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Serum Adiponectin and C-Reactive Protein Profiles in Metabolic Syndrome patients with Metabolic Associated Fatty Liver Disease

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Abstract

Metabolic syndrome (MetS) encompasses a cluster of metabolic abnormalities that increase the risk of cardiovascular and liver diseases, notably non-alcoholic fatty liver disease (NAFLD) and metabolic-associated fatty liver disease (MAFLD). Methods: This cross-sectional analytical study assessed the prevalence of MAFLD and biomarker profile, focusing on serum adiponectin and C-reactive protein (CRP), in 118 MetS patients with NAFLD at the University of Calabar Teaching Hospital. Participants were recruited via convenience sampling, and demographic, clinical, and laboratory data were analysed using SPSS version 25. NAFLD prevalence was high (72.9%), with most patients aged 50–70 years (mean 58.1 ± 9.7) and a female predominance (ratio 1.81:1). Fatigue was the most frequently reported symptom. Over 80% of the NAFLD cases demonstrated abnormal biomarker profiles, characterised by either elevated CRP levels or reduced adiponectin concentrations.; however, neither showed an independent association after adjustment. Hypertriglyceridemia emerged as the sole biochemical predictor. NAFLD frequently co-exists with obesity, hypertension, and diabetes, reflecting shared metabolic risk factors. Conclusion: These findings highlight the growing burden of NAFLD in our setting, the central role of triglyceride metabolism, and the need for early intervention through lifestyle modification and targeted lipid management. Further longitudinal research is warranted to clarify the role of CRP and adiponectin in disease progression and refine risk-stratification strategies.

Keywords: Adiponectin, Diabetes Mellitus, C-reactive protein, Non-alcoholic fatty liver disease (NAFLD), Metabolic Associated Fatty Liver Disease (MAFLD), Metabolic Syndrome (MetS).

Introduction

Metabolic syndrome (MetS) is not classified as a disease in itself, but rather represents a cluster of interrelated metabolic abnormalities—including abdominal obesity, hyperglycemia, hypertension, low levels of high-density lipoprotein (HDL) cholesterol, and hypertriglyceridemia (Paschos et al., 2009). These components were formally defined by the National Cholesterol Education Program's Adult Treatment Panel III (NCEP ATP III) in 2001, which outlined five criteria for diagnosis (Lemieux et al., 2020). The presence of any three of these five risk factors is sufficient for a MetS diagnosis (Wang et al., 2020).

Although insulin resistance is central to the pathophysiology of MetS, it is not an explicit criterion in the NCEP ATP III framework, which assigns equal diagnostic weight to all five components, making it clinically practical (Wang et al., 2020). MetS significantly elevates the risk of several chronic conditions, including type 2 diabetes mellitus (T2DM), cardiovascular disease (CVD), and chronic kidney disease (Paschos et al., 2009; Wang et al., 2020). It is also associated with a pro-inflammatory and prothrombotic state, as well as non alcoholic fatty liver disease (NAFLD), cholesterol gallstone disease, and reproductive dysfunction (Wang et al., 2020).

Non Alcoholic Fatty Liver Disease is defined as the presence of fat in the liver on imaging and/or on liver biopsy, after exclusion of another obvious cause of liver damage (e.g., no excessive alcohol consumption, hepatotoxic medication, toxins, viral infections, genetic hepatic diseases). The term NAFLD, by definition, denotes non-alcohol-related liver injury, but it does not reflect the underlying metabolic dysfunction or the associated cardiovascular risks (Boccatonda et al., 2023). NAFLD is broadly categorised into two forms: simple hepatic steatosis a generally benign and non-progressive condition, and non-alcoholic steatohepatitis (NASH), an inflammatory form that can progress to cirrhosis and hepatocellular carcinoma (HCC) (Ng et al., 2022).

In 2020, an international expert panel considered a new nomenclature metabolic dysfunction-associated fatty liver disease (MAFLD) to replace NAFLD, which had been previously defined by exclusion. The MAFLD definition requires evidence of hepatic steatosis (via imaging or histology), along with at least one of the following: obesity, type 2 diabetes mellitus (T2DM), or metabolic dysregulation (Boccatonda et al., 2023). MAFLD is specifically defined as hepatic steatosis in the presence of obesity (BMI >25 kg/m² for Caucasians and >23 kg/m² for Asians), type 2 diabetes mellitus, or at least two of the following conditions: increased waist circumference; elevated high-sensitivity serum C-reactive protein levels; prediabetes; elevated blood pressure; reduced HDL-cholesterol levels; elevated triglyceride levels; and a homeostasis model assessment (HOMA)-insulin resistance score of ≥2.5 (Boccatonda et al., 2023). The likelihood of developing systemic end-organ complications such as CVD, stroke, and chronic kidney disease appears to be slightly higher in MAFLD than in NAFLD (EASL et al., 2024; Godoy-Matos et al., 2020). This observation reinforces the rationale for adopting the updated nomenclature and enhancing risk stratification for individuals at increased risk.

Furthermore, the adoption of the MAFLD definition importantly considers beyond the exclusion of alternative causes of chronic liver disease, such as alcohol or viral hepatitis (Ng et al., 2022). The proposed advantages of the terminology change from NAFLD to MAFLD include a clearer representation of the underlying disease process, reduced stigmatisation through the removal of the term *"non-alcoholic"*, and enhanced research opportunities, particularly in the context of coexisting liver diseases (European Association for the Study of the Liver -EASL, 2024; Godoy-Matos et al., 2020). Potential limitations of this terminology change include the potential for disruption to ongoing NAFLD clinical trials, biomarker discovery studies, and research into lean or non-obese NAFLD phenotypes (Ng et al., 2022). Significantly, the revised nomenclature aims to address the significant alterations in disease trajectory observed in individuals with concurrent hepatic steatosis and viral hepatitis, an overlap that can complicate the management of each condition (Fernandez et al., 2024).

Chronic hepatitis B and C viral infection, when present alongside MAFLD, have been shown to act synergistically to accelerate liver disease progression. This occurs through a multifactorial mechanism

involving hepatocyte injury, inflammation, fibrosis, and hepatocellular carcinoma (HCC), mediated by activation of cellular immune pathways, release of pro-inflammatory cytokines, stimulation of de novo lipogenesis in hepatocytes, and modulation by host genetic factors (Fernandez et al., 2024). Given the emerging recognition of NAFLD as a heterogeneous disorder, the international consensus panel's decision to adopt a terminology that better reflects disease associations is well justified (Eslam et al., 2020). This is particularly relevant in settings such as ours, where the prevalence of HBV and HCV remains high and is compounded by the growing burden of non-communicable diseases (2018 National AIDS Indicator and Impact Survey [NAIIS]; Bello-Ovosi et al., 2018).

The rapid urbanisation occurring across sub-Saharan Africa including Nigeria has brought about technological advancement, but also a marked shift toward sedentary lifestyles, westernised diets, and increased alcohol and tobacco use, contributing to the rise in non-communicable metabolic-related diseases (Muazu et al., 2019). MetS is a known precursor to both NAFLD and CVD (Paschos et al., 2009), and growing evidence suggests that even mild hepatic steatosis increases the risk of CVD and all-cause mortality, particularly when compounded by T2DM (Kim et al., 2024). The burden of MetS in Nigeria is considerable and regionally variable. In North-West Nigeria, the prevalence among urban residents was 35.1%, with a higher rate in females (42.83%) compared to males (27.36%) (Sabir et al., 2016). In rural South-West Nigeria, the prevalence was lower at 12.1%, with a slight male predominance (Adegoke et al., 2010). Meanwhile, in South-East Nigeria, MetS affected 38.2% of the population, again showing a higher prevalence in females (Chukwurah et al., 2019).

While most Nigerian studies on fatty liver disease have been based on the older nomenclature – NAFLD, their findings are consistent with global evidence, demonstrating strong associations with T2DM, obesity, hypertension, and dyslipidemia (Chukwurah et al., 2019; Obasi et al., 2022; Sabir et al., 2016). A recent study from Ebonyi State in South-East Nigeria, neighbouring Cross River State reported a NAFLD prevalence of 12.3% among individuals with MetS (Obasi et al., 2022). This study further alluded to the pivotal roles of morbid obesity, low HDL levels, and T2DM in the development of NASH (Obasi et al., 2022).

There remains a significant paucity of research in our setting addressing the recently adopted terminology, MAFLD, and the broader pathophysiological mechanisms underlying NAFLD. In particular, the potential contributions of pro-inflammatory cytokines, genetic predisposition, and environmental exposures (factors that may play a critical role in the onset and progression of the disease). This pilot study aimed to determine the prevalence of NAFLD and MAFLD among MetS patients and to evaluate serum adiponectin and C-reactive protein (CRP) levels within the NAFLD cohort. Considering the evolving conceptual shift from NAFLD to MAFLD and the pressing need for region-specific data, this study aims to generate preliminary insights into the inflammatory and metabolic profiles of MetS patients with NAFLD, thereby providing a foundation for future large-scale investigations and informing targeted interventions in the Nigerian context.

Methods

Study location: This study was conducted in the Gastroenterology, Cardiology, Diabetic, and Metabolic clinics of the University of Calabar Teaching Hospital (UCTH). This tertiary health centre is situated in Calabar, the capital of Cross River State (CRS), located in Nigeria's South-South rainforest region. The University of Calabar Teaching Hospital is located within the same vicinity as the University of Calabar, the pioneer tertiary educational institution in the state. It is a 600-bed tertiary healthcare facility located in Calabar South Local Government Area. It serves as a major referral centre for residents of Cross River State and surrounding states, including Akwa Ibom, Abia, and Benue. Additionally, it also receives referrals from Cameroon, a neighbouring country.

Study design and population: This was a cross-sectional analytical study, spanning twelve months. Informed consent was obtained from prospective study participants (aged eighteen years and above). Using

the NCEP: ATP III guidelines, the diagnosis of Metabolic Syndrome was made in the presence of at least three out of the five components listed below (Huang, 2009; Paschos et al., 2009).

1. **Presence of central obesity**: i.e., waist circumference ≥ 102cm in men or 88cm in women,
2. **Triglyceride levels (TG)**: fasting TG level ≥ 1.69mmol/L
3. **High-density lipoprotein (HDL) cholesterol levels**: ≤1.03mmol/L in males, or ≤1.29mmol/L in females.
4. **Fasting Blood sugar (FBS)**: FBS ≥ 5.5mmol/L.
5. **Blood pressure (BP)**: ≥ 130/85 mmHg.

The diagnosis of **NAFLD** in study participants with MetS was established based on a combination of clinical history (e.g., vague right upper quadrant pain), physical examination findings (hepatomegaly), radiologic evidence (detailed below), and relevant laboratory abnormalities (such as dyslipidemia and elevated liver enzymes) (El-Kader, 2015).

The abdominal ultrasound findings of fatty liver include;

- Diffuse or focal parenchymal echogenicity of the liver, higher than the renal cortex and spleen due to fatty infiltration. Focal involvement appeared as areas of increased echogenicity in the liver with geographic or straight borders.
- Three grades of steatosis/ fatty infiltration were described.
  - Grade 1: when the echogenicity is just increased.
  - Grade 2: when the echogenic liver obscures the echogenic walls of the portal vein branches.
  - Grade 3: when the echogenic liver obscures the diaphragmatic outline (Kolawole et al., 2024; Onyekwere et al., 2015)

While **MAFLD** was diagnosed in study participants with MetS who satisfied the following criteria:

1. Hepatic steatosis confirmed sonographically in participants with coexisting obesity, defined as a body mass index (BMI) greater than 25 kg/m².
2. Type 2 diabetes mellitus **OR**
3. ≥2 of the following conditions:

i. *Increase in waist circumference;*
ii. *Elevated highly sensitive serum C-reactive protein level;*
iii. *Pre-diabetes;*
iv. *Elevated blood pressure;*
v. *Decreased HDL-cholesterol levels;*
vi. *Increased triglyceride levels and*
vii. *Homeostasis model assessment (HOMA)-insulin resistance score ≥2.5*

Additionally, following current recommendations, the diagnosis of MAFLD in this study also accounted for alternative causes of chronic liver disease, such as alcohol-related liver disease and viral hepatitis B and C (Ng et al., 2022).

Study inclusion & Exclusion criteria: Eligible participants were adults aged 18 years and above who provided informed consent, had sonographic evidence of fatty liver on abdominal ultrasound, and met the diagnostic criteria for both MetS and NAFLD. Patients were excluded if they were jaundiced, had a clinically or sonographically shrunken liver, or had any form of malignancy. Additional exclusion criteria included current use of medications known to predispose to or cause secondary steatosis such as

amiodarone, corticosteroids, or methotrexate or a history of jejunoileal bypass surgery or extensive small bowel resection. Pregnant women, individuals younger than 18 years, and patients with severe comorbid conditions, including congestive heart failure, advanced liver disease, thyroid disease, or chronic kidney disease, were also excluded.

Sample size determination: The sample size was determined using Cochran's formula for large populations (>10,000), with an assumed prevalence of 12.3% based on Obasi et al, a 95% confidence level, and a 5% margin of error (Obasi et al., 2022). This yielded a minimum sample size of 166, which was adjusted to 183 to account for a projected 10% non-response rate. As the study population was fewer than 10,000, the figure was further refined using the Taro Yamane adjustment, based on an estimated clinic population of 320 patients over a six-month recruitment period. This calculation resulted in a final minimum sample size of 117 participants. Using a convenience sampling approach, consecutive patients attending the Gastroenterology, Cardiology, and Diabetic Clinics of the University of Calabar Teaching Hospital who fulfilled the diagnostic criteria for MetS were recruited. These participants were subsequently evaluated for the presence of NAFLD.

Data collection: A semi-structured, pre-tested, interviewer-administered questionnaire was employed to collect information from participants regarding their bio-data, vague right upper quadrant pain, fatigue, jaundice, history of diabetes, alcohol consumption, history of abdominal surgery, drug history, and family history of diabetes, liver disease, and cardiovascular disease. To ensure the validity, reliability, and clarity of the research instrument, a pilot test was conducted. This phase involved administering the questionnaire to a small representative sample, constituting 10% of the target population (12 participants). The purpose of this pilot testing was to identify and eliminate any ambiguities in the questionnaire, detect potential biases or errors, and pinpoint areas for improvement. A comprehensive clinical examination was conducted for each participant to assess stigmata of chronic liver disease and non-hepatic manifestations of NAFLD. Blood pressure was measured in a seated position after at least 15 minutes of rest and before blood sampling, using a mercury sphygmomanometer (Accoson, England). Weight (in kilograms) and height (in centimetres) were recorded using the RGZ-120 health scale stadiometer, with participants dressed in light clothing and having removed shoes, hats, or caps. Body mass index was calculated using the formula: *Weight (kg)/Height² (m²)*. Waist circumference was measured in centimetres using a flexible, non-stretchable measuring tape at the midpoint between the lower margin of the last palpable rib and the superior border of the iliac crest. While, venous blood samples were collected into plain bottles for biochemical analyses, including fasting blood glucose, fasting lipid profile, liver function tests, hepatitis B and C serology, serum adiponectin, and high-sensitivity C-reactive protein (hs-CRP). Hepatitis B surface antigen (HBsAg) and hepatitis C virus antibody (anti-HCV) were screened using One Step Biocheck rapid diagnostic kits, which are qualitative, highly sensitive direct-binding tests providing results within 10–20 minutes, read visually without instrumentation. Serum adiponectin was quantified using an enzyme-linked immunosorbent assay (ELISA) kit (Elabscience, USA), and hs-CRP was measured using an ELISA kit (Monobind, Lake Forest, CA, USA).

Data analysis plan: Statistical analysis was performed to examine the relationship between various factors and the prevalence of NAFLD among patients with Met-S at UCTH, Calabar. Data was exported from Microsoft Excel to SPSS version 25.0 for cleaning and analysis. Descriptive statistics summarized socio-demographic characteristics, past medical history, anthropometric measurements, and laboratory parameters. Results were presented as means with standard deviations, frequencies, percentages, and graphical displays where appropriate. The prevalence of NAFLD and MAFLD in the study population was illustrated using pie charts. NAFLD status was defined as the dependent variable, while independent variables included socio-demographic characteristics, anthropometric indices, and biochemical parameters. Associations between these independent variables and NAFLD were first evaluated using bivariate analysis. The Chi-square test (or Fisher's exact test where expected cell counts were <5) was used to assess statistical associations, with significance set at $p<0.05$. Independent variables that demonstrated statistically significant associations in the bivariate analysis were further assessed using multivariate binary logistic

regression to identify independent predictors of NAFLD among Met-S patients. Multivariate results were reported with 95% confidence intervals, and statistical significance was maintained at the 5% level.

Ethical consideration: The study received approval from the Health Research Ethics Committee (HREC) of UCTH (protocol number: UCTH/HREC/33/Vol. III/118). Written informed consent was obtained from all participants. Three patients declined participation, and one patient died during recruitment. The study adhered to the ethical principles outlined in the Declaration of Helsinki.

Results

Demographic and Clinical Characteristics: A total of 118 patients with MetS were evaluated. Females constituted the majority (64.4%), while males accounted for 35.6%. Most patients were within the 45–65 years age group (76.3%), followed by those over 65 years (20.3%), and a small proportion (3.4%) aged 18–45 years. Occupational distribution showed that 35.6% of patients were in the "Others" category, followed by business owners (27.1%), civil servants (21.2%), and public servants (16.1%). These findings suggest that the typical Met-S patient in our study was a middle-aged female engaged across various occupational sectors. The most commonly reported symptom was fatigue (83.1%), followed by right upper quadrant pain (25.4%). Leg swelling (5.9%) and abdominal distension (5.1%) were infrequent.

Anthropometric Profile: The majority of patients had a BMI within the overweight range (25.0–29.9 kg/m²; 30.5%), followed by those classified as obese class I (30.0–34.9 kg/m²; 27.1%). Waist circumference was elevated in more than half (52.5%) of the MetS patients, indicating a high prevalence of central obesity.

Biochemical Findings: Biochemical assessment included measurement of alanine aminotransferase (ALT), fasting blood sugar (FBS), fasting lipid profile, hs-CRP, and serum adiponectin. ALT was elevated in 48.3% of participants, while elevated FBS was observed in 73.7%. Lipid profile abnormalities comprised elevated total cholesterol (53.4%), elevated low-density lipoprotein (LDL) cholesterol (54.2%), low high-density lipoprotein (HDL) cholesterol (29.7%), and elevated triglycerides (40.7%). Inflammatory marker evaluation showed elevated hs-CRP in 43.2% and reduced adiponectin levels in 39.0% of participants.

Prevalence and Associated Conditions: Eighty-six patients (72.9%) were diagnosed with NAFLD, while MAFLD was identified in 89 (75.4%) of the cohort. The highest prevalence occurred among individuals with abnormal BMI (73.1%), hypertension (72.6%), and diabetes mellitus (72.0%). These results indicate that the majority of patients with metabolic syndrome had either NAFLD or MAFLD.

Bivariate analysis revealed no statistically significant associations between NAFLD and BMI ($p = 0.076$), waist circumference ($p = 0.243$), alanine aminotransferase (ALT) levels ($p = 0.546$), HDL-cholesterol ($p = 0.259$), C-reactive protein ($p = 0.109$), or adiponectin ($p = 0.057$). LDL-cholesterol showed a borderline association ($p = 0.054$). Significant associations were however identified with total cholesterol ($p = 0.041$), triglycerides ($p = 0.012$), and fasting blood sugar ($p = 0.031$). In the multivariate binary logistic regression model, which included total cholesterol, triglycerides, and fasting blood sugar, triglycerides emerged as the only statistically significant independent predictor of NAFLD (adjusted odds ratio [AOR] = 2.046; 95% confidence interval [CI]: 1.025–4.086; $p = 0.042$). Total cholesterol (AOR = 1.251; 95% CI: 0.942–1.660; $p = 0.122$) was not significant. Fasting blood sugar demonstrated a trend toward significance with a potential inverse association (AOR = 0.837; 95% CI: 0.700–1.002; $p = 0.052$).

Discussion

This cross-sectional analytical study, involving 118 consecutive MetS patients attending the medical outpatient clinic of the University of Calabar Teaching Hospital, CRS, Nigeria found that, using conventional diagnostic criteria, NAFLD and MAFLD could not be clinically distinguished. Both conditions exhibited the hallmark feature of hepatic fat accumulation, with or without secondary causes. In line with recent diagnostic updates, which no longer require the exclusion of secondary causes such as viral hepatitis or alcohol use for a MAFLD diagnosis (Ng et al., 2022), the prevalence increased slightly from 72.9% (n = 86) for NAFLD to 75.4% (n = 89) for MAFLD, with three patients testing positive for hepatitis B. Ng et al. (2022) in their study similarly found a slightly higher prevalence of MAFLD than NAFLD.

Their work also reported that up to 30–40% of patients with chronic hepatitis B may present with concurrent hepatic steatosis, which were cases previously excluded from NAFLD classification. When occurring concurrently with MAFLD, chronic hepatitis B and C infections have been shown to work in concert to hasten the progression of liver disease (Fernandez et al., 2024). In Nigeria, where the burden of viral hepatitis and non-communicable diseases continues to rise, the adoption of this new nomenclature holds particular relevance (Eslam et al., 2020; Bello-Ovosi et al., 2018). In light of the ongoing shift from NAFLD to MAFLD terminology, this pilot study suggests a potentially higher burden of MAFLD in our setting, underscoring the need to further understand the disease pathophysiology, identify at-risk individuals, and encourage further research, particularly in those with coexisting liver diseases.

This study demonstrated a clear female predominance (64.4% female vs. 35.6% male), yielding a female-to-male ratio of 1.81:1. The majority of participants (76.3%) were aged between 50 and 70 years, with a mean age of 58.1 ± 9.7 years. Age is a key determinant of NAFLD severity, with individuals over 50 years being more susceptible to advanced disease and insulin resistance (Obasi et al., 2022). Ageing is associated with impaired autophagy, increased oxidative stress, mitochondrial dysfunction, and chronic low-grade inflammation, all of which contribute to hepatic steatosis development and progression (Obasi et al., 2022).

In this study, fatigue emerged as the most common symptom, reported by over three-quarters (83.1%) of MetS patients with NAFLD, while one-quarter (25.4%) experienced right hypochondrial pain. Leg and abdominal swelling were less frequent. Pouwels et al. reported that though NAFLD patients are mostly asymptomatic, when symptoms do occur, they may range from fatigue to right upper quadrant discomfort, hepatomegaly, to obvious dermatological manifestations such as; acanthosis nigricans, and lipomatosis (Pouwels et al., 2022). Similarly, most patients with NASH remain asymptomatic, with the diagnoses often made incidentally during routine medical assessments (Pouwels et al., 2022). Clinical stigmata of chronic liver disease are uncommon in NAFLD, and diagnoses are more often triggered by abnormal liver function tests, particularly elevated aminotransferases (ALT and AST) or an incidental radiologic detection of hepatic steatosis (Pouwels et al., 2022). The clinical pattern observed in this study is consistent with findings from other Nigerian studies (Onyekwere et al., 2011; Onyia et al., 2024).

Among MetS patients with sonographic evidence of fatty liver, hypertension (99.2%), type 2 diabetes mellitus (84.7%), and elevated BMI (82.2%) were the most prevalent comorbidities, a pattern also reported in both local and international studies (Nouri-Keshtkar et al., 2023; Seerat & Jain, 2012; Onyekwere et al., 2011; Sabir et al., 2016). In these studies, women were more likely to exhibit MetS-related features such as higher BMI, central obesity, and lower HDL cholesterol levels (Seerat & Jain, 2012). Furthermore, non-diabetic women tended to have higher BMI and 2-hour postprandial glucose levels than men (Seerat & Jain, 2012). The high prevalence of hypertension and T2DM among our MetS patients reflects the central role these metabolic conditions play in defining MetS (Huang, 2009; Paschos et al., 2009).

A history of stroke was reported in 87.5% (7 out of 8) of MetS patients with NAFLD. This finding aligns with existing literature indicating that individuals with NAFLD have a 1.1- to 2.5-fold higher risk of stroke compared to those without NAFLD (Canillas et al., 2022; Hu et al., 2021; Wang et al., 2022).

Although not statistically significant, this study found that well-educated, middle-aged women who mostly engaged in 'other' occupations, e.g. farming or business/ trading, were more likely to present with NAFLD. Similar trends were described by Chukwurah et al. (2019), who reported increasing NAFLD prevalence from the fourth decade of life, likely driven by urbanisation and westernised dietary habits. The rising prevalence of obesity among women may partly explain their heightened risk of MetS and NAFLD (Seerat & Jain, 2012). Hormonal influences, including lower sex hormone-binding globulin levels in women, have also been linked to increased MetS risk, whereas testosterone levels in men have not demonstrated a similar association (Obasi et al., 2022). Interestingly, NAFLD prevalence was lower in elderly participants, consistent with Onyia et al. (2024), who observed a midlife peak followed by a decline in older age groups. The reasons for this pattern remain unclear and merit further population-based investigation.

Laboratory analyses revealed that close to 50% of NAFLD patients had elevated ALT, though this was not statistically significant. ALT is often used as a surrogate marker of hepatocellular injury; its elevation may indicate progression to NASH (Pearce et al., 2013). However, normal ALT levels do not exclude NASH, as histological findings have demonstrated a full NAFLD spectrum in patients with normal enzyme levels (Pearce et al., 2013). Liver biopsy remains the gold standard but is invasive, costly, and subject to sampling error, necessitating the development of reliable, non-invasive biomarkers. The invasive nature of liver biopsy has necessitated the development and utilization of non-invasive tools (NITs) to accurately evaluate NAFLD severity in otherwise healthy individuals. The American Gastroenterological Association (AGA) clinical practice update expert review, broadly describes these NITs into serum-based and imaging-based biomarkers. They recommend NITs that are readily available, cost-effective, and offer point-of-care assessment to risk stratify patients with NAFLD for advanced fibrosis (Wattacheril et al., 2023). Concerning the biomarkers assayed in this study, more than two-thirds of NAFLD patients in this study exhibited combined abnormalities, with elevated CRP observed in 51 patients (43.2%) and low adiponectin levels in 46 patients (39%). Although these alterations were notable, neither showed a statistically significant association with NAFLD following bivariate analysis. CRP, a pro-inflammatory marker linked to obesity and insulin resistance, has been investigated for its potential to distinguish simple steatosis from NASH; however, its diagnostic utility remains uncertain due to inconsistent findings across studies (Jamialahmadi et al., 2023; Hui et al., 2004). Moreover, factors such as statin use and the inherently low specificity of CRP may confound its clinical relevance (Zimmermann et al., 2011).

Similarly, low adiponectin—an adipokine with anti-inflammatory and insulin-sensitising properties, inversely related to obesity was not significantly associated with NAFLD in this cohort (Adolph et al., 2017). The leptin–adiponectin ratio has been proposed as a more reliable predictor of MetS risk than either marker alone (Adejumo et al., 2019). In our study, medication use, including PPARγ agonists, may have influenced adiponectin levels, potentially masking any true association.

Bivariate analysis in this study demonstrated significant associations between NAFLD and elevated total cholesterol, LDL, triglycerides (TG), and fasting blood sugar. However, multivariate regression identified hypertriglyceridaemia as the sole independent predictor, consistent with findings from other studies (Chukwurah et al., 2019; Tomizawa et al., 2014).

Hypertriglyceridaemia is strongly linked to NAFLD, particularly in individuals consuming high-carbohydrate diets and in those with T2DM, who have an increased propensity for endogenous triglyceride production (Ahmad et al., 2018). Tomizawa et al. (2014) identified triglyceride levels as the strongest predictor of NAFLD when compared with blood glucose and HbA1c, noting a stronger correlation between hypertriglyceridaemia and NAFLD than with hyper-LDL cholesterolaemia or hypo-HDL cholesterolaemia. They further alluded that high-carbohydrate diets substantially contribute to triglyceride accumulation in hepatocytes.

Given that most NAFLD patients in our cohort also had T2DM, increased endogenous triglyceride production may plausibly account for this observation. Notably, previous reports indicate that elevated serum triglyceride levels remain an independent risk factor for the development of T2DM, even after adjusting for BMI and other associated risk factors (Ahmad et al., 2018).

In this study, the absence of a significant association between NAFLD and certain risk factors, such as dyslipidemia (hyper-LDL cholesterolaemia or hypo-HDL cholesterolaemia) and diabetes, may be attributable to the ongoing use of statins or hypoglycemic agents among participants. While statins and, less frequently, fibrates are standard therapies for managing dyslipidemia in individuals with MetS, the use of fibrates remains uncommon in local settings due to limited availability (Ascaso et al., 2007). This limited access may partly account for the persistent elevation of triglyceride levels observed in treated patients.

Conclusion

This pilot study reflects a high burden of both NAFLD and MAFLD in MetS patients in our setting. This was characterised by a marked female predominance and a midlife peak in NAFLD prevalence, with hypertriglyceridaemia emerging as the only independent biochemical predictor following multivariate analysis. The observed demographic trends may be influenced by age-related susceptibility, hormonal factors, lifestyle patterns, and central obesity. Persistent triglyceride elevation could indicate heightened endogenous production in predisposed individuals and suboptimal therapeutic control, highlighting gaps in current metabolic management. Although elevated CRP levels and reduced adiponectin were common, neither showed independent associations, suggesting a complex interaction between inflammatory pathways, adipokine regulation, and pharmacological effects. Overall, the findings underscore that NAFLD in MetS patients arises from multifactorial metabolic derangements, with disordered triglyceride metabolism as a central driver.

This study identifies several practical and research priorities as recommendations for addressing NAFLD and MAFLD in patients with MetS. Targeted screening should focus on middle-aged women over 50 years of age and individuals with hypertriglyceridemia, even when low-density lipoprotein cholesterol and glucose levels are well controlled. Protocols for healthcare would benefit from an expanded lipid management strategy that incorporates triglyceride-lowering therapies such as fibrates or omega-3 fatty acids where appropriate. Similarly, efforts should advance the development and validation of non-invasive composite biomarkers, including indices such as the leptin–adiponectin ratio, to enhance early detection and risk stratification. Lifestyle interventions for at-risk individuals remain essential, with particular emphasis on programmes that promote locally sourced dietary modifications and increased physical activity among urbanised, sedentary middle-aged populations, tailored to local dietary patterns and environmental contexts. Furthermore, longitudinal studies are warranted to elucidate the influence of medication use, survivor bias, the role of genetics and age-related hormonal changes on the progression of NAFLD.

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