication characterized by elevated blood glucose levels, which can affect the health of both the mother and fetus. This study aims to evaluate the impact of physical exercise on blood glucose levels in pregnant women with gestational diabetes mellitus. We reviewed studies published over the past ten years from PubMed, Cochrane, and Science Direct. Our analysis includes randomized controlled trials exploring the role of physical activity in blood glucose management among gestational diabetes mellitus patients, examining both aerobic and anaerobic exercise interventions. We extracted data on maternal characteristics, intervention details, and outcomes post-intervention. Fasting and postprandial blood glucose levels were our primary results. Diabetes mellitus is a complication during pregnancy marked by high blood glucose levels, which can impact both the mother and the unborn child. This study finds that physical exercise positively influences metabolism in women with gestational diabetes mellitus, particularly in controlling and reducing blood glucose levels. Exercise significantly affected postprandial blood glucose levels.

Keywords: Fasting Blood Glucose Level, Gestational Diabetes Mellitus, Insulin, Physical Activity, Postprandial Glucose Level

1. Introduction

The hallmark of diabetes mellitus is high blood glucose levels due to either an insulin secretion deficiency or biological dysfunction in humans (Xia et al., 2021). Diabetes complications are a significant contributor to the high mortality rates of this illness, which is third on the list of "silent killers" after cancer and cardiovascular diseases (Kodikonda & Naik, 2017). Diabetes mellitus is a multifactorial metabolic disease defined by chronic hyperglycemia and altered carbohydrate, lipid, and protein metabolism resulting from insulin production abnormalities (Beyuo et al., 2015). According to their causes, diabetes mellitus can be divided into two main categories: An immune system attack on the pancreatic islet cells' proteins causes type 1 diabetes. In addition to genetics, which can cause members of the family to have issues with insulin secretion, type 2 diabetes is also a

result of environmental factors like stress, obesity, overeating, and inactivity (Ozougwu, 2013). Another special kind of diabetes that is different from Type 1 and Type 2 is gestational diabetes (GDM). GDM frequently improves after birth, giving those affected optimism even though its symptoms and treatment approaches may be comparable. This implies that diabetes mellitus can strike anyone, including expecting moms. Although its symptoms and therapeutic strategies may be similar, GDM often improves after delivery, offering hope to those affected. This suggests that anyone, including expectant mothers, can get diabetes mellitus. (Woodside & Bradford, 2021).

Pregnancy involves normal physiological variations that lead to a pseudodiabetogenic state, marked by increased insulin resistance and decreased insulin sensitivity. This mechanism helps ensure sufficient nutrient supply to the fetus (Mottola & Artal, 2016). Consequently, the prevalence of diabetes mellitus, including Type 1, Type 2, and GDM, increases during pregnancy (Murphy et al., 2017). GDM is a common complication during pregnancy (Ming et al., 2018), characterized by elevated glucose levels exceeding the normal range during pregnancy and associated with high health risks for both mother and child (Kim et al., 2021).

With an estimated median prevalence of 12.9%, ranging from 8.4% to 24.5%, the Middle East and North Africa have the most significant prevalence of gestational diabetes mellitus (GDM) worldwide. Southeast Asia and the Western Pacific are next, with a median prevalence of 11.7%, then South and Central America (11.2%), Africa (8.9%), North America, and the Caribbean (7.0%). The lowest prevalence is in Europe, where the median incidence is 5.8% (1.8% to 22.3%) (Zhu et al., 2019).

Among the risk factors that contribute to the development of GDM include maternal age, obesity, a history of GDM, a family history of diabetes, and a previous history of macrosomia (Kouhkan et al., 2021). Even though diet and exercise are effective therapy and preventative strategies, being overweight or obese is a substantial risk factor for GDM. Numerous studies have examined how well these medications manage or prevent GDM (Chiefari et al., 2017).

Physical activity has several advantages for general well-being and is essential for maintaining a healthy lifestyle. Numerous chronic diseases can be effectively prevented and treated with exercise (Hegde, 2018). Frequent exercise is crucial for managing and maintaining metabolic syndrome, which is characterized by the co-occurrence of many risk factors for atherosclerosis. Significant factors include glucose intolerance, impaired fasting glucose, obesity, dyslipidemia, and hypertension (Ko et al., 2016). Exercise and other physical activity also have significant positive health effects on expectant mothers.

2. Methods

2.1 Research Methodology

We presented the results of our systematic review and meta-analysis following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) standards.

2.2 Search Strategy

We looked for papers published between February 2014 and February 2024 using ScienceDirect, PubMed, and the Cochrane Library. The search used a combination of the following keywords: ('activit*' OR 'exercise' OR 'physical activit*' OR 'physical exercise') AND ('pregnancy' OR 'wom*') AND ('GDM' OR 'gestational diabetes mellitus' OR 'Gestational diabetes') AND ('insulin level' OR 'postprandial blood glucose level' OR 'fasting blood glucose level'). To find further research that might have gone unnoticed, we also looked through the reference lists of pertinent publications.

2.3 Study Selection

These requirements had to be met by the included research: 1) they were randomized controlled trials (RCTs); 2) the interventions involved at least one type of exercise; and 3) participants in both the intervention and control groups were pregnant women with GDM. Publications were excluded if they: 1) were published more than 10 years ago; 2) were not in English; 3) were literature reviews, case reports, or protocols; 4) only published abstracts or conference content; or 5) did not provide specific data.

2.4 Data Extraction

Each of the three authors searched the literature and retrieved information from relevant studies. All participating writers conducted a thorough review and discussion to settle any differences in data extraction. The following information was among the extracted data: 1) study attributes (authors, year of publication, nation, sample size, and gestation period); 2) type, frequency, duration, and intensity of exercise intervention; and 3) blood glucose and insulin change outcomes (fasting, postprandial, and insulin levels). A reduction in fasting blood glucose was the primary result, with reductions in postprandial blood glucose and insulin levels being secondary results.

2.5 Risk of Bias Assessment

The Cochrane Guide for Systematic Reviews of Interventions. recommendations were adhered to during the quality assessment process. We evaluated the selected RCTs' quality using the Risk of Bias Tool version 2 (RoB2) for randomized trials, focusing on five areas: 1) bias in the process of randomization; 2) bias arising from deviations from deliberate interventions; 3) bias arising from incomplete outcome data; 4) bias in the measurement of outcomes; and 5) bias in the selection of results that were presented.

2.6 Data Synthesis

Review Manager version 5.4.1 (RevMan 5.4.1) was used for data analysis. To evaluate the total effect magnitude, a 95% CI and a mean difference (MD) were computed. For continuous outcomes such as postprandial blood glucose levels and fasting, the mean difference was provided. Heterogeneity was evaluated using Cochran's Q-statistic ($P < 0.1$), and the level of heterogeneity was quantified using the Higgins I^2 statistic. A p-value of less than 0.05 in this two-tailed test indicated statistical significance.

3. Results

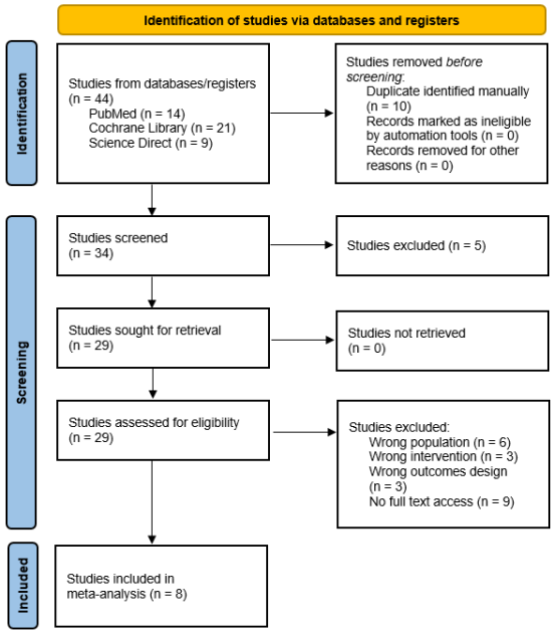
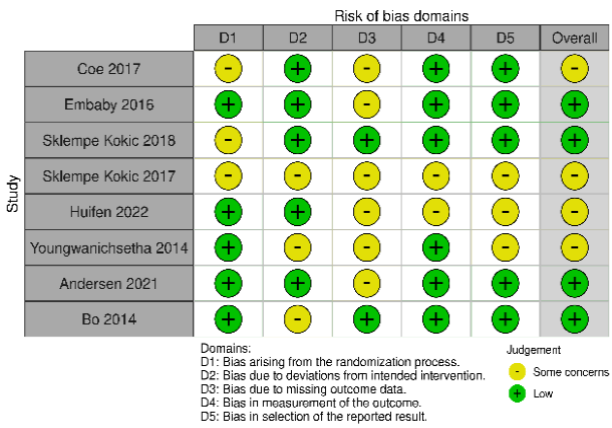


Figure 1: PRISMA Flow Diagram

Table 1: Randomized Control Trial Assessment Bias



After conducting the literature search, we identified 44 studies relevant to the topic and filtered them based on the publication date within the past ten years. As shown in Figure 1, the 44 studies were evaluated based on specific inclusion and exclusion criteria, ultimately resulting in eight studies that met the inclusion criteria (Bo et al., 2014; Dawn Coe, Scott Conger, Jo Kendrick, Bobby Howard, Dixie Thompson, David Bassett, 2017; Embaby et al., 2016; I. Sklempe Kokic et al., 2018; Iva Sklempe Kokic et al., 2018; Xie et al., 2022; Youngwanichsetha et al., 2014). Of these eight studies, two were from Croatia, while the others originated from the United States, Saudi Arabia, China, Thailand, Denmark, and Italy. The general characteristics of each included study are detailed in Table 2.

Overall, the bias assessment domains outlined in Table 1 showed that four studies had a low risk of bias (Andersen et al., 2021; Bo et al., 2014; Embaby et al., 2016; I. Sklempe Kokic et al., 2018), while the remaining four raised some concerns but were not at high risk of bias (Dawn Coe, Scott Conger, Jo Kendrick, Bobby Howard, Dixie Thompson, David Bassett, 2017; Iva Sklempe Kokic et al., 2018; Xie et al., 2022). Among the included studies, none exhibited high risk in any specific bias domain. In the randomization process domain, five studies

demonstrated a low risk of bias (Andersen et al., 2021; Bo et al., 2014; Embaby et al., 2016; Xie et al., 2022; Youngwanichsetha et al., 2014). Likewise, five studies showed low risk for deviations from intended interventions (15) (Andersen et al., 2021; Embaby et al., 2016; I. Sklempe Kokic et al., 2018; Xie et al., 2022). For missing outcome data, two studies exhibited the lowest risk of bias (Bo et al., 2014; I. Sklempe Kokic et al., 2018). In the outcome selection domain, five studies had a low risk of bias (Andersen et al., 2021; Bo et al., 2014; Dawn Coe, Scott Conger, Jo Kendrick, Bobby Howard, Dixie Thompson, David Bassett, 2017; Embaby et al., 2016; I. Sklempe Kokic et al., 2018). Finally, in the outcome measurement domain, six studies had a low risk of bias, with two studies presenting some concerns (Andersen et al., 2021; Bo et al., 2014; Dawn Coe, Scott Conger, Jo Kendrick, Bobby Howard, Dixie Thompson, David Bassett, 2017; Embaby et al., 2016; I. Sklempe Kokic et al., 2018; Youngwanichsetha et al., 2014).

The included studies encompassed 488 participants in total, 244 in the intervention groups and 248 in the control groups. One study utilized a crossover design, resulting in 14 participants in both intervention and control groups (Andersen et al., 2021).

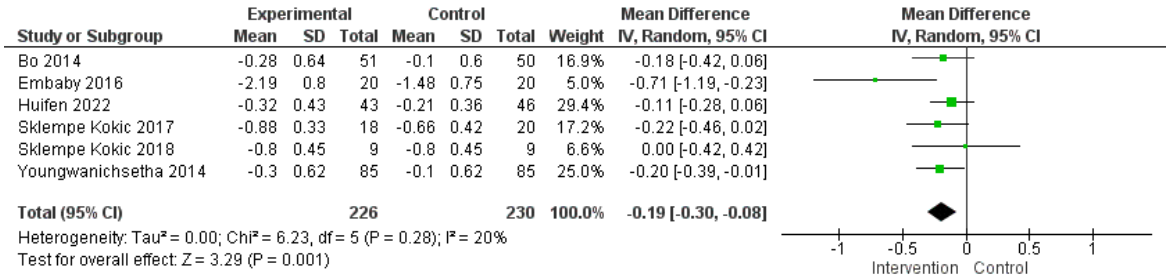


Figure 2: Meta-Analysis of Changes in Fasting Blood Glucose Levels

This review and meta-analysis were divided into subgroups to obtain more specific data based on the desired outcomes. Six of the eight studies were grouped in the first subgroup as they provided data on fasting blood glucose levels (FBG) before and after the intervention (Bo et al., 2014; Embaby et al., 2016; I. Sklempe Kokic et al., 2018; Iva Sklempe Kokic et al., 2018; Xie et al., 2022; Youngwanichsetha et al., 2014). The meta-analysis revealed a more significant reduction in FBG in the intervention group (MD = -0.19; 95% CI [-0.30, -0.08]; P=0.28; I2= 20%) (Figure 2). In this subgroup, the study by Huifen et al. (Xie et al., 2022) held the most significant weight at 29.4%, though its FBG reduction (-0.11 [-0.28, 0.06]) was not more significant than those of other studies.

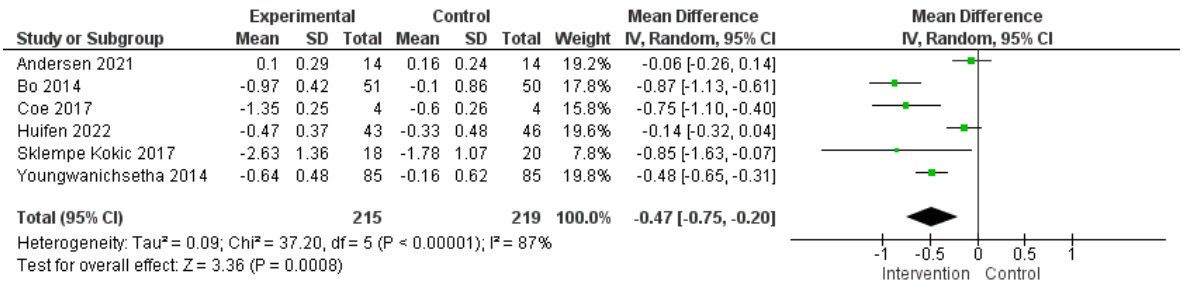


Figure 3: Meta-Analysis of Changes in Postprandial Blood Glucose Levels

The following subgroup analysis focused on the impact of exercise on changes in postprandial blood glucose levels (PPBG). Six studies provided PPBG data (Andersen et al., 2021; Bo et al., 2014; Dawn Coe et al., 2017; Iva Sklempe Kokic et al., 2018; Xie et al., 2022; Youngwanichsetha et al., 2014). The meta-analysis showed a significant reduction in PPBG, with the intervention group exhibiting a more significant decrease compared to the control group (MD = -0.47; 95% CI [-0.75, -0.20]; P < 0.00001; I2 = 87%) (Figure 3). Study weights in this subgroup ranged from 15.8% to 19.8%, with the study by Sklempe Kokic et al. (Iva Sklempe Kokic et al., 2018) in 2017 holding the most negligible weight at 7.8% yet yielding the second-largest significant reduction at -0.85 [-1.63, 0.07].

In the second half of pregnancy, skeletal muscle and adipose tissue become insulin-resistant. Given the metabolic effects of exercise, it proves to be an effective approach to preventing or managing GDM (Hamidreza Sheikhi, Mojtaba Jahromi, Alireza Sheikhi, 2017). Both aerobic exercise and resistance training, or a combination of the two, can be effective in improving fitness (Laredo-Aguilera et al., 2020). Physical activity increases glucose uptake by muscles, thereby requiring less insulin, which can help reduce PPBG (ACOG Practice Bulletins, 2018). Additionally, exercise improves insulin sensitivity by modifying adipokine parameters or lowering intermediate intramuscular lipid concentrations, such as various ceramides and diacylglycerols, which otherwise disrupt insulin signaling (Gu et al., 2022).

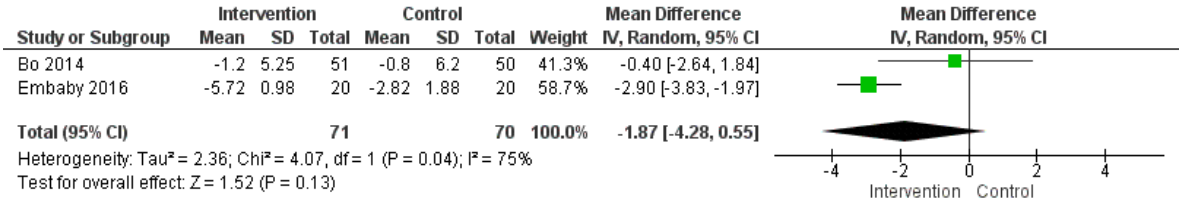


Figure 4: Meta-Analysis of Changes in Insulin Levels in the Blood

The final subgroup meta-analysis assessed the effect of exercise on insulin levels in the blood, comparing the intervention and control groups. Only two studies provided eligible data for this outcome (Bo et al., 2014; Embaby et al., 2016). Results showed a reduction in insulin usage as a metabolic function, particularly in the intervention group (MD = -1.87; 95% CI [-4.28, 0.55]; P = 0.04; I2= 75%) (Figure 4). Of the two studies, Embaby et al. (Embaby et al., 2016) had the largest weight at 58.7% and reported a change of -2.90 [-3.83, -1.97], which had a substantial impact on the overall results.

Table 2: Data Extraction

Author, Year	Country	Subject			Description of Intervention					Results
		Total		Pregnancy Duration (Weeks)	Intervention Type	Interval	Duration (minutes /day)	Frequency (days /weeks)	Intensity	
		Intervention	Control							
Anderson et al., 2021	Denmark	14	14	30.5–33.1	Interval walking after meals	4 days	3 x 20	4	Moderate	Postprandial interval walking effectively controls postprandial blood glucose
Bo et al., 2014	Italy	51	50	24-26	Brisk walking	Up to 38 weeks of gestation	20	7	Moderate	Exercise can reduce postprandial blood glucose but is not significant for fasting blood glucose
Coe et al., 2017	United States	4	4	24-35	Walking on a treadmill	Once	30	1	Moderate	The reduction in postprandial blood glucose levels is greater in the intervention group
Embaby et al., 2016	Saudi Arabia	20	20	20-24	Walking on a treadmill	Up to 37 weeks of gestation	45	3	Moderate	Fasting blood glucose levels decreased significantly in the intervention group

Huifen et al., 2022	China	46	46	24-31	Resistance training	Up to 37 weeks of gestation	50-60	3	Moderate	After the exercise period, blood glucose levels in the intervention group were lower than in the control group
Skelmpe Kokic et al., 2017	Croasia	20	20	≤30	Resistance, aerobic, and stretching exercises	6 weeks	50-55	2	Moderate	Postprandial blood glucose in the intervention group was lower, while the difference in fasting blood glucose was not significant
Skelmpe Kokic et al., 2018	Croasia	9	9	Not stated	Resistance, aerobic, and stretching exercises	Up to 36 weeks of gestation	50-55	2	Moderate	There was a reduction in blood glucose levels in both groups with a less significant difference
Youngwan ichsetha et al., 2014	Thailand	85	85	24-30	Yoga exercises	8 weeks	15-20	5	Mild	The intervention group showed a significant reduction in both fasting and postprandial blood glucose levels

4. Discussion

These findings are consistent with several studies indicating that women who tend to be less active at the beginning of pregnancy may increase their risk of developing gestational diabetes mellitus (GDM) (do Nascimento et al., 2019). Research in China also showed that increased physical activity during pregnancy is associated with a reduced risk of GDM, whereas a sedentary lifestyle is associated with an increased risk of GDM among pregnant women (Leng et al., 2016).

For more than a decade, healthcare professionals have focused on exercise for overweight/obese women during pregnancy in relation to GDM, although a substantial proportion of women with GDM have a normal pre-pregnancy BMI (Ming et al., 2018). Moderate-intensity physical activity can lower fasting blood glucose levels in mothers with GDM and is recommended as part of the treatment plan for GDM patients. Common activities such as walking for 10-15 minutes are also recommended to control fasting blood glucose (ACOG Practice Bulletins, 2018).

Exercise may influence adipokine profiles by increasing adiponectin, a protein that enhances cellular sensitivity to insulin (Wang et al., 2016). It also raises the expression of GLUT4, a glucose transporter that moves glucose from the bloodstream into cells, lowering blood glucose and reducing insulin resistance, thus alleviating pancreatic strain on the mother. Additionally, exercise boosts antioxidant levels, countering oxidative stress, a contributor to GDM, and decreases inflammatory markers linked to insulin resistance, potentially reducing GDM risk by decreasing maternal insulin resistance (Wang et al., 2016).

Based on data extraction results, the study by Youngwanichsetha et al. (Youngwanichsetha et al., 2014), with the highest sample size of 85 participants in both groups, showed significant reductions in FBG and PPBG. This study's intervention involved exercise sessions of 15–20 minutes, five times a week, over eight weeks, resulting in a longer intervention period than other studies. Conversely, Bo et al. (Bo et al., 2014) provided a 20-minute daily exercise session until 38 weeks of gestation. Although this study showed a significant reduction in PPBG in the intervention group, the FBG reduction was less pronounced.

5. Conclusion

This study demonstrates that pregnant women with gestational diabetes mellitus (GDM) can engage in light to moderate-intensity physical exercise, including resistance training, aerobic exercises, or yoga. Physical exercise positively influences metabolism in women with GDM, particularly in controlling and reducing blood glucose levels. Exercise significantly affected postprandial blood glucose levels (PPBG) compared to fasting blood glucose levels (FBG). Additionally, it may help regulate insulin levels, further supporting glucose control.

Moderate-intensity exercises, such as walking, and low-intensity activities like yoga, yielded notable benefits. Exercises that do not strain the mother excessively and promote relaxation are well-suited for managing blood glucose levels. An essential factor in exercising for pregnant women with GDM is to engage in regular, well-measured activity under supervision to ensure both safety and effectiveness.

Author Contributions: Conceptualization, F.A., D.A.R.D., G.B.N.K.T.S., and A.K.M.; Methodology, F.A., D.A.R.D.; Software, G.B.N.K.T.S., and A.K.M.; Validation, F.A., G.B.N.K.T.S., and A.K.M..; Formal Analysis, F.A., G.B.N.K.T.S., and A.K.M.; Resources, F.A., G.B.N.K.T.S., and A.K.M.; Data Curation, F.A., G.B.N.K.T.S., and A.K.M.; Writing – Original Draft Preparation, F.A., G.B.N.K.T.S., and A.K.M.; Writing – Review & Editing, R.S., D.A.R.D.; Visualization, A.A., F.U., and A.R.; Supervision, D.A.R.D., L.I.T.W.; Project Administration, R.S., A.A.

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The Effectiveness of Wolbachia Deployment as a Dengue Control Method: A Systematic Review

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Abstract
As a neglected tropical disease, dengue significantly impacts global health. World Health Organization data shows that approximately 390 million people are infected with the dengue virus each year, with 96 million cases manifesting clinically. Various innovations have been pursued to control dengue virus infections, one of which is the use of *Wolbachia*, a bacterium with high potential to address this issue. *Wolbachia* can reduce and even halt dengue virus transmission by mosquitoes by inhibiting the virus's development and replication within the *Aedes aegypti* mosquito. This study explores the effectiveness of *Wolbachia* in reducing dengue incidence across different regions. The method used in this study follows the PRISMA guidelines. Data sources include PubMed, ScienceDirect, and Cochrane, yielding 585 studies screened and narrowed down to four studies meeting inclusion criteria: one study in Malaysia, one in Brazil, and two in Yogyakarta, Indonesia. Each study's risk of bias was assessed using RoB2 and ROBINS-I according to its methodology. Success rates were evaluated based on the prevalence of *Wolbachia*-infected mosquitoes and the reduction in dengue incidence over a defined period. The results show that *Wolbachia* prevalence can reach 100%, with the highest reduction in dengue incidence reaching up to 77%. This outcome indicates that *Wolbachia* is an effective tool for controlling dengue.

Keywords: *Aedes Aegypti*, Control, Dengue, Neglected Tropical Diseases, *Wolbachia*

1. Introduction

Neglected Tropical Diseases (NTDs) comprise a diverse group of 20 diseases that disproportionately affect impoverished populations, particularly in tropical and subtropical regions (Montresor, 2023). These diseases thrive in areas with inadequate sanitation, limited access to clean water and healthcare, and environments where people live close to animals and vectors of infectious diseases, such as remote rural areas, informal settlements, or conflict zones (Engels & Zhou, 2020). NTDs impose substantial social and economic burdens, impacting over one billion

people worldwide and resulting in more than 200,000 deaths per year from snake bites, rabies, and dengue (Montresor, 2023). Addressing NTDs is critical to obtaining universal health coverage. The global response to NTDs aims to support impoverished populations and address their health and economic challenges (Engels & Zhou, 2020).

As previously mentioned, dengue is classified as one of the NTDs. It is an acute viral infection transmitted between humans by the *Aedes aegypti* mosquito. The role of environmental factors in dengue transmission, such as temperature, rainfall, and seasonal variations, cannot be overstated. These factors significantly impact the presence of the *Aedes aegypti* mosquito (Cattarino et al., 2020). Dengue is the most common human arbovirus infection, with an estimated 105 million infections globally each year, of which 51 million are symptomatic (Asish et al., 2023). According to WHO, there are approximately 390 million dengue virus infections annually, with 96 million clinical cases, and about 3.9 billion people are at risk. Dengue is now endemic in over 100 countries in WHO regions, including Africa, America, Eastern Mediterranean, Southeast Asia, and Western Pacific.

The current strategy for controlling dengue infection focuses on reducing adult and immature mosquito populations by using insecticides and educating the public on how to remove breeding grounds. Maintaining low mosquito populations is still challenging despite massive resource efforts, which results in recurring seasonal outbreaks (Pinto et al., 2021). Therefore, research and health innovations are necessary to help reduce and control these dengue outbreaks.

Several studies have been conducted to innovate dengue outbreak control. Research has demonstrated that *Aedes aegypti* mosquitoes infected with *Wolbachia* have a lower potential for transmitting human arboviruses such as dengue, Zika, and chikungunya (Tantowijoyo et al., 2020). *Wolbachia* represents a recent innovation aimed at curbing the spread of dengue within communities. In recent years, *Wolbachia* has become a primary focus of research efforts to mitigate mosquito-borne outbreaks (Caragata et al., 2021).

Wolbachia is a type of bacterium commonly found in insects (Asri Nuraeni, 2020). It is an intracellular endosymbiotic bacterium, naturally present in around 60% of insect species, including several mosquitoes (Dorigatti et al., 2018). *Wolbachia* can inhabit various tissues within its host, including the ovaries and testes, allowing it to be maternally inherited. This bacterium is under continuous study to assess its success and effectiveness in controlling infectious diseases, often spread by arthropods like mosquitoes. *Wolbachia* is an obligate endosymbiotic bacterium that cannot survive outside its host cells and is transmitted vertically through the female (Li & Liu, 2021). *Wolbachia* from *Drosophila melanogaster* has been successfully isolated into the eggs of *Aedes aegypti* mosquitoes, where it establishes a stable symbiosis and is passed on to subsequent generations. *Wolbachia* does not genetically modify mosquitoes, meaning *Aedes aegypti* is not genetically engineered. Research shows that *Wolbachia* inhibits the development and replication of the dengue virus, reducing transmission, with some programs reporting an 86% reduction in dengue spread (Suwantika et al., 2020).

2. Methods

2.1 Guidelines

This systematic review was conducted following the PRISMA guidelines specifically designed for systematic reviews and meta-analyses. PRISMA offers a framework that aids researchers in achieving accurate and reliable data selection for systematic reviews. This systematic review developed a pertinent scientific question using the established guidelines.

2.2 Formulating the Scientific Question

The scientific question for this systematic review was developed using the PICO framework (Population, Intervention, Comparison, Outcome). PICO is a tool that assists researchers in constructing a suitable scientific question based on three core concepts: population or problem, intervention, comparison, and outcome. In this

review, the three primary aspects considered are humans (population), *Wolbachia* (intervention), and dengue (outcome).

2.3 Systematic Search Strategy

The systematic search involved three main steps: identification, screening, and inclusion (Figure 1).

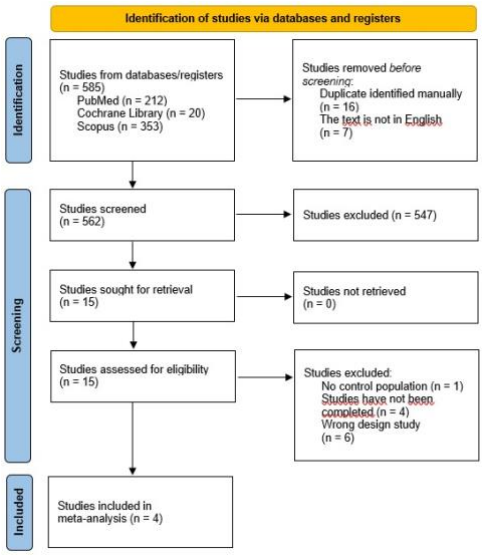

Figure 1: PRISMA Flow Chart

2.4 Identification

The identification process included searching for synonyms, medical subject headings (MeSH), and related terms within the categories of humans, *Wolbachia*, and dengue. Databases used included PubMed, Scopus, and Cochrane. This search yielded a total of 585 articles, with 16 duplicates and 7 non-English articles removed, leaving 562 articles.

2.5 Screening

The screening was conducted for the remaining 562 articles by categorizing them from each database. Articles that were journal articles, written in English, and contained both qualitative and quantitative data were required to meet the Inclusion criteria. Systematic reviews and articles with inconsistent findings were excluded. This process excluded 547 articles, leaving 15 suitable articles. Further manual screening was conducted to assess intervention results, excluding studies without a control population, incomplete studies, and those with incompatible study designs, ultimately resulting in 4 eligible studies.

2.6 Data Extraction

Data extraction involved detailed analysis of each study's abstract, methodology, and results. Extracted data were then organized into a data extraction table for analysis, identifying patterns within the data available.

3. Results

Of the four included studies, one was a cluster-randomized trial (Utarini et al., 2021), and the other three were quasi-experimental trials (Anders et al., 2020; Nazni et al., 2019; Pinto et al., 2021). Two studies were conducted in Indonesia (Anders et al., 2020; Utarini et al., 2021), one in Brazil (Pinto et al., 2021), and one in Malaysia (Nazni et al., 2019). The methods for disseminating *Wolbachia* differed, with two studies using mosquito eggs (Anders et al., 2020; Utarini et al., 2021) and two using adult mosquitoes directly (Nazni et al., 2019; Pinto et al.,

2021). All studies showed a reduction in dengue cases, but the percentage decrease varied, ranging from 40.3% to 77%.

Table 1: Data Extraction Results from Four Studies

No	Author	Location (Year)	Method	Release Zone	*Wolbachia* Deployment Technique	*Wolbachia* Prevalence	Results
1	(Utarini A, Indriani C, Ahmad RA, Tantowijoyo W, Arguni E, 2021)	Yogyakarta, Indonesia (2021)	Cluster Randomized Trial	There were 12 intervention clusters where *Aedes aegypti* mosquitoes infected with wMel were released, and 12 control clusters with no releases, covering a total area of 26 km² and a population of 311,700.	Mosquito eggs were placed in intervention clusters from March to December 2017, with each cluster receiving between 9 and 14 deployment cycles.	The average monthly prevalence of wMel per cluster was 95.8% over a 27-month clinical survey period.	Dengue incidence reduced by 77%.
2	(Nazni et al., 2019)	Kuala Lumpur, Malaysia (2019)	Quasi-Experimental Trial	Release of *Wolbachia*-carrying *Aedes aegypti* was conducted in 6 locations across Kuala Lumpur with high endemic dengue transmission.	Mosquitoes were released weekly in the morning across pre-defined grids, with *Wolbachia* frequency monitored approximately 4 weeks post-release.	After releases ended, *Wolbachia* frequency remained stable and high: 98% at Mentari Court and 95% in other areas.	A 40.3% reduction in dengue cases across all intervention areas.
3	(Pinto et al., 2021)	Brazil (2021)	Quasi-Experimental Trial	Release took place in four zones with a total area of 83 km² and a population of 373,000.	*Wolbachia*-infected adult mosquitoes were deployed weekly over 40 km² for 35 months, from February 2017 to December 2019, using mobile vehicles.	Weekly screenings of a minimum sample of 168 mosquitoes showed a wMel prevalence of 100% every week except for 3 screenings, with prevalence never dropping below 97%.	Dengue incidence reduced by 69% with *Wolbachia* intervention .
4	(Anders et al., 2020)	Yogyakarta, Indonesia (2022)	Quasi-Experimental Trial	Intervention area covering 5 km² with an adjacent population of 65,000, and a 3 km² area with a population of 34,000 as the non-intervention zone.	*Wolbachia*-infected mosquito eggs were released using mosquito release containers (MRCs), which were placed outside houses, sheltered from direct sunlight and rain, from August 2016 to March 2017.	Median *Wolbachia* prevalence was 73% (range 67-92%) one week post-deployment and reached 100% (range 96-100%) two years after deployment.	Dengue incidence reduced by 73%.

4. Discussion

4.1 Methods of Deployment of Wolbachia

Based on four selected and analyzed journals, there are two main methods for disseminating *Wolbachia*. The first method involves releasing eggs of mosquitoes infected with *Wolbachia*. This process entails collecting eggs of the *Aedes aegypti* mosquito infected with *Wolbachia* and placing them in a designated intervention area. Two research journals from Yogyakarta using this method reported a prevalence of 67-95.8%. However, one of the journals indicated an increase in prevalence that could reach up to 100% (Anders et al., 2020).

The second method involves directly releasing *Aedes aegypti* mosquitoes infected with *Wolbachia* into the intervention area (Nazni et al., 2019; Pinto et al., 2021). This release can occur at several points within a container or from a moving vehicle. The prevalence in this case ranges from 95% to 100%. This demonstrates that spreading *Wolbachia* through the direct release of adult mosquitoes yields a higher prevalence more quickly than using eggs.

4.2 Data Calculation of Prevalence of Wolbachia-Infected Mosquitoes

In all included studies, *Aedes aegypti* mosquitoes carrying *Wolbachia* exhibited a high prevalence with a relatively diverse range of percentages. The monitored prevalence of *Wolbachia* after the cessation of releases will serve as a reference for controlling the spread of *Wolbachia* in the intervention areas. This prevalence can provide information on whether the mosquito distribution was carried out correctly and successfully and whether there is a need for further release of *Wolbachia* in areas with low prevalence.

This also helps determine the duration of *Wolbachia* screening in *Aedes aegypti* mosquitoes if necessary. For instance, in the second Yogyakarta study, testing was conducted weekly when *Wolbachia* prevalence was <80%, biweekly when ≥80%, and every four weeks when ≥90%. The study showed rapid *Wolbachia* establishment in the intervention area, with continuous increases in infected *Aedes aegypti* prevalence during the first-year post-release. The median *Wolbachia* prevalence was 73% (67-92%) one week after release ceased and 100% (96-100%) two years after placement. Additionally, the average monthly cluster prevalence rate of wMel was 95.8% (interquartile range, 91.5 to 97.8) over 27 months of clinical surveillance (Anders et al., 2020).

A study in Malaysia showed an increase in *Wolbachia* frequency to over 80% at all intervention sites. After the cessation of mosquito releases, the frequency of *Wolbachia* remained stable and high (98% at 12 months after releases stopped). In some areas, the frequency exceeded 95%, but fluctuations occurred over time after the cessation (Nazni et al., 2019). Screening for wMel infection was conducted weekly in the Brazil study using a minimum sample of 168 mosquitoes from the release colony, employing quantitative polymerase chain reaction (qPCR). A prevalence of wMel was found to be 100% at all screening times, except for three screening times, but the results stayed below 97% (Pinto et al., 2021).

4.3 Effectiveness of Wolbachia in Reducing Dengue Incidence

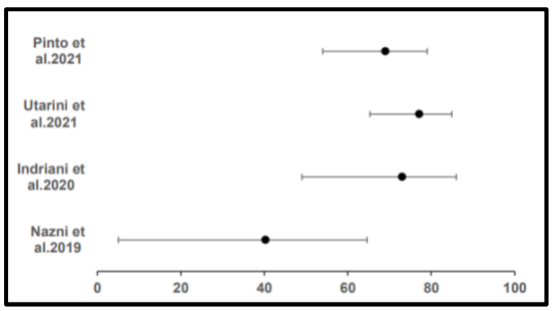

Figure 2: The reduction in dengue incidence (indicated by black dots) was assessed with 95% CI (horizontal lines)

The reduction in dengue incidence in areas with *Wolbachia*-infected mosquito releases has shown positive results. The study in Yogyakarta revealed a significant difference in dengue incidence, with only 67 cases reported among 2905 participants (2.3%) in the intervention area, compared to 318 cases among 3401 participants (9.4%) in the control area. These results indicate a protective efficacy of 77.1% (95% CI, 65.3 - 84.9) (Utarini et al., 2021). The second study in Yogyakarta showed a 73% reduction in dengue cases derived from an interrupted time series (ITS) analysis reporting monthly dengue cases from January 2006 to March 2019. Furthermore, an analysis conducted 6 months after intervention until September 2019 demonstrated an enhancement in reducing dengue incidence to 76% (Anders et al., 2020).

In Brazil, a release of *Aedes aegypti* infected with *Wolbachia* was conducted in Niterói. This area was divided into zones 1, 2, 3, 4, and a control zone. Using an Interrupted Time Series (ITS) analysis, a reduction in dengue cases was observed starting from 46% in zone 3, with the most significant reduction in zone 2 at 75.9% and an average reduction of 69.4% of cases occurring in Niterói (Pinto et al., 2021). Subsequently, a study conducted in Malaysia differed from the other areas as it utilized the wAlbB strain, while the previous three studies used the wMel strain. The results, derived from comparing dengue incidence from 2013 to 2019 in mosquito release and control areas

based on data from the Malaysian National Dengue Surveillance System, revealed a reduction in dengue incidence of 40.3% across all intervention areas using a Bayesian time series model (Nazni et al., 2019).

5. Conclusion

There are still many limitations in the studies, particularly regarding some data needing more control cases for comparison, indicating a need for further studies to ensure the accuracy of the analytical data obtained. Both methods used for disseminating *Wolbachia* in *Aedes aegypti* mosquitoes demonstrated similarly positive results. However, the direct dispersal of *Wolbachia* using adult mosquitoes can yield higher results more quickly than releasing through mosquito eggs. The *Wolbachia* prevalence observed after the cessation of releases yielded high outcomes in each intervention area without significant hindrances or disruptions. Analyses conducted on four studies across different countries found that employing *Wolbachia* as a dengue control strategy positively inhibited and reduced the spread of the dengue virus.

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Literature Reviews on Orthostatic Hypotension and Its Effect on the Quality of Life of the Elderly

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Abstract
The substantial drop in blood pressure that happens when a person moves from a seated or supine position to a standing one is known as orthostatic hypotension (OH). At least 10 mmHg in diastolic blood pressure or 20 mmHg in systolic blood pressure has been dropped. Because OH causes neurodegenerative abnormalities of the autonomic nervous system and decreased baroreceptor sensitivity, it is one of the diseases that increases morbidity and death in the aged. This decline in physical, psychological, and cognitive functions affects the quality of life of the elderly. The life quality index for person with OH and non-OH significantly differs in several aspects including physical, psychological, independence, pain, and discomfort in performing daily activities. Hence, realizing this issue, this literature review particularly aims to assess the current state and advancements in the management of OH.

Keywords: Review, Orthostatic Hypotension, Elderly, Quality of Life

1. Research Background

Orthostatic hypotension (OH) refers to the substantial drop in blood pressure that appears when a person alters position from lying or sitting to standing. This drop in blood pressure is at least 20 mmHg in systolic blood pressure or at least 10 mmHg in diastolic blood pressure (Magkas *et al.*, 2019). OH is a common health issue found in the elderly. As we age, changes in various bodily systems become more frequent. Many changes lead to a decrease in the function of various organ systems. OH is one of the many diseases that cause morbidity and mortality in the elderly (Nurullita, 2015). OH can be detected by quantify blood pressure after an individual has been in a supine position for five minutes, followed by measuring it again three minutes after moving to a standing position (Kim and Farrell, 2022).

Orthostatic hypotension is generally occur in the elderly. It is related to the reduced baroreflex response, decreased cardiac compliance, and weakness of vestibulosympathetic reflexes. The elderly who live in their own homes or with family tend to have lower rates of orthostatic hypotension, around 6%. Whereas, the elderly who live in healthcare facilities, such as nursing homes or similar facilities, have a much higher rate of OH incidence, between

54% and 68%. This could be due to various health conditions and medications commonly used in such care facilities (Freeman, 2008).

Orthostatic hypotension often becomes the cause of admission of elderly patients to hospital. Approximately a quarter of patients who come to the emergency department for fainting have orthostatic hypotension. About 36 out of every 100,000 adults require hospitalization due to orthostatic hypotension. This number can increase 233 out of every 100,000 patients over the age of 75. The hospital mortality rate from this condition is 0.9%. About 60% of hospitalized elderly patients have orthostatic hypotension. Moreover, this condition is also an indicator of the increased risk of death in patients (Palma and Kaufmann, 2017).

1.1 Etiology

The causes of orthostatic hypotension are categorized into two types: primary and secondary. Primary orthostatic hypotension is uncommon and typically results from pure autonomic failure, multiple system atrophy, Parkinson's disease, and other severe neurodegenerative diseases. Secondary orthostatic hypotension, on the other hand, is more prevalent and can be brought on by a number of contributing factors, including the usage of specific drugs, dehydration, vein buildup, heart problems, diabetes, renal failure, autoimmune diseases, and endocrine disorders. (Tzur, Izhakian and Gorelik, 2019).

There are two types of orthostatic hypotension: neurogenic and non-neurogenic. Medication use may also be a contributing factor. Autonomic nervous system instability brought on by neuropathic, neurodegenerative, or aging conditions is known as neurogenic orthostatic hypotension. Diabetes, cholinergic receptor autoantibodies, and familial dysautonomia are examples of neuropathic causes. Parkinson's disease, multiple system atrophy, and pure autonomic failure are examples of neurodegenerative factors. Conversely, a drop in blood volume brought on by dehydration frequently causes non-neurogenic orthostatic hypotension. Additionally, it is also necessary to consider orthostatic hypotension that can be triggered by the use of antihypertensive drugs, especially in polypharmacy situations in the elderly (Ringer M, 2023) (Ricci, De Caterina and Fedorowski, 2015).

Orthostatic hypotension, resulting from the use of certain medications, accounts for about 1.3% of adverse drug reactions, particularly in the elderly. This is caused by drugs that can interfere with the body's response to changes in position, for example by reducing vasoconstriction or increasing venous build-up. Elderly people are more prone to this condition due to the physical changes that occur with age, which can affect the way their body processes drugs. The elderly are also more susceptible to orthostatic hypotension due to other factors like concurrent illnesses, taking many drugs at once, and a decline in physical fitness.(Rivasi *et al.*, 2020).

1.2 Risk Factors

Atrial fibrillation 5.9%, diabetes mellitus 22%, and hypertension 60% are risk factors for orthostatic hypotension in the elderly. The prevalence of orthostatic hypotension in the elderly should receive particular attention because it may raise their risk of falling. (Ga Mudamakin, Aryana, and Suastika, 2018).

Age is the primary cause of orthostatic hypotension. At age ≥70 years, the prevalence of orthostatic hypotension rises from less than 5% in the fifth decade of life to 20%. Carotid artery disease, diabetes, Parkinson's disease, and hypertension are additional risk factors. The autonomic processes that control blood pressure may be hampered by any of these risk factors. In particular, under these circumstances, baroreflex function is reduced (Shibao and Biaggioni, 2010).

As people age, orthostatic hypotension becomes more common. In middle-aged persons, it can vary from 5 to 10%, while in those over 60, it can surpass 20%. Although the exact cause of the higher prevalence of orthostatic hypotension in the elderly is still unknown, potential causes include an increased risk of autonomic nerve disease, the use of numerous medications that exacerbate the condition, poor nutrition, deteriorating physical health, and

age-related changes in the body, such as a less-than-ideal reaction to changes in body position and nerve damage that frequently happens with aging. (Lei, Chew and Raj, 2020).

Orthostatic hypotension commonly occurs in women due to biological and physiological differences that affect the body's response to changes in position. Women tend to have smaller bodies, including a smaller heart, which can affect the heart's ability to maintain blood circulation when standing. Moreover, the lower Center Of Gravity (COG) in women causes blood accumulation in the lower part of the body, interfering with blood circulation back to the heart when standing. Responses of the autonomic nervous system in women to changes in body position also tend to be less efficient, which can lead to a rapid drop in blood pressure. Hormonal changes, such as during menopause, also have the potential to affect the body's response to blood pressure and overall heart function. These factors combined increase women's susceptibility to orthostatic hypotension when compared to men (Cheng *et al.*, 2011). Orthostatic hypotension affects around 10.7% of the elderly, and up to 30% of outpatients over 65 have the condition. Epidemiological research findings indicate that orthostatic hypotension is frequently linked to myocardial infarction, Parkinson's disease, short-lived stroke episodes, high blood pressure, and aberrant ECG readings. Conversely, the prevalence of orthostatic hypotension is only around 7% in older adults who are healthy, have normal blood pressure, and have no other risk factors.(Potocka-Plazak and Plazak, 2001).

1.3 Epidemiology

As people age, orthostatic hypotension becomes more common. Patients 65 years of age and older are more likely to have the condition, which is partially brought on by a loss in baroreceptor sensitivity. Orthostatic hypotension was identified in 5% of people aged 45–49, 15% of people aged 65–69, and over 25% of people aged 85 and older, according to two large-scale investigations carried out in the United States (Ringer M, 2023). 12.6% of Indonesians aged 40 years and above experience orthostatic hypotension (Setiati and Prodjosudjadi, 2004).

In the ARIC (Atherosclerosis Risk In Communities) study, which included a prospective cohort of 15,792 middle-aged adults between the ages of 45 and 64, it was discovered that approximately 5% of the participants had orthostatic hypotension. About 30% of people with type 1 diabetes and 25% to 30% of people with type 2 diabetes suffer with orthostatic hypotension, a prevalent symptom in diabetic patients. Up to 64% of these patients may have orthostatic hypotension when they need to be admitted to the hospital (Freeman *et al.*, 2018). The prevalence of orthostatic hypotension in adults aged 40 years and above in Indonesia reached 12.6% (Setiati and Prodjosudjadi, 2004).

The prevalence of orthostatic hypotension in the elderly in China is 0.76%, which is much lower than the rates reported in other countries. For example, a study in Malaysia showed a hypotension prevalence rate of 29.3% in community-dwelling elderly, while in Estonia, the prevalence was 11.1% in people aged 65 years and above who had orthostatic hypotension. The large difference in prevalence rates may also be due to differences in the definition of hypotension. The prevalence rate of orthostatic hypotension showed a significant difference between men and women, with women having a higher rate of 27.95% compared to men at 14.46%. This indicates a greater tendency for women to experience the condition of orthostatic hypotension compared to men. However, the correlation between gender and cognitive impairment is still debatable. This may be related to the decrease in estrogen levels in the female body after menopause (Zhu *et al.*, 2016).

1.4. Pathophysiology

Reduced blood pressure is the outcome of orthostatic hypotension, which happens when blood vessels are unable to adapt to the position change from lying to standing. This is brought on by alterations in the blood arteries and a reduction in the amount of blood that pools in the lower body. As a result, there is less blood flowing to the brain, which makes the blood vessels less effective at responding to the brain's need for more blood flow (Nurullita, 2015).

The autonomic nervous system, which helps to keep blood flowing to the heart, leg muscle contractions, and other intricate processes are all part of the body's reaction to standing. When blood pressure falls, the body's baroreceptors sense it and alert the brain to raise sympathetic nerve activity. In order to keep blood flowing to the brain, this causes vasoconstriction and an elevated heart rate. Disturbances in the autonomic nervous system prevent this compensatory mechanism in neurogenic orthostatic hypotension, which results in a prolonged reduction in cardiac output and may cause syncope and brain hypoperfusion. Orthostatic hypotension in the elderly is frequently caused by neurodegenerative diseases, including multi-system atrophy, Parkinson's disease, and Lewy body dementia. Moreover, autonomic nerve abnormalities that lead to orthostatic hypotension can also be brought on by diabetes, HIV, and a few other illnesses (Dani *et al.*, 2021).

1.5 Diagnosis

Blood pressure is measured using a blood pressure measuring device following the standard. Measurements are taken twice in a lying position and an upright sitting position. Blood pressure measurement while lying down is performed after the patient has rested for 10 minutes in a lying position. The arm is kept in a horizontal position during the measurement. When blood pressure drops by at least 20 mmHg in the systolic or at least 10 mmHg in the diastolic within three minutes of standing up from a sitting or reclining posture, orthostatic hypotension is diagnosed(Setiati and Prodjosudjadi, 2004) (Robertson, 2008).

1.6 Supporting Examination

Supporting examination to identify orthostatic hypotension involves a series of important measures. These include laboratory tests to measure blood components such as hemoglobin, electrolytes, glucose, creatinine and thyroid hormone (TSH). Cardiovascular health is assessed through electrocardiogram (ECG) recording, long-term monitoring with telemetry or Holter-ECG, as well as echocardiographic examination for visual images. Furthermore, an ECG during physical exercise is also performed. If needed, brain imaging is performed to gain a deeper understanding of the neurological condition, especially when there is a history of head trauma or neurological symptoms that need to be examined. All of these steps aim to provide a comprehensive insight into the patient's condition (Ricci, De Caterina and Fedorowski, 2015).

1.7 Management

The management approach for patients is mostly determined by the etiology. Relieving symptoms and avoiding negative health outcomes are the primary objectives of treatment. The literature indicates that, with the exception of Parkinson's disease, people who do not exhibit symptoms are usually left without specialized therapy. Due to their increased risk of falls and declining quality of life, these individuals require screening. Eliminating the cause and improving the treatment strategy are the initial steps for individuals with drug-use-related illnesses. In order to treat diseases like diabetes, hypertension, Parkinson's disease, and others, a multidisciplinary approach is frequently necessary. Patients who are dehydrated require prompt volume resuscitation. The use of abdominal belts, compression stockings on the legs, the significance of drinking enough water, monitoring salt intake, and fall prevention techniques are all necessary for patients with orthostatic hypotension brought on by neurogenic causes. Non-pharmacological methods have proven successful in treating this illness. (Ringer M, 2023).

Non-pharmacological approaches

Several non-pharmacological measures can be taken to manage orthostatic hypotension (Ringer M, 2023), including:

a. Make slow and gradual changes in body position when moving from lying to sitting, and then standing. Avoid sudden changes in position.
b. Ensure the body stays hydrated with enough fluids.
c. Avoid alcohol, hot environments, heavy meals, and hot baths that can affect blood pressure.
d. Raising the head of the bed as you sleep can help lower your risk of hypotension
e. Do an exercise program to maintain physical health.

f. After standing up, gradually strengthen the muscles of the legs and hips.
g. Use compression on the lower extremities.
h. In order to prevent hypotension, consider to using an abdominal binder

Pharmacological approaches
Pharmacological treatment is recommended after non-pharmacological interventions are deemed to have failed in reducing symptoms. Consequently, a pharmacological treatment approach becomes relevant. Fludrocortisone and midodrine remain the main options, along with other pharmacologic therapies such as pyridostigmine. Midodrine serves as an alpha-1 agonist, pyridostigmine as an acetylcholinesterase inhibitor, and fludrocortisone as an aldosterone analog. Each of these three medications increases vascular tone in a different way. The current study's findings demonstrate that midodrine is more effective than pyridostigmine at reducing symptoms. Midodrine's efficacy against other forms of orthostatic hypotension is unknown, though, and it is only advised for individuals with orthostatic hypotension brought on by autonomic dysfunction. Another option for treating orthostatic hypotension is droxidopa, though further research is needed to confirm its efficacy. (Ringer M, 2023).

1.8. Prognosis

Although frequently asymptomatic or with only mild symptoms, orthostatic hypotension increases the risk of death and the likelihood of heart attack, heart failure, stroke, and heart rhythm disorders. Heart and vascular disease may also explain why there is an increased risk of death associated with orthostatic hypotension, as it is associated with heart attacks, brief ischemic attacks, abnormalities in electrocardiogram recording, and narrowing of the carotid arteriesWhen the heart is at rest, blood passes through the left coronary artery. Consequently, when the heart is at rest, coronary blood flow may be decreased in patients with orthostatic hypotension, which could ultimately lead to poor survival chances (Ringer M, 2023). No studies have yet revealed whether treatment for orthostatic hypotension can improve the prospects of recovery. However, comorbid conditions that often occur in patients with orthostatic hypotension are realized to also increase the risk of heart problems, especially diabetes and hypertension. Therefore, it is imperative that strategies to reduce orthostatic hypotension need to be carried out with caution to avoid worsening these additional disease conditions (Wieling *et al.*, 2022).

2. Discussion

Commonly, after entering the elderly phase, an individual tends to experience a decline in cognitive and psychomotor functions. Cognitive functions include processes such as learning, perceiving, understanding, comprehending, focusing, and others, resulting in slower reactions and behavior of the elderly. Meanwhile, psychomotor functions include aspects related to movement control and coordination of actions, thus the elderly become less dexterous in their activities (Kesehatan et al., 2019).

The decline in physical, psychological and cognitive functions occurred in the elderly with OH can reduce the level of health and potentially affect their quality of life. The elderly level of health and quality of life are perceptions of well-being related to health, personal independence, status and the role of individuals in the community. Measuring the level of quality of life in the elderly can be done by evaluating the impact of medical conditions on the well-being felt by the elderly (Cheng et al., 2023). In a research conducted by Kin et al. (2020), it is also stated that the quality of life index of individuals with OH and non-OH significantly differs in the aspects of physical, psychological, independence, pain, and discomfort in carrying out daily activities (Kim et al., 2020).

In physical and psychological aspects, the elderly groups with OH and non-OH are significantly different. Influencing aspects include the presence of OH symptoms that can increase levels of anxiety and depression. The types and occurrences of orthostatic symptoms are dizziness, fatigue, memory decline, difficulty concentrating, blurred vision, vibration sensation, vertigo, pale facial skin, feelings of anxiety, increased heart rate, cold and moist skin, and nausea. When the elderly groups with OH and non-OH are compared, the elderly group with OH has quite extreme problems from these variables (Kim et al., 2020).

In previous research by Moon et al. (2016), each orthostatic symptom has a clinically significant difference.

Moreover, patients with orthostatic intolerance can experience depression and decreased quality of life that tends to be excessive, including those with minimal symptoms (Moon et al., 2016).

Patients with OH are mostly people with older age, lower education, and more comorbidities (Kim et al., 2020). As it is commonly known, older people will experience a decrease in physiological function. This decrease in physiological function will certainly affect an individual's quality of life in all aspects. Low education can also affect an individual's level of health. FCT (Fundamental Cause Theory) argues that social factors such as education are 'fundamental' causes of health and disease because they determine access to many material and non-material resources such as income, a safe environment, or a healthier lifestyle, all of which have the effect of protecting or improving health (Zajacova & Lawrence, 2018). By realizing a disease, which in this context is OH, starting from preventive, curative, and rehabilitative stages, it is expected that individuals can take care of themselves from the disease, thus they can live more prosperously in their old age. Along with the aging process, individuals will also face challenges from a number of other diseases, especially those that are degenerative such as dementia, hypertension, stroke and DM. OH itself is often associated with an increased risk of death in a number of populations (Fedorowski et al., 2014) (Zhu et al., 2016). The lower comorbidity levels in individuals with OH will also reduce its impact, thus lessening its effect on the quality of life of the elderly (Ricci, Fedorowski, et al., 2015).

Orthostatic hypotension (OH) frequently occurs in frail elderly individuals and can be caused by various medical conditions, such as decreased intravascular volume, varicose veins, severe anemia, antihypertensive therapy, and decreased physical function. The prevalence of OH commonly increases in patients over >65 years, although only 2% of them show symptoms (Raber et al., 2022). When OH occurs in middle-aged patients without volume depletion or drug effects, the OH encountered is usually neurogenic due to impaired norepinephrine release from sympathetic postganglionic neurons. This occurs in about one-third of patients with OH. Neurogenic OH is best understood as a neurotransmitter disorder and this condition has a fairly high prevalence in the United States, occurring in less than 200,000 people. Nonetheless, the prevalence of neurogenic orthostatic hypotension may be underestimated, as blood pressure measurements are not always taken in an upright position (Palma & Kaufmann, 2017).

3. Conclusion

Orthostatic hypotension in the elderly is a common condition and affects their quality of life. Therefore, accurate diagnosis of the disease is crucial, by considering safety, effectiveness, individual traits, and a multidisciplinary approach as the key to enabling the elderly to live a healthy, high-quality life.

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