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# Reference Interval of Plasma Potassium: A Port Harcourt Based Study

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## Abstract

**BACKGROUND:** Plasma potassium concentration is influenced by dietary intake of potassium when all other parameters that control potassium homeostasis are normal. Studies have shown significantly different potassium means across regions and since blood potassium concentration is important in the management of kidney, heart and organ transplant patients among others, it is, therefore, important to determine our own population-based reference interval. **AIM:** This study was to determine the reference interval of plasma potassium in this geographical region. **METHODS:** This was a retrospective study where results from the laboratory day sheets of patients who met the inclusion criteria were selected over a period of six months. This results were determined using ISE LWE60E by Landwind. This results were ranked and outliers removed and the mean calculated. The 2.5<sup>th</sup> percentile was calculated and used as the lower limit while the 97.5<sup>th</sup> percentile was determined and used as the upper limit. **RESULTS:** The mean age and result of the study population were 45.2 years and 4.3mmol/l, respectively. The reference interval was 2.4- 4.7mmol/l. **CONCLUSION:** The reference interval so determined in this study is about the same with those determined from other locations in Nigeria but significantly different from that of Caucasians. Most of the lower limits of the reference interval determined in Nigeria were below 3.0mmol/l. This is significant as it calls for a re-definition of grading hypokalaemia.

**Keywords:** Non-Parametric, Ions Selective Electrodes, Hypokalaemia

## INTRODUCTION

Potassium is an electrolyte that can be found in blood. This is a very small percentage when compared with the concentration located within the cells ( Agarwal, Afzalpurkar & Fordtran. 1994). The blood potassium is measured and this is used to assess the body potassium concentration. Basically, blood potassium is a balance between potassium intake and the amount excreted, which in this case is mainly through the kidney in the urine and through body sweat (Castrop & Schiefl. 2014).

Still, the blood potassium concentration can be determined by factors that control the shift of potassium from intracellular space into the blood and vice versa (Viera & Wouk. 2015). A shift from intracellular into the blood

would falsely increase blood potassium (pseudo hyperkalaemia) while a shift from blood into cells will cause a false decrease of plasma potassium (pseudo hypokalaemia). Apart from the above mentioned homeostatic mechanism, plasma concentration of potassium is mainly determined by dietary intake in the presence of normal renal function (Penton, Czogalla & Loffing, 2015). While the excretion of potassium depends mainly on subject's renal status, the influence of potassium intake on the plasma concentration, depends on the type of diet. This was shown in a study where the difference in potassium means across geographical regions were found to be significant, which was attributed to the type of diet of the people (Reidenberg, et al. 1993) Other studies have also shown that potassium deficiency is a global problem (Dobermann, et al. 1998) and this may be due to changes in soil potassium across the world (Bengtsson, et al. 2003). Plasma potassium concentration of a subject is influenced by the amount of potassium rich diet when other parameters are normal (Harris. 1998).

A normal potassium blood concentration is necessary for normal heart and muscles activities among others (Bengtsson, et al. 2003). The determination of the reference interval of potassium is made even more significant with the very narrow reference range of the normal value. Since every laboratory is encouraged to determine its own population base reference interval, (Harris. 1998) the dietary influence on plasma potassium and the narrow range of potassium reference interval have therefore made it even more necessary to determine the reference interval of potassium in this region.

## METHODS

Data of potassium results from a tertiary hospital in southern Nigeria, were collected from patients between the ages of 10- 80 years, who had no renal disorders, gastro intestinal disorders, cardiac disorders or on drugs that affect plasma potassium concentration. (ACE inhibitors, nonsteroidal anti-inflammation drugs, potassium sparing diabetics, laxatives, insulin among others). The plasma potassium values were determined using ion-selective electrode (ISO) LWE60E by land wind, results so generated were ranked and outliers were removed using the Dixon method (Horn, et al. 2001). from both sides of the data. The mean age and result of the data were calculated. The non-parametric method of determining reference intervals was used due to the skewedness of the data. The 2.5<sup>th</sup> and the 97.5<sup>th</sup> percentiles were determined and used as the lower and upper reference limits respectively (Solberg. 1993). The data were again grouped according to age groups of tens and the mean of each group was calculated.

## RESULTS

Table 1: Results of age-related means of plasma potassium

<u>Age group</u>	<u>Mean (SD)</u>
10- 19	4.3/0.6
20- 29	4.2/0.6
30- 39	4.2/0.6
40- 49	4.3/0.6
50- 59	4.3/0.6
60- 69	4.3/0.6
70- 79	4.5/0.6
80- 89	4.5/0.8

\*Differences across age groups are not statistically significant. (P-value greater than 0.05)

Table 2: Results of data

<u>Parameter</u>	<u>Results</u>
Mean age of subjects (years)	45.2
Standard error	0.0
Mean result	4.3mmol/L
Standard deviation	0.6
Range	3.9
Lowest result	1.8mmol/l
Highest result	5.7mmol/l

2.5 <sup>th</sup> percentile	2.4
97.5 <sup>th</sup> percentile	4.7
Reference interval	2.4 -4.7mmol/l

## RESULTS

A total of 2200 urea results were collected from one thousand (1000) males and one thousand two hundred (1200) females who met the inclusion criteria over a period of six months. The mean age was 45.2 years while the mean of the total result was 4.3mmol/l. The lowest potassium result was 1.8mmol/l while the highest plasma potassium result was 5.7mmol/l. The 2.5<sup>th</sup> percentile was 2.4mmol/l while the 97.5<sup>th</sup> percentile was 4.7mmol/l and this gave a potassium reference interval of 2.4-4.7mmol/l.

## DISCUSSION

The potassium results collected were grouped according to the ages of the patients and the mean potassium result for each group was determined as seen in table 1. There was no noticeable age-related variation in the means till the age of 70 years. This showed that plasma potassium concentration of this study population was not necessarily affected by the ageing process until the age of 70years. This observation can be said to be due to the gradual organs failure associated with aging (Weidmann, et al. 1975). The glomerular filtration rate (GFR) has been shown to decrease with age and this may explain the increase (Danziger, et al. 1990). Though aging is arguably associated with decreased food intake (John. 2001), the reduced plasma potassium concentration expected with decreased intake is seen to be overwhelmed by the gradual decrease in renal potassium excretion. Again most elderly people are physically inactive and their sweat glands are failing in their functions and so are expected to sweat less thereby reducing potassium loss through sweating (Laure, et al. 2016 & Buono, McKenzie & Kasch. 1991). Organs that produce hormones (adrenal gland) are affected by the aging process and are therefore associated with a reduction in plasma concentration of these hormones and, in this case aldosterone (Weidmann, et al. 1975). Aldosterone controls the potassium pump at the cellular membrane, thereby controlling the shift between intracellular and extracellular potassium (Wanzhu, et al. 2017). Though aging is associated with decreased intake of diets in general (potassium diet), the decreased sweating, decrease urinary loss due to decreased GFR and slight reduction of plasma aldosterone activity could cumulatively explain the increase of plasma potassium associated with aging.

A slight renal disorder may be associated with slight metabolic acidosis (Frassetto, Sebastian & Morris Jr. 1996), which may also explain the slight age-related increase in plasma potassium. Cortisol activity is slightly increased in the elderly, this high cortisol has an aldosterone-like effect, since it stimulates the sodium pump thereby increasing intracellular sodium and this displaces intracellular potassium into the plasma to maintain electrochemical neutrality (Terker, et al. 2015). This means that the potassium moves from the cells into plasma (pseudo hyperkalaemia). All these factors that cause hyperkalaemia in the elderly are believed to outweigh and overwhelm the effect of reduced intake of potassium.

The reference interval of potassium in this study was 2.4-4.7mmol/l and is different from the one in use by the laboratory, which is 3.5-5.7mmol/l, believed to have been from manufacturers of potassium measuring kits. The reference interval determined in this study was also found to be about the same from a study done in Minna, Niger state of Nigeria which had a reference interval of 2.9-5.0mmol/l (Makun, et al. 2001) An Abeokuta study of children and adolescents residing in Abeokuta and its environs had a reference interval of 2.5-4.9mmol/l (Ajose. 2004). One thing was common in all the Nigerian studies and that is the lower reference limit below 3.0 mmol/l that is 2.4 mmol/l for the Abeokuta study, 2.4mmol/l in this study and 2.9mmol/l for the Minna study. While the upper reference limit is 4.7mmol/l in this study, 4.9mmol/l in the Abeokuta study and 5.0mmol/l in the Minna study, showing an upper reference limit of 5 mmol/l and below. These low values seen in the lower limit can be attributed to the effect of diet since most of the Caucasians reference interval had higher lower and higher limits above 3.0 and 5.0 mmol/l and above (Reidenberg, et al. 1993, Pagana, Pagana & Pagana. 2019, Jia, et al. 2015, Rustad, et al 2004 ). This, therefore, means that, it may be necessary to review the cut-off for hypokalaemia in this area and other economically non-viable areas.

Since a normal potassium reference interval has a narrow range, and potassium plasma concentration is very important when managing patients with acute or chronic renal failures, cardiac/adrenal disorders, and dialysis and transplant rejections among others have made the determination of potassium reference interval very important. A study of these reference values determined in various geographical locations in Nigeria has also made it important to re-evaluate the plasma concentration values referred to as low, mild, and severe hypokalaemia. To further buttress this point is a study that showed regional differences in the mean value of plasma potassium and found that the Chinese had the lowest mean value of 3.8mmol/l. Next were the Brazilians with 4.06mmol/l while the Australians had 4.14mmol/l the Americans had the highest mean of 4.3mmol/l followed by the Dominicans with a mean of 4.37mmol/l (Reidenberg, et al. 1993). These findings were attributed to the type of food intake of the people. Another study carried out in south-east Asia due to the sudden and unexpected deaths of young adults during sleep was also attributed to low plasma potassium due to low intake since the urine potassium concentration was found to be normal (Tosukhowong, et al. 2001). These findings have made the determination of potassium reference interval a must for every region and call for re-evaluation of the classification of hypokalaemia.

## CONCLUSION

The reference interval of plasma potassium generated in this study was found to be about the same with those from other Nigerian studies but had a significantly different lower reference limit from that of Caucasians. It may, therefore, be necessary to re-evaluate the value of hypokalaemia in this area and other economically non-viable regions for better management of patients.

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