Original Article

Population-Based Reference Intervals for Some Chemical Pathology Analytes in Lagos Communities

Adeyemi Oluwaseun Dada[1], Akinsegun Abdujaleel, Akinbami [2], Uduak Akpan Ikpegbu. [3], Halimat Oyindamola Shasore [4], Ebele Ifeayinwa Uche[2], Kikelomo Ololade Wright[5], Mayowa Emmanuel Adekiitan[6].

[1]Department of Chemical Pathology, Lagos State University College of Medicine, Lagos. Nigeria. [2]Department of Haematology and Blood Transfusion, Lagos State University College of Medicine, Lagos. Nigeria. [3]Department of Pathology, General Hospital Lagos (ODAN), Lagos. Nigeria. [4]Department of Chemical Pathology, Lagos State University Teaching Hospital, Lagos. Nigeria. [5]Department of Community Health and Primary Health Care, Lagos State University College of Medicine. [6]Department of Pathology, University of Northern Dakota, United States.

Abstract

Background: The need to avoid misleading reference intervals (RI) which can affect clinical decisions about the management of patients led this study aimed at determining the population-based RI of some chemical pathology analytes among adults in Lagos State, Nigeria. **Methods:** This was a population-based, cross-sectional study conducted in August 2022 on selected residents in all the five divisions of Lagos State. Blood samples of Apparently healthy three hundred and forty-one (341) participants aged 18-89 years were analyzed for sodium, potassium, chloride, bicarbonate, calcium, phosphates, magnesium, creatinine, uric acid, albumin, total protein, total bilirubin, direct bilirubin, aspartate transaminase, alanine transaminase, alkaline phosphatase, triglycerides and total cholesterol using Miura 200 machine. Data were analyzed with Statistical Package for Social Sciences, Inc., Chicago, Ill version 26.0. The median, 2.5th and 97.5th percentiles and gender-specific data were obtained. **Results:** The mean age of the 341 participants was 50.1 ±14.4 years. There were 189 (55.4%) females and 152 (44.6%) males. The male-to-female ratio was 1:0.8. The majority of the parameters had similar median, 2.5th and 97.5th percentiles across the genders while most of the analytes had a wide RI relative to known values. **Conclusion:** A wider RI found in this study with no gender disparity suggests that caution should be exercised in interpreting biochemical results of South West Nigerians in order to avoid the error of wrong diagnosis and management.

Keywords: Reference Interval, Clinical decisions, Population Study, Lagos State

INTRODUCTION

Reference Intervals (RI) or reference limits are clinical laboratory measurements of an apparently healthy population and they have been described as a set of results that can be obtained in 95 percent of an apparently healthy reference population. [1,2] Reference intervals are different from decision limits, [1] and should not be called 'normal values' or 'normal ranges' as incorrectly

Correspondence:

Adeyemi Oluwaseun Dada, [1]
Department of Chemical Pathology,
Lagos State University College of Medicine, Lagos. Nigeria.
Email: Adeyemi.dada@lasucom.edu.ng

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used in the past and do not represent the definition of RI.[3] It has been reported that RI can be affected by race, geographical location, socio-economic circumstances, age and gender. [4] Several authors have reported that RIs are less useful in judging individual patients if the inter-individual variability is much larger than intra-individual variability. [5] When an inappropriate RI is used in the management of patients, poor management outcome is expected with attendant complications. [6] In line with the European Union directive regarding in vitro diagnostic medical devices [7] many laboratories in low and medium-resource countries rely on RI provided by diagnostic manufacturers who supply them with assay platforms and reagents, as well as internet sources.

These RI are expected to be periodically verified by each laboratory as directed by the International Organization for Standardisation (ISO) 15189,[3] however, the expensive, time-consuming and complex nature of the exercise are some reasons why many laboratories do not undertake this task. [1] In addition, physicians also complement their resources for RI with the information from textbooks, journals and other studies that do not realistically reflect the true nature of RI in the region. [3]

Reference Intervals have been described as one of the ways of turning figures into information and are important for calling the clinician's awareness towards additional or further care in a particular patient. It offers a basis for the interpretation of patients' results for efficient management. [8] Two approaches have been described in the establishment of the RI. These approaches include the traditional or direct approach and the indirect approach. In the direct approach, the RI is typically defined as the interval between the two reference limits (2.5th and 97.5th percentiles) derived from the distribution of results obtained from a sample of the reference population [9] The indirect approach on the other hand involves the use of routine clinical pathology databases for the purpose of establishment of RI. [9]

The need to avoid misleading RI led us to undertake this task of determining the population-based RI of some chemical pathology analytes among adults in Lagos State, Nigeria.

MATERIALS AND METHODS

The study was carried out in Lagos State, in the southwest geographic zone of Nigeria. This study was a population-based, descriptive, and cross-sectional study with study participants recruited from communities within the five divisions of Lagos State i.e., Ikeja, Ikorodu, Lagos Island, Epe, and Badagry (Figure 1) in August 2022.

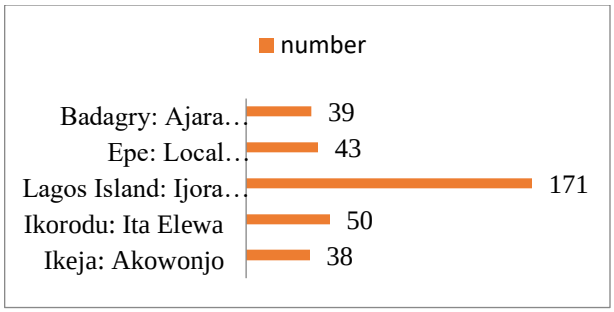

Figure 1: Divisions of the 341 study participants within Lagos state, Nigeria

Sampling Technique

A multistage sampling technique was used. In the first stage, all five divisions were included in the study. Subsequently, communities were divided into clusters as the sampling units in the five divisions from which communities were randomly selected in each of the divisions. Participants in the houses, shops within the sampling units were recruited consecutively as they consented to participate in the study.

Inclusion criteria include consenting adults willing to participate in the study while adults with severe known co-morbidities such as diabetes mellitus, obesity, hypertension; conditions like pregnancy, breastfeeding, recent history of blood donation, hospitalization and or surgery in the previous three months before enrollment, individuals living with human immunodeficiency virus, hepatitis B virus, and hepatitis C virus were excluded from the study. In addition, individuals with history of smoking, alcohol or substance abuse or use of oral contraceptives were not included.

An interviewer-administered questionnaire was used to collect socio-demographic and anthropometric data from each participant, including weight, height, body mass index, and waist circumference. Clinical information such as age, medical history including blood transfusions and drug use, was also recorded. In addition, random capillary blood glucose (RBS) levels were measured using point of care accu-chek active device by Roche Germany; blood pressure was taken, and screening tests were done: for β-hCG using laborex test strips China, Determine strips by Abbott for HIV, Promed test strips China for HBsAg and HCV.

Sample Size Calculation

The minimum requirement for this study is a sample size of one hundred and twenty healthy participants. [10] The sample size was determined using the statistical formula that applies to surveys [11]. Numeric outcome (mean)

$$N=Z_{\alpha}^2\ \sigma^2/\partial^2$$

N=Sample size
Z_α= Normal Standard Deviate for α-error =1.960
σ =variance =50% (0.5)
ð =Precision level assumed at 5% (0.05)
N= $(1.96)^2$ * $(0.5)^2$/ $(0.05)^2$
=3.84*0.25/0.0025=0.96/0.0025=384

Sample Collection

Four and a half milliliters of fasting venous blood were collected from each study participant under aseptic techniques. This was dispensed into lithium heparin (LH) specimen bottles. In order to prevent the pre-analytic effect of false elevation on analytes like potassium, the samples were transported in ice packs from the field to the laboratory where they were centrifuged at 4000rpm for 5minutes. The supernatant plasma was separated and stored at -80^{0}C pending analysis while the infra-natant was discarded through the hospital medical waste disposal unit. Each parameter was analyzed in batches with levels 1 and 3 quality control material from randox laboratories included in each analytic run.

Out of the 384 participants enrolled for the study, only 341 samples were eligible for analysis. The samples were transported to, and run at the Chemical Pathology Laboratory of Lagos State University Teaching Hospital, Ikeja using ISE 6000 (SFRI, France) for the electrolytes (Sodium- Na, Potassium- K, Chloride- Cl, Bicarbonate- HCO_3) and Miura 200 autoanalyzer (I.S.E S.R.L, Italy) which is a closed system for albumin, total protein- TP, calcium- Ca, phosphate- PO_4, magnesium- Mg, aspartate transaminase- AST, alanine transaminase- ALT, alkaline phosphatase- ALP, total bilirubin- TB, direct bilirubin- DB, uric acid- UA, urea- U, creatinine- Cr, total cholesterol- TC and fasting triglycerides- Tg. Methodologies used for each analyte have been listed out in Table 1.

Statistical Analysis

The data in this study were analyzed using SPSS version 26.0 (Statistical Package for Social Sciences, Inc., Chicago, Ill). There were no missing data. Reference intervals were computed independently for male and female participants. The median and dispersion (2.5th and 97.5th percentiles) were generated using a non-parametric method of analysis. Gender stratification was made for each parameter, but there was no test of statistical significance.

Ethical Considerations

Ethics committee approval was obtained from the Health Ethics and Research Committee of Lagos State University Teaching Hospital with a reference number LREC/06/10/1886. The participants were informed about the study, as well as their rights and benefits. Written informed consent was obtained from each participant using voluntarily signed consent forms and No participant was coerced in any way to participate in this study, which was at no cost to them.

RESULTS

A total of Three Hundred and eighty-four (384) participants were recruited, however, following data

Table 1: Summary Of Methodologies Used for Each Analyte

SN	Biochemical Analytes	Methodology
1	Sodium, Na (mmol/L)	Potentiometry, ISE 6000
2	Potassium, K (mmol/L)	Potentiometry, ISE 6000
3	Chloride, Cl (mmol/L)	Potentiometry, ISE 6000
4	Bicarbonate, HCO3 ((mmol/L)	Potentiometry, ISE 6000
5	Calcium, Ca	Spectrophotometry, Arsenazo III
6	Phosphate, PO4	Spectrophotometry, UV Phosphomolybdnate method
7	Magnesium, Mg	Spectrophotometry, Xylidyl blue method
8	Urea, U	Spectrophotometry, L-glutamate dehydrogenase method
9	Creatinine, Cr	Spectrophotometry, Jaffe Kinetic method
10	Uric acid, UA	Spectrophotometry, Uricase enzymatic method
11	Albumin, Alb	Spectrophotometry, Bromocresol green
12	Total Protein, TP	Spectrophotometry, Biuret tartrate method
13	Total Bilirubin, TB	Spectrophotometry, VB reaction - Azobilirubin
14	Direct Bilirubin, DB	Spectrophotometry, VB reaction - Azobilirubin
15	Aspartate Transaminase, AST	Spectrophotometry, ASAT enzymatic activity IFCC
16	Alanine Transaminase, ALT	Spectrophotometry, ALAT enzymatic activity IFCC
17	Alkaline Phosphatase, ALP	Spectrophotometry, DGKC enzymatic method
18	Triglyceride, Tg	Spectrophotometry, GPO Tinder method
19	Total Cholesterol, TC	Spectrophotometry, CHOP enzymatic method

ISE- ion selective electrode; UV- ultraviolet; VB- van den bergh reaction; IFCC- International Federation of Clinical Chemists; ASAT- Aspartate amino transferase; ALAT- Alanine amino transferase; DGKC- Deutsche Gesellschaft Fur Klinische Chemie; GPO- Glycerol Phosphate Oxidase; CHOP- Cholesterol oxidase Peroxidase

Table 2: Median and percentiles of the various analytes for the general population, Male and Female participants
CI=Confidence Interval, P= p-value for the median differences between males and females for the analytes

SN	Biochemical Analytes	Median (2.5th, 97.5th) for General population N=341	CI@90%	Median (2.5th, 97.5th) for Males N= 152	Median (2.5th, 97.5th) for Females N=189	P value
1	Sodium, Na (mmol/L)	138 (131, 167)	(141 -144)	138 (122, 170)	139 (122, 167)	0.121
2	Potassium, K (mmol/L)	4.3 (3.6, 5.5)	(4.3 - 4.4)	4.3 (3.6, 5.5)	4.3 (3.6, 5.4)	0.736
3	Chloride, Cl (mmol/L)	101 (90, 119)	(102 -104)	101 (88, 119)	102 (92, 118)	0.056
4	Bicarbonate, HCO3 (mmol/L)	21 (16, 27)	(20.6 - 21.3)	21 (16, 27)	21 (16, 27)	0.897
5	Calcium, Ca (mmol/L)	2.4 (2.05, 2.87)	(2.4 – 2.5)	2.4 (2.1, 2.7)	2.4 (2.0, 2.9)	0.959
6	Phosphate, PO4 (mmol/L)	1.3 (1.0, 1.5)	(1.2 – 1.3)	1.3 (1.0, 1.6)	1.3 (1.0, 1.5)	0.982
7	Magnesium, Mg (mmol/L)	0.5 (0.3, 1.0)	(0.58 – 0.6)	0.5 (0.2, 1.0)	0.5 (0.3, 1.0)	0.333
8	Urea, U (mmol/L)	4.0 (1.8, 8.5)	(6.6 - 7.2)	4.0 (1.9, 8.1)	4.2 (1.8, 8.5)	0.595
9	Creatinine, Cr (µmol/L)	88 (53, 141)	(89.1 – 97.2)	88 (53, 140)	88 (62, 141)	0.082
10	Uric acid, UA (µmol/L)	333 (162, 607)	(506 - 543)	342 (161, 553)	333(161, 631)	0.244
11	Albumin, Alb (g/L)	47 (36, 54)	(46 - 47)	47 (36, 54)	47 (35, 54)	0.220
12	Total Protein, TP (g/L)	80 (60, 90)	(77 - 79)	80 (60, 90)	80 (59, 90)	0.299
13	Total Bilirubin, TB (µmol/L)	10 (3.4, 40)	(13 - 16)	10 (3.4, 40)	8.5 (3.4, 48)	0.455
14	Direct Bilirubin, DB (µmol/L)	3.4 (1.7, 6.8)	(3.3 – 3.6)	3.4 (1.7, 10)	3.4 (1.7, 6.8)	0.619
15	Aspartate Transaminase, AST (U/L)	19 (8, 32)	(18.8 - 20.4)	18 (8, 30)	19 (8, 35)	0.453
16	Alanine Transaminase, ALT (U/L)	9 (4, 25)	(10.8 - 13.3)	9 (3, 22)	9 (4, 28)	0.907
17	Alkaline Phosphatase, ALP (U/L)	154 (93, 243)	(157 - 168)	154 (94, 245)	153 (87, 244)	0.825
18	Triglyceride, Tg (mmol/L)	0.6 (0.3, 1.1)	(0.59 – 0.7)	0.6 (0.3, 1.1)	0.6 (0.3, 1.1)	0.578
19	Total Cholesterol, TC (mmol/L)	2.8 (1.7, 5.2)	(3 – 3.2)	2.9 (1.6, 5.2)	2.8 (1.8, 5.2)	0.845

Table 3: Comparison of median and percentiles of the various analytes with Nigerian and African studies

SN	Biochemical Analytes		Median and RI This study	Median and RI Ayemoba et al*	Median and RI Miri-Dashe et al*
1	Sodium, Na (mmol/L)	M	138 (122-170)	133 (114-144)	136 (132-149.4)
		F	139 (122-167)	133 (114-144)	133 (120-156)
2	Potassium, K (mmol/L)	M	4.3 (3.6-5.5)	4.0 (2.7-7.0)	4.6 (4.0-7.5)
		F	4.3 (3.6-5.4)	4.1 (2.8-7.0)	4.7 (4-7.7)
3	Chloride, Cl (mmol/L)	M	101 (88-119)	93 (80-100)	100 (98-108.4)
		F	102 (92-118)	93 (80-100)	101 (98-110)
4	Bicarbonate, HCO3	M	21 (16-27)	NA	24.0 (22-32)
	(mmol/L)	F	21 (16-27)		17.0 (14-29)
5	Calcium, Ca (mmol/L)	M	2.4 (2.1-2.7)	2.3 (1.6- 2.7)	NA
		F	2.4 (2.0-2.9)	2.3 (1.6- 2.7)	NA
6	Phosphate, PO4	M	1.3 (1.0-1.6)	1.3 (0.6- 4.8)	NA
	(mmol/L)	F	1.3 (1.0-1.5)	1.3 (0.6- 4.6)	NA
7	Magnesium, Mg	M	0.5 (0.2- 1.0)	NA	NA
	(mmol/L)	F	0.5 (0.3-1.0)		NA
8	Urea, U (mmol/L)	M	4.0 (1.9- 8.1)	3.6 (1.2-9)	2.7 (2.2-4.8)
		F	4.2 (1.8-8.5)	3.4 (1.3-7.2)	3.2 (2.5-5.8)
9	Creatinine, Cr (µmol/L)	M	88 (53-140)	88 (46-132)	86 (76.3-111.1)
		F	88 (62-141)	90 (48-136)	76 (63-117.8)
10	Uric acid, UA (µmol/L)	M	342 (161, 553)	274 (141-460)	NA
		F	333 (161- 631)	273 (140-400)	NA
11	Albumn, Alb (g/L)	M	47 (36-54)	45.8 (34.8-53.0)	NA
		F	47 (35-54)	45.9 (33.9-54.2)	NA
12	Total Protein, TP (g/L)	M	80 (60-90)	79.5 (52.2- 98.0)	NA
		F	80 (59- 90)	79.3 (54.5- 97.4)	NA
13	Total Bilirubin, TB	M	10 (3.4- 40)	8.8 (1.5 - 33.8)	6.8 (3.4-17.1)
	(µmol/L)	F	8.5 (3.4-48)	8.9 (1.4 - 41.2)	2.3 (0.3-10.6)
14	Direct Bilirubin, DB	M	3.4 (1.7-10)	4.3 (0.4-16.9)	NA
	(µmol/L)	F	3.4 (1.7-6.8)	4.3 (0.2- 19.6)	NA
15	Aspartate Transaminase,	M	18 (8-30)	18.3 (2.9 - 52.0)	31 (26-49.4)
	AST (U/L)	F	19 (8-35)	19.0 (3.2-47.4)	31 (22-58.4)
16	Alanine Transaminase,	M	9 (3- 22)	16 (3.5- 63.2)	22 (17.3-48.4)
	ALT (U/L)	F	9 (4 - 28)	16.6 (4.5- 63.0)	23 (19-38)
17	Alkaline Phosphatase,	M	154 (94-245)	162 (79-338)	NA
	ALP (U/L)	F	153 (87-244)	152 (86-327)	NA
18	Triglyceride, Tg	M	0.6 (0.3-1.1)	0.8 (0.5-1.8)	(0.7-2.2)
	(mmol/L)	F	0.6 (0.3- 1.1)	0.7 (0.4-1.6)	0.8 (0.6- 2.1)
19	Total Cholesterol, TC	M	2.9 (1.6-5.2)	4.0 (2.4-6.2)	3.7 (3.2-5.3)
	(mmol/L)	F	2.8 (1.8-5.2)	4.0 (2.2-6.3)	3.8 (3.1-5.6)

NA, Not available; RI Reference Interval

Table 4: Comparison of median and percentiles of the various analytes with American and European studies

SN	Biochemical Analytes	RI in this study	RI by Dosso et al* (Ghana) [22]	RI by Kibaya et al* (Kenya) [23]	RI for Americans-tietz [14, 15]	RI for British-NHS [16]
1	Sodium, Na (mmol/L)	131-167	135-150	141.4-152.5	137-143	133-146
2	Potassium, K (mmol/L)	3.6-5.5	3.6- 5.2	3.9-5.8	3.8-4.9	3.5-5.3
3	Chloride, Cl (mmol/L)	90-119	102-114	100.5-111.7	101-108	95-108
4	Bicarbonate, HCO_3 (mmol/L)	16-27	NA	17.7-28.5	19- 26	22-29
5	Calcium, Ca (mmol/L)	2.05-2.87	NA	NA	2.3-2.56	2.2-2.6
6	Phosphate, PO_4 (mmol/L)	1.0-1.5	0.7-1.5	NA	0.95-1.57	0.8-1.5
7	Magnesium, Mg (mmol/L)	0.3-1.0	NA	NA	0.66- 1.07	0.7-1.0
8	Urea, U (mmol/L)	1.8-8.5	0.9-5.7	1.4-4.6	2.9- 8.6	2.5-7.8
9	Creatinine, Cr (µmol/L)	53-141	49-118	55-102	52-150	45-104
10	Uric acid, UA (µmol/L)	162- 607	91-399	NA	218- 459	140-360
11	Albumn, Alb (g/L)	36-54	33.0-49	35.8-48.1	39- 50	35-50
12	Total Protein, TP (g/L)	60- 90	50.6-86.7	NA	68-83	60-80
13	Total Bilirubin, TB (µmol/L)	3.4-40	2.9-25.8	4.9-39.9	1.0-19.9	0-21
14	Direct Bilirubin, DB (µmol/L)	1.7-6.8	0.8-4.0	1.1-8.8	1.9-7.1	NA
15	Aspartate Transaminase, AST (U/L)	8- 32	14- 51	13.8-42.3	0-35	10-40
16	Alanine Transaminase, ALT (U/L)	4-25	7-51	9.6-52.0	0-45	10-50
17	Alkaline Phosphatase, ALP (U/L)	93- 243	85-241	NA	56-167	30-130
18	Triglyceride, Tg (mmol/L)	0.3- 1.1	0.4-2.2	0.4-2.6	0.4-3.4	0-1.7
19	Total Cholesterol, TC (mmol/L)	1.7- 5.2	2.0-5.4	2.6-5.7	2.59-7.10	0-5.0

NA, Not available; RI – Reference Interval (2.5^{th} – 97.5^{th})

cleaning, 43 participants with RBG greater than 11.1mmol/L, those with abnormal parameters of unknown causes, those with haemolyzed samples, and those with history of smoking and alcohol ingestion were excluded from the analysis, only three hundred and forty-one (341) healthy participants who were all of South Western origin were left. The minimum and maximum ages of participants were 18 and 89 years respectively with a mean age of 50.1 ±14.4 years. About 50% of the participants were between the ages 40-60years, 22.3% of the participants were less than 40years and 27% were above 60years. The distribution in terms of gender includes 189 (55.4%) females and 152 (44.6%) males. The median, 2.5^{th} percentile (known as lower limit –LL) and 97.5^{th} percentile (known as upper limit –UL) for the biochemical analytes in the general population, male and female populations are presented in Table 2. In Table 3, the median, LL and UL in this study was compared with other studies in Nigeria while Table 4 shows the comparison of our study with other African studies, American and British RI.

DISCUSSION

certain biochemical analytes among participants from communities in Lagos State Nigeria. Overall, plasma Na, K, Cl, HCO_3, UA, Ca, TP, Alb, Cr, Mg, U, TB, ALP had a wider RI while PO_4, DB, AST, ALT, Tg, Tc had a lower RI compared to values quoted by the laboratory which is traceable [3, 12] and transferred [13] from standard RI established among Caucasian populations as presented in textbooks of clinical chemistry and other sources. [14, 15, 16]

This study set out to determine reference intervals for Plasma Na, K, Cl, HCO_3, UA, Ca, TP, Alb, had a wider RI with higher UL and a lower LL. Total bilirubin, urea, creatinine, alkaline phosphatase have a wider RI with higher UL while magnesium, urea, direct bilirubin, triglyceride, and total cholesterol have reduced LL when compared with Caucasian RI. In addition, the UL for bicarbonate, phosphate, magnesium, urea, creatinine, albumin, direct bilirubin, AST and total cholesterol compares with the UL of some Caucasian values. [14, 15, 16] When compared with Caucasian RI, the LL for phosphates, creatinine, total bilirubin, and ALP in our study were higher.

There was no difference between the median values for the analytes across gender groups in this study suggesting that single RI can be used for both genders. Factors that may be responsible for our findings could include traditional practices such as the use of herbal concoctions and alternative/traditional medicine which are common practices among citizens in Nigeria as a first line of treatment against minor and serious ailments which at times have various underlying causes. [17] The effects that some of the herbal components have on the body's physiology and their half-life in the body cannot be verified. Despite designing our methodology to exclude these factors during the process of recruitment of

the participants, the authors note that it may not be completely easy to eradicate this possibility.

To our knowledge, a few studies have been done to determine reference intervals of clinical chemistry analytes among Nigerians and outside the hospital environment. One of such studies looked at the RI of Nigerians within the age limits of 18-26years spanning the geopolitical zones, across the 36 states and Federal Capital Territory which cuts across many tribes. [18] This study by Ayemoba et al, focused on young people, while our study had wider age coverage with more than half of the participants being in middle age. Another study was conducted in Jos, north central Nigeria which focused on voluntary blood donors as well as pregnant women between the ages of 18 and 65 years. [19]

The gender ratio in our study was almost equal compared to some of the other studies noted. [15, 17] What is quite consistent between our study and other Nigerian studies is the wider RI for most of the analytes when compared with Caucasian values. The majority of the analytes which had a lower LL in our study were also low in the other two studies (Table 4) but with varying values.[18, 19] There was however some similarities in median values with some analytes such as K, Ca, PO_4, Cr, Alb, TP, TB, and AST. The age spectrum could have accounted for the difference in the sodium concentration between our study and the other studies. [18, 19]

Selecting suitable reference individuals and preparing these individuals for data collection as well as blood sample collection in a standard way were very important aspects of our study just as was the processing, analysis of the samples in a quality-controlled environment to generate quality results that are suitable for clinical use. [20, 21] When compared with RI generated by a study in Ghana [22] and Kenya [23] as shown in Table 4, our study had wider RI for the majority of the parameters except for K, PO_4, albumin, ALP, TB and TC which had some similarity with one or the two studies. The study done in middle-belt of Ghana had similar findings with the one done in Akuapem. [12, 22] had parameters like AST, ALT and triglycerides having a wider RI when compared with our study. These findings of increased RI for liver enzymes in the Ghanaian study were attributed to possible sub-clinical viral infections or the use of herbs. The RI in our study is more similar to the British RI [16] compared to the American RI as seen in Table 4. According to a study that compared RI for some common laboratory parameters among Asians, Blacks, Hispanics and Whites in the United States, [24] significant racial differences were found in almost all the 38 laboratory parameters assayed with Blacks noted to have significantly higher RI in TP, and lower RI in TC, Tg.

Limitations

A study limitation is the reliability of information provided by the participants regarding the history of medication especially those that have an effect on the analytes. Secondly, we were not able to eliminate pre-analytical factors that affect certain analytes like food, traditional practices such as the use of herbs etc which could have impacted the results obtained, however, abnormal results of unknown causes were excluded from the overall data during data cleaning.

CONCLUSION

What is Known of this Topic

- There are some published studies on reference intervals among certain age groups in Nigeria, Africa and the World in general
- Secondly, majority of the laboratories in Nigeria rely on the reference limits provided with equipment, reagents, obtained from textbooks and internet sources.

What this Topic Adds

- This study provides the reference intervals for some biochemical analytes in communities in Lagos state, south west Nigeria which to the best of our knowledge, is the first study focusing on reference intervals of these analytes among adults.
- Secondly, this study provides some insight into possible differences that exist between the RI among south west population and other geographical locations in Nigeria, across some countries in Africa and Caucasian population.

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REFERENCES

1. Ozarda, Y., Higgins, V., and Adeli, K. "Verification of reference intervals in routine clinical laboratories: practical challenges and recommendations" Clinical Chemistry and Laboratory Medicine (CCLM), 2019; 57(1): pp. 30-37. https://doi.org/10.1515/cclm-2018-0059
2. Sikaris KA. Physiology and its importance for reference intervals. Clin Biochem Rev. 2014; 35(1):3-14. PMID: 24659833; PMCID: PMC3961997
3. International Organization for Standardization. ISO 15189:2012 (E) Medical laboratories – Requirements for quality and competence, Third edition, 2012-11-01.
4. Ichihara K, Itoh Y, Lam CWK, Poon PMK, Kim J-H, Kyono H, et al. Sources of variation of commonly measured serum analytes in 6 Asian cities and consideration of common reference intervals. Clin Chem. 2008; 54(2):356–65.
5. Andersen TB, Erlandsen EJ, Frøkiaer J, Eskild-Jensen A, Brøchner-Mortensen J. Comparison of within- and between-subject variation of serum cystatin C and serum creatinine in children aged 2-13 years. Scand J Clin Lab Invest. 2010;70:54-9
6. Ichihara K, Ceriotti F, Tam TH, Sueyoshi S, Poon PMK, Thong ML, et al. The Asian project for collaborative derivation of reference intervals: (1) strategy and major results of standardized analytes. Clin Chem Lab Med 2013; 51(7):1429–42.
7. Directive 98/79/EC OF European Parliament and the Council of 27 October 1998 on the in vitro diagnostic medical devices. Official J Eur Commun 7 December 1998; L331/1-L331/37.
8. CLSI. Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline. 3rd ed. CLSI EP28-A3c. Wayne, Pennsylvania: Clinical and Laboratory Standards Institute; 2010.
9. Jones G, Horowitz G, Katayev A, Fleming JK, Luo D, Fisher AH, et al. Reference intervals data mining: getting the right paper. Am J Clin Pathol. 2015; 144(3):526-7. doi: 10.1309/AJCP26VYYHIIZLBK. PMID: 26276785.
10. Sasse Edward A, Doumas Basil T, D'Orazio Paul E, Evans Susan A, Graham Gary A, Myers Gary L, et al. How to Define and Determine Reference Intervals in the Clinical Laboratory; Approved Guideline—Second Edition. National Committee for Clinical Laboratory Standards. (NCCLS Document C28-A); 2000.
11. Bolarinwa OA. Sample size estimation for health and social science researchers: The principle and considerations for different study designs. Niger Postgrad Med. J.: 2020:27:67-75
12. Koram KA, Addae MM, Ocran JC, Adu-Amankwah S, Rogers WO, Nkrumah FK. Population-based reference intervals for common blood haematological and biochemical parameters in the Akuapem north district. Ghana Med J. 2007;41(4): 160–166.
13. Tate JR, Yen T, Jones GR. Transference and validation of reference intervals. Clinical Chemistry. 2015 Aug;61(8):1012-1015. DOI: 10.1373/clinchem.2015.243055. PMID: 26089382.
14. Adeli K, Ceriotti F and Nieuwesteeg M. Reference Information for the Clinical Laboratory. In: Rifai N, Horvath A, Wittwer C. editors. Tietz Textbook of Clinical Chemistry and Molecular Diagnostics. 6th edition. Elsevier Inc, 2018. P1745–1789.
15. Roberts WL, McMillin GA, and Burtis CA. Reference Information for the Clinical Laboratory. In: Tietz Textbook of Clinical Chemistry and Molecular Diagnostics; Editors: Burtis CA, Ashwood ER and Bruns DE. 5th edition. Elsevier Inc, 2012. P2131–2188.
16. Munro J. Clinical Biochemistry Reference Ranges Handbook; NHS Trust. 2021 BIJ-11 Issue 14 (V2.2) 1–17
17. Ojua TA, Ishor DG, and Ndom PJ. African cultural practices and health implications for Nigeria rural development. IRMBR 2013; 2(1):176-183.
18. Ayemoba O, Okeji N, Hussain N, Umar T, Ajemba-Life A, Kene T, et al. Reference intervals of common clinical biochemistry analytes in young Nigerian adults. PLOS ONE 2021; 16(3): e0247672. https://doi.org/10.1371/journal.pone.0247672)
19. Miri-Dashe T, Osawe S, Tokdung M, Daniel N, Choji RP, Mamman I,et al. Comprehensive Reference Ranges for Hematology and Clinical Chemistry Laboratory Parameters Derived from Normal Nigerian Adults. PLOS ONE. 2014; 9(5): e93919. https://doi.org/10.1371/journal.pone.0093919
20. Solberg, Helge Erik. "The IFCC recommendation on estimation of reference intervals. The RefVal Program" Clinical Chemistry and Laboratory Medicine (CCLM), vol. 42, no. 7, 2004, pp. 710-714. https://login.research4life.org/tacsgr1doi_org/10.1515/CCLM.2004.121.
21. Ozarda Y, Ichihara K, Barth JH, Klee G. Protocol and standard operating procedures for common use in a worldwide multicenter study on reference values. Clin Chem Lab Med [Internet]. 2013 [cited 2015 Oct 19]; 51(5):1027–40.
22. Dosso DK, Kayan K, Adu-Gyasi D, Kwara E, Ocran J, Osei-Kwaye K, et al. Haematological and Biochemical Reference Values for Healthy Adults in the Middle Belt of Ghana. Plos ONE. 2012; 7(4) e36308. https://doi.org/10.1371/journal.pone.0036308 PMID: 22558429.
23. Kibaya RS, Bautista CT, Sawe FK, Shaffer DN, Sateren WB, Scott PT, et al. Reference ranges for the clinical laboratory derived from a rural population in Kericho, Kenya. PLoSOne3 2008: e3327.
24. Lim E, Miyamura J, Chen JJ. Racial/Ethnic-Specific Reference Intervals for Common Laboratory Tests: A Comparison among Asians, Blacks, Hispanics, and White. Hawaii J Med Public Health. 2015;74(9):302-10. PMID: 26468426; PMCID: PMC4578165.