REFERENCE VALUES FOR SOME PARAMETERS OF LIVER FUNCTION TESTS IN ADULT NIGERIANS RESIDENT IN URBAN LAGOS

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SUMMARY

OBJECTIVES: *This study is aimed at establishing reference values for some of the liver function tests commonly requested for in the management of patients in this environment. With the acknowledged differences between Africans and Caucasians, it has become imperative to produce local reference values for Nigerians. This report is for adult Nigerians in urban Lagos as a part of a larger effort aimed at establishing biochemical reference baseline data for Nigeria.*

SUBJECTS/MATERIALS/METHODS: *One thousand two hundred Nigerians, resident in Lagos, with ages ranging between 21-59 years, were enrolled in this study. There were 600 males, average age 37.7±6.5 years (mean±SD), and 600 females, average age 36.8±8.6 years. Fasting plasma was chemically analysed by methods previously established for total bilirubin, TBIL, and direct bilirubin, DBIL, transaminases, alkaline phosphatase, ALP, and gamma-glutamyl transpeptidase, GGT, on the Synchron CX5 (Beckman, USA, marketed by Darlez Nigeria Limited, Lagos). The Epi info statistical package of the CDC, USA, was used to calculate the means, standard deviations and ranges.*

RESULTS: *The reference values obtained were as follows for males, females and combined group: -TBIL (mmol/L): 6.9-19.1, 2.0-20.1 and 2.6-20.4; DBIL (mmol/L): 0.2-2.8, 0.0-3.0, and 0.0-3.0; ALT (iu/L): 12-66, 12-61, and 12-64; AST (iu/L): 10-43, 9-37, and 10-40; GGT (iu/L): 13-74, 13-75, and 13-75; ALP (iu/L): 41-149, 37-138, and 38-148. The males had non-significantly higher means for TBIL, DBIL, ALT, AST and ALP. The females had non-significantly higher GGT mean .The females had a wider range for bilirubin, TBIL and DBIL, while the males had wider ranges for the transaminases, ALT and AST. For the membrane enzymes, the females had a wider range for GGT, while the males recorded a wider range for ALP.*

CONCLUSION: *This study has established reference values for bilirubin, transaminases and liver membranous enzymes among Nigerians in urban Lagos. Non-significant differences were found between sexes in all parameters, and these have been explained. It is recommended that larger studies, involving rural Lagos, be done to further enrich the quality of result interpretation in this environment. Furthermore, the ages not covered here would need to be studied to widen the data base.*

INTRODUCTION

The liver carries out metabolic processes. The combination of anabolic and catabolic activities are mediated by a plethora of enzymes, including aspartate transaminase (AST), alanine transaminase(AST), alkaline phosphatase (ALP) and gamma-glutamyl transpeptidase (GGT).

The transaminases, such as AST, transfer amine groups, and are important to the citric-urea cycles of Kreb, amongst others(1), while ALP catalyzes the removal of inorganic phosphate groups from organic esters. The assay of these enzymes is commonly requested for in hepatic disorders in Nigeria. While the ALT is mainly found in the cytosol, the AST is of unique isomorphology, being found both in the cytosol and in the mitochondrial fluids(2,3). The AST is, thus, unique also in the assessment of the depth of penetration of any injury to the liver cell, as seen in viral infection and toxicology of phenacetin and carbon tetrachloride, amongst other associated pharmaceutical products.

Both ALP and GGT are traditional membrane enzymes, found in the linings of the canaliculi (4). Alkaline phosphatase transfers

phosphate groups at alkaline pH, while GGT transfers the amine group attached to the gamma carbon of amino acids. These enzymes naturally derive their importance from their behaviour in obstructive liver conditions as well as in alcoholic affectations, when their serum levels become very high (5).

Bilirubin, from senescent erythrocytes, is an ever present toxic waste. However, the liver's conjugating process renders it harmless, converting indirect or unconjugated forms to the water soluble or direct bilirubin. In an environment with high infection rate, bilirubin assay is also a common request. Besides this, certain drugs like dicumarol and phenacetin displace bilirubin from binding sites on albumin, thus, raising serum levels to fatal levels, especially in neonates.

This study is part of an effort to develop local reference biochemical data (6,7,8). Though these parameters have been measured for many decades in Nigeria, baseline reference data are scanty, with Caucasian values still guiding result interpretation. Errors are common in such carry-overs; while the Caucasian AST/ALT ratio is always under 1(9), the Nigerian ratio has been found to be above 1 (10,11). This study sets out to establish normal or reference values for these liver-related analytes among Nigerians to guide result interpretation in our environment.

SUBJECTS/MATERIALS/ METHODS

The study was guided by the recommendations of the International Federation of Clinical Chemistry for the establishment of reference values (12-17). One thousand two hundred healthy Nigerians, resident in Lagos, with age range between 21-59 years, were enrolled in this study. There were 600 males, average age 37.7±6.5 years (mean±SD) and 600 females, average age 36.8±8.6 years. These were sourced from amongst medical students, other hospital staff, bank executives, media men and women, relations of patients, artisans, housewives, etc.

Fasting blood was drawn at the ante-cubital vein into heparinized bottles, spun (3000g, 10 min) and plasma separated into plain plastic bottles for storage overnight at 4 °C, if analysis was not done the same day. Chemical analysis by methods previously established for bilirubin(18), transaminases(19), ALP (20), and GGT (21), was done by automation on the Synchron CX5 (Beckman, USA, marketed by Darlez Nigeria Limited, Lagos).

The Epi info statistical package of the CDC, USA, was used to calculate the means and standard deviation (SD).

RESULTS

The result of the study is presented in Tables 1-3.

Table 1 showed that the males had non-significantly higher means in TBIL (12.17±3.51 vs. 11.08±4.62) mmol/L, in DBIL (1.28±0.76 vs. 1.08±0.97) mmol/L, in ALT (39.03±13.93 vs. 36.63±12.54) iu/L, in AST (26.25±8.46 vs. 22.98±6.98) iu/L, and in ALP (94.81±27.51 vs. 90.50±27.30) iu/L. The females had non-significantly higher GGT mean compared to the males (43.45±15.35 vs. 44.23±15.83) iu/L.

Table3 showed the females had a wider range for TBIL and and for DBIL, with both male ranges falling within the female ranges. The males, on the other hand, had wider ranges for the transaminases, ALT and AST, also recording higher upper limits of normal (ULN) than the females. While the females had a wider range for GGT, the males recorded a wider range for ALP; the sex with the higher range also recording the higher ULN.

Table 1: The means and the 0.025 to 0.975 or 95% intervals (mean±1.96SD) in brackets.

Analyte	Males(n=600)	Female(n=600)	General(n=1200)
TBIL µmol/L	**12.17 ± 3.51** (6.88 - 19.05)	**11.08 ± 4.62** (2.03 - 20.14)	**11.50 ± 4.53** (2.62 - 20.38)
DBIL µmol/L	**1.28 ± 0.76** (0.21 - 2.77)	**1.08 ± 0.97** (0.0 - 2.98)	**1.19 ± 0.94** (0.0 - 3.03)
ALT ui/L	**39.03 ± 13.93** (11.73 - 66.33)	**36.63 ± 12.54** (12.05 - 61.21)	**37.90 ± 13.12** (12.19 - 63.62)
AST "	**26.25 ± 8.46** (9.67 - 42.83)	**22.98 ± 6.98** (9.29 - 36.66)	**24.67 ± 7.75** (9.48 - 39.86)
GGT "	**43.45 ± 15.35** (13.36 - 73.54)	**44.23 ± 15.83** (13.20 - 75.26)	**43.88 ± 15.71** (13.02 - 74.67)
ALP "	**94.81 ± 27.51** (40.89 - 148.73)	**90.50 ± 27.30** (36.99 - 138.01)	**92.90 ± 28.10** (37.82 - 147.98)

Table 2: The 0.025 to 0.975 or 95% intervals (bold) and 90% confidence intervals

Analyte	Males(n=600)	Female(n=600)	General(n=1200)
TBIL µmol/L	**6.88 - 19.05**	**2.03 - 20.14**	**2.62 - 20.38**
	6.44 18.61	1.44 19.55	2.21 19.97
	7.32 19.49	2.61 20.72	3.02 20.78
DBIL µmol/L	**0.21 - 2.77**	**0.0 - 2.98**	**0.0 - 3.03**
	0.11 2.67	0.0 2.85	0.0 2.94
	0.30 2.86	0.12 3.10	0.08 3.11
ALT ui/L	**11.73 - 66.33**	**12.05 - 61.21**	**12.19 - 63.62**
	9.97 64.57	10.47 59.63	11.77 63.20
	13.48 68.08	13.12 62.78	12.60 64.03
AST "	**9.67 - 42.83**	**9.29 - 36.66**	**9.48 - 39.86**
	8.60 41.76	8.41 35.78	8.79 39.17
	10.73 43.89	10.16 37.53	10.16 40.54
GGT "	**13.36 - 73.54**	**13.20 - 75.26**	**13.02 - 74.67**
	11.43 71.61	11.21 73.27	11.62 73.27
	15.28 75.46	15.18 77.24	14.41 76.06
ALP "	**40.89 - 148.73**	**36.99 - 138.01**	**37.82 - 147.98**
	37.43 145.27	33.55 134-57	35.32 145.48
	44.34 152.18	40.42 141.44	40.31 150.47

Table 3: The reference limits for the 0.025 to 0.975 or 95% intervals in males, females and group studied

Analyte	Males(n=600)	Female(n=600)	General(n=1200)
TBIL µmol/L	6.9 - 19.1	2.0 20.1	2.6 - 20.4
DBIL µmol/L	0.2 - 2.8	0.0 - 3.0	0.0 - 3.0
ALT ui/L	12 - 66	12 - 61	12 - 64
AST "	10 - 43	9 - 37	10 - 40
GGT "	13 - 74	13 - 75	13 - 75
ALP "	41 - 149	37 - 138	38 - 148

DISCUSSION

This study has yielded normal, or reference, values for total and direct bilirubin, the transaminases and the membrane enzymes in this Nigerian population of urban dwellers. The values calculated for males and females have characteristics, which are further discussed on the basis of the parameters studied.

The total bilirubin mean was higher in males, while the range was wider in the females. The wider range is statistically derived from the wider scatter, or higher SD, obtained in the females. This same pattern was observed with direct bilirubin; the females recording the higher ULN. The differences were small, however, and hardly lend themselves to further explanations. This pattern was also reported in Caucasians by Wilding et al(22).

Both transaminases had male values higher than obtained in females, with ranges also being wider in males. This also agrees with Caucasian findings(22). The males have larger liver mass, which is important in determining the serum levels of the transaminases(10). The Nigerian AST and ALT ranges were similar to the Caucasian findings(23). However, both LLN and ULN for Nigerian ALT are 2 iu/L and 5 iu/L higher than the respective Caucasian values. The AST ULN for Nigerians, on the other hand, was 2 iu/L lower than Caucasian values. Further studies may provide an explanation for these observations on transaminases.

The membrane enzymes defined different patterns for the sexes. While the mean of ALP was higher for the males, the GGT mean was higher in females. The GGT range was wider in females, while the ALP range was wider in males. The Nigerian values would agree with the Caucasian findings as far as ALP was concerned(22). Why these membrane enzymes show sex variation in Nigerians would need further study. The range for the Nigerian population was wider for both GGT and ALP. The LLN for GGT in Nigerians was 4 iu/L higher than Caucasian values, while the ULN for Nigerians was 25 iu/L above Caucasian values. The Caucasian range of 42-121 iu/L for ALP was well within the Nigerian range of 38-148 iu/L. Possibly, some inapparent canaliculi membrane irritants may be in operation in the Nigerians, accounting for these large differences.

In conclusion, reference values for bilirubin, transaminases and liver membranous enzymes have

been established for the Nigerians in urban Lagos Non-significant differences between males and females were found for all parameters, and explained. It is recommended that larger studies, involving rural Lagos, be done to further enrich the quality of result interpretation in this environment.

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