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Original Research Article

Prevalence and Associations of Metabolic Dysfunction-Associated Steatotic Liver Disease in Type 2 Diabetic Out-Patients in a Nigerian Tertiary Health Facility: A Cross-Sectional Study

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Abstract: ***Background*:** Metabolic dysfunction-associated Steatotic liver disease (MASLD) is the most common chronic liver disease that has become a leading health problem globally. ***Objectives*:** To determine the prevalence, grades and associated risk factors for MASLD in type 2 diabetes mellitus (T2DM) subjects at NAUTH, Nnewi, Nigeria. ***Materials and Methods*:** This was a cross-sectional study that was carried out among stable T2DM out-patients at NAUTH. Anthropometric and blood pressure (BP) measurements were done. Glycated haemoglobin and fasting lipid profile were assayed. Abdominal ultrasonography was performed to diagnose and stage MASLD. Data was analysed using SPSS version 25. Results of categorical variables were presented as frequencies and percentages, in tables. The mean values and standard deviation for the continuous variables were calculated. Chi-square test was used to determine the association between MASLD and MASLD stages with the risk factors. The level of significance was set at $p < 0.05$. ***Results*:** A total of 142 T2DM subjects with complete results were analysed. The prevalence rate of MASLD was 46.5% among the subjects, with 47.9%, 35.2%, 14.1% and 2.8% of them having grades 0, 1, 2 and 3 MASLD, respectively. A statistically significant association was found between MASLD and educational levels ($X^2 = 20.732$; $p = 0.000$), DM duration ($X^2 = 5.509$; $p = 0.019$), global obesity ($X^2 = 6.079$; $p = 0.014$) and anti-hypertensive medications use ($X^2 = 5.938$; $p = 0.015$). Equally, significant association was found between MASLD grades and marital status ($X^2 = 9.181$; $p = 0.027$), educational level ($X^2 = 25.492$; $p = 0.02$), DM duration ($X^2 = 8.083$; $p = 0.044$), abdominal obesity in the male subjects ($X^2 = 11.786$; $p = 0.003$), global obesity ($X^2 = 9.736$; $p = 0.021$) and diastolic hypertension ($X^2 = 14.509$; $p = 0.002$) in the subjects. ***Conclusion*:** The prevalence of MASLD from the study was high and thus showed a high burden of the disease in T2DM subjects. MASLD and it stages showed significant associations with some of the risk factors evaluated.

Keywords: Associations, Cross-Sectional, Facility, Metabolic dysfunction-associated liver disease, Type 2 Diabetes Mellitus, Tertiary.

INTRODUCTION

Diabetes mellitus is defined as a metabolic disorder of multiple aetiologies characterized by chronic hyperglycaemia with disturbances of carbohydrate, protein and fat metabolism resulting from defects in insulin secretion, insulin action or both [1]. Diabetes is aetiologically classified into: type 1, type 2, gestational DM and others [1].

Diabetes mellitus is approaching a pandemic level and constituting a healthcare burden globally. According to the International Diabetes Federation (IDF), an estimated 366 million people had DM globally with an estimated prevalence of 8.3% as of 2011 [2]. This figure is projected to hit 552 million by the year 2030, giving a prevalence rate of 9.9% [2].

Metabolic dysfunction-associated steatotic liver disease (MASLD) formerly referred to as nonalcoholic

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fatty liver disease (NAFLD) results from excess fat accumulation in the liver that is not linked to a heavy alcohol use. Liver steotosis that results from a heavy alcohol consumption is referred to as alcoholic fatty liver disease or alcohol-associated liver disease. MASLD has been prevalent and is still rising steadily, globally and is the most common chronic liver disease that has become a leading health problem globally [3-5]. The specific cause of MASLD is unknown but its known risk factors include obesity, hypercholestrolaemia, T2DM, and metabolic syndrome. MASLD is mainly asymptomatic but in rare cases may manifest with fatigue, pain and weight loss. Equally, no precise treatment exists for MASLD as the remedy involves treating the predisposing risk factors [3-5]. MASLD if unmanaged, may over time progress to inflammation (steatohepatitis) and scarring (cirrhosis).

MASLD is the most common liver disorder affecting about 20% to 40% of the adults in the general population, with the prevalence rates differing according to the diagnostic method, age, sex, and ethnicity [6, 7]. Review of literature showed that one-third to two-thirds of the people with T2DM have MASLD [7]. Equally MASLD is present in up to 75% of the people that were overweight and in over 90% of the subjects with severe obesity [8, 9]. MASLD affects people of all ages, children inclusive; although its prevalence is known to increase with age [10]. Almost 10% of children aged between 2 and 19 years in the United States of America (USA) had MASLD. MASLD equally affects all races, although it had been found to be more common among Hispanic individuals and less common among non-Hispanic blacks [11, 12]. Currently, some of the racial and ethnic differences in MASLD prevalence are attributable to genetic variations [11, 12]. The association between MASLD and T2DM is bidirectional. MASLD contributes to the onset of insulin resistance in T2DM and studies had reported an association between the presence of MASLD and an increased risk of developing T2DM [13, 14]. Equally, T2DM and "prediabetes" (including impaired glucose tolerance and impaired fasting glucose) are strong risk factors for the development of MASLD. The mechanisms underlying MASLD-induced predisposition to T2DM and "prediabetes" involve several mediators that include lipotoxicity, inflammation and oxidative stress [15].

When obesity, insulin resistance, or hyperglycaemia were combined with MASLD, T2DM risk increased dramatically [16]. MASLD can be diagnosed via a two-step process: identification of fatty infiltration of the liver (hepatic steotosis) on ultrasonographic evaluation or histology and the exclusion of secondary causes of liver steotosis that include significant alcohol consumption, hepatitis B and C viral antibody positivity. The decision on the extent of the initial blood work-up for the evaluation of MASLD has not been reached among guidelines [17]. Notwithstanding the fact that alanine transaminase (ALT) levels had been shown to have the best single biochemical correlation with hepatic steatosis, liver enzymes levels could be normal, fluctuating or elevated in patients with MASLD [18]. This is the reason why liver enzyme assay is not a sinequanon in the diagnostic protocol for MASLD. Although more complex and costly diagnostic tools like transient elastography and magnetic resonance imaging mass spectroscopy could be valuable in the early detection of MASLD and prediction of fibrosis, ultrasonography offers the extra advantage of being the simplest, most affordable, easily available and noninvasive assessment tool for the diagnosis and staging of MASLD and thus is well suited for resource-poor settings typical of the sub-Saharan African [19].

The prevalence of MASLD in western parts of Nigeria was 16.7% and 1.2% in T2DM subjects and non-diabetic control subjects, respectively [20]. Also, central obesity and dyslipidaemia were found to be independently associated with MASLD in male subjects with T2DM [20]. Onyekwere *et al*., found that the prevalence of MASLD was 9.5% and 4.5% among diabetic and non-diabetic subjects, respectively [21]. They equally found that central obesity (increased waist circumference "WC") was significantly more in persons with MASLD compared with those without [21]. In the South-eastern Nigeria, Onyia *et al*., found that the prevalence of MASLD was 36.4% in obese subjects and 0.4% in the non-obese control subjects [22]. According to them, the degree of obesity, levels of transaminases, total cholesterol (TC), diastolic hypertension, fasting plasma glucose (FBG) and WC were significantly associated with higher prevalence of MASLD [22]. Afolabi *et al*., in Nigeria found that the prevalence of MASLD was 68.8% among their T2DM subjects. Of these, they found that 25%, 16.3%, 32.5% and 20% of the subjects had grade 1, grade 2 and grade 3 MASLD respectively [23]. It is evident that the prevalence of MASLD was very high and is still soaring geometrically in subjects with T2DM, just as T2DM, the major Risk factor for MASLD is equally rising exponentially. MASLD doubles both as a cause and a consequence of T2DM and if left untreated could progress to steatohepatitis and ultimately to cirrhosis, marking it out as an important cause of chronic liver disease and cardiovascular morbidity and mortality, especially in subjects with type 2 diabetes mellitus [20]. Hence this co-morbid association between MASLD, T2DM and even obesity makes them constitute a public health concern, generally and a serious health challenge specifically to patients patients suffering from their scourge. The multiple threats and danger posed by MASLD notwithstanding, there is still a dearth of locally published data on this very challenging disease.

This study aimed at evaluating the prevalence and ultrasonographic grades of MASLD as well as their association with the traditional metabolic and socio-clinical risk factors of T2DM at Nnamdi Azikiwe

University Teaching Hospital (NAUTH), Nnewi in South-Eastern Nigeria.

MATERIALS AND METHODS

This was a Cross-sectional, descriptive study that was carried out at the diabetes out-patient clinic at NAUTH. A total of 150 consenting T2DM subjects aged 18 years and above were recruited for participation in this study. A total of 5 subjects dropped out of the study, while 3 subjects had incomplete data and were not analysed. At the end, 142 subjects with complete results were analysed. Ethical clearance for the study was obtained from the Research Ethics Committee of the Nnamdi Azikiwe University Teaching Hospital, Nnewi before the commencement of the study, with the ethical code: NAUTH/CS/66/VOL.15/VER.3/077/2022/038.

The Subjects were recruited for participation in the study via a simple random sampling method. During each clinic consultation each of the consenting subjects that qualified for the study was made to pick a card randomly from a pool of cards, each of which was labelled: "Yes" or "No", folded and put in a pot. All the subjects that picked "Yes" were recruited consecutively into the study.

Inclusion Criteria: all consenting subjects with T2DM aged 18 years and above.

Exclusion criteria:

Subjects who were less than 18 years of age, subjects with type 1 DM, subjects with a previous history of hepatitis B or C infection or those who have stigmata of chronic liver diseases, subjects whose score depicted hazardous drinking or alcohol use disorder based on the abbreviated Alcohol Use Disorders Identification Test (AUDIT C) questionnaire and those who were very sick [24].

Data extraction was done with a pre-tested researcher-structure questionnaire and an AUDIT C questionnaire that has been validated and used in several Nigerian studies [25]. Blood sample collection was done via venipuncture of the cubital vein following aseptic procedure. The researcher had two contacts with the subjects on two separate clinic days.

At the first contact, informed consent was obtained, a focused history was taken, anthropometric and blood pressure measurements were done, as well as abdominal ultrasound scanning. At the second meeting, 5ml of venous blood was collected from each subject. This was after they had observed a fast of about 8 - 14 hours based on the instructions they were given during the first meeting. 1 ml of blood from each subject was stored in ethylenediaminetetraacetic acid (EDTA) bottle and used for glycated haemoglobin (HbA1c) assay. The remaining 4 ml of blood was stored in plain bottle and used for fasting lipid profile assay. HbA_{1C} was measured using the boronate affinity chromatography method using the automated CLOVER A1c Analyzer (Infopia, Korea) and CLOVER A1c Self-Test Cartridge [26].

High density lipoprotein (HDL-C) was obtained by a precipitation technique [27].

Total cholesterol level was determined using the kit employing the enzymatic and the 4-hydroxybenzoate/4-aminophenazone systems (BioSystems) [28].

Triglyceride level was determined using a kit employing enzymatic hydrolysis of triglyceride with lipases (Randox) [29]. Low density lipoprotein cholesterol (LDL-C) was measured using a kit employing a precipitation technique (MyBioSource – MBS023682 kit. San Diego, California) [30].

The AUDIT-C score ranges from 0 to 12. A score of less than 4 means non-harmful drinking, that of greater than or equal to 4, but less than 5 means hazardous drinking (risk of physical or physiological harm) and that of greater than or equal to 5 shows alcohol use disorder [24].

Abdominal ultrasonography was performed for the evaluation of MASLD by an experienced radiologist at the NAUTH Radiology Department using a Mindray ultrasound machine model: DC-32 SN: 9Q-98000221; manufactured in China.

Weight and height were measured using Stadiometer (RGZ-120), waist circumference measured with a measuring tape and blood pressure measured using Accoson mercury sphygmomanometer [31].

DEFINITION OF TERMS AND CRITERIA

Hypertension was defined as systolic BP ≥ 140mmHg and or diastolic BP ≥ 90 mmHg, measured on at least 2 separate occasions or if a patient is already on anti-hypertensive medications [32].

Diabetes mellitus was defined by fasting plasma glucose of ≥ 7.0 mmol/l (126 mg/dl) measured on at least 2 separate occasions or the patient is already on glucose lowering agents [1].

Type 1 DM was defined as subjects with DM who are dependent on insulin for survival and are at risk for ketoacidosis [1].

Type 2 DM was defined as patients with DM on diet therapy either alone or in combination with oral glucose lowering agent(s) for glycaemic control [1].

Dyslipidaemia was taken as HDL-C <1.04 mmol/L(males) or < 1.3 mmol/L or TG ≥ 1.7 mmol/L or LDL-C ≥ 2.6 mmol/L or total cholesterol (TC) ≥ 5.2 mmol/L or if the patient is on lipid lowering agents [33].

Young age was taken as 18-44 years, middle age as 45-64 years and old age as 65 years and above [34].
Poor glycaemic control was taken as (glycated haemoglobin) $HbA_{1C} \geq 7.0\%$ [1].
Global obesity was defined by body mass index (BMI) >30 (kg/M^2) [1].
Central obesity was defined by Central obesity was defined by waist circumference (WC) > 94 cm in men and > 80 cm in women [1].

Statistical Analysis

Data collected was entered into spreadsheet using Microsoft Office Excel, and then analyzed using Statistical Package for Social Sciences (SPSS) version 25. Results of categorical variables were presented in tables as frequencies and percentages. The mean values and standard deviation for the continuous variables were calculated. Chi-square test was used for determining the association between MASLD and risk factors. The level of significance for all tests was set at $p < 0.05$.

RESULTS

A total of 142 subjects had complete results and were analysed in this study,

1. Socio-Demographic Characteristics

The age range of the subjects was 32 to 80 years and the mean age was 59.15 ± 11.37 years. Majority of the subjects were of middle age (54.9%), 35.2% were elderly and only 9.9% were of young age. There were more female subjects (57.7%) than male subjects (42.3%), and the majority (94.4%) of the subjects were married. Regarding educational attainment, 40.8%, 18.3% and 39.4% of the subjects had tertiary education, secondary education and Primary education, respectively, while 1.4% had no formal education (details in table 1) [35].

Table 1: Socio-demographic characteristics [35]

Variable	Frequency	Percentage
Age (years)		
18-44	14	9.9
45-64	78	54.9
≥65	50	35.2
Mean = 59.15 ± 11.37		
Sex		
Male	60	42.3
Female	82	57.7
Marital status		
Single	0	0
Married	134	94.4
Divorced	0	0
Widowed	8	5.6
Educational level		
No formal	2	1.4
Primary	56	39.4
Secondary	26	18.3
Tertiary	58	40.8

2. Mean Values of Some Biochemical Determinants among the Subjects

The mean value of glycated haemoglobin (HbA1c) was 8.30 ± 2.26 %), while the mean values of total cholesterol (TC), triglyceride (TG), high density lipoprotein (HDL) and low density lipoprotein (LDL) were: 4.45 ± 0.94 mmol/L, 1.24 ± 0.83 mmol/L, 1.12 ± 0.36 mmol/L and 2.72 ± 0.81 mmol/L respectively (details in table 2).

Table 2: Mean values of some biochemical determinants among the subjects

Variable	Minimum	Maximum	Mean	SD
HbA1c (%)	4.50	15.50	8.30	2.26
Total cholesterol (mmol/L)	2.60	7.11	4.45	0.94
Triglyceride (mmol/L)	0.40	4.79	1.24	0.83
High density lipoprotein (mmol/L)	0.24	3.09	1.12	0.36
Low density lipoprotein (mmol/L)	4.76	4.76	2.72	0.81

3. Results of the Liver Ultrasonography in the Subjects

Ultrasonography of the liver showed that 46.5% of the subjects had MASLD and 47.9%, 35.2%, 14.1% and 2.8% of them had grades 0, 1, 2 and 3 MASLD respectively.

Also, 53.5% of the subjects had increased liver echogenicity, 2.8% had nodule(s) in their liver, 19.3%

had portal vein blurring, and 14.1% had portal vein dilatation (details in table 3).

Table 3: Results of the ultrasonography of the liver

Variable	Frequency	Percentage (%)
MASLD		
Present	76	46.5
Absent	66	53.5
MASLD grades		
0	68	47.9
1	50	35.2
2	20	14.1
3	4	2.8
Liver echogenicity		
Increased	76	53.5
Normal	66	46.5
Nodule(s)		
Present	4	2.8
Absent	138	97.2
Portal vein blurring		
Present	26	18.3
Absent	116	81.7
Portal vein dilatation		
Present	20	14.1
Absent	122	85.9

4. Association between MASLD and Socio-Demographic Factors

A statistically significant association was found between MASLD and the education levels of the subjects ($X^2 = 20.732$; $p = 0.000$) and the duration of diabetes mellitus ($X^2 = 5.509$; $p = 0.019$) among the subjects.

A higher prevalence of MASLD was found among subjects who had secondary education (69.2%), tertiary education (69.0%) and short duration of diabetes mellitus (68.2%).

There were no significant association between the prevalence of MASLD and some other socio-demographic factors that included age, sex and marital status ($p > 0.05$ in these cases) (details in table 4).

Table 4: Association between MASLD and socio-demographic factors

Factor	MASLD		X^2	p-value
	Present	Absent		
Age (years)				
18-44	8 (57.1)	6 (42.9)	0.948	0.622
45-64	44 (56.4)	34 (43.6)		
≥65	24 (48.0)	26 (52.0)		
Sex				
Male	34 (56.7)	26 (43.3)	0.413	0.520
Female	42 (51.2)	40 (48.8)		
Marital status				
Single	0	0	1.572	0.210
Married	70 (52.2)	64 (47.8)		
Divorced	0	0		
Widowed	6 (75.0)	2 (25.0)		
Educational level				
No formal	0	2 (100)	20.732	0.000*
Primary	18 (32.1)	38 (67.9)		
Secondary	18 (69.2)	8 (30.8)		
Tertiary	40 (69.0)	18 (31.0)		
Duration of Diabetes mellitus				
Short	30 (68.2)	14 (31.8)	5.509	0.019*
Long	46 (46.9)	52 (53.1)		

5. Association between MASLD and Clinical Factors

A statistically significant association was found between MASLD and global obesity (X^2 = 6.079; p = 0.014) and anti-hypertensive medications use (X^2 = 5.938; p = 0.015).

A higher prevalence of MASLD was found among subjects who had global obesity (70.0%), and among the subjects taking anti-hypertensive medications (62.5%).

No significant association was found between the prevalence of MASLD and some other clinical factors that included abdominal (central) obesity, glycaemic control, hypertension, dyslipidaemia, treatment for DM and the use of lipid-lowering medications (p > 0.05 in these cases) (details in table 5).

Table 5: Association between MASLD and clinical factors

Factor	MASLD		X^2	p-value
	Present	Absent		
Abdominal obesity (males)				
Present	16 (57.1)	12 (42.9)	0.005	0.944
Absent	18 (56.3)	14 (43.8)		
Abdominal obesity (females)				
Present	36 (51.4)	34 (48.6)	0.008	0.927
Absent	6 (50.0)	6 (50.0)		
Global obesity				
Present	28 (70.0)	12 (30.0)	6.079	0.014*
Absent	48 (47.1)	54 (52.9)		
Glycaemic control				
Good	20 (50.0)	20 (50.0)	0.278	0.598
Poor	56 (54.9)	46 (45.1)		
Systolic hypertension				
Present	26 (54.2)	22 (45.8)	0.012	0.912
Absent	50 (53.2)	44 (46.8)		
Diastolic hypertension				
Present	26 (61.9)	16 (38.1)	1.685	0.194
Absent	50 (50.0)	50 (50.0)		
Treatment for Diabetes				
Diet alone	0	0	0.361	0.835
OADs	52 (55.3)	42 (44.7)		
Insulin	4 (50.0)	4 (50.0)		
Both	20 (50.0)	20 (50.0)		
Dyslipidaemia				
Present	66 (52.4)	60 (47.6)	0.584	0.445
Absent	10 (62.5)	6 (37.5)		
Exercise				
Yes	14 (53.8)	12 (46.2)	0.880	0.644
No	62 (53.0)	54 (47.0)		
Anti-hypertensive medication(s) use				
Yes	50 (62.5)	30 (37.5)	5.938	0.015*
No	26 (41.9)	36 (58.1)		
Lipid lowering medication(s) use				
Yes	48 (51.1)	46 (48.9)	0.675	0.411
No	28 (58.3)	20 (41.7)		

6. Association between MASLD Grading and Socio-Demographic Factors

There was significant association between the MASLD grades and marital status (X^2 = 9.181; p = 0.027), education level (X^2 = 25.492; p = 0.02) and the duration of diabetes mellitus (X^2 = 8.083; p = 0.044) amongst the subjects.

A higher percentage of the subjects that were married had grade 0 of MASLD. Grade 2 NAFLD was more prevalent among the subjects that had secondary (23.1%) and tertiary education (20.7%), while grade 0 was more among those subjects that had primary education (67.9%). Grades 0 and 1 MASLD were more prevalent among the subjects that had long duration

(55.1%) and short duration (50.0%) of DM, respectively (details in table 6).

Table 6: Association between MASLD grading and socio-demographic factors

Factor	MASLD grading				X^2	p-value
	0	1	2	3		
Age (years)						
18-44	6 (42.9)	6 (42.9)	0	2 (14.3)	10.848	0.093
45-64	36 (46.2)	28 (35.9)	12 (15.4)	2 (2.6)		
≥65	26 (52.0)	16 (32.0)	8 (16.0)	0		
Sex						
Male	26 (43.3)	26 (43.3)	8 (13.3)	0	5.365	0.147
Female	42 (51.2)	24 (29.3)	12 (14.6)	4 (4.9)		
Marital status						
Single	0	0	0	0	9.181	0.027*
Married	66 (49.3)	48 (35.8)	16 (11.9)	4 (3.0)		
Divorced	0	0	0	0		
Widowed	2 (25.0)	2 (25.0)	4 (50.0)	0		
Educational level						
No formal	2 (100)	0	0	0	25.492	0.002*
Primary	38 (67.9)	14 (25.0)	2 (3.6)	2 (3.6)		
Secondary	8 (30.8)	10 (38.5)	6 (23.1)	2 (7.7)		
Tertiary	20 (34.5)	26 (44.8)	12 (20.7)	0		
Duration of Diabetes						
Short	14 (31.8)	22 (50.0)	6 (13.6)	2 (4.5)	8.083	0.044*
Long	54 (55.1)	28 (28.6)	14 (14.3)	2 (2.0)		

7. Association between MASLD Grades and Clinical Factors

There was significant association between the MASLD grades and abdominal obesity in male subjects ($X^2 = 11.786$; $p = 0.003$), global obesity ($X^2 = 9.736$; $p = 0.021$) and diastolic hypertension ($X^2 = 14.509$; $p = 0.002$) amongst the entire subjects. A higher percentage of the male subjects that had abdominal obesity (42.9%) had grade 0 MASLD, while their counterparts without abdominal obesity had more of Grade 1 MASLD (56.3%). Majority of the subjects who had global obesity (40.0%) had Grade 1 MASLD, while the subjects without global obesity had more of grade 0 MASLD. Similarly, the subjects with diastolic hypertension had more of grade 0 (42.9%) and Grade 1 MASLD, respectively (42.9%), while those without diastolic hypertension (50.0%) had more of grade 0 MASLD (details in table 7).

Table 7: Association between MASLD grades and clinical factors

Factor	MASLD grades				X^2	p-value
	0	1	2	3		
Abdominal obesity (males)						
Present	12 (42.9)	8 (28.6)	8 (28.6)	0	11.786	0.003*
Absent	14 (43.8)	18 (56.3)	0	0		
Abdominal obesity (females)						
Present	36 (51.4)	18 (25.7)	12 (17.1)	4 (5.7)	4.811	0.186
Absent	6 (50.0)	6 (50.0)	0	0		
Global obesity						
Present	12 (30.0)	16 (40.0)	10 (25.0)	2 (5.0)	9.736	0.021*
Absent	56 (54.9)	34 (33.3)	10 (9.8)	2 (2.0)		
Glycaemic control						
Good	20 (50.0)	12 (30.0)	6 (15.0)	2 (5.0)	1.457	0.692
Poor	48 (47.1)	38 (37.3)	14 (13.7)	14 (13.7)		
Systolic hypertension						
Present	24 (50.0)	18 (37.5)	4 (8.3)	2 (4.2)	2.347	0.504
Absent	44 (46.8)	32 (34.0)	16 (17.0)	2 (2.1)		
Diastolic hypertension						
Present	18 (42.9)	18 (42.9)	2 (4.8)	4 (9.5)	14.509	0.002*
Absent	50 (50.0)	32 (32.0)	18 (18.0)	0		
Treatment for DM						

Diet alone OADs Insulin Both	0 44 (46.8) 4 (50.0) 20 (50.0)	0 30 (31.9) 4 (50.0) 16 (40.0)	0 16 (17.0) 0 4 (10.0)	0 4 (4.3) 0 0	5.334	0.502
Dyslipidaemia						
Present Absent	62 (49.2) 6 (37.5)	42 (33.3) 8 (50.0)	18 (14.3) 2 (12.5)	4 (3.2) 0	2.066	0.559
Exercise						
Yes No	12 (46.9) 56 (48.7)	12 (46.2) 38 (32.2)	2 (7.7) 18 (15.7)	0 4 (3.5)	4.923	0.554
Anti-hypertensive medication(s) use						
Yes No	32 (40.0) 36 (58.1)	32 (40.0) 18 (29.0)	14 (17.5) 6 (9.7)	2 (2.5) 2 (3.2)	5.156	0.161
Lipid-lowering medication(s) use						
Yes No	48 (51.1) 20 (41.7)	28 (29.8) 22 (45.8)	14 (14.9) 6 (12.5)	4 (4.3) 0	5.081	0.166

DISCUSSIONS

A total of 142 T2DM subjects with complete data were analysed. Their mean age was 59.15 ± 11.37 years. Majority of the participants were female subjects (57.7%), had tertiary education (40.8%) and were of middle age (54.9%), respectively. The overall prevalence rate of MASLD among the subjects was 46.5%. With respect to the grades of MASLD, the prevalence rates of grades 0, 1, 2 and 3 NAFLD were 47.9%, 35.5%, 14.1% and 2.8%, respectively. Additionally, 53.5% of the subjects had increased liver echogenicity, 2.8% had nodule(s) in the liver, 19.3% had blurring of the portal vein, and 14.1% had dilatation of the portal vein.

Afolabi *et al*., and Aransiola *et al*., in Western Nigeria found that the prevalence rates of MASLD among their T2DM subjects were 68.8%, and 46.0% respectively [23-36]. Afolabi *et al*., equally found that 25.0%, 16.3%, 32.5% and 20.0% of their subjects had grades 0, 1, 2 and 3 MASLD, respectively [23]. Olusanya *et al*., and Onyekwere *et al*., also found that the prevalence rates of MASLD in their T2DM subjects were 16.7% and 9.5% compared with 1.2% and 4.5% found in the non-diabetic counterparts [20, 21]. Finally, Onyia *et al*., found that the prevalence rate of MASLD in obese patients was 36.4% as against 0.4% in the non-obese control subjects while Odenigbo *et al*., found a prevalence rate of MASLD of 31.0% among the general medical out-patients [22-37].

The prevalence rate of MASLD in patients with T2DM found by Aransiola *et al*., (46.0%) was very comparable to the 46.5% found by this study [36]. Both studies were recent, Nigerian and adopted similar methodologies that included similar method of evaluation for and diagnosis of MASLD and also the fact that they studied a very comparable sample size; 139 and 142 T2DM subjects by Aransiola *et al*., and the index work, respectively [36]. Afolabi *et al*., contrastingly, found that prevalence rate of MASLD in T2DM subjects was 68.8% and additionally, that grade 2 MASLD had the highest prevalence (32.5%), followed by grade 0 (25.0%) and 3 (20.0%), respectively, while the index study recorded the highest prevalence rate for grade 0 (47.9%), followed by grade 1 (35.2%) and lastly grade 3 NAFLD (2.85%) among the subjects, respectively [23]. The fact that both studies were Nigerian notwithstanding, Afolabi et al's work was older and the sample size smaller (80 T2DM subjects) when compared to this study that evaluated 142 T2DM subjects [23]. Furthermore, increasing adoption of the modern trends in the management of DM in our clime, that include the use of the sodium glucose co-transporter 2 inhibitors And the other weight-reducing medications, as well emphasis on life style modifications, including habitual exercise for weight loss in the obese type 2 diabetic patients could have impacted on the MASLD prevalence in the T2DM subjects in the index study [38-40]. Obesity and metabolic syndrome have been closely associated with the rising prevalence of MASLD [41, 42]. Similarly, the disparity between Onyekwere et al's finding and that of the index study could be explained by the long interval of time between the two studies, as well as the difference in the methodologies adopted by the two studies. Onyekwere et al's research work was done over a decade ago and they evaluated 106 T2DM subjects [21].

Sinha *et al*., comparably found that the prevalence of MASLD was 57.0% in T2DM subjects, their sample size was 132 T2DM subjects, which was still close to that of the index study [43]. Younossi *et al*., in a systematic review and meta–analysis found a higher global pooled prevalence of MASLD of 65.33% among T2DM subject [7]. They analysed studies that deployed varying diagnostic tools and modalities for the evaluation of MASLD. Lastly, Alsabaani *et al*., found a higher prevalence rate of MASLD of 72.8% in their T2DM subjects in the Middle-east compared with the index study [44]. Their sample size of 245 was far above that of the index study.

This study found a significant association between MASLD and educational level, duration of DM, global obesity and the use of anti-hypertensive medication(s). Equally, ultrasound grades of MASLD

showed significant association with marital status, educational level, Duration of DM, abdominal obesity, global obesity and diastolic hypertension. Most subjects with higher educational levels tend to adopt western life style that predisposes to obesity and the metabolic syndrome with their attendant sequelae, including MASLD. Long duration of T2DM was found to be associated with an increased rate of MASLD as well mortality in patients with MASLD [45]. On the other hand, MASLD diagnosis could be made at the level of impaired fasting glucose, antedate the diagnosis of T2DM or be present early in the course of T2DM as was the case in the index study. Zhang *et al*., found increased risks of MASLD and of the different grades of MASLD in diabetic individuals [45]. The finding of significant association between the incidence of MASLD, the grades of MASLD and obesity by the index study was as expected, patients with obesity had higher odds of MASLD [46, 47]. Obesity was also a strong predictor of MASLD [23-48]. Afolabi *et al*., and Abangah *et al*., found that the prevalence of MASLD and its grades in T2DM varied significantly with BMI (global obesity) [23-48].

The relationship between hypertension and MASLD is bidirectional; MASLD contributes independently to the development of hypertension and vice versa and this occurs via mechanisms postulated to result from Insulin resistance and inflammation, with the activation of the sympathetic nervous system or the rennin-angiotensin-aldosterone system [49].

Finally, Fu *et al*., and Li *et al*., found that hypertension was associated with higher prevalence of liver steatosis and fibrosis [50, 51].

CONCLUSION

The prevalence rate of MASLD in subjects with T2DM at NAUTH, Nnewi, found by this study was high and showed the huge burden of this disease in this group of subjects. This study also found a significant association between MASLD and educational level, duration of DM, global obesity and the use of anti-hypertensive medication(s). Additionally, the index study found found significant association between the ultrasound grades of MASLD and the marital status, educational level, duration of DM, obesity and diastolic hypertension. These findings underscore the need for early and routine screening for MASLD in subjects with T2DM and timely adoption of total life style modifications, including weight reduction and blood pressure control by the obese and hypertensive type 2 Diabetic subjects, respectively.

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AUTHORS' CONTRIBUTIONS

Data Availability

The data that support the findings of this study would be made available by the corresponding author upon reasonable request.

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Conflict of Interests: None declared.

Ethical Approval

Ethical clearance was obtained from the Research Ethics Committee of Nnamdi Azikiwe University Teaching Hospital, Nnewi before the commencement of the study. A written informed consent was gotten from the study participants before they were enrolled to participate in the study. Participation was entirely voluntary and patients were allowed to withdraw from the study if they wanted without any official notification to the researchers.

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