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Serum Lipid Profile, Liver Function Indices and Electrolyte Levels in Diabetics and Subjects with Hepatic Impairment in the University of Port Harcourt Teaching Hospital

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ABSTRACT: This study investigated serum lipid profile, liver function indices and electrolyte levels in diabetics and hepatitics in the University of Port Harcourt Teaching Hospital. 210 subjects comprising 70 subjects each for diabetics, hepatitics, and control matched for age and sex were sampled for the purpose of the study based upon specified criteria. 45 each were males while 25 each were females. Mean alanine and aspartate aminotransferases (ALT and AST), alkaline phosphatase (ALP) and gamma glutamyltransferase (GGT) activities, respectively, were significantly elevated ($p<0.05$) in the diabetics (22 U/L, 30 U/L, 91 U/L, and 12 U/L respectively) and hepatitics (86 U/L, 161 U/L, 113 U/L, and 50 U/L respectively); mean triglycerides (TG), total cholesterol (TC) and low density lipoprotein-cholesterol (LDL-C) levels respectively, were significantly elevated ($p<0.05$) in the diabetics (1.8 mmol/L, 4.6 mmol/L, and 2.6 mmol/L respectively) and hepatitics (1.4 mmol/L, 3.6 mmol/L, and 1.8 mmol/L respectively) except the hepatitics mean LDL-C level, whereas mean high density lipoprotein-cholesterol (HDL-C) level was significantly reduced ($p\geq0.05$) in the diabetics (1.2 mmol/L) and hepatitics (1.0 mmol/L). Mean sodium and potassium levels were significantly reduced ($p\geq0.05$) in the diabetics (135 mmol/L and 3.5 mmol/L respectively). Mean sodium level was reduced in the hepatitics while mean potassium level was elevated in the hepatitics. Mean bicarbonate level was significantly elevated ($p<0.05$) in the diabetics (28 mmol/L) but slightly elevated in the hepatitics. Conclusively, differences in lipids, electrolyte levels and liver function indices found in diabetics and hepatitics have a great potential as a diagnostic means in clinical practice.

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Key words: Lipid profile, Diabetics, Hepatitics, Diagnostic means, Clinical practice.

Diabetes mellitus (DM) is associated with pervading alteration in lipid profile (Arora, 2010). Research has indicated that diabetics have a higher occurrence of liver and renal function dysfunction, besides production of free radicals due to glucose oxidation, non-enzymatic glycosylation of proteins and subsequent degeneration of glycated proteins produced by oxidation, proceeding to a reduction in antioxidant defence mechanisms activity and destruction of cellular organelles and enzymes, increased lipid peroxidation and insulin growth resistance (Arora, 2010). Hepatitis is arisen from noxious or contagious factors, of which hepatomegaly is a characteristic feature (Mathew *et al*., 2016). Various observational studies assessing the relationship between diabetes and hepatitis have been published (Negro and Alaei, 2009). The proposal that hepatitis C virus (HCV) may be associated with type 2 diabetes mellitus (T2DM) was first made by Allison in 1994. Nevertheless, researchers have provided inconclusive results, with a few researchers supporting the excess T2DM risk with HCV infection compared with non-HCV infected controls (Allison *et al*., 1994), and a few researchers indicated variations (Chehadeh *et al.*, 2009). Both diabetes and hepatitis are widespread, globally. The burden of HCV consistently increases due to hepatitis C-related disorders. From studies, 33% of HCV subjects develop, minimally, an extra-hepatic manifestation (Jacobson *et al.*, 2010). A further similar previous study aimed at determining the links was conducted. It was based on an engrossing report (Marzouk *et al*., 2007). The authors sampled subjects and narrated the widespread of both diabetes and hepatitis. Previous studies suggested that HCV and diabetes result in elevated triglyceride (TG) level in humans with a higher elevation in diabetics (Perlemuter *et al*., 2002). It is directly related to the present study due to its connection by the study of TG in both as the determination of the state of the fatty liver is pertinent in the present. In this study, the serum lipid profile, liver function indices, and electrolyte levels of the diabetics and subjects with hepatic impairment (test groups) alongside the

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control were investigated and compared. The research objectives were to ascertain the blood biochemical parameters levels in the diseases conditions under investigation for the management of these ailments, and to evaluate dyslipidaemia in sampled subjects. This study intends to make available some scientific information on lipid profile, liver and renal function statuses of diabetics and subjects with hepatic impairment.

MATERIALS AND METHODS

Study Area: The study was conducted in the Chemical Pathology Department of the University of Port Harcourt Teaching Hospital located in Choba, near Alakahia junction in Obio Akpor local government area (LGA), a LGA in Port Harcourt, the capital city of Rivers State, Nigeria. Rivers State was formed in 1967 by the Federal Government of Nigeria. Rivers State covers a land area of 21,850 sq. km.

*Equipment/Instruments***:** BSA 3000 Chemistry Analyzer (Model – 3000, Manufacturer – SFRI, France).
UNISCOPE laboratory water bath (Model – Sm0147 Water Bath Cabinet Model SM-8B, Manufacturer - Surgifriend Medicals, England).
Universal 320 laboratory centrifuge (Model – Hettich Refrigerated Benchtop Centrifuge Model Universal 320 R, Manufacturer - Hettich, Germany).
Test-tubes, test- tube racks, pipette (5 ml, 10 ml), micropipette (0-100 µl, 100-1000 µl), micropipette tips, sample containers, plain bottles, syringes and needles, cotton wool, methylated spirit and tourniquette.

TABLE 1 Experimental design for control, diabetic and subjects with hepatic impairment (hepatitic subjects) in different age groups for the male subjects.

Age Group	Type Of Sample	Number Of Subjects	Control	Diabetic	Hepatitic
15-29	Venous blood	45	15	15	15
30-44	Venous blood	45	15	15	15
45-59	Venous blood	45	15	15	15
60-74	Venous blood	45	15	15	15

TABLE 2. Experimental design for control, diabetic and hepatitic in different age groups for the female subjects.

Age Group	Type Of Sample	Number Of Subjects	Control	Diabetic	Hepatitic
15-29	Venous blood	25	9	8	8
30-44	Venous blood	25	8	8	9
45-59	Venous blood	25	8	9	8
60-74	Venous blood	25	8	9	8

Hepatitis and diabetes status were observed in patients seen in the University of Port Harcourt Teaching Hospital (UPTH) in 2017. Chart of diabetics and subjects with hepatic impairment was reviewed. 70 diabetic subjects (diabetics), 70 subjects with hepatic impairment, and 70 normal subjects (control), matched for age and sex were sampled for the purpose of the study based upon the following criteria:

*Inclusion criteria***:** All subjects aged between 15 to 74 years attending the routine clinic at UPTH, and at the Medical Out-Patient (MOP) department that presented themselves. All subjects who agreed to participate in the research.

Exclusion criteria: Subjects with co-infection with hepatitis delta (D) or other metabolic disorders.

Ethical clearance: The proposal for the research was approved by the Research and Ethics Committee of both the University and UPTH before the research was commenced. Participating subjects/each participant provided consent on the available consent form. Subjects who suffered from diabetes or hepatitis were counselled appropriately.

Experimental Subjects: A total of two hundred and ten (210) subjects were sampled for the purpose of the experiment. They consisted of seventy (70) subjects each for diabetics, hepatic impairment, and control matched for age and sex, and satisfying the eligibility criteria which was hepatitis and diabetes positivity in blood for a minimum of five months; exclusion of subjects with co-infection with hepatitis D; and inclusion of subjects between the ages of five (5) to eighty (80) who agreed to participate in the study after being given the informed consent form.

Sample Collection and Preparation: Subjects were issued or given consent form to fill after listening to a detailed explanation from the researcher. 3-4 ml of blood samples were obtained by venipuncture using 5 ml syringes and deposited into plain bottles. The samples were placed inside sample racks and incubated at 25^{o}C for a minimum of 30 minutes. The

serum samples were centrifuged for 5 minutes to obtain a completely clear sample.

Lipid Profile Assays: Determination of serum triglyceride (TG) level was done using the Agappe test kits for triglycerides. Normal range of TG in serum is ≤2.3mmol/l (Thefeld *et al*., 1994). Concerning total cholesterol (TC) determination, blood cholesterol level was determined using the serum and Agappe test kits for cholesterol. Reference range of TC level in serum is ≤5.2mmol/l (Thefeld *et al.*, 1994). Determination of high density lipoprotein-cholesterol (HDL-C) level was done using the serum and Agappe test kits for HDL-C. Normal range of HDL-C in serum is 0.9 -1.6mmol/l (Thefeld *et al*., 1994). The serum low density lipoprotein-cholesterol (LDL-C) was calculated by Friedewald equation. Normal range of LDL-C in serum is 1.3 -2.6mmol/l (Thefeld *et al.*, 1994).

Enzyme Assays: Determination of the serum aspartate aminotransferase (AST) activity was done at 37ºC using the Agappe test kits by measuring the amount of oxaloacetate formed in the presence of L-aspartate and alpha-ketoglutarate as reported by Thefeld *et al*., (1994). Normal range of AST in serum is 1-46U/l (Thefeld *et al*., 1994). For alanine aminotransferase (ALT), L-alanine replaced L-aspartate whereas pyruvate replaced oxaloacetate. Determination of the serum ALT activity was done using Agappe test kits (Thefeld *et al*., 1994). Normal range of ALT present in serum is 1-49U/l (Thefeld *et al*., 1994). Normal range of gamma glutamyltransferase (GGT) in serum is 5-32U/l in female, and 7-45U/l in male (Thefeld *et al*., 1994). Determination of the serum GGT activity was done using Agappe test kits whereas the serum alkaline phosphatase (ALP) activity was determined using the Agappe test kits and monitored the amount of inorganic phosphate released from p-nitrophenyl phosphate following the procedure of Thefeld *et al*., (1994). Normal range of ALP in serum is 64-306U/l for women, and 80-306U/l for men (Thefeld *et al.*, 1994).

Electrolyte Assays: The determination of sodium ion (Na^+) in the serum samples was performed at 25ºC by colorimetric method. Sodium and proteins are precipitated together by magnesium uranyl acetate as uranyl magnesium sodium acetate salt. Excess of uranyl salt reacts with potassium ferrocyanide to produce a brownish colour. The intensity of the colour is inversely proportional to the sodium concentration in the specimen and is measured photometrically at 530 nm. Normal range of Na^+ in serum is 135-145 mmol/l (Thefeld *et al*., 1994). The determination of potassium ion (K^+) in the serum samples was performed at 25ºC by turbidometric method based on the principle of reacting sodium-tetraphenylborate with K^+ to yield potassium-tetraphenylborate and Na^+ (Engelbrecht and McCoy, 2002). The extent of turbidity is proportional to the potassium concentration and is measured photometrically at 578 nm (Engelbrecht and McCoy, 2002). Normal range of K^+ in serum is 3.5-5.5 mmol/l (Thefeld *et al.*, 1994). The determination of bicarbonate ion (HCO_3^-) in the serum samples was also performed at 25ºC using the back titration method which involves a simple reaction between acid and base. The bicarbonate reagent utilizes the enzymatic method (Tietz, 1990). In this procedure, bicarbonate (HCO_3^-) and phosphoenolpyruvate (PEP) are converted to oxaloacetate and phosphate in the reaction catalyzed by phosphoenolpyruvate carboxylase (PEPC). Malate dehydrogenase (MDH) catalyzes the reduction of oxaloacetate to malate with the concomitant oxidation of reduced nicotinamide adenine dinucleotide (NADH). This oxidation of NADH results in a reduction in absorbance of the reaction mixture measured bichromatically at 380/410nm proportional to the bicarbonate content of the sample. Normal range of HCO_3^- in serum is 24-30 mmol/l (Thefeld *et al.*, 1994).

Statistical Analysis: All data were subjected to statistical analysis. Statistical analysis was performed using SPSS version 20.0 (IBM, U.S.A). The data were analyzed using one-way analysis of variance (ANOVA) and significant differences were determined using post Hoc Duncan multiple comparison test ($p<0.05$). The results were considered significant at 95% confidence level. The values are represented as mean ± standard deviation (SD).

RESULTS AND DISCUSSION

The results obtained for the serum lipid profile, liver function indices, and electrolyte levels of the various parameters determined are presented in Figures 1-10. The reduction of HDL-C level in subjects with hepatic impairment in this research was compatible with previous researchers (Cicognani *et al.,* 1997).

Due to the fact that much of the measured HDL-C was synthesized in the liver, major damages to hepatocytes, such as those caused by alcohol consumption or chronic viral hepatitis may generate anomalous liver function and moderate reduction in HDL-C and TC levels (Cicognani *et al.,* 1997). Lipids have been observed to play a significant role in immune host response to infections (Grunfeld and Feingold, 1992).

For diabetics, low HDL-C level was equivalent to high TC level. Diabetic patients had elevated liver marker enzymes values that were within the normal range. Diabetes does not indicate liver damage but can elevate the possibility of chronic liver disease independent of viral hepatitis, as the prevalence of elevated liver marker enzymes in diabetic patients was considerably higher than expected (Kim *et al.*, 2004). Electrolytes such as sodium and potassium assist in the maintenance of the body electrolyte and water balance (Nguyen and Kurtz, 2004).

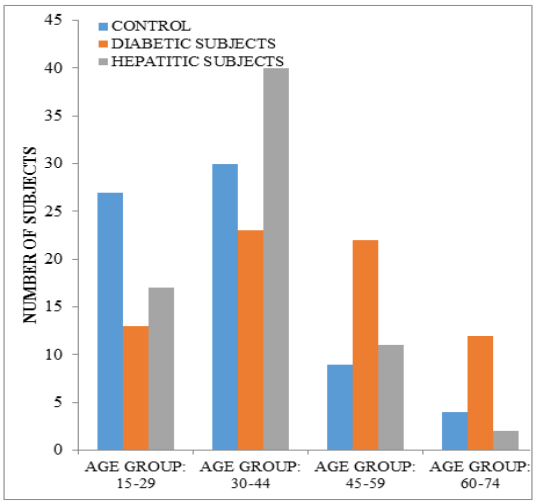

Fig 1: Descriptive report on the age groups of the diabetic subjects (diabetics) and hepatitic subjects (subjects with hepatic impairment). This figure shows the number of subjects in the various age groups listed above. The number of subjects in age group 45-59 is a direct opposite of that in age group 15-29 while the number of subjects in age group 60-74 is a direct opposite of that in age group 30-44.

Elevated ALT value was noted in 42.7% of the diabetics and in 58.6% of the hepatitic subjects. ALT performs the catalysis of the reversible transamination between L-alanine and α-ketoglutarate to yield pyruvate and L-glutamate as such possessing a relevant function in amino acid metabolism and gluconeogenesis. The reaction remains reversible, but the ALT reaction equilibrium favours L-alanine formation. ALT activity is found primarily in the liver (Mathur *et al.*, 2016). Further elucidation may be up-regulation of ALT activity. Among the amino acids, the utmost effective precursor for gluconeogenesis is alanine. Gluconeogenesis is elevated in T2DM subjects due to increased substrate delivery (e.g., alanine) and an increased conversion of alanine to glucose. ALT may thus be up-regulated as a remediable response to the diminished effect of hepatic insulin signalling or, in an alternative way, might leak more comfortably away from the hepatocytes due to fatty infiltration and subsequent destruction (Schindhelm *et al.*, 2006).

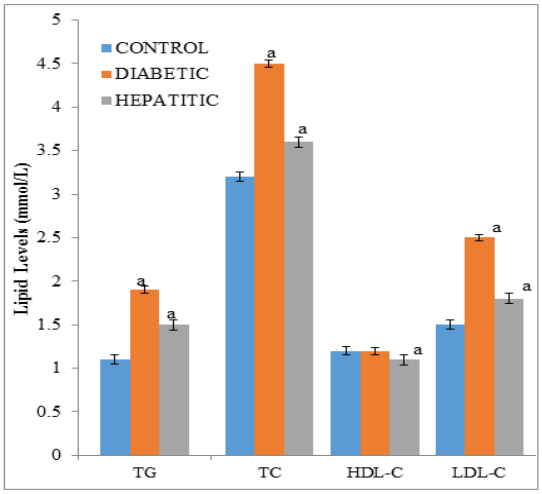

Fig 2: Serum lipid profile in the diabetics and hepatitics (subjects with hepatic impairment). Values are mean ± standard deviation (SD). Values with the same superscript (a) are significantly different ($p<0.05$) compared with the control.

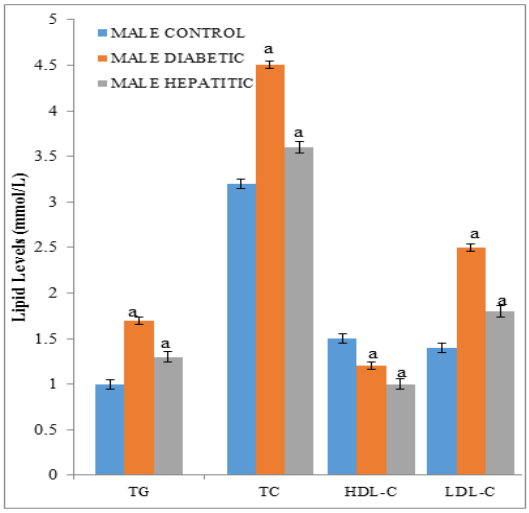

Fig 3: Serum lipid profile in the male diabetics and hepatitics (subjects with hepatic impairment). Values are mean ± standard deviation (SD). Values with the same superscript (a) are significantly different ($p<0.05$) compared with the control.

Elevated AST value was noted in 50.4% of the diabetics and in 68.6% of the hepatitic subjects (Mathur *et al.*, 2016). The activity of AST, an aminotransferase, is frequently measured; this enzyme role is customarily to transfer the amino group from an amino acid, aspartate in the case of AST, to a keto acid, yielding oxaloacetate and pyruvate, respectively. It is seen in hepatocyte cytoplasm; an alternative type of AST is also seen in hepatocyte mitochondria. Notwithstanding that both aminotransferases; AST, and ALT, are generally circulated in further body tissues, AST activities outside the liver are reduced and, thus, considered to be more specific for hepatocellular destruction (Boon *et al.*, 2006).

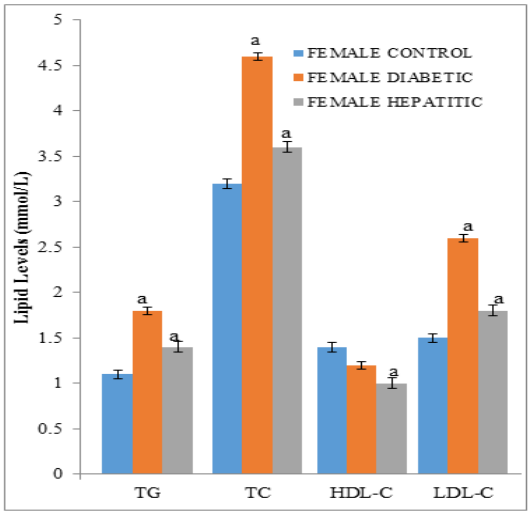

Fig 4: Serum lipid profile in the female diabetics and hepatitics (subjects with hepatic impairment). Values are mean ± standard deviation (SD). Values with the same superscript (a) are significantly different (p<0.05) compared with the control.

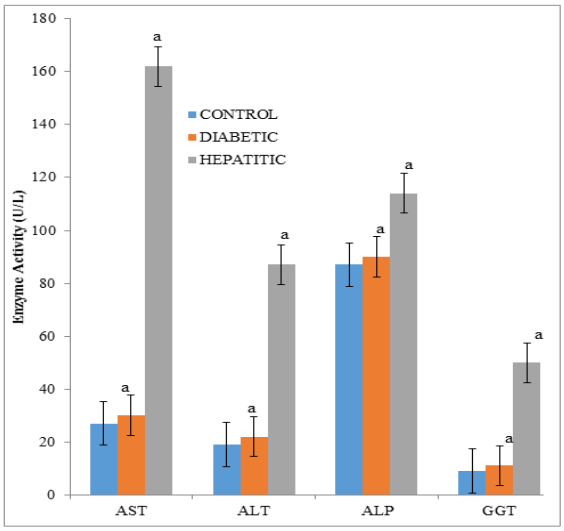

Fig 5: Serum liver marker enzymes activity (liver function index) in the diabetics and hepatitics (subjects with hepatic impairment). Values are mean ± standard deviation (SD). Values with the same superscript (a) are significantly different (p<0.05) compared with the control.

Elevated ALP value was noted in 41.1% of the diabetics and in 49.4% of the hepatitic subjects. T2DM exists as a metabolic syndrome in which fat metabolism is dysregulated and there is consequent increase of FFA resulting in subsequent fatty liver. ALP is seen to be associated with cell membrane which connects the bile canaliculus, and so highly elevated serum concentration of the liver isoenzyme signifies cholestasis preferably to barely destruction to the hepatocytes (Mathur *et al.*, 2016). According to a study by Southampton University hospitals, 60 diabetics stabilized on oral hypoglycaemic agents or insulin, and routine tests, specifically saw their ALP level rise anomalously although barely to more than twice the normal upper limit. It may be concluded that this notable liver function disease is rare among stabilized diabetics (Foster *et al.*, 2013).

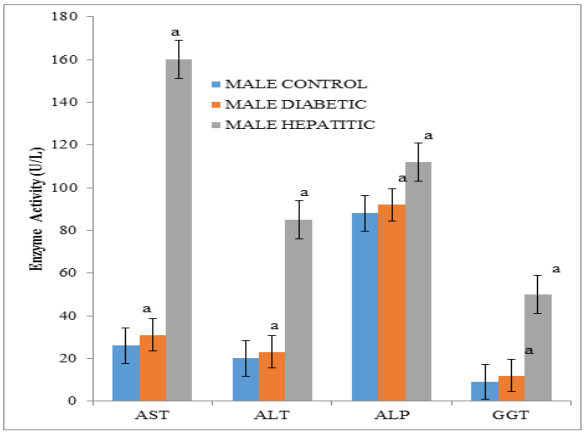

Fig 6: Serum liver marker enzymes activity (liver function index) in the male diabetics and hepatitics (subjects with hepatic impairment). Values are mean ± standard deviation (SD). Values with the same superscript (a) are significantly different (p<0.05) compared with the control.

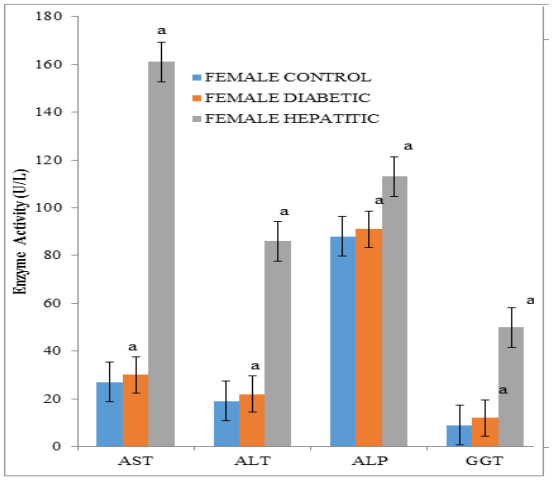

Fig 7: Serum liver marker enzymes activity (liver function index) in the female diabetics and hepatitics (subjects with hepatic impairment). Values are mean ± standard deviation (SD). Values with the same superscript (a) are significantly different (p<0.05) compared with the control.

Elevated GGT value was noted in 48.9% of the diabetics and in 59.2% of the hepatitic subjects (Mathur *et al.*, 2016). Elevated TG value was noted in 75.6% of the diabetics and in 58.3% of the hepatitic subjects (Tietz, 1990). Elevated TC value was noted in 82.7% of the diabetics and in 60.5% of the hepatitic subjects (Third Report of the NCEP, 2001). Reduced HDL-C value was noted in 4.3% of the diabetics and in 30.7% of the hepatitic subjects (Third Report of the NCEP, 2001). Elevated LDL-C

value was noted in 93.8% of the diabetics and in 4.9% of the hepatitic subjects (Third Report of the NCEP, 2001). Reduced Na^+ value was noted in 71.8% of the diabetics and in 73.4% of the hepatitic subjects (Tietz, 1990). Reduced K^+ value was noted in 78.6% of the diabetics and in 82.2% of the hepatitic subjects (Tietz, 1990). Elevated bicarbonate value was noted in 53.5% of the diabetics and in 4.7% of the hepatitic subjects (Tietz, 1990).

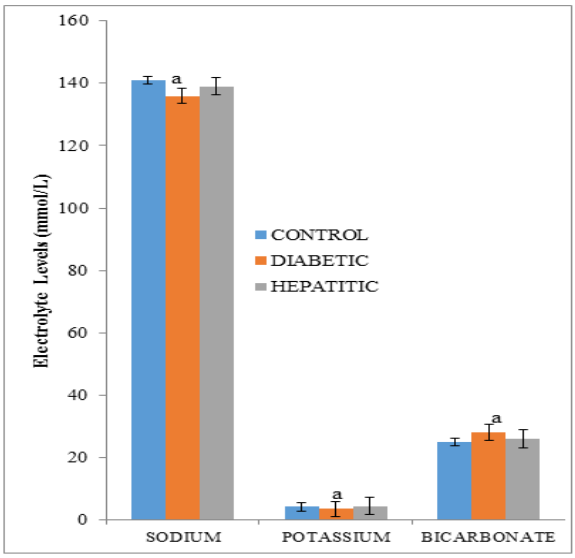

Fig 8: Serum electrolyte levels in the diabetics and hepatitics (subjects with hepatic impairment). Values are mean ± standard deviation (SD). Values with the same superscript (a) are significantly different ($p<0.05$) compared with the control.

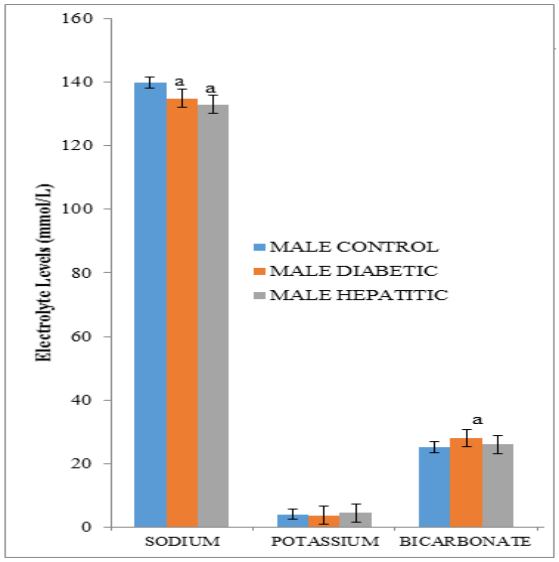

Fig 9: Serum electrolyte levels in the male diabetics and hepatitics (subjects with hepatic impairment). Values are mean ± standard deviation (SD). Values with the same superscript (a) are significantly different ($p<0.05$) compared with the control.

Type 2 diabetic subjects were shown to be associated with large occurrence of anomalous tests compared with non-diabetic subjects, with elevated ALT values being the most usual anomaly. A cross sectional study from Iran demonstrated ALT and AST elevation which was 10.4% and 3.3% respectively in type 2 diabetics (Meybodi *et al*., 2008). Based on a research conducted in Sudan, where 50 diabetic subjects and 30 normal control subjects were tested for liver function, ALT, AST, and GGT mean values were shown to be significantly elevated among diabetic subjects compared with the control. However, the values were within the normal range (Idris *et al*., 2011). Based on Vozarova *et al*., the liver marker enzymes; ALT, AST and ALP were estimated to be significantly elevated in diabetics in comparison to the control (Vozarova *et al*., 2002).

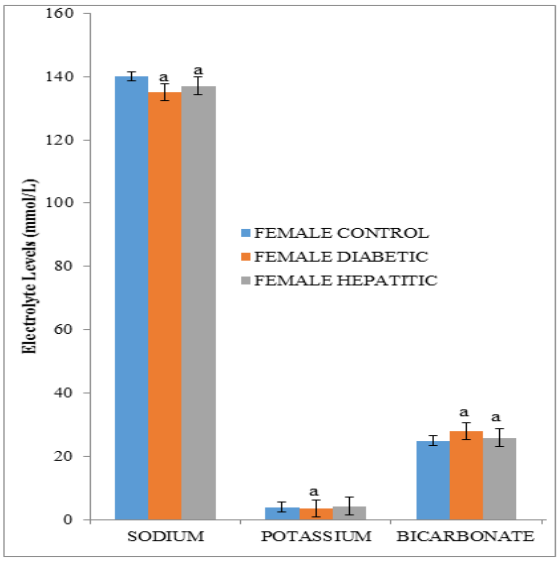

Fig 10: Serum electrolyte levels in the female diabetics and hepatitics (subjects with hepatic impairment). Values are mean ± standard deviation (SD). Values with the same superscript (a) are significantly different ($p<0.05$) compared with the control.

Electrolyte balances derangement may occur in DM, arising from hyperglycaemia, hyperketonaemia, and insulin deficiency. The present study showed a majorly significant reduction in Na^+ and K^+ serum values in DM. This result was consistent with those reported in previous studies. Below physiologic conditions, most of Na^+ is reabsorbed in the kidneys' proximal tubule (Guyton and Hall, 2006). The relative insulin deficiency present in DM decreases lipoprotein lipase action effect and leads to reduced HDL-C levels and elevated TG levels, which may be improved with enhanced glycemic control (Brunzell and Chait, 1997).

*Conclusion***:** An elevation in mean serum potassium in hepatitics was observed due to damage by the hepatitis virus which could lead to glomerular filtration pattern change since potassium is much involved in the glomerular basement membrane and reabsorbed in the tubules. Hepatitis appeared to produce a more dysfunctional state to subjects compared with diabetes despite the complications associated with diabetes. Differences in lipids, electrolyte levels and liver function indices found in diabetics and hepatitics have a great potential as a diagnostic means in clinical practice.

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*Compliance with Ethical Standards***:** The ethics committee of University of Port Harcourt and University of Port Harcourt Teaching Hospital respectively approved this study (REC numbers: UPH/CEREMAD/REC/04 and UPTH/ADM/90/S.II/VOL.XI/361 respectively) before the commencement of the research work.

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