Original Article

Clinical Significance of Lipoprotein and Ceruloplasmin Variations in Type 2 Diabetes Mellitus: A Cross-Sectional Study in Owo, Nigeria

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Abstract

Background

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder characterized by insulin resistance leading to hyperglycemia, dyslipidemia, and oxidative stress. Ceruloplasmin (CP), the major oxidase and copper-binding protein, has recently been under investigation as an indicator of metabolic dysfunction. Increased CP levels cause oxidative stress and inflammation and thus promote numerous cardiovascular and renal complications. Determination of CP could serve as an early reliable biomarker for timely intervention in the holistic management of T2DM. The present study was designed to compare lipoprotein levels, CP, and oxidative stress markers between participants with diabetes and those without diabetes.

Methods

Fifty patients with T2DM were evaluated along with 30 age- and sex-matched non-diabetic controls visiting Federal Medical Centre, Owo. Standard enzymatic and ELISA techniques assessed biochemical parameters such as fasting blood sugar (FBS), total cholesterol (TC), triglycerides (TG), high-density lipoprotein (HDL), low-density lipoprotein (LDL), very low-density lipoprotein (VLDL), CP, malondialdehyde (MDA), and total antioxidant status (TAS). Data were analyzed by SPSS Version 25. The independent t-test was then used to determine the difference between group means in the biochemical markers. Spearman's correlation was applied to establish relationships, and the level of significance was set at $p<0.05$.

Results

The FBS, CP, TC, TG, HDL, VLDL, and MDA levels were all statistically significant in patients with T2DM, while TAS decreased remarkably ($p<0.05$). Obese participants showed exacerbated dyslipidemia and oxidative stress. Positive correlations were observed between CP and lipid parameters, while MDA negatively correlated with TAS.

Conclusion

Ceruloplasmin was raised in T2DM, dyslipidemia, and lowered antioxidant capability were early markers that prompt intervention for oxidative stress and biochemical derangements in patients with T2DM. In this regard, CP could potentially emerge as a novel marker to monitor the progression of complications in T2DM.

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Keywords: Diabetes Mellitus, Lipoproteins, Malonaldehyde, Total antioxidant, Ceruloplasmin

Introduction

Type 2 Diabetes Mellitus (T2DM) is characterized by a state of chronic exposure of hyperglycemia accompanied by metabolic derangements on the carbohydrate, lipid, and protein metabolisms, thus rendering the patient liable to both microvascular and macrovascular complications.[1,2,3] The prevalence of diabetes is rapidly rising globally in 2019, with some 463 million people affected, occurring mostly amongst the less privileged in middle to low-income countries.[4,5] In Nigeria, the prevalence of diabetes is 5.8% and constitutes a vast public health and economic burden.[6,7]

Lipoproteins and CP have a paramount role in the pathophysiology of T2DM and its complications. The classical diabetic dyslipidemia is characterized by elevated triglycerides (TG), low high-density lipoprotein (HDL), and increased low-density lipoprotein (LDL), possibly increasing the risk of cardiopathy.[8,9,10] However, this suggests skepticism about HDL's quantity in diabetes, thereby questioning its functionality. Diabetes can even moderate the production of dysfunctional HDL, thus eliminating its protective property against cardiovascular risk.[11]

Ferroxidase ceruloplasmin, an antioxidant enzyme that eliminates iron overload and possesses a truly unique ferroxidase function, and its associated antioxidant capacity have potentially been proposed as markers of oxidative damage in T2DM.[12] Elevated CP parallels the increased glycemia in oxidative stress, with increased oxidative damage known to significantly contribute to the advancement of diabetic foot ulcers, nephropathy, retinopathy, and cardiomyopathy among others.[13] The CP, besides defending the neutrophils from oxidative damage by oxidizing toxic ferrous ions (Fe^{2+}) into non-toxic ferric ions (Fe^{3+}), is also a prominent biomarker for systemic inflammation and metabolic dysfunction and might also feature prominently in T2DM.[14,15]

Although the roles of ceruloplasmin and certain lipoproteins in the pathogenesis of T2DM have been widely recognized, the critical piece of information is absent in the Nigerian data on the specific nature of CP and its relation to lipids in this population. In some international studies, diabetes patients presented with higher CP concentrations and activities than their non-diabetic controls.[16] Nevertheless, data from Nigeria are scarce on CP, even in the face of other investigation forms on trace metal and antioxidant status in diabetes.[17] This gap requires further investigation for assessing the significance of CP as a clinical biomarker for early intervention in diagnosing T2DM. This study therefore hypothesised that the levels of serum CP are significantly higher in Nigerian patients who have T2DM than in those without diabetes and that CP positively correlates with markers of oxidative stress and dyslipidemia in these patients.

This study aimed to assess the levels of lipoproteins and CP among patients with T2DM at the Federal Medical Centre, Owo. Specifically, it sought to: determine the lipid profile (HDL, LDL, TC, TG) in T2DM subjects compared to controls, assess CP levels in T2DM subjects relative to controls, compare the relationship between lipoproteins and CP in T2DM subjects, and evaluate the association between CP, MDA, and TAS.

Methods

Study Design and Participant

This was a hospital-based analytical cross-sectional study conducted at the Federal Medical Centre, Owo from January to August 2024. A total of 80 participants were recruited consecutively from the outpatient clinics and the laboratory unit during their visits using convenience sampling methods. The study population consisted of 50 patients with confirmed T2DM and 30 apparently healthy non-diabetic controls. The controls who were selected from related individuals were appropriately matched with the cases for age (±5 years) and sex to minimize any confounding influences.

Eligible participants were adults aged 30 years and above who gave informed consent. The influence of adiposity on lipid profile and ceruloplasmin (CP) levels was examined with Body Mass Index (BMI). Continuous variables were expressed as mean ± standard deviation (SD), SD being the variability of observations away from the mean.

Inclusion criteria

Participants were adults aged ≥ 30 years diagnosed with T2DM who provided informed consent to participate. This also ensured that the selected population reflected the clinic context of T2DM.

Exclusion criteria

Exclusion criteria included individuals who declined to sign informed consent and those in whom medical conditions or factors that are potential confounding variables were present (e.g. renal or hepatic diseases, active infections, drugs interfering with lipid or glucose metabolism). The exclusion criteria ensured that the study was restricted to the population of interest and would not be interfered with by possible confounding factors.

Sample size determination

The sample size of the study was determined based upon the given prevalence of 5.8% in Nigeria [7] at a confidence level of 95%, and a margin of error of 5% using Fisher's formula, n = Z2(p*q)/d2; where n =desired sample size, Z=standard normal deviation (1.96) that corresponds with 95% confidence level. So, from the above calculation, 80 individuals (50 with T2DM and 30 without diabetes as controls) were used as the required sample size. This sample was regarded to be sufficient to generate enough statistical power so that significant differences could be detected among groups.

Data collection

Through structured questionnaires, data concerning demographic details and medical history of all the study subjects were collected.

The blood sampling procedure was aseptic and carried out by a phlebotomist skilled in the art with a 5 mL sample. Blood was drawn from the antecubital vein with the prior application of a tourniquet and was stored in lithium heparin anticoagulant bottles. Plasma was obtained by centrifugation at 4000 rpm for 5 min and stored at −20°C until analysis.

Laboratory assays

Biochemical analyses were performed at the Chemical Pathology Laboratory of the FMC, Owo, utilising various standard methodologies. Lipoprotein profiling was conducted by measuring TC, TG, and HDL levels with standard enzymatic spectrophotometric techniques using reagents provided by Randox Laboratories Ltd. (UK). The LDL and VLDL were calculated using the Friedewald equation accordingly. [18] For CP quantification, levels were determined through a quantitative enzyme-linked immunosorbent assay (ELISA) kit from Melsin Medical Company, USA. The assay was carried out as per the manufacturer's instructions. Intra-assay coefficient of variation (CV) was <6% and inter-assay CV was <10%. We used OxiSelect™ TBARS Assay Kit, Catalog STA-330 (for MDA quantitation). The assay involves reacting the sample with TBA under acidic and heated conditions, producing a coloured MDA-TBA adduct measured spectrophotometrically at 532 nm.[19] Intra-assay CV was <5% and inter-assay CV was <10%. TAS was measured to evaluate the overall systemic antioxidant capacity by the 1,1-diphenyl-2-picrylhydrazyl (DPPH) Method as used by Bondet et al.[20] Intra-assay CV was <5% and inter-assay CV was <10%.

Statistical analysis

Data entry and statistical analysis were performed using the IBM SPSS Statistics for Windows version 25.0 (IBM Corp, Armonk, NY, USA). Normality was assessed using the Shapiro-Wilk test. For normally distributed data, parametric tests (independent t-test, $t(78) = 3.14$, $p = 0.002$) were used; non-parametric tests (Mann-Whitney U, $U = 230.5$, $p = 0.045$) were applied for non-normal data.

The p-values were considered statistically when they were less than 0.05. Effect sizes (Cohen's d = 0.58, rank-biserial correlation = 0.35) and 95% confidence intervals were calculated. Spearman's correlation (ρ = 0.43, p = 0.03) assessed relationships due to the non-normal distribution of some data.

Potential confounder variables such as BMI, medication use, diabetes duration, age, and sex were adjusted in the analysis to accurately estimate the relationship between CP levels, lipoproteins, and oxidative stress. These potential confounders were controlled using multiple regression to account for their effects on the final results.

Ethical considerations

The study was endorsed by the Research Ethics Committee of FMC, Owo, with the approval number FMCOWO/HREC/2024/032. Written consent in detail was received from all participants before they were incorporated into the study. All of the participants were informed concerning the purpose, procedures, and potential risks of the study, and their participation was voluntary.

Results

Demographic and baseline characteristics of study participants

Demographic and baseline characteristics between patients with T2DM and controls were compared. Significant differences were found in BMI (p=0.02), blood pressure (systolic, p<0.001; diastolic, p=0.001), and hypertension (p=0.01) (Table 1).

Table 1. Demographic and baseline characteristics of study participants

Characteristic	Patients With T2DM (n=50)	Controls (Patients Without T2DM) (n=30)	P- Value
Age (years)	Mean ± SD: 55.2 ± 8.4	Mean ± SD: 54.1 ± 9.0	0.45
Age group (years)			N/A
30-39	8 (16%)	30-39: 6 (20%)	
40-49	12 (24%)	40-49: 9 (30%)	
50-59	18 (36%)	50-59: 10 (33%)	
60-69	12 (24%)	60-69: 5 (17%)	
Sex distribution			1.00
Male	25 (50%)	15 (50%	
Female	25 (50%)	15 (50%)	
BMI (kg/m²)	Mean ± SD: 28.3 ± 5.2	Mean ± SD: 26.1 ± 4.1	0.02
BMI categories			0.08
Obese	30 (60%)	12 (40%)	
Non-obese	20 (40%)	18 (60%)	
Duration of diabetes (years)	Mean ± SD: 6.3 ± 4.1	N/A	N/A
Blood pressure			0.001
Systolic	142.1±10.2	120.4±8.3	
Diastolic)	88.3 ± 9.5	78.2 ± 7.4	0.001
Medication use			
Insulin (%)	30 (60%)	N/A	N/A
Metformin (%)	40 (80%)		
Lipid-lowering drugs (%)	25 (50%)		
Lifestyle Factors			
Smoking (%)	10 (20%)	5 (17%)	0.75
Alcohol use (%)	15 (30%)	10 (33%)	0.80
Comorbidities			
Hypertension (%)	35 (70%)	12 (40%)	0.01
Cardiovascular disease History (%)	10 (20%)	4 (13%)	0.38

Abbreviations: T2DM, Type 2 Diabetes Mellitus; SD, standard deviation; Level of significance: P≤0.05

Evaluation of biochemical parameters between participants with diabetes and controls

The patients with T2DM had elevated FBS (170.84 ± 48.76 mg/dL), CP (35.91 ± 1.95 mg/dL), and lipid parameters (TC, TG, HDL, and VLDL), while TAS was significantly lower (2.45 ± 0.42 U/L) compared to controls. The LDL levels, though higher in patients with T2DM, they were not statistically significant (Table 2).

Table 2. Comparison of the mean concentration of the measured biochemical parameters between participants with diabetes and controls (N=80, independent t-test)

Parameters	Patients With T2DM (n=50)	Controls (Patients Without T2DM) (n=30)	*P* -Value
FBS (mg/dL)	170.84 ± 48.76	61.08 ± 12.63	0.001
CP (mg/dL)	35.91 ± 1.95	25.34 ± 1.49	0.001
TC (mg/dL)	205.27 ± 52.20	159.42 ± 36.16	0.001
TG (mg/dL)	178.54 ± 65.52	118.05 ± 59.08	0.001
HDL (mg/dL)	59.89 ± 20.35	38.68 ± 10.02	0.001
LDL (mg/dL)	110.93 ± 33.85	97. 31 ± 21.97	0.053
VLDL (mg/dL)	35.70 ±13.11	23.61 ± 11.82	0.001
MDA (μmol/L)	2.88 ± 0.67	1.82 ± 0.28	0.001
TAS (u/L)	2.45 ± 0.42	4.17 ± 1.07	0.001

Abbreviations: FBS, fasting blood sugar; TC, total cholesterol; TG, triglycerides;HDL, high-density lipoprotein; LDL, low-density lipoprotein; VLDL, very low-density lipoprotein; CP, ceruloplasmin; MDA, malondialdehyde; TAS, total antioxidant status. Level of significance: P≤0.05

Stratified HDL levels by medication use, sex, and obesity status

Stratification by statin use revealed that statins may significantly elevate HDL levels in patients with T2DM (p=0.03, explaining the higher-than-expected HDL results (Table 3).

Table 3. Stratified HDL levels by medication use, sex, and obesity status (N=80, independent t-test)

Factor	Patients withT2DM (n=50)	Controls (Patients Without T2DM) (n=30)	P-Value
Statin Use	Statin: Mean ± SD = 60.5 ± 21.4	Statin: Mean ± SD = 42.8 ± 10.9	0.03
	Non-statin: Mean ± SD = 56.2 ± 20.6	Non-statin: Mean ± SD = 34.1 ± 9.5	0.04
Sex	Male: Mean ± SD = 62.3 ± 18.3	Male: Mean ± SD = 41.5 ± 12.3	0.02
	Female: Mean ± SD = 55.3 ± 19.4	Female: Mean ± SD = 35.6 ± 7.6	0.03
Obesity Status	Obese: Mean ± SD = 58.1 ± 22.7	Obese: Mean ± SD = 36.2 ± 9.3	0.05
	Non-obese: Mean ± SD = 59.5 ± 19.8	Non-obese: Mean ± SD = 41.4 ± 11.5	0.07

Abbreviation: SD, standard deviation. Level of significance: P<0.05

Evaluation of biochemical parameters among participants with diabetes in relation to their BMI

Sex and obesity status also influenced HDL levels, with males (p=0.02) and non-obese individuals (p=0.07) showing higher HDL concentrations. Obese participants showed significantly higher CP, TC, TG, HDL, VLDL, and MDA levels and reduced TAS compared to non-obese counterparts (Table 4).

Table 4. Comparison of the mean concentration of the biochemical parameters among participants with diabetes in relation to their BMI (n=50, independent t-test)

Parameters	Obese Mean ± SD (n=21)	Non-Obese Mean ± SD (n=29)	*P* -Value
FBS (mg/dL)	181.50 ± 62.09	163.11 ± 35.50	0.191
CP (mg/dL)	37.83 ± 0.68	34.52 ± 1.26	0.001
TC (mg/dL)	222.97 ± 54.68	192.45 ± 47.20	0.040
TG (mg/dL)	212.91 ± 73.65	153.66 ± 45.94	0.001
HDL (mg/dL)	67.82 ± 18.09	54.15 ± 20.23	0.017
LDL (mg/dL)	121.71 ± 40.02	103.13 ± 26.67	0.054
VLDL (mg/dL)	42.58 ± 14.74	30.72 ± 9.18	0.001
MDA (µmol/L)	3.12 ± 0.71	2.70 ± 0.60	0.027
TAS (u/L)	2.27 ± 0.35	2.58 ± 0.43	0.009

Abbreviations: FBS, fasting blood sugar; CP, ceruloplasmin; TC, total cholesterol; TG, triglycerides; HDL, high-density lipoprotein; LDL, low-density lipoprotein; VLDL, very low-density lipoprotein; MDA, malondialdehyde; TAS, total antioxidant status; SD, standard deviation. Level of significance: P<0.05

Correlation between the measured parameters and CP level among diabetic participants

Correlation analysis was performed to assess the relationship between CP and metabolic parameters among participants with T2DM. Serum CP showed significant positive correlations with FBS (r = 0.798, p < 0.001), TC (r = 0.445, p < 0.001), TG (r = 0.454, p < 0.001), HDL (r = 0.544, p < 0.001), LDL (r = 0.235, p = 0.036), and VLDL (r = 0.454, p < 0.001) (Figure 1 & 2).

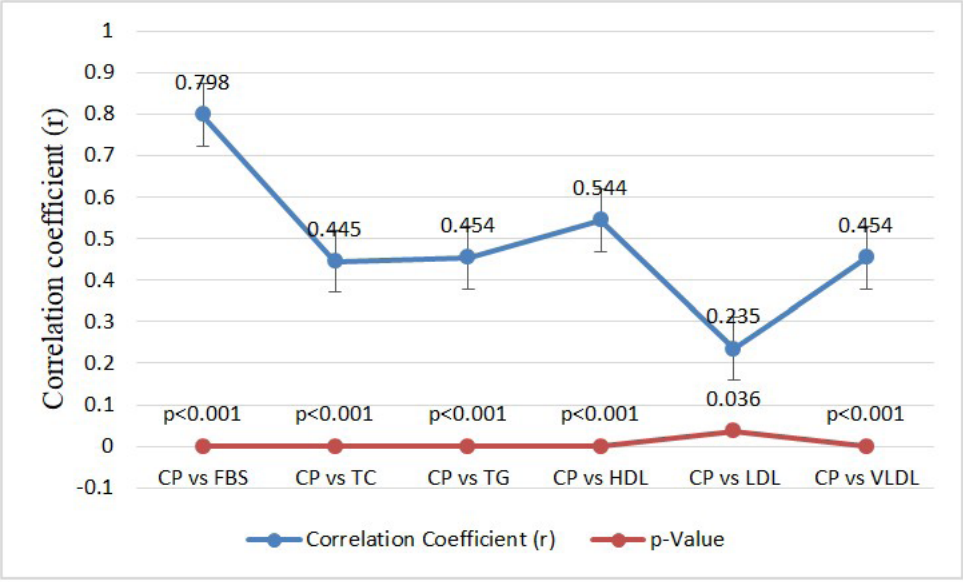

Figure 1. Correlation coefficients between serum ceruloplasmin and metabolic parameters among diabetic study participants

Abbreviations: CP, ceruloplasmin; FBS, fasting blood sugar; TC, total cholesterol; TG, triglycerides; HDL, high-density lipoprotein; LDL, low-density lipoprotein; VLDL, very low-density lipoprotein. Level of significance p<0.05.

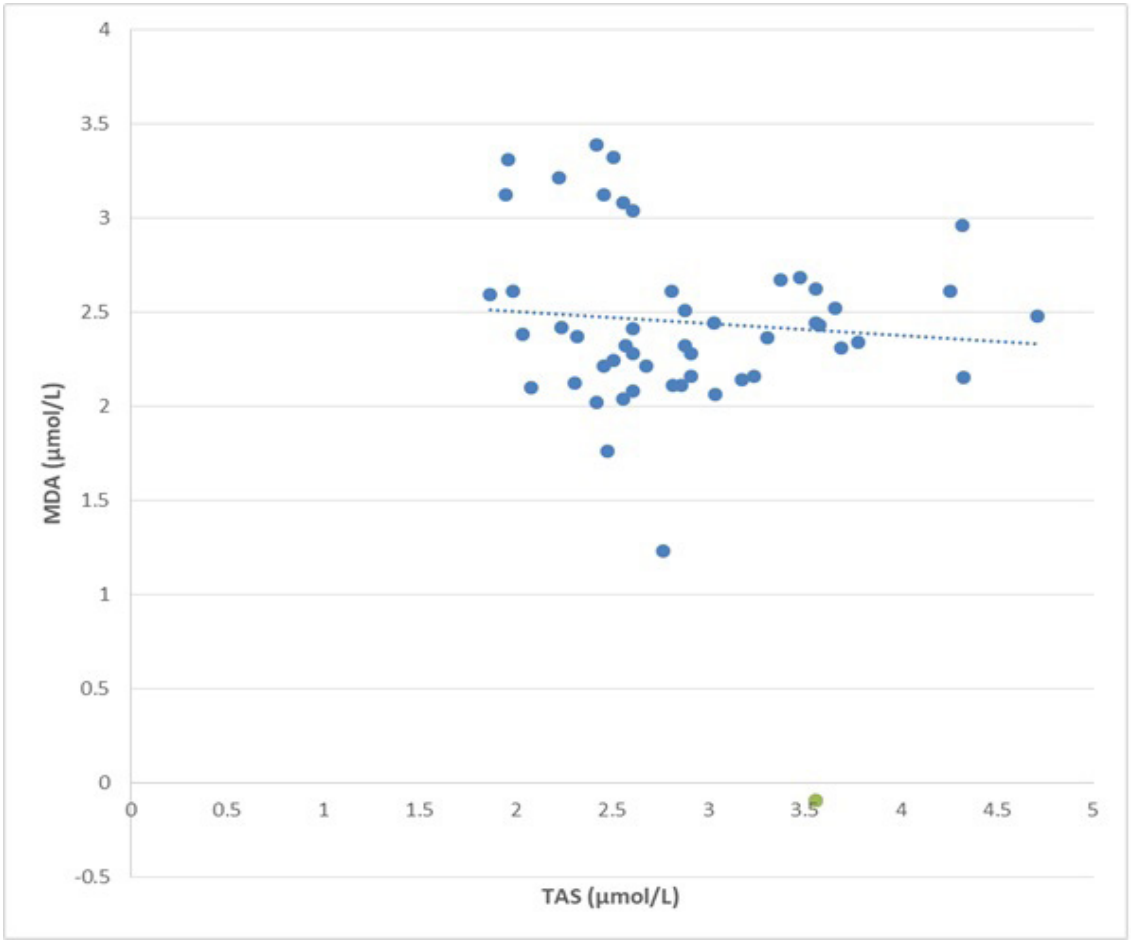

Figure 2. Scatter plot showing correlation of MDA vs TAS among diabetic participants
Abbreviations: MDA, malondialdehyde; TAS, total antioxidant status.

Discussion

This study investigated the differences in lipoprotein profiles and levels of serum ceruloplasmin between individuals with T2DM and controls and the relationship of ceruloplasmin with selected metabolic parameters. The findings revealed that diabetic subjects had significantly increased serum cesuloplasmin concentrations and dyslipidaemia compared with the non-diabetic control subjects. Serum ceruloplasmin is significantly associated with fasting blood glucose as well as total cholesterol, triglycerides, HDL, LDL and VLDL concentrations in the diabetic subjects. The complex correlations between insulin resistance and oxidative stress, as well as disorder in T2DM, have been shown in this study. A considerable increase in fasting blood sugar levels in T2DM cases when compared with normal controls does suggest a reduced secretion of insulin.

Reduced insulin secretion can occur in T2DM, but it is usually relative to the degree of insulin resistance and becomes more prominent as β-cell function declines over time.[3,21] Moreover, the association of dyslipidemia, characterized by elevated TC, TG, and VLDL levels, with reduced TAS among the participants with diabetes subjects suggests that these lipid abnormalities may contribute to increased oxidative stress and inflammatory processes in diabetes.[8,22] In this study, higher levels of HDL were observed in patients with T2DM than in controls. In exploring this anomaly, we performed stratified analyses by statin use, sex, and obesity status. Stratification according to treatment with a specific lipid-lowering drug resulted in a statistically significant elevation of serum HDL in patients with T2DM (P=0.03), which is consistent with the observed elevated HDL levels.

Additional analysis performed on participants not receiving lipid therapy also confirmed an increased level of HDL in patients with T2DM (mean HDL_T2DM = 60.5 ± 21.4 vs. controls = 42.8 ± 10.9; t = X, p = X), implying that such elevation might be induced due to any alteration in the composition or function of HDL and not just by an increase in the amount of HDL. [23,24] Gender and obesity also affect HDL levels, with men exhibiting considerably higher HDL than women (P=0.02), with non-obese individuals harboring elevated HDL than the obese (P=0.07). These results challenge the usually seen diabetic dyslipidemia, suggesting instead, that factors like medication use, sex, and obesity have significant effects on HDL variations in patients with T2DM.[25]

The significant decrease in TAS and significantly high levels of MDA in the patients with T2DM, reflecting a severe oxidative stress status, may be a causative factor in functional alterations. ROS induces oxidative stress, generates free radicals, initiates fatty acid peroxidation reaction, and impairs the balance between oxidative stress and antioxidant systems, all of which are responsible for increased cardiovascular risk in T2DM.[22,26] These statements are supported by a report that found an inverse correlation between MDA and TAS, further indicating that oxidative damage exacerbates as antioxidant defense levels become diminished.

Moreover, the rise in the CP level in patients with T2DM might reflect the involvement of CP as an APP and marker for chronic inflammation and oxidative stress. The ferroxidase activity of CP decreases iron-mediated oxidative injury, and yet paradoxically promotes oxidative injury (via the catalysis of oxidative modification of LDL) which is an early detection of atherogenesis. [27,28] Interestingly our results also showed the involvement of CP with the lipid indices TC, TG, HDL, and VLDL in patients with T2DM, suggesting that CP might serve as a biomarker of dyslipidemia and metabolic disturbances in T2DM.

Obesity, a prevalent comorbidity in patients with T2DM that exacerbates metabolic disturbances, fosters higher concentrations of CP, TC, TG, HDL, VLDL, and MDA, compared to non-obese participants with diabetes, in addition to lower concentrations of TAS (P<0.001). This clearly suggests that the synergistic effects of obesity and T2DM might aggravate oxidative stress and dyslipidemia.[29,30] The fact that bursting BMI has such an action on all these points strongly points to a keen opportunity to focus on targeted interventions, which may consequently address metabolic and weight issues related to diabetes care in a more comprehensive manner.

The previously mentioned outcome reiterated the conclusion from a few other investigations showing that CP had a strong correlation with poor glycemic control, oxidation, and cardiovascular complications in patients with T2DM.[15,31,32] It was found that there was a significant positive correlation between ceruloplasmin levels in blood and TC, TG, HDL, and VLDL of T2DM, and so were implicated in metabolic dysfunction. The correlation between TG and CP (r = 0.45, 95% CI 0.20 to 0.64, p = 0.001) and a negative correlation between MDA and TAS (r = -0.47; 95% CI,-0.67 to -0.26, p < 0.001) indicate that oxidation is involved in the progression of T2DM and thus makes the molecules depict it as mostly relevant. Meta-analytical observations suggest a consistent pattern of increased lipid peroxidation and decreased antioxidant capacity in T2DM. Formation of more MDA and TAS in clinical terms sheds much insight into oxidative damage and the capacity versus antioxidant activities to save the subject from oxidative stress, which is critical in provoking metabolic dysfunction and facilitating the progression of T2DM complications.[33,34]

The CP is an acute-phase protein (APP) that plays a role in the nonspecific phase of the body's inflammatory response. The levels of CP increase during inflammation and have been shown to undergo an association with T2DM.

The copper-handling capacity of CP is a key player in redox reactions, where copper is a cofactor in enzymes participating in oxidative stress modulation, for example, cytochrome c oxidase and superoxide dismutase (SOD). Under oxidative stress, CP could possibly transform from an antioxidant to a pro-oxidant, thus playing a part in the facilitation of lipid peroxidation and causing damage to cells.[35] The copper residing in the structure of CP would involve the formation of reactive oxygen species (ROS) in serious oxidative conditions, which could cause serious tissue damage and aid the pathogenesis of diabetic complications in particular diabetic nephropathy.[27]

Moreover, it has been noted that CP can positively predict the progression of complications like diabetic nephropathy, even though it does not have any association with the severity of other complications, retinopathy for example.[27,36] In the study, the HDL levels were significantly increased in patients with T2DM (p=0.03) and this elevation remained even after excluding patients on lipid-lowering therapy, suggesting that such enhanced HDL maybe related to altered HDL function, rather than the increased HDL itself, probably through a pathway of oxidative stress or inflammation.[15] This is in line with observations about dysfunctional HDL in diabetes where antioxidants are rendered ineffective, while cholesterol efflux is also blunted, now giving it a proinflammatory role, as opposed to a protective role.[37,38]

Furthermore, gender (P=0.02) and obesity status (non-obese, P=0.07) exhibit highly specific HDL values, which make lipid metabolism, oxidative stress, and inflammation an instrumental confounding factor for T2DM.[25] These suggest CP to be a marker of such metabolic dysregulation in T2DM. However, further evidence must depend on prospective research into its justice-associated complications with diabetes and its potential role as a target for therapy.

Strengths and limitations of the study

This study has several strengths. The cross-sectional design enabled comparison between diabetic and non-diabetic groups within the same setting. Age- and sex-matched controls improved internal validity. Standardized laboratory methods supported the reliability and consistency of the outcome, while several biomarkers enhanced comprehensive assessment.

This study has provided us with considerable information, yet there are several limitations. The FBS was used as a long-term hyperglycemia marker rather than a very precise measure of glycemic control for a much longer-term, implicating in HbA1c-metered presence of blood sugar for the past 2-3 months. The use of FBS was simply because it is easily amenable and often used clinically. Maintaining a concurrent measurement of HbA1c in future studies to assess glucose control might provide a more effective and comprehensive evaluation of the complications of T2DM.

Furthermore, the cross-sectional design of the described work encumbers causal inferences among the lipoproteins, ceruloplasmin, and glycemic control. A longitudinal study should give much better clarification about the timeline related to these biomarkers and the interface of T2DM. It is also important to note that the study was conducted in a single centre, which could challenge its generalizability to other regions or various populations.

Conclusion

This study disclosed the status of CP and lipid profile parameters in the consequent state of metabolic and oxidative stress in T2DM cases. The high values of CP and dyslipidemia concomitantly with low values of TAS favour the metabolic evaluation against the backdrop of T2DM, which again stands with the pillars of prevention protocol. These abnormalities are further and more significantly inflated by the burgeoning epidemic of obesity, driving the point for the search of possible weight management

strategies and combating oxidative stress. On that scale, CP emerges as among the stronger candidate biomarkers for early detection and monitoring of therapy in T2DM. Incorporating these findings into patient care may improve metabolic control as well as reduce the burden of diabetic complications. In the future, research establishing these initial findings in larger longitudinal cohorts and testing targeted therapeutics should be given priority.

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Authors' contribution
AAD and NOP conceived the research and prepared the initial draft of the manuscript. OMO, KYA and AAA contributed to the conceptualization and critically evaluated the intellectual content of the final manuscript. All authors actively contributed to the development of the final draft and share responsibility for ensuring its accuracy and integrity.

Conflict of interest
The authors declare no conflicts of interest.

Generative AI statement
The authors used a generative AI tool for language editing only. All scientific content, interpretation, and conclusions were independently verified and approved by the authors.

References

1. Saeedi P, Petersohn I, Salpea P, Malanda B, Karuranga S, Unwin N, et al. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas, 9th edition. *Diabetes Res Clin Pract.* 2019;157:107843. https://doi.org/10.1016/j.diabres.2019.107843
2. Stamouli M, Pouliakis A, Mourtzikou A, Skliris A, Panagiotou I, Mournianakis E, et al. Evaluation of the lipid profile in type 2 diabetes mellitus patients in Greece. *Clin Lab.* 2014;60(10):1593–600. https://doi.org/10.7754/clin.lab.2013.130919
3. Akalu Y, Birhan A. Peripheral Arterial Disease and Its Associated Factors among Type 2 Diabetes Mellitus Patients at Debre Tabor General Hospital, Northwest Ethiopia. *J Diabetes Res.* 2020;2020:9419413. https://doi.org/10.1155/2020/9419413
4. Wang S, Lu Z, Wang Y, Zhang T, He X. Metalloproteins and apolipoprotein C: candidate plasma biomarkers of T2DM screened by comparative proteomics and lipidomics in ZDF rats. *Nutr Metab.* 2020;17:66. https://doi.org/10.1186/s12986-020-00488-2
5. Ugwueze CV, Nnolim BI, Anikpo NC, Onyekachi KE, Onah CK, Chukwu OE, et al. Risk assessment for type 2 diabetes mellitus among participants in a market survey at Ebonyi State, South East Nigeria, using Finnish diabetes risk score questionnaire. *Niger J Med.* 2022;31:530–4. https://doi.org/10.4103/NJM.NJM_79_22
6. Uloko AE, Musa BM, Ramalan MA, Gezawa ID, Puepet FH, Uloko AT, et al. Prevalence and Risk Factors for Diabetes Mellitus in Nigeria: A Systematic Review and Meta-Analysis. *Diabetes Ther.* 2018;9(3):1307–16. https://doi.org/10.1007/s13300-018-0441-1

7. Olamoyegun MA, Alare K, Afolabi SA, Aderinto N, Adeyemi T. A systematic review and meta-analysis of the prevalence and risk factors of type 2 diabetes mellitus in Nigeria. *Clin Diabetes Endocrinol.* 2024 ;10(1):43. https://doi:10.1186/s40842-024-00209-1
8. Goldberg IJ. Clinical review 124: Diabetic dyslipidemia: causes and consequences. *J Clin Endocrinol Metab.* 2001;86(3):965–71. https://doi.org/10.1210/jcem.86.3.7304
9. Rye KA, Barter PJ, Cochran BJ. Apolipoprotein A-I interactions with insulin secretion and production. *Curr Opin Lipidol.* 2016;27(1):8–13. https://doi.org/10.1097/MOL.0000000000000253
10. Feingold KR. Dyslipidemia in Patients with Diabetes. [Updated 2023 Dec 4]. In: Feingold KR, Anawalt B, Blackman MR, et al., editors. *Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc.;* 2000. https://www.ncbi.nlm.nih.gov/books/NBK305900/
11. Zhang P, Gao J, Pu C, Zhang Y. Apolipoprotein status in type 2 diabetes mellitus and its complications (Review). *Mol Med Rep.* 2017;16(6):9279–86. https://doi.org/10.3892/mmr.2017.7831
12. Linder MC. Ceruloplasmin and other copper-binding components of blood plasma and their functions: an update. *Metallomics.* 2016;8(9):887–905. https://doi.org/10.1039/c6mt00103c
13. Sharma VK, Tumbapo A, Pant V, Aryal B, Shrestha S, Yadav BK, et al. Ceruloplasmin, a potential marker for glycemic status and its relationship with lipid profile in Type II diabetes mellitus. *Asian J Med Sci.* 2018;9:13–8. https://doi.org/10.3126/AJMS.V9I2.19003
14. Fox PL, Mazumder B, Ehrenwald E, Mukhopadhyay CK. Ceruloplasmin and cardiovascular disease. *Free Radic Biol Med.* 2000;28(12):1735–44. https://doi.org/10.1016/s0891-5849(00)00231-8
15. Arenas de Larriva AP, Limia-Pérez L, Alcalá-Díaz JF, Alonso A, López-Miranda J, Delgado-Lista J. Ceruloplasmin and Coronary Heart Disease-A Systematic Review. *Nutrients.* 2020;12(10):3219. https://doi.org/10.3390/nu12103219
16. Satyanarayana G, Keisham N, Batra HS, V SM, Khan M, Gupta S, Mahindra V. Evaluation of Serum Ceruloplasmin Levels as a Biomarker for Oxidative Stress in Patients With Diabetic Retinopathy. *Cureus.* 2021 Feb 2;13(2):e13070. https://doi.org/10.7759/cureus.13070
17. Mabayoje VO, Akanni EO, Arinola GO, Hassan RO. Plasma transferrin and caeruloplasmin levels in Nigerians with diabetes mellitus. *Int J Trop Med.* 2010;5(1):6–9. https://doi.org/10.3923/ijtmed.2010.6.9
18. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clin Chem.* 1972;18(6):499–502. https://doi.org/10.1093/clinchem/18.6.499
19. Ohkawa H, Ohishi N, Yagi K. Assay for lipid peroxides in animal tissues by thiobarbituric acid reaction. *Anal Biochem.* 1979;95(2):351–8. https://doi.org/10.1016/0003-2697(79)90738-3
20. Bondet V, Brand-Williams W, Berset C. Kinetics and Mechanisms of Antioxidant Activity using the DPPH. Free Radical Method. *LWT Food Sci Technol.* 1997;30:609–15. https://doi.org/10.1006/fstl.1997.0240
21. Atere AD, Chukwuemeka CE, Oluwatuyi KO, Olupeka BT. Serum amyloid A as acute phase protein and its association with dyslipidemia in type 2 diabetes. *Biomed Biotechnol Res J.* 2023;7:195–200. https://doi.org/10.4103/bbrj.bbrj_27_23
22. Kosmas CE, Rodriguez Polanco S, Bousvarou MD, Papakonstantinou EJ, Peña Genao E, Guzman E, et al. The Triglyceride/High-Density Lipoprotein Cholesterol (TG/HDL-C) Ratio as a Risk Marker for Metabolic Syndrome and Cardiovascular Disease. *Diagnostics (Basel).* 2023;13(5):929. https://doi.org/10.3390/diagnostics13050929

23. McTaggart F, Jones P. Effects of statins on high-density lipoproteins: a potential contribution to cardiovascular benefit. *Cardiovasc Drugs Ther.* 2008 Aug;22(4):321-38. https://doi.org/10.1007/s10557-008-6113-z
24. Rossini E, Biscetti F, Rando MM, Nardella E, Cecchini AL, Nicolazzi MA, Covino M, Gasbarrini A, Massetti M, Flex A. Statins in High Cardiovascular Risk Patients: Do Comorbidities and Characteristics Matter? *Int J Mol Sci.* 2022; 23(16):9326. https://doi.org/10.3390/ijms23169326
25. Vekic J, Zeljkovic A, Stefanovic A, Jelic-Ivanovic Z, Spasojevic-Kalimanovska V. Obesity and dyslipidemia. *Metabolism.* 2019 Mar;92:71-81. https://doi.org/10.1016/j.metabol.2018.11.005
26. Černiauskas L, Mažeikienė A, Mazgelytė E, Petrylaitė E, Linkevičiūtė-Dumčė A, Burokienė N, et al. Malondialdehyde, Antioxidant Defense System Components and Their Relationship with Anthropometric Measures and Lipid Metabolism Biomarkers in Apparently Healthy Women. *Biomedicines.* 2023;11(9):2450. https://doi.org/10.3390/biomedicines11092450
27. Lee MJ, Jung CH, Kang YM, Jang JE, Leem J, Park JY, et al. Serum Ceruloplasmin Level as a Predictor for the Progression of Diabetic Nephropathy in Korean Men with Type 2 Diabetes Mellitus. *Diabetes Metab J.* 2015;39(3):230–9. https://doi.org/10.4093/dmj.2015.39.3.230
28. Satyanarayana G, Keisham N, Batra HS, SM V, Khan M, Gupta S, et al. Evaluation of Serum Ceruloplasmin Levels as a Biomarker for Oxidative Stress in Patients With Diabetic Retinopathy. *Cureus.* 2021;13(2):e13070. https://doi.org/10.7759/cureus.13070
29. Atere AD, Ajani OF, Alade OG, Ajani LA, Moronkeji AI. Evaluation of diagnostic performance of serum copeptin in correlation with dyslipidemia in Obesed and Non-Obesed type 2 diabetes mellitus (T2DM). *Al Ameen J Med Sci.* 2020;13(4):226–33.
30. Khadka B, Pandey S, Kafle D. Dyslipidemia among Patients with Type 2 Diabetes Mellitus Visiting a Tertiary Care Centre. *JNMA J Nepal Med Assoc.* 2023;61(266):758–61. https://doi.org/10.31729/jnma.7662
31. Nowak M, Wielkoszyński T, Marek B, Kos-Kudła B, Swietochowska E, Siemińska L, et al. Antioxidant potential, paraoxonase 1, ceruloplasmin activity and C-reactive protein concentration in diabetic retinopathy. *Clin Exp Med.* 2010;10(3):185–92. https://doi.org/10.1007/s10238-009-0084-7
32. Inoue K, Sakano N, Ogino K, Sato Y, Wang DH, Kubo M, et al. Relationship between ceruloplasmin and oxidative biomarkers including ferritin among healthy Japanese. *J Clin Biochem Nutr.* 2013;52(2):160–6. https://doi.org/10.3164/jcbn.12-122
33. Matough FA, Budin SB, Hamid ZA, Alwahaibi N, Mohamed J. The role of oxidative stress and antioxidants in diabetic complications. *Sultan Qaboos Univ Med J.* 2012;12(1):5–18. https://doi.org/10.12816/0003082
34. Oguntibeju OO. Type 2 diabetes mellitus, oxidative stress and inflammation: examining the links. *Int J Physiol Pathophysiol Pharmacol.* 2019;11(3):45–63.
35. Jia D, Liu L, Liu W, Li J, Jiang X, Xin Y. Copper metabolism and its role in diabetic complications: a review. *Pharmacol Res.* 2024;206:107264. https://doi.org/10.1016/j.phrs.2024.107264
36. Wada J, Makino H. Inflammation and the pathogenesis of diabetic nephropathy. *Clin Sci (Lond).* 2013;124(3):139–152. https://doi.org/10.1042/CS20120198
37. Navab M, Yu R, Gharavi N, Huang W, Ezra N, Lotfizadeh A, Anantharamaiah GM, Alipour N, Van Lenten BJ, Reddy ST, Marelli D. High-density lipoprotein: antioxidant and anti-inflammatory properties. *Curr Atheroscler Rep.* 2007;9(3):244–248. https://doi.org/10.1007/s11883-007-0026-3
38. Rader DJ. New therapeutic approaches to the treatment of dyslipidemia. *Cell Metab.* 2016;23(3):405–412. https://doi.org/10.1016/j.cmet.2016.01.005