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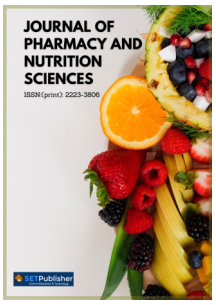

Anthropometry and Liver Function Parameters in Individuals with Metabolic Syndrome

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Abstract:

Metabolic syndrome (MS) is a metabolic condition commonly associated with central adiposity and altered liver function parameters (LFPs). Several studies have suggested these altered LFPs as a result of fatty liver diseases (e.g., non-alcoholic fatty liver diseases) often prevalent in MS. Since altered LFPs are very common in MS, there is a possibility they can be used as predictors of MS. However, only a few studies have been carried out to evaluate this possibility. This study, therefore, aimed to evaluate the potential of LFPs as predictors or risk factors of MS. The study groups included 50 individuals diagnosed with MS (case group) and 50 apparently normal individuals (control) from Ibadan, Oyo State, Nigeria. Anthropometric measurements, phlebotomy, liver function tests, and lipid profile estimations were done using standard procedures. (The result and conclusion section has been omitted).

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INTRODUCTION

Metabolic syndrome (MS) is a cluster of conditions that occur together, thereby increasing the risk of heart disease and other health problems (e.g. stroke and diabetes) [1]. MS is commonly associated with central adiposity and can be characterized by the presence of three or more of the following components: hypertension (diastolic blood pressure (DBP) >85 mmHg, systolic blood pressure (SBP) >130 mmHg or on antihypertensive drug treatment), elevated triglycerides (TG) (>150 mg/dl or on drug treatment for raised triglycerides), decreased high-density lipoprotein cholesterol (HDL-C) level (<50 mg/dl in women, <40 mg/dl in men or on drug treatment for reduced HDL-C), impaired fasting plasma glucose (FPG) (100 - 125 mg/dl or on anti-diabetic drug treatment), and abdominal obesity (waist circumference (WC) >88 cm in women, >102 cm in men) [2].

Several studies have suggested liver enzymes to be significantly related to high risk of metabolic syndrome [1,3], while alanine aminotransferase (ALT) and aspartate aminotransferase (AST) have been said to positively correlate significantly with body mass index (BMI) [4,5]. Among hepatic enzymes, ALT has been suspected to be the most specific indicator of hepatic pathology [6]. Previous studies have also described an inverse correlation between serum total protein and liver disease [7]. An inverse correlation has been suspected to exist between serum albumin and body mass index (BMI) [8]. Glycated albumin has been reported to be negatively associated with obesity in non-diabetic children [9,10], and more recently in non-diabetic adults [9].

Liver enzymes such as aspartate aminotransferase (AST), alanine aminotransferase (ALT), and gamma-glutamyltransferase (GGT) are considered as surrogate markers of liver function. Recently, an elevated serum GGT level has been reported as an important risk factor in the development of impaired fasting glucose (IFG), type 2 diabetes mellitus (T2DM), cardiovascular disease, and metabolic syndrome. AST and ALT have also been reported to be associated with MS and T2DM [11].

The diagnosis of MS is made using the International Diabetes Federation (IDF) parameters [12], however, there is a need for enhanced accuracy in the diagnosis of the condition. Several studies have reported altered liver function parameters (LFPs) in MS [3,13,14], therefore, there is a possibility that they can be included as indirect markers of MS.

Abdominal obesity is a known component of MS, and according to the Joint Interim Statement of the International Diabetes Federation Task Force on Epidemiology and Prevention [12], it can be estimated using the waist circumference. Several studies have linked altered plasma LFPs with waist circumference [3,11]. Not enough studies, however, have compared the plasma LFPs with other anthropometry parameters and components of MS. This study, therefore, aimed to evaluate the relationship between LFPs, and anthropometry parameters and components of MS, to further contribute to the pool of knowledge on the potential of LFPs as predictors of MS.

MATERIALS AND METHOD

Sample Collection

After ethical approval has been obtained from the Joint Ethical Committee of the University of Ibadan/ University College Hospital, Ibadan, Nigeria (UI/UCH), 788 individuals were picked randomly from different locations in Ibadan. Several laboratory tests and anthropometric measurements were carried out to confirm those that fall within the measures of MS according to the Joint Interim Statement (JIS) criteria, 2009 [12]. Consent forms and questionnaires were given to each member of the study groups before sample collection. The questionnaire was divided into 5 sections i.e., gender, age, anthropometric parameters, residential, and health sections. The survey was to ensure there was no recent history of alcohol or drug abuse, bone defect/problem, chronic illness, immune and metabolic disorders, cancer or tumour, and/or liver disease (e.g. hepatitis) among the study groups.

Sample Size Determination

The prevalence of MS in Nigeria ranges from 12.1 - 33.1% [15,16] and globally the prevalence is 37.4% [17].

SAMPLE SIZE: $N = \frac{2(Z\alpha + Z\beta)^2 X\pi(1-\pi)}{(P1-P2)^2}$

Where $\pi = \frac{P1-P2}{2}$

Zα = standard normal deviate of α =1.96

Zβ = standard normal deviate of β = (z-β) = 80% of power = 0.84

P_1= prevalence of MS in Nigeria = 12.1% [15].

P_2= Expected prevalence of MS in general population. (Arbitrary estimate & assumption, general population) = 37.4% [17].

$$\pi = \frac{p1 - p2}{2} = \frac{0.121 + 0.374}{2} = 0.2475$$

$$N = \frac{2(1.96 + 0.84)^2 \times 0.2475 \times 0.7525}{0.064}$$

N = 46

Therefore, 100 individuals (66 females), aged 31 to 80 years were randomly picked from the above-mentioned population (788 individuals), and divided into case (50 individuals diagnosed with MS with no recent history of alcohol or drug abuse, or any other illness) and control (50 apparently normal individuals) groups.

Blood Sample Collection and Preparation

Ten ml of venous blood was aseptically obtained by venepuncture from the patients. This was achieved by applying a tourniquet of 4-6 inches (10-15 cm) above the intended puncture site to avoid the return of venous blood to the heart and the distended vein. The puncture spot, the median cubital vein in the antecubital fossa, was first cleansed with an alcohol swab, and the blood was then collected with new disposable pyrogen-free needles and syringes after the skin had been air-dried. The sample was dispensed into a covered anticoagulant free bottle. The blood was left at room temperature undisturbed for 20 min and the clot formed was removed by centrifugation at 1,000 g for 10 min after which the serum was extracted and stored at -20 ^{o}C until analysis was done.

Determination of Anthropometric Parameters

The anthropometric measurements (height, waist and hip circumferences, BMI, body weight, and waist/hip ratio (WHR)) of each individual were done according to the international guidelines for anthropometric research using standard procedures [18].

Estimation of % Body Fat

Based on population studies, the percentage of body fat is approximately equal to the body adiposity index (BAI) which is calculated using height and the HC [19,20]. The formula is as follows:

$$BAI = \frac{100 \times hip\ circumference\ in\ m}{Height\ in\ m \times \sqrt{height}} - 18$$

Laboratory Procedures

Estimation of Serum ALP Activity

The serum ALP activity was estimated using a kinetic method as described by Emam *et al*. [21]. 1 ml of para-nitrophenyl phosphate (pH 9.8) was pipetted into a cuvette containing 0.1 ml of non-haemolysed serum sample. The colourless para-nitrophenyl phosphate is hydrolysed by alkaline phosphatase at pH 9.8 and 25 ˚C to form yellow free para nitrophenol. The initial absorbance (A_0) was measured at 410 nm/min and 25 ˚C, the reading was taken again after 1, 2 and 3 min respectively.

The mean value of the differences between the absorbances (△A) was calculated as follows:

$$\Delta A = \frac{(A_1 - A_0) + (A_2 - A_1) + (A_3 - A_2)}{3}$$

The ALP activity was then calculated using the following formulae:

U/L = 1158 x △A

The normal reference range of ALP for an adult is 60 - 180 U/L.

Estimation of Serum Aspartate Aminotransferase (AST) Activity

The AST activity was estimated using the colorimetric method as described by Obi *et al*. [22]. Aspartate transaminase catalyses the interconversion of two amino acids: L-aspartate and L-glutamate to their corresponding ketoacids (i.e., oxaloacetate and ∝-ketoglutarate). The oxaloacetate then reacts with 2, 4-dinitrophenylhydrazine to produce a brownish coloured solution which can be measured spectrophotometrically.

L-aspartate + ∝-ketoglutarate ⇔ oxaloacetate + L-glutamate

About 0.6 ml of the reagent blank (0.5 ml of reagent 1 (buffer containing 100 mmol/l phosphate buffer (pH 7.4), 100 mmol/l L-aspartate and 2 mmol/l ∝-ketoglutarate) and 0.1 ml of distilled water) and 0.6 ml of the sample [0.5 ml of reagent 1 and 0.1 ml of the sample (non-haemolysed serum)] were pipetted into different test tubes and incubated for exactly 30 min at 37 ˚C. In addition, 0.5 ml of reagent 2 (2mmol/l of 2,4-dinitrophenylhydrazine) was pipetted into each test tube, mixed and allowed to stand for exactly 20 min at 25 ˚C. After 20 min, 5 ml of sodium hydroxide was then

added to each test tube to stop the reaction. The solution in each test tube was mixed, and the absorbance of the sample (A_{sample}) was read against the sample blank after 5 min.

Estimation of Serum ALT Activity

The ALT activity was estimated using the colorimetric method as described by Obi *et al*. [22]. ALT catalyses the transfer of amino group between L-alanine and L-glutamate to form their corresponding ketoacids (i.e., ∝-ketoglutarate and pyruvate). The pyruvate then reacts with 2, 4-dinitrophenylhydrazine to produce pyruvate hydrazone a brownish coloured solution that can be measured spectrophotometrically.

∝-ketoglutarate + L-alanine ⇔ L-glutamate + pyruvate

About 0.6 ml of the reagent blank (0.5 ml of reagent 1 (buffer containing 100 mmol/l phosphate buffer (pH 7.4), 200 mmol/l of L-alanine and 2 mmol/l ∝-ketoglutarate) and 0.1 ml of distilled water) and 0.6 ml of the sample (0.5 ml of reagent 1 and 0.1 ml of the sample (non-haemolysed serum)) were pipetted into different test tubes and incubated for exactly 30 min at 37 ˚C. The rest of the procedure is as found in AST above.

Estimation of Total Protein

The total serum protein was estimated using the method described by Roy and Bandyopadhyay, [23]. In an alkaline solution, proteins form a purple complex with cupric ions. The reaction is named after the basic compound biuret, which has a similar reaction. The strength of the purple colour is determined at 540 nm on the spectrophotometer and compared with the standard serum of the known protein concentration.

About 5.5 ml of the reagent blank (containing 2.5 ml of 0.154 M sodium chloride diluent and 3 ml of biuret reagent (0.2 M sodium hydroxide, 0.032 M sodium potassium tartrate, 0.019 M copper sulphate and 0.054 M potassium iodide)), standard 1 (S1) (containing 2.45 ml sodium chloride diluent, 0.05 ml standard, and 3 ml biuret reagent), standard 2 (S2) (containing 2.4 ml sodium chloride diluent, 0.1 ml standard, and 3 ml biuret reagent), standard 3 (S3) (containing 2.35 ml sodium chloride diluent, 0.15 ml standard, and 3 ml biuret reagent), test sample (containing 2.4 ml sodium chloride diluent, 0.1 ml test sample (non-haemolysed serum), and 3 ml biuret reagent), and quality control (containing 2.4 ml sodium chloride diluent, 0.1 ml quality control sample, and 3 ml biuret reagent) were pipetted into different test tubes. The solution was thoroughly mixed and incubated at room temperature (25-35 °C) for 15 min. The spectrophotometer was set to zero at 540 nm with a blank, and the absorbances of standards, test, and quality control (QC) were measured. The absorbance values of standards (S1, S2, and S3) were plotted against their respective concentrations, once linearity had been proved, the test samples were then calculated for using standard S2 and the formula:

$$\frac{Test\ absorbance}{Standard\ absorbance} \times Concentration\ of\ S2 \ldots\ldots\ldots\ldots \frac{g}{dl}$$

The normal reference range for normal serum total protein is 6.5 –8.5 g/dl.

Estimation of Serum Albumin

Serum albumin estimation was done using the method described by Sani *et al*. [24]. At pH 4.15, albumin combines quantitatively with bromocresol green, resulting in a green colour that can be measured using a 630 nm/red filter [24].

To dilute with distilled water, 2 ml of 5.3%, 11.1%, 17.6%, 25%, 11.1%, and 11.1% of standards (S1, S2, S3, & S4), test and quality control samples respectively were each pipetted into appropriately labelled 13 x 100 mm tubes. The solution was well mixed. Then 2.6 ml of standard 1 (S1) (containing 0.1 ml distilled water and 2.5 ml BCG solution), standards 2 (S2), 3 (S3) and 4 (S4) (each containing 0.1 ml diluted standard and 2.5 ml BCG solution), test sample (containing 0.1 ml diluted test sample and 2.5 ml BCG solution), and the quality control (containing 0.1 ml diluted quality control sample and 2.5 ml BCG solution) were each pipetted into another set of appropriately labelled 18 x 50 mm test tubes. The tubes were gently vortexed and incubated at room temperature (25 – 35 ˚C) for 10 min. The spectrophotometer was set to zero using blank at 630 nm and the absorbance of standards, test & QC were measured. The absorbance values of standards (S1, S2, S3, and S4) were plotted against their respective concentrations. Once linearity is proved, the test samples were then calculated for using standard S2 and the formula:

$$\frac{Test\ absorbance}{Standard\ absorbance} \times Concentration\ of\ S2 \ldots\ldots\ldots\ldots \frac{g}{dl}$$

The normal reference range for normal Serum albumin is 3.5 – 5.0 g/dl.

Data Analysis

All completed questionnaires were collected and screened for completeness and all blood samples collected from the respondents were analysed in the laboratory. Relationships between data obtained from the questionnaire and laboratory parameters were analysed by using the Mann-Whitney and the Spearman rank correlation tests after distributions of all the test results have been checked for normality using the Anderson-Darling test. Data were analysed at a 5% level of significance.

RESULTS

Comparison of means of the MS components, anthropometry, and liver function parameters of the case and control groups were depicted in Figures **1**, **2** & **3** respectively. Except for total cholesterol (TC), Figure **1** shows significantly higher MS components in the case group than the control. Increased anthropometry parameters and altered LFPs were also observed in the case group compared to the control which was apparently normal (Figures **2** & **3**).

The results showed no significant correlation between the LFPs of the case group and their respective % body fat, height, hip circumference (HC) and waist/hip ratio (Tables **1**, **2**, **6**, & **7**). However, significant positive correlations were observed between ALT and BMI and waist circumference respectively (Tables **4** & **5**). Table **3** also showed a significant positive correlation between body weight and total protein (Table **3**).

% body fat, BMI, waist circumference, and waist/hip ratio showed no significant correlation with the components of MS in the case group (Tables **1**, **4**, & **7**). There were, however, significant inverse correlations

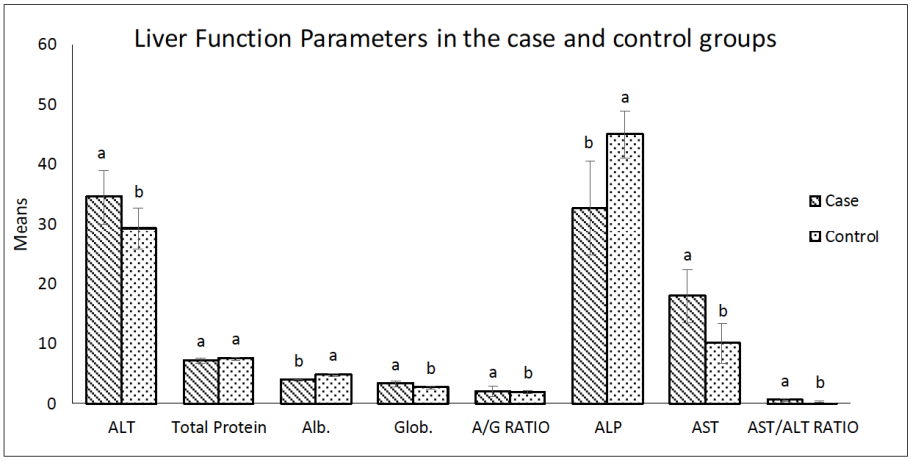

Figure 1: Comparison of means of the liver function parameters in the case and control groups. Columns with different alphabets within the same parameter are significantly different ($p < 0.05$).

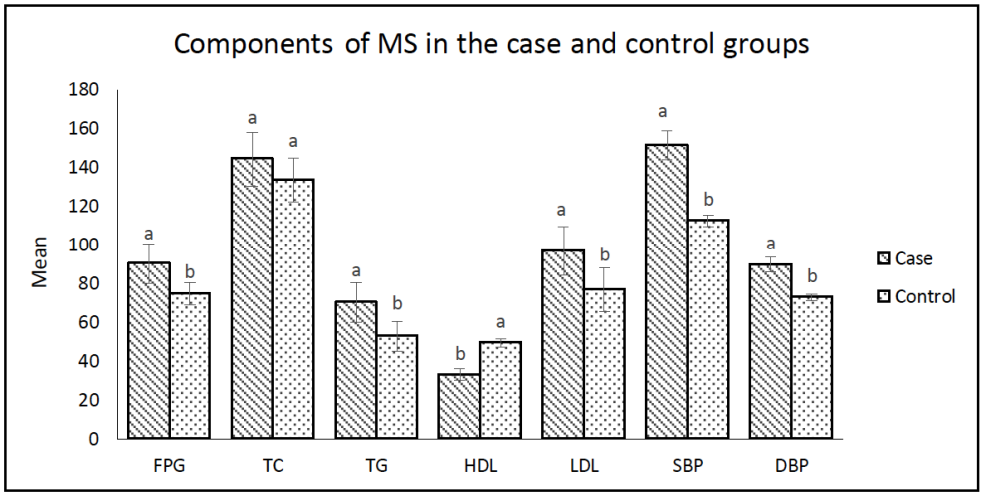

Figure 2: Comparison of means of the components of MS in the case and control groups. Columns with different alphabets within the same component are significantly different ($p < 0.05$).

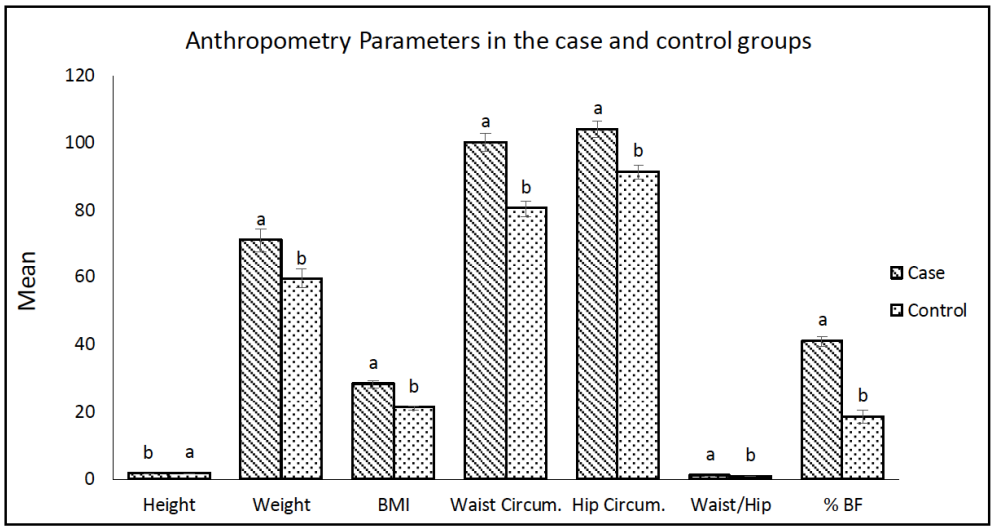

Figure 3: Comparison of means of the anthropometric parameters in the case and control groups. Columns with different alphabets within the same parameter are significantly different ($p < 0.05$).

Table 1: Spearman Correlation between % Body Fat and Liver Function Parameters and Components of Metabolic Syndrome in the Case and Control Groups

	% body fat			
	Case		Control	
	r_s	p-value ($p < 0.05$)	r_s	p-value ($p < 0.05$)
Liver function parameters				
ALP (U/L)	0.148	0.321	-0.268	0.066
AST (U/L)	0.135	0.354	-0.088	0.599
ALT (U/L)	0.266	0.062	0.522	0.000*
AST/ALT Ratio	-0.064	0.659	-0.124	0.457
Total Protein (g/dl)	0.226	0.115	-0.274	0.066
Albumin (g/dl)	-0.000	0.997	-0.326	0.027*
Globulin (g/dl)	0.228	0.111	-0.103	0.496
Albumin/globulin ratio	-0.248	0.082	-0.131	0.386
Components of Metabolic Syndrome				
FPG	-0.135	0.350	-0.462	0.001*
Total cholesterol (mg/dL)	0.252	0.077	-0.195	0.175
Triacylglycerol (mg/dL)	-0.215	0.134	0.099	0.496
HDL cholesterol (mg/dL)	0.173	0.229	0.283	0.046*
LDL cholesterol (mg/dL)	0.261	0.067	-0.227	0.113
SBP (mm Hg)	0.207	0.148	0.073	0.612
DBP (mm Hg)	0.160	0.268	-0.225	0.116

[1]BMI, body mass index; FPG, fasting plasma glucose; SBP, systolic blood pressure; DBP, diastolic blood pressure.
[2]Analysed by using Spearman rank correlation.
Number of participants = 50.

Table 2: Spearman Correlation between Height and Anthropometric Parameters and Components of Metabolic Syndrome in the Case and Control Groups

	Height			
	Case		Control	
	r_s	p-value ($p < 0.05$)	r_s	p-value ($p < 0.05$)
Liver function parameters				
ALP (U/L)	-0.112	0.455	0.447	0.002*
AST (U/L)	0.112	0.445	0.361	0.026*
ALT (U/L)	0.261	0.067	-0.230	0.109
AST/ALT Ratio	-0.025	0.864	0.305	0.035*
Total Protein (g/dl)	0.097	0.501	0.095	0.514
Albumin (g/dl)	0.140	0.333	0.339	0.017*
Globulin (g/dl)	0.018	0.903	-0.106	0.468
Albumin/globulin ratio	0.039	0.786	0.322	0.024*
Components of Metabolic Syndrome				
FPG	-0.104	0.472	0.138	0.341
Total cholesterol (mg/dL)	0.320	0.023*	0.284	0.046*
Triacylglycerol (mg/dL)	0.237	0.097	-0.090	0.536
HDL cholesterol (mg/dL)	0.104	0.471	-0.307	0.030*
LDL cholesterol (mg/dL)	0.266	0.062	0.332	0.019*
SBP (mm Hg)	-0.125	0.388	0.355	0.012*
SBP (mm Hg)DBP (mm Hg)	-0.049	0.737	0.296	0.037*

[1]BMI, body mass index; FPG, fasting plasma glucose; SBP, systolic blood pressure; DBP, diastolic blood pressure.
[2]Analysed by using Spearman rank correlation.
Number of participants = 50.

Table 3: Spearman Correlation between Weight and Anthropometric Parameters and Components of Metabolic Syndrome in the Case and Control Groups

	Weight			
	Case		Control	
	r_s	p-value ($p < 0.05$)	r_s	p-value ($p < 0.05$)
Liver function parameters				
ALP (U/L)	-0.041	0.783	0.460	0.001*
AST (U/L)	0.140	0.337	0.176	0.290
ALT (U/L)	0.338	0.016	-0.029	0.839
AST/ALT Ratio	-0.078	0.591	0.175	0.234
Total Protein (g/dl)	0.281	0.048*	0.111	0.446
Albumin (g/dl)	0.024	0.870	0.257	0.074
Globulin (g/dl)	0.266	0.062	-0.038	0.793
Albumin/globulin ratio	-0.252	0.077	0.184	0.206
Components of Metabolic Syndrome				
FPG	-0.289	0.042*	-0.276	0.053
Total cholesterol (mg/dL)	0.364	0.009*	0.298	0.035*
Triacylglycerol (mg/dL)	-0.100	0.488	0.182	0.206
HDL cholesterol (mg/dL)	0.220	0.125	-0.173	0.230
LDL cholesterol (mg/dL)	0.331	0.019*	0.345	0.014*
SBP (mm Hg)	0.096	0.507	0.540	0.000*
DBP (mm Hg)	0.175	0.225	0.192	0.183

[1]BMI, body mass index; FPG, fasting plasma glucose; SBP, systolic blood pressure; DBP, diastolic blood pressure.
[2]Analysed by using Spearman rank correlation.
Number of participants = 50.

Table 4: Spearman Correlation between BMI and Anthropometric Parameters and Components of Metabolic Syndrome in the Case and Control Groups

	BMI			
	Case		Control	
	r_s	p-value ($p < 0.05$)	r_s	p-value ($p < 0.05$)
Liver function parameters				
ALP (U/L)	0.099	0.509	0.358	0.015*
AST (U/L)	0.118	0.418	-0.002	0.991
ALT (U/L)	0.305	0.031*	0.291	0.041*
AST/ALT Ratio	-0.096	0.505	0.153	0.301
Total Protein (g/dl)	0.238	0.095	0.050	0.731
Albumin (g/dl)	0.007	0.960	-0.003	0.986
Globulin (g/dl)	0.240	0.093	0.058	0.693
Albumin/globulin ratio	-0.265	0.063	-0.093	0.525
Components of Metabolic Syndrome				
FPG	-0.151	0.294	-0.596	0.000*
Total cholesterol (mg/dL)	0.234	0.102	0.182	0.207
Triacylglycerol (mg/dL)	-0.230	0.107	0.380	0.006*
HDL cholesterol (mg/dL)	0.190	0.187	-0.138	0.341
LDL cholesterol (mg/dL)	0.238	0.096	0.277	0.051
SBP (mm Hg)	0.212	0.140	0.389	0.005*
SBP (mm Hg)DBP (mm Hg)	0.189	0.188	-0.145	0.315

[1]BMI, body mass index; FPG, fasting plasma glucose; SBP, systolic blood pressure; DBP, diastolic blood pressure.
[2]Analysed by using Spearman rank correlation.
Number of participants = 50.

Table 5: Spearman Correlation between Waist Circumference and Anthropometric Parameters and Components of Metabolic Syndrome in the Case and Control Groups

	Waist Circumference			
	Case		Control	
	r_s	p-value ($p < 0.05$)	r_s	p-value ($p < 0.05$)
Liver function parameters				
ALP (U/L)	-0.035	0.816	0.284	0.055
AST (U/L)	0.134	0.360	-0.164	0.325
ALT (U/L)	0.311	0.028*	0.279	0.050
AST/ALT Ratio	-0.064	0.661	0.038	0.800
Total Protein (g/dl)	0.057	0.693	-0.127	0.384
Albumin (g/dl)	0.120	0.405	-0.131	0.369
Globulin (g/dl)	-0.005	0.971	-0.029	0.845
Albumin/globulin ratio	0.021	0.883	0.018	0.901
Components of Metabolic Syndrome				
FPG	-0.198	0.168	-0.349	0.013*
Total cholesterol (mg/dL)	0.175	0.225	0.444	0.001*
Triacylglycerol (mg/dL)	-0.118	0.413	0.290	0.041*
HDL cholesterol (mg/dL)	0.171	0.236	-0.041	0.777
LDL cholesterol (mg/dL)	0.147	0.310	0.482	0.000*
SBP (mm Hg)	0.081	0.576	0.366	0.009*
SBP (mm Hg)DBP (mm Hg)	0.110	0.446	0.118	0.413

[1]BMI, body mass index; FPG, fasting plasma glucose; SBP, systolic blood pressure; DBP, diastolic blood pressure.
[2]Analysed by using Spearman rank correlation.
Number of participants = 50.

Table 6: Spearman Correlation between the Hip Circumference and Anthropometric Parameters and Components of Metabolic Syndrome in the Case and Control Groups

	Hip Circumference			
	Case		Control	
	r_s	p-value ($p < 0.05$)	r_s	p-value ($p < 0.05$)
Liver function parameters				
ALP (U/L)	0.087	0.562	0.111	0.462
AST (U/L)	0.054	0.714	-0.019	0.908
ALT (U/L)	0.177	0.220	0.233	0.104
AST/ALT Ratio	-0.023	0.874	-0.001	0.996
Total Protein (g/dl)	0.136	0.348	-0.100	0.496
Albumin (g/dl)	-0.118	0.414	-0.100	0.496
Globulin (g/dl)	0.217	0.131	-0.039	0.789
Albumin/globulin ratio	-0.241	0.092	0.021	0.887
Components of Metabolic Syndrome				
FPG	-0.434	0.002*	-0.443	0.001*
Total cholesterol (mg/dL)	0.371	0.008*	0.220	0.125
Triacylglycerol (mg/dL)	-0.018	0.901	0.338	0.017*
HDL cholesterol (mg/dL)	0.265	0.063	0.059	0.686
LDL cholesterol (mg/dL)	0.357	0.011*	0.234	0.103
SBP (mm Hg)	0.026	0.859	0.332	0.018*
DBP (mm Hg)	0.054	0.709	0.128	0.377

[1]BMI, body mass index; FPG, fasting plasma glucose; SBP, systolic blood pressure; DBP, diastolic blood pressure.
[2]Analysed by using Spearman rank correlation.
Number of participants = 50.

Table 7: Spearman Correlation between Waist/Hip Ratio and Anthropometric Parameters and Components of Metabolic Syndrome in the Case and Control Groups

	Waist/Hip Ratio			
	Case		Control	
	r_s	p-value ($p < 0.05$)	r_s	p-value ($p < 0.05$)
Liver function parameters				
ALP (U/L)	-0.071	0.635	0.284	0.056
AST (U/L)	0.088	0.547	-0.236	0.154
ALT (U/L)	0.127	0.380	0.297	0.036*
AST/ALT Ratio	0.004	0.978	-0.075	0.613
Total Protein (g/dl)	-0.009	0.952	-0.142	0.332
Albumin (g/dl)	0.186	0.195	-0.234	0.105
Globulin (g/dl)	-0.162	0.260	-0.041	0.779
Albumin/globulin ratio	0.238	0.096	-0.034	0.819
Components of Metabolic Syndrome				
FPG	0.252	0.077	-0.157	0.276
Total cholesterol (mg/dL)	-0.132	0.359	0.555	0.000*
Triacylglycerol (mg/dL)	-0.073	0.614	0.205	0.152
HDL cholesterol (mg/dL)	-0.133	0.356	-0.081	0.576
LDL cholesterol (mg/dL)	-0.159	0.269	0.576	0.000*
SBP (mm Hg)	0.063	0.665	0.212	0.140
DBP (mm Hg)	0.036	0.803	0.000	0.999

[1]BMI, body mass index; FPG, fasting plasma glucose; SBP, systolic blood pressure; DBP, diastolic blood pressure.
[2]Analysed by using Spearman rank correlation.
Number of participants = 50.

Table 8: Spearman Correlation between Liver Functions Parameters and Components of Metabolic Syndrome in the Case and Control Groups

		FPG		Total cholesterol (mg/dL)		Triacylglycerol (mg/dL)		HDL cholesterol (mg/dL)		LDL cholesterol (mg/dL)		SBP (mm Hg)		DBP (mm Hg)	
		r_s	p-value	r_s	p-value	r_s	p-value	r_s	p-value	r_s	p-value	r_s	p-value	r_s	p-value
ALP (U/L)	Case	-0.072	0.632	0.065	0.663	0.156	0.295	0.036	0.810	0.046	0.758	-0.249	0.092	-0.237	0.109
	Control	-0.088	0.562	0.144	0.338	0.133	0.379	-0.242	0.106	0.137	0.362	0.343	0.020*	-0.243	0.104
AST (U/L)	Case	0.140	0.337	0.206	0.155	0.093	0.523	-0.211	0.145	0.239	0.097	0.106	0.470	0.014	0.924
	Control	0.028	0.868	-0.218	0.188	0.002	0.993	-0.237	0.153	-0.178	0.286	0.077	0.645	-0.045	0.786
ALT (U/L)	Case	-0.116	0.423	0.171	0.235	-0.041	0.776	-0.159	0.270	0.223	0.119	0.063	0.666	0.109	0.451
	Control	-0.194	0.177	0.209	0.145	0.125	0.387	0.025	0.861	0.285	0.045*	-0.025	0.861	0.201	0.161
AST/ALT Ratio	Case	0.177	0.220	0.178	0.215	0.252	0.077	-0.070	0.627	0.168	0.243	0.065	0.654	-0.094	0.517
	Control	-0.063	0.669	-0.227	0.120	-0.049	0.740	-0.213	0.147	-0.099	0.502	-0.086	0.561	-0.414	0.003*
Total protein (g/dl)	Case	0.093	0.522	0.262	0.067	0.090	0.535	0.171	0.235	0.198	0.169	0.299	0.035*	0.272	0.056
	Control	-0.131	0.371	-0.157	0.282	-0.185	0.203	-0.395	0.005*	0.031	0.833	0.292	0.042*	0.118	0.419
Albumin (g/dl)	Case	0.065	0.656	-0.113	0.435	0.015	0.917	-0.072	0.619	-0.177	0.219	0.214	0.135	0.248	0.083
	Control	0.027	0.854	0.025	0.863	-0.076	0.605	-0.487	0.000*	0.146	0.315	0.269	0.062	0.116	0.426
Globulin (g/dl)	Case	-0.020	0.892	0.298	0.036*	0.035	0.809	0.235	0.101	0.270	0.058	0.149	0.301	0.153	0.289
	Control	-0.152	0.298	-0.236	0.102	-0.199	0.171	-0.110	0.453	-0.100	0.496	0.126	0.389	0.119	0.417
A/G ratio	Case	0.097	0.505	-0.258	0.071	0.074	0.609	-0.298	0.035*	-0.252	0.077	-0.038	0.792	-0.055	0.703
	Control	0.280	0.051	0.299	0.037*	0.075	0.610	-0.033	0.821	0.164	0.261	-0.024	0.872	0.062	0.670

[1]A/G, albumin/globulin ratio; FPG, fasting plasma glucose; SBP, systolic blood pressure; DBP, diastolic blood pressure.
[2]Analysed by using Spearman rank correlation. Number of participants = 50.

between FPG and body weight and hip circumference, respectively (Tables **3** & **6**). Significant positive correlations were also found between TC and height, body weight and hip circumference respectively (Tables **2**, **3**, & **6**). Bodyweight and hip circumference also showed significant positive correlations with LDL cholesterol (Tables **3** & **6**).

The LFPs and the components of MS were analysed for significance using Spearman correlation (Table **8**). Significant positive correlations were observed between total protein and SBP, and globulin and TC. Albumin/globulin ratio also showed a significant negative correlation with HDL-cholesterol.

DISCUSSION

A total number of 100 participants were included in this work. There were 2 groups with 50 participants in each, viz: apparently normal individuals (no diabetes, MS, or obesity) (control group) and individuals with metabolic syndrome (case group). Figures **1**, **2** and **3** show the comparison of means of the MS components, liver function parameters (LFPs) and anthropometry parameters, respectively. According to the Joint Interim Statement of the International Diabetes Federation Task Force on Epidemiology and Prevention, (2009), at least three out of five components (hypertension, elevated triglycerides, decreased HDL-cholesterol level, impaired fasting plasma glucose, and abdominal obesity) must be positive for an individual to be diagnosed of MS [2]. This research constituted the case and control groups using the above diagnostic procedure, and as shown in Figure **1**, except for TC, the case group had significantly higher MS components than the control group.

According to the findings of Sajithya Perera *et al*. [3], obese Thai Men and women with ALT concentrations in the extreme quartiles (>40 units/L and >23 units/L), had a 2.77-fold and 2.55-fold increased risk of MS, respectively. They, therefore, suggested a relationship between increased anthropometry parameters, elevated liver enzymes, and the risk of MS [3,14]. Those findings were corroborated in this study, as significantly increased anthropometry parameters (Figure **2**) and altered LFPs (Figure **3**) were observed in the case group (compared to the control which lies within the normal range). The findings of this study, therefore, support the suggestion of LFPs as risk factors of MS.

According to Sajithya Perera *et al*. [3] and Hampe *et al*. [14], metabolic syndrome is commonly accompanied by altered LFPs and increased anthropometry parameters, these were confirmed in this study as increased anthropometry parameters (Figure **2**) and altered LFPs (Figure **3**) were observed in the case group compared to the control which lies within the normal range.

Previous studies found strong associations between ALT, and body mass index (BMI) and waist circumference [3,13,25,26]. Measures of central obesity (e.g. waist circumference) have also been found to have strong associations with elevated plasma ALT levels and cirrhosis-related death or hospitalization to a higher degree than body mass index (BMI) [27,28]. ALT is more specific to the liver, therefore, the significant positive correlations observed between ALT and BMI, and waist circumference (Tables **4** & **5**) in this study suggest possible liver injury with every increase in BMI or WC (Tables **4** and **5**) and reinforce previous studies' suggestions of BMI and waist circumference as risk factors of fatty liver disease. The corresponding increases in plasma ALT levels in this study with body weight and waist circumference in the MS individuals suggest elevated plasma ALT also as an indicator of MS.

Like in ALT, serum elevation of AST among the case group (Figure **1**) is also an indication of liver dysfunction, however, the elevation may also be due to extrahepatic disorders, e.g., celiac sprue, muscle disorders, thyroid disorders, and haemolysis [29,30].

Low albumin levels may be a sign of advanced liver disease, protein-calorie malnutrition and/or intestinal malabsorption syndromes [31]. The significant decrease in serum albumin observed in the case group compared with the controls (Figure **1**) suggests possible end-stage liver disease among the case group. This is like the work done by Ghosh & Suryawanshi, [32] in which a sharp fall in serum albumin was observed in the uncontrolled obese diabetic rats. Hypoalbuminemia is a common issue in people with diabetes, and it is usually caused by diabetic nephropathy [32]. However, another study has suggested inhibition of the albumin promoter as a cause for the reduced protein synthesis in the liver of diabetic rats [32].

A study of the relationships between the anthropometric parameters and the components of MS revealed a significant positive correlation between TC and height. Bodyweight and hip circumference also showed significant positive correlations with TC and LDL cholesterol. These suggest increases in height,

body weight and hip circumference as risk factors in the development of hypercholesterolemia and atherosclerosis in MS individuals.

The elevation of globulin in the case group (Figure **1**) suggests chronic low-grade inflammation and elevated serum levels of systemic inflammatory markers commonly found in obesity-related insulin resistance, type 2 diabetes, and metabolic syndrome [29,30]. This inflammation is suspected to be because of hypercholesterolemia which was found in this study to be significantly positively correlated with globulin (Table **8**). The entry and retention of low-density lipoprotein (LDL) particles within the arterial wall trigger several inflammatory responses, culminating in the expression of adhesion molecules by the endothelium and the local secretion of cytokines and chemokines, which ultimately contribute to the accumulation of macrophages and other inflammatory cells in the subendothelial space [33]. This lipid-inflammation interface reunites enough elements for setting up a proper soil for atherosclerosis initiation and oftentimes, atherosclerosis progression [33]. The observed significant corresponding increase in plasma total proteins with bodyweight is suspected to be due to the increased globulins and inflammatory agents.

Kälsch *et al*. [13] described insulin resistance and diabetes as key features of the metabolic syndrome, this agreed with the elevated plasma FPG levels found in this study (Figure **2**). However, further studies need to be done to explain the observed FPG's inverse correlations with bodyweight and hip circumference (Tables **3** & **6**).

A low A/G ratio has been suggested to be a sign of an autoimmune disorder, a tumour of the bone marrow, kidney disease or cirrhosis, while the elevation of A/G ratio may be a sign of liver, kidney, or intestinal disease [34]. The significant negative correlation observed between the A/G ratio and HDL cholesterol (Table **8**), therefore, further suggests liver dysfunction in the case group. Further studies, however, need to be done to fully understand this phenomenon.

CONCLUSION

Obesity, especially central obesity, in MS may cause ectopic storage of fats in the liver. This may result in NAFLDs (which range from mild steatosis to steatohepatitis) which if left unchecked may progress to liver cirrhosis or complete liver failure. Routine evaluation of the plasma liver enzymes, total protein, and albumin of an MS individual in the laboratory often reflects altered liver functions. MS is therefore often accompanied by altered LFPs. This study suggests plasma ALT as the most effective predictor of MS among the LFPs. Increased globulin, total protein and A/G ratio are also suggested as risk factors of MS and/or inflammation in MS. This study suspects alteration in the LFPs to be a result of hepatic dysfunction, however, altered LFPs alone are not enough to arrive at this diagnosis. We, therefore, recommend further studies to compare the LFPs in MS with ultrasound or ultrasonographic results to establish a sound picture of the liver's histology.

CONFLICTS OF INTEREST

The author declares that there are no conflicts of interest regarding the publication of this paper.

ETHICAL APPROVALS

Ethical clearance was obtained from the National Health Research Ethics Committee (NHREC/TR/02/06/2007a), University of Ibadan, Ibadan, Nigeria before the commencement of this research.

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