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ORIGINAL ARTICLE

Clinical Correlates of Non-alcoholic Steatohepatitis in Nigerian Patients with Metabolic Syndrome

Corrélats Cliniques de la Stéatohépatite Non Alcoolique chez les Patients Nigérians Atteints du Syndrome Métabolique

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ABSTRACT

BACKGROUND: Non-alcoholic steatohepatitis (NASH) is a progressive form of non-alcoholic fatty liver disease (NAFLD). NASH is frequently associated with metabolic syndrome (MetS) and its prevalence is increasing due to rising global epidemics of MetS. This study aimed at determining the prevalence, risk factors and correlates of NASH in patients with MetS in a tertiary hospital in Nigeria.

METHODS: We caried out a hospital based cross-sectional study of 81 subjects with MetS. The diagnosis of NASH was made by ultrasound evidence of hepatic steatosis, and exclusion of significant consumption of alcohol as well as histologic evidence of NASH on liver biopsy. Subjects gave informed consent and ethical approval was obtained from the ethics committee of the hospital. Data obtained were entered into SPSS version 20 and analyzed using simple and inferential statistics. A p-value of < 0.05 was considered statistically significant.

RESULTS: Total of 81 subjects with MetS were studied, males 36(44.4%), females 45(55.6%), mean age(SD) of 49.77 (12.08) years. Ten (12.3%) subjects were diagnosed with NASH. Subjects with NASH had significant association with obesity, dyslipidaemia, and poor glycemic control. Regression analysis showed that morbid obesity, low HDL and presence of type 2 diabetes mellitus were independent risk factors for the development of NASH.

CONCLUSION: NASH is common in Nigerian patients with MetS and its presence is significantly associated with obesity, dyslipidemia, and type 2 diabetes mellitus. **WAJM 2022; 39(4): 407–414.**

Keywords: NASH, metabolic syndrome, clinical correlates, prevalence.

RÉSUMÉ

CONTEXTE: La stéatohépatite non alcoolique (NASH) est une forme progressive de stéatose hépatique non alcoolique (NAFLD). La NASH est fréquemment associée au syndrome métabolique (MetS)et sa prévalence augmente en raison de la montée des épidémies mondialesde MetS. Cette étude visait à déterminer la prévalence, le risqué facteurs et corrélats de la NASH chez les patients atteints de MetS dans un tertiaire hôpital au Nigeria.

MÉTHODES: Nous avons créé un hôpital transversal étude de 81 sujets atteints de MetS. Le diagnostic de NASH était fait par échographie des signes de stéatose hépatique et d'exclusionde consommation importante d'alcool ainsi que d'histologique signes de NASH sur biopsie du foie. Les sujets ont donné informéle consentement et l'approbation éthique ont été obtenus de l'éthique comité de l'hôpital. Les données obtenues ont été saisies dans SPSSversion 20 et analysée à l'aide de statistiques simples et inférentielles.Une valeur de p de < 0.05 a été considérée comme statistiquement significative.

RÉSULTATS: Au total, 81 sujets atteints de MetS ont été étudiés, hommes36(44.4%), femmes 45(55.6%), âge moyen (ET) de 49.39 + 11.67années. Dix (12.3%) sujets ont reçu un diagnostic de NASH.Les sujets atteints de NASH avaient une association significative avec l'obésité,dyslipidémie et mauvais contrôle glycémique. Analyse de regression ont montré que l'obésité morbide, un faible taux de HDL et la présence de type 2le diabète sucré était un facteur de risque indépendant pour le développement de la NASH.

CONCLUSION: La NASH est fréquente chez les patients nigérians atteints deMetS et sa présence est significativement associée à l'obésité,dyslipidémie et diabète sucré de type 2. **WAJM 2022; 39(4): 407–414.**

Mots-clés: NASH, Syndrome métabolique, Corrélats cliniques, Prévalence.

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Abbreviations: METS, Metabolic Syndrome; **NAFLD,** Non-alcoholic Fatty Liver Disease; **NASH,** Non-alcoholic steatohepatitis.

INTRODUCTION

Non-alcoholic steatohepatitis (NASH) is part of the spectrum of non-alcoholic fatty liver disease (NAFLD) and it is characterized by the presence of excess fat in the liver (steatosis), variable liver cell inflammation, hepatocyte death with or without scarring (fibrosis) in the absence of significant alcohol consumption.[1]

Metabolic syndrome, according to the US National Cholesterol Education Program and Adult Treatment Panel 111(NCEP: ATP 111) Criteria,[2] is defined as the presence of any three of the following: (i). Waist Circumference of >102cm in men or > 88cm in women. (ii). Triglyceride ≥150mg/dl (1.7mmol/l). (iii). High density Lipoprotein (HDL) Cholesterol< 40mg/dl(1.0mmol/l) in men and < 50mg/dl(1.3mmol/l) in women. (iv). Blood pressure of ≥130/85 mmHg or in someone that is on anti-hypertensive medications and (v). Fasting plasma glucose ≥ 100mg/dl (6.1 mmol/l).

Over the years, NASH has gained worldwide prominence as an important public health condition because of its propensity to progress to hepatocellular carcinoma (HCC), liver failure and end-stage liver disease.[2,3] NASH is the third most common risk factor for HCC after viral hepatitis and alcohol.[4] NASH associated liver cirrhosis accounts for approximately 13% of all cases of hepato-cellular carcinoma.[5] It has been suggested that NAFLD represents the hepatic component of the metabolic syndrome.[6] NAFLD is closely associated with type 2 diabetes mellitus, obesity, arterial hypertension, and hyperlipidaemia.[2,7] NASH cirrhosis is the second leading indication for liver transplantation in the United States of America.[8]

Most studies in Nigeria have been prevalence studies, one of such puts the prevalence of NAFLD at 8.7%.[9] There is paucity of data on NASH, especially histologically proven NASH, in patients with metabolic syndrome in Nigeria. This study therefore aimed at identifying the prevalence and risk factors associated with the development of NASH in patients with metabolic syndrome.

METHODS

This was a hospital-based cross-sectional study carried out in the Gastroenterology and Endocrinology Clinics of Obafemi Awolowo University & Obafemi Awolowo University Teaching Hospitals Complex, Ile Ife, South West, Nigeria. The study period was from October 2018 to October 2019. Participants gave informed consent and ethical approval was obtained from the hospital Ethics and Research Committee (approval numbers IRB/IEC/0004553 NATIONAL and NHREC/27/02/2009a). Adults aged 18 years and above with metabolic syndrome were recruited consecutively. Metabolic syndrome was diagnosed using the US National Cholesterol Education Program and Adult Treatment Panel 111(NCEP: ATP 111) Criteria.[10] The study excluded those with intake of alcohol of ≥ 140g/week for men and ≥ 70g/week for women.[2] Those with myocardial infarction, end-stage renal disease, congestive cardiac failure, chronic obstructive pulmonary disease (COPD), diabetic coma, hepatitis C and B infection and those on drugs that could result into fat accumulation in the liver were also excluded. Sample size was calculated using Fisher's statistical formula[12] $n = Z^2pq / d^2$ Where n = desired sample size where the population is more than 10,000) Z = Standard deviation usually set at 1.96, corresponding to 95% confidence interval (CI). P = Best estimated prevalence of Metabolic syndrome from literature review which is 12.1%.[11]) This puts the sample size at 81 after addition of the 10% attrition rate and further addition to improve the strength of the study. Body mass index was calculated and classified according to the WHO Criteria.[13] Waist-Hip Ratio was calculated by dividing the waist circumference by the hip circumference.[13] Biochemistry analysis was done to obtain total cholesterol using the modified method of Liebermann-Burchard.[14], HDL-Cholesterol was obtained by the precipitation method.[15] Triglyceride was done using a kit that employed enzymatic hydrolysis of triglycerides with lipases[16] and LDL-C was calculated using Friedwald's formula,[17] as LDL-C = (TCHOL- HDL-C) – TG/5 when serum cholesterol is more than 400mg%.[10] Glycated haemoglobin was measured using Hemo-One autoanalyzer (ISE srl companies, Italy) via antigen (HBA1C) and antibody (anti-HbA1C) reaction in whole blood and fasting blood glucose was measured using Accu-chek® Aviva nano (Roche diagnostics, Basel, Switzerland) through glucose oxidase-glucose and ferricyanide reactions. Liver biochemistry assay for aspartate transaminase (AST) and alanine transaminase (ALT) were done using an automated system (using measurement of the enzyme activity by the kinetic methods as recommended by the International Federation of Clinical Biochemistry).[18] Serological tests for hepatitis B and C viral markers were done using Immuno-comb kit. Abdominal ultrasonography was done for all subjects after an overnight fast by an experienced Radiologist using a 3.5 MH_z probe Mind ray DP 9900 scanning machine looking for evidence of significant hepatic steatosis which includes increased echogenicity of the hepatic parenchyma, hepatomegaly and blurring of vascular margin.[19] Liver biopsy was carried out on 22 patients that were fit for the procedure and had evidence of hepatic steatosis on ultrasound. NASH CRN NAFLD activity scoring system was used for the histologic classification of NASH.[20] Brunt fibrosis staging was used to stage fibrosis in the histology slides of the subjects.[47] Data obtained were entered into and analyzed using statistical package for social sciences (SPSS) version 20 software (SPSS Inc, Chicago IL). Simple descriptive and inferential statistics were performed.

The results were presented as frequency tables and pie chart. Categorical data were summarized as frequencies and percentages while continuous data were summarized as mean ± standard deviation. Chi-Square test was used to compare the relationship between two qualitative variables. Binary logistic regression was conducted to assess associations between presence of NASH and risk factors for development of NASH. A p-value of < 0.05 at a confidence interval of 95% was considered statistically significant.

RESULTS

A total of eighty-one (81) subjects with metabolic syndrome were recruited

and studied. Age range for participants was 18 and 80 years. The mean age (SD) of the subjects was 49.77 (12.08) years. There was a higher proportion of females 45(55.6%) than males 36(44.4%) with a female to male ratio of 1.25:1 (Table 1). Twenty-two (22) of the subjects with metabolic syndrome who had hepatic steatosis on ultrasound with no contraindications to liver biopsy had liver biopsy. Liver histology confirmed 10 of the 22 (45.5%) subjects with hepatic steatosis as having NASH with varying histological grades; 9 (40.9%) had moderate, 9 (40.9%) severe, and 3 (13.6%) had mild and 1 (4.5%) very severe fatty infiltration respectively. Also, 12 (54.5%) had none, 9 (40.9%) had 2–4 foci and 1 (4.5%) had more than 4 foci of lobular-inflammation respectively. The NASH Clinical Research Network NAFLD Activity Scores of the subjects with hepatic steatosis were none in 12 (54.5%), borderline in 2 (9.1%) and definitive in 8 (27.8%) respectively. Fibrosis was absent in 7 (31.8%), mild in 9 (40.9%), moderate zone-3 peri-sinusoidal in 3(13.6%), Portal/periportal in 2(9.1%) and severe in 1(4.5%) respectively.

The overall prevalence of NASH in subjects with metabolic syndrome in this study was 12.3% (Figure1). Comparing patients with NASH and those without NASH, the mean BMI, waist circumference and waist hip ratio were significantly higher in subjects with NASH than in those without NASH (39.78 ± 5.21, 115.82 ± 9.96 and 1.056 ± 0.56) vs. (26.55 ± 5.35, 106.18 ± 9.35 and 1.019 ± 0.44) ($p<0.05$) respectively. The mean LDL was also significantly higher in subjects with NASH than in those without NASH (142.06 ±33.72 vs.112.2 ± 18.72 $p=0.002$) while the mean HDL was significantly lower in subjects with NASH than in those without NASH (38.9 ±11.77 vs. 44.57 ± 9.39, $p=0.04$) respectively. The mean ALT and AST were also significantly higher in subjects with NASH than in those without NASH (13.71±4.75 and 20.24 ± 6.24) vs. (7.84 ± 6.02 and 8.26 ± 4.79) ($p<0.001$) respectively (Table 3). Bivariate analysis of the factors associated with NASH showed that central obesity, waist-circumference, presence of type 2 DM, elevated LDL and TG, were significantly

Table 1: Socio-demographic Characteristics of the Study Participants

Variables	Frequency N=81	Percent (%)
Age Groups (years)		
18 – 30	2	(2.5)
31 – 50	43	(53.1)
51 – 70	32	(39.5)
>70	4	(4.9)
Gender		
Male	36	(44.4)
Female	45	(55.6)
Level of Education		
Primary	16	(19.8)
Secondary	19	(23.5)
Tertiay	46	(56.8)
Ethnicity		
Yoruba	76	(93.8)
Igbo	4	(4.9)
Idoma	1	(1.2)
Marital Status		
Single	5	(6.2)
Married	73	(90.1)
Widowed	3	(3.7)
Religion		
Christianity	71	(71.7)
Islam	10	(12.3)
Occupation		
Civil Servants	32	(39.5)
Artisans	24	(29.6)
Traders	18	(22.2)
Unemployed	7	(8.6)

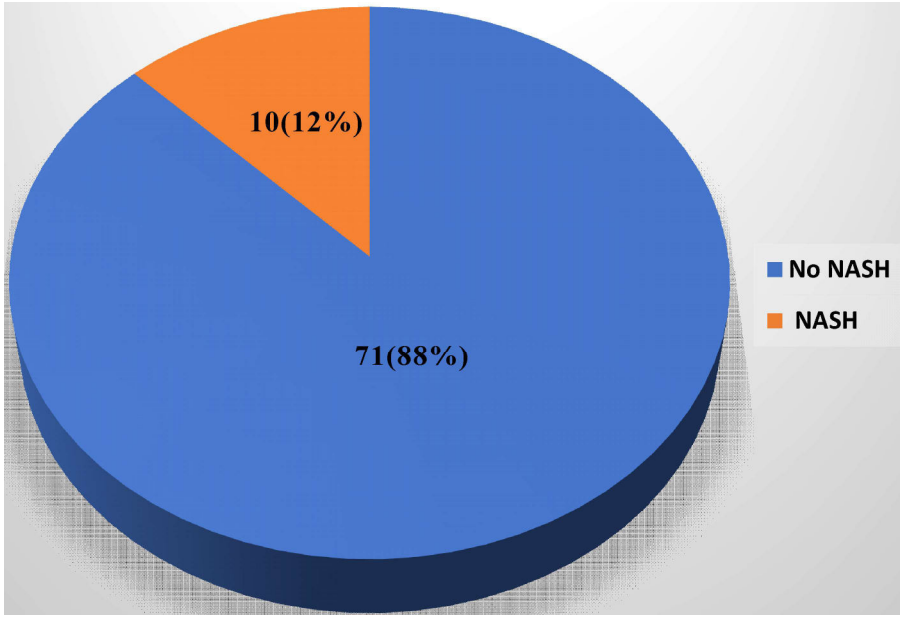


Fig. 1: Prevalence of NASH in Metabolic Syndrome

Table 2: Comparison of Clinical Presentations of Subjects with Metabolic Syndrome with and without NASH

Variable	NASH N=10, N (%)	No NASH N=71, N (%)	Statistics	*p-value*
Symptomatic				
Yes	8 (80.0)	22 (31.0)	χ^2 = 9.030	0.003*
No	2 (20.0)	49 (69.0)	df= 1	
Abdominal Pain				
No	1 (10.0)	55 (77.5)	χ^2 = 18.697	0.001*
Yes	9 (90.0)	16 (22.5)	df= 1	
Easy Tiredness				
No	0 (0.0)	65 (91.5)	χ^2 = 46.347	0.001*
Yes	10 (100.0)	6 (8.5)	df= 1	
Malaise				
No	2 (20.0)	65 (91.5)	χ^2 = 31.387	0.001*
Yes	8 (80.0)	6 (8.5)	df= 1	
Hepatomegaly				
No	1 (10.0)	58 (81.7)	χ^2 = 4.605	0.032*
Yes	9 (90.0)	13 (18.3)	df= 1	
Liver Tenderness				
No	6 (60.0)	70 (98.6)	FE = 22.539,	0.001*
Yes	4 (40.0)	1 (1.4)	df= 1	

*LR,Likelihood ratio; χ^2, Chi-square test; FE, Fisher's exact test; *, Statistically significant.*

Table 3: Comparison of the Demographics, Anthropomethric and Biochemical Charactersitics of the Subjects with and those without NASH

Variable	NASH (Mean ± SD) N (%) N=10	No NASH (Mean ± SD) N (%) N–71	Statistics	*P*-value
Age(years)	51.17 ± 12.87	49.39 ±11.94	t-test	0.591
BMI(Kg/m2)	39.78 ± 5.21	26.55 ± 5.35	t-test	<0.001*
WC(cm)	115.82 ± 9.96	106.18 ± 9.35	t-test	<0.001*
WHR	1.056 ± 0.56	1.019 ± 0.44	t-test	0.004*
Total cholesterol(mg/dl)	203.35± 47.39	202.96 ± 31.96	t-test	0.969
HDL(mg/dl)	38.9 ±11.77	44.57 ± 9.39	t-test	0.04*
LDL(mg/dl)	142.06 ±33.72	112.2 ± 18.72	t-test	0.002*
Triglyceride(mg/dl)	120.11±32.17	111.36 ± 25.94	t-test	0.311
FBS(mmol/L)	6.81 ± 2.18	5.56 ± 2.098	t-test	0.034*
2HPP(mmol/L)	10.45 ± 4.04	9.38 ± 8.15	t-test	0.603
HBAIC(%)	5.92 ± 1.23	4.72 ± 1.20	t-test	0.001*
SBP(mmHg)	145.7 ±11.58	115.8 ± 19.8	t-test	0.052
DBP(mmHg)	93.24 ± 8.5	89.53 ± 31.96	t-test	0.061
ALP(IU/L)	131.35 ±41.72	115.92 ± 44.34	t-test	0.201
AST(IU/L)	20.24 ± 6.24	8.26 ± 4.79	t-test	<0.001*
ALT(IU/L)	13.71±4.75	7.84 ± 6.02	t-test	<0.001*

**, Statistically significant*

BMI, Body mass index; LDL-C, Low Density Lipoprotein Cholesterol; WC, Waist circumference; HDL-C, High Density Lipoprotein Cholesterol; WHR, Waist-hip ratio; FBS, Fasting blood sugar; 2HPP, 2 Hours post-prandial; HbA1c, HemoglobinA1c; SBP, Systolic blood pressure; DBP, Diastolic blood pressure; ALP,Alkaline phosphatase; AST, Aspartate Aminotransferase; ALT, Alanine Aminotransferase.

associated with NASH compared with those without NASH (p< 0.05.) (Table 4).

Logistic regression analysis between presence of NASH and risk factors for NASH showed that subjects with morbid obesity were 41.9 times more at risk of having NASH than in those with normal weight (OR=41.90, 95% CI=1.86–942.76, P<0.019). Also subjects with low serum HDL level were 17.9 times more at risk of development of NASH than in those with normal serum HDL level (OR=17.90, 95% CI=2.49-128.93, P=0.004) and subjects with type 2 diabetes mellitus were 7 times more at risk of developing NASH than in those without diabetes mellitus (OR=7.00, 95% CI=1.06–46.04, p=0.043) (Table 5).

DISCUSSION

Majority of the subjects (patients with metabolic Syndrome) in this study fall within age group of 31–50 years 43 (53.1%) and this agrees with other studies in Nigeria.[21,22] However, Ford, *et al*.[23] noted increasing prevalence of metabolic syndrome in younger adults in the USA. Ageing is a risk factor for MetS due to some effects of ageing lipo-peroxidation, generation of free radicals and physiological declines in growth hormones.[24] Many MetS parameters such as obesity, insulin resistance increase in prevalence with advanced age.[25]

Majority of the subjects with MetS in this study were females, this agrees with other studies in Nigeria.[21,22] A study however reported that the prevalence was equal in both sexes.[24] The variations in gender may be mediated by the female sex hormones and lifestyles. Bhasin, *et al.*[26] in the Framingham Heart Study found that sex hormone-binding globulin is independently associated with increased risk of metabolic syndrome whereas testosterone is not.

The spectrums (NAFLD, NASH with or without fibrosis) of NAFLD obtained from this study differs from those reported in other studies in Nigeria.[14,16] Onyekwere *et al*[9] reported only one diabetic subject with elevated aminotransferases as NASH. Their study ultilized ultrasonography and liver biochemistry as evidence of NASH, whereas this present study relied on ultrasonography, liver biochemistry and liver histology.

Table 4: Bivariate Analysis of Clinical and Biochemical Factors associated with NASH in Subjects with Metabolic Syndrome

Variables	NASH N (%)N=10	NO NASH N (%)N=71	Statistics	*p*-value
Waist Circumference				
Normal	0 (0.0)	14 (19.7)	χ^2= 4.079	0.043*
Abnormal	10 (100.0)	57 (80.3)	df= 1	
Type 2 Diabetes Mellitus				
No	3 (30.0)	57 (80.3)	χ^2= 11.540	0.001*
Yes	7 (70.0)	14 (19.7)	df= 1	
Systemic Hypertension				
No	1 (10.0)	29 (40.8)	χ^2= 3.576	0.059
Yes	9 (90.0)	42 (59.2)	df= 1	
Total Cholesterol(mg/dl)				
Normal	5 (50.0)	30 (42.3)	χ^2= 0.214	0.643
Elevated (≥200)	5 (50.0)	41 (57.7)	df= 1	
HDL-C (mg/dl)				
Low (<40males,<50females)	9 (90.0)	42 (59.2)	χ^2= 3.576	0.059
Normal	1 (10.0)	29 (40.8)	df= 1	
Triglyceride (mg/dl)				
Normal	7 (70.0)	65 (91.5)	χ^2= 4.121	0.042*
Elevated (≥150)	3 (30.0)	6 (8.5)	df= 1	
LDL-C (mg/dl)				
Elevated (≥100)	9 (90.0)	27 (38)	χ^2= 5.704	0.017*
Normal	1 (10.0)	40(62)	df= 1	
Gender				
Male	6(60)	31(43.7)	χ^2= 0.941	0.332
Female	4(40)	40(56.3)	df= 1	
ALT (IU/L)				
Elevated (≥12)	7(70)	13(18.3)	χ^2= 10.73	0.001*
Normal (<12)	3(30)	58(81.7)	df= 1	
BMI				
Underweight	0 (0.0)	1 (1.1)		
Normal	31 (43.7)	22 (24.7)	LR = 12.385	0.015*
Overweight	10 (14.1)	29 (32.6)	df= 4	
Obesity	24 (33.8)	33 (37.1)		
Morbid Obesity	6 (8.5)	4 (4.5)		

*LR, Likelihood ratio; χ^2, Chi-square test; *, Statistically significant; HDL-C, High density lipoprotein cholesterol; LDL-C, Low density lipoprotein cholesterol; BMI, Body mass index; ALT, Alanine aminotransferase; IGT, Impaired glucose tolerance.*

The overall prevalence of NASH in subjects with metabolic syndrome in this study was 12.3%. Previous studies in Nigeria did not determine the prevalence of NASH in NAFLD.[14,16] The prevalence of NASH in MetS in this study is similar to that by Kruger *et al*[27] in South Africa, but lower than that in Europe,[28,29] Asia[30] and North America.[2,31] The reasons for the lower prevalence of NASH in MetS in this study include genetic factors, lower levels of serum triglycerides in Africans, older age population in Hispanics and Caucasians. A post-mortem study in the USA in NAFLD/ NASH between Caucasians and minority racial groups also showed low prevalence in African Americans, therefore this may be peculiar to Blacks.[32] Genetic disparity involved in lipid metabolism and lower prevalence of metabolic syndrome were the major explanation for the lowest incidence of NASH and NAFLD in African-Americans.[32] Genome wide association studies revealed that single nucleotide polymorphisms are associated with the development of NASH. Patatin-like phospholipase domain-containing protein 3 gene variant 1148M associated with the development and progression of NAFLD/NASH to hepatic fibrosis and HCC. These occur less frequently in Blacks than other races.[33]

This study showed severe metabolic disorder in those with NASH evident by the higher number of components of MetS in patients with NASH compared with those without. These findings support another study by Marchesini, *et al*[34] in Italy and Kanwar *et al*[35] in the USA. A study in Nigeria,[9] also reported similar finding in subjects with NAFLD. This therefore means that most components of MetS are independent risk factors for the development of NASH.[36] The mean age of patients with NASH agrees with other studies in Nigeria and elsewhere.[37,9,27,38,29] It has been shown from studies that age of more than 50 years is a known risk factor for advanced NAFLD.[39] and insulin resistance, the pathologic hallmark of the NAFLD and a major component of the MetS.[39] Advanced age is associated with central obesity, insulin resistance, generation of proinflammatory cytokines and activation of nuclear factor-κB pathways.[40] Ageing also leads to impaired autophagy, accumulation of lipofuscin, increased reactive oxygen species generation, decreased area of smooth endoplasmic reticulum and a declining number and dysfunction of mitochondria.[40]

This study showed that NASH occurred predominantly among male gender and this agreed with other studies in Nigeria and USA,[37,29] but differs from studies that showed no sex predilection, [9] and another study with a higher female predilection.[48] The reason why males are more affected has been attributed to consumption of non-diet soda by most males than females.[29] Sex-hormones and varying fat distribution have also been said to play a role.[39]

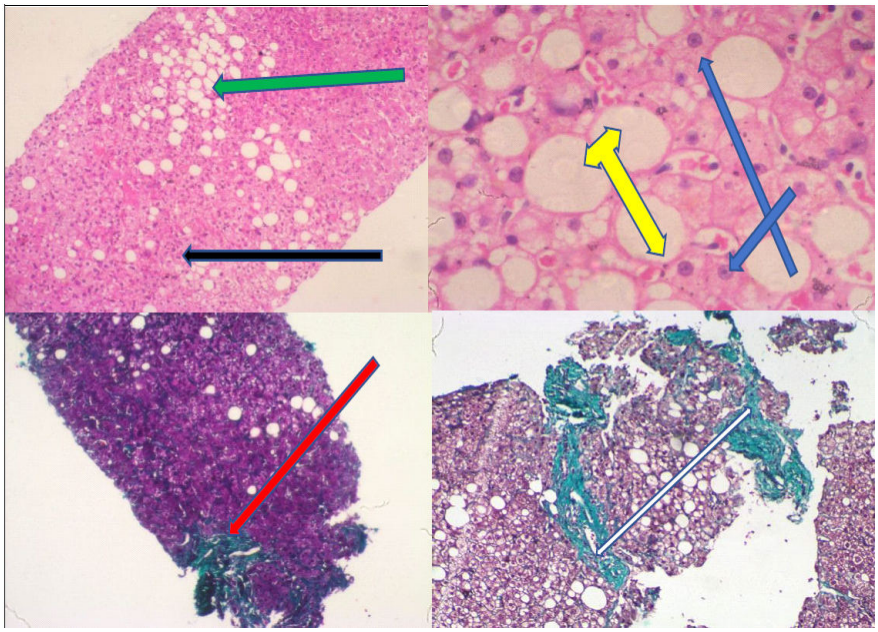
The mean BMI, waist circumference, waist hip ratio, FBS, serum triglyceride and LDL-cholesterol were significantly higher in subjects with NASH than in those without NASH. These findings are comparable to what was reported by studies in Nigeria,[9,16] Europe and USA.[29,32] Factors significantly associated with the

Table 5: **Binary Logistic Regression between Presence of NASH and Risk Factors for NASH**

Variables	Odd Ratio	p-value	95% Confidence Interval
BMI			
Normal	Ref.		
Overweight	1.60	0.685	0.14 – 21.11
Obese	2.10	0.529	0.21 – 21.98
Morbid Obesity	41.90	0.019*	1.86 – 942.76
Triglyceride			
Normal	Ref.		
Elevated	1.50	0.696	0.19 – 11.98
HDL-C			
Normal	Ref.		
Low	17.90	0.004*	2.49 – 128.93
Diabetes Mellitus			
No	Ref.		
Present	7.00	0.043*	1.06 – 46.04
Hypertension			
No	Ref.		
Present	2.30	0.313	0.45 – 12.10

BMI, Body mass index; HDL-C, High density lipoprotein cholesterol;
**, Statistically significant.*

APPENDIX IV
Photomicrograph of Some Subjects with Hepaic Steatosis/NASH



Green arrow: Hepatic steatosis.
Red arrow: Periportal fibrosis.
White arrow: Bridging fibrosis
Black arrow: Lobular inflammation.
Blue arrow: Hepatocyte ballooning
Yellow arrow: Macrovesicular steatosis

presence of NASH in subjects with MetS include obesity (high BMI), central obesity (increased WC), dyslipidemia (low HDL, high LDL and high triglyceride), presence of type 2 DM, elevated ALT and AST. Diabetes mellitus was identified in higher proportion of MetS subjects with NASH than those without NASH and this also agrees with reports from other studies.[37,32,29] Type 2 DM and NASH in terms of pathogenesis both shared insulin resistance. Diabetes in NAFLD is a risk factor for progression to NASH, cirrhosis, and mortality and poor glycemic control increases the risk of fibrosis in NASH.[41] The high prevalence of components of MetS and Type 2 Diabetes mellitus in NASH suggests that risk stratification and aggressive treatment is needed to control the risk of fibrosis, cirrhosis, HCC, CVD and other possible comorbidities in these patients.[2] Binary analysis showed that morbid obesity, dyslipidemia and presence of type 2 diabetes mellitus were independently associated with development of NASH in subjects with MetS. Another study in Nigeria by Olusanya, *et al*[37] similarly identified central obesity, dyslipidemia and presence of type 2 diabetes mellitus as independently associated with the development of NAFLD but did not diagnose NASH.[37] Other studies also found systemic hypertension to be an independent risk factor for the development of NASH.[52,7,42,49] The relationship between metabolic syndrome components, diabetes mellitus and development of NAFLD/NASH could be related to their common pathophysiologic mechanisms.[39]

CONCLUSION

The prevalence of NASH in subjects with MetS in this study was 12.3%. NASH was found to be common in middle-aged patients. The factors significantly associated with development of NASH included type 2 diabetes mellitus, central obesity, dyslipidemia, higher number of components of MetS and elevated aminotransferases. The study also showed that type 2 diabetes mellitus, morbid obesity and dyslipidemia are independent risk factors for the development of NASH. This study hereby recommends i. routine screening

for NAFLD and NASH in subjects with metabolic syndrome. ii. Aggressive prevention and treatment of obesity, dyslipidemia, type 2 diabetes mellitus, systemic hypertension in patients especially metabolic syndrome subjects with or without NALD/NASH.

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