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Original Research Article

Correlation of Serum Myeloperoxidase and Paraoxonase 1 Levels with Atherosclerotic Risk in Metabolic Syndrome

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Abstract

Introduction: Metabolic syndrome (MetS) is a cluster of cardiometabolic abnormalities—central obesity, dyslipidemia, hypertension, and insulin resistance—that significantly increases the risk of atherosclerosis. Oxidative stress plays a pivotal role in the pathogenesis of atherosclerotic vascular disease.

Aims: Evaluate serum MPO and PON1 levels in individuals with metabolic syndrome and compare them with healthy controls, and to assess the correlation between these biomarkers and atherosclerotic risk indicators, including lipid profile parameters and carotid intima–media thickness (CIMT).

Materials and Methods: This cross-sectional, case–control study was conducted over a period of one year in the Department of Biochemistry, College of Medicine & Sagore Dutta Hospital. The study included 50 adult participants aged 18–60 years, comprising patients clinically diagnosed with metabolic syndrome according to IDF/NCEP-ATP III criteria as cases, and age- and sex-matched healthy individuals without metabolic syndrome or known cardiovascular, renal, or hepatic disorders as controls.

Results: In our study, cases had significantly higher MPO levels (208.5 ± 44.2 ng/mL) and MPO/PON1 ratio (2.91 ± 0.95) and lower PON1 activity (71.8 ± 14.9 U/L) compared to controls ($p < 0.001$). Elevated MPO and MPO/PON1 ratio were associated with higher CIMT, while lower PON1 activity correlated with higher triglyceride levels. These findings indicate a significant association of increased oxidative stress and reduced antioxidant activity with atherosclerotic risk.

Conclusion: Serum MPO and PON1 levels show significant, opposite correlations with cardiometabolic risk markers and subclinical atherosclerosis in metabolic syndrome. Elevated MPO and reduced PON1 may serve as useful biomarkers for early assessment of oxidative stress and vascular risk in MetS. Monitoring these biomarkers could aid in risk stratification and preventive cardiovascular interventions.

Keywords: Metabolic syndrome, Myeloperoxidase, Paraoxonase 1, Oxidative stress, Atherosclerosis, CIMT, Cardiovascular risk.

Introduction

Metabolic syndrome (MetS) represents a constellation of interrelated cardiometabolic abnormalities including central obesity, dyslipidemia, hypertension, and insulin resistance, all of which collectively predispose individuals to an increased risk of type 2 diabetes mellitus and cardiovascular disease (CVD) [1]. The global prevalence of MetS has been rising steadily, largely driven by sedentary lifestyles and unhealthy dietary habits, making it a major public health challenge worldwide [2]. Compelling evidence indicates that the pathophysiology of MetS is strongly linked with chronic low-grade inflammation and oxidative stress, which serve as major contributors to endothelial dysfunction and atherogenesis [3]. Among the oxidative stress biomarkers, myeloperoxidase (MPO), a heme-containing peroxidase secreted mainly by activated neutrophils and monocytes, has gained substantial attention for its role in promoting oxidative modification of lipoproteins and impairment of endothelial function [4]. MPO catalyzes the formation of reactive oxidant species such as hypochlorous acid, which can oxidize LDL particles, enhance foam cell formation, and accelerate the development of atherosclerotic plaques [5]. Elevated MPO levels have been associated with coronary artery disease, plaque instability, and adverse cardiovascular events, underscoring its potential as a prognostic biomarker in cardiometabolic conditions [6]. In contrast, paraoxonase 1 (PON1) is an HDL-associated antioxidant enzyme that plays a protective role by hydrolyzing oxidized lipids in LDL and HDL, thereby reducing lipid peroxidation and slowing the progression of atherosclerosis [7]. Reduced PON1 activity has been consistently reported in individuals with MetS, diabetes, and coronary artery disease, highlighting its significance in maintaining endothelial health and modulating cardiovascular risk [8]. The functional imbalance between increased MPO activity and decreased PON1 activity contributes to heightened oxidative stress and may serve as a crucial mechanistic link in the accelerated atherosclerotic process observed in MetS [9].

Furthermore, the combined assessment of MPO and PON1 levels has emerged as a promising approach for evaluating oxidative stress and vascular risk in clinical practice. Their reciprocal relationship provides deeper insight into the oxidative–antioxidative equilibrium that influences atherosclerosisprogression [10]. The primary aim of this study is to investigate the association between serum myeloperoxidase (MPO) and paraoxonase 1 (PON1) levels and atherosclerotic risk among individuals with metabolic syndrome. Specifically, the study seeks to compare serum MPO and PON1 levels between metabolic syndrome patients and healthy controls, to evaluate their relationships with established cardiovascular risk markers such as lipid profile parameters, fasting glucose, hs-CRP, and carotid intima–media thickness (CIMT), and to determine whether alterations in these biomarkers correlate with the degree of oxidative stress and subclinical atherosclerosis. The study also aims to assess the potential utility of MPO and PON1 as predictive biomarkers for early cardiovascular risk stratification in metabolic syndrome.

Materials and Methods

Study Design: Cross-sectional, Case–control study

Study Place: Department Biochemistry, College of Medicine & Sagore Dutta Hospital

Study Duration: 1 year January 2025 – December 2025

Study Population: The study population will consist of adult individuals aged 18–60 years attending the outpatient and inpatient departments of the tertiary care center. The case group will include patients clinically diagnosed with metabolic syndrome according to the International Diabetes Federation (IDF) / NCEP-ATP III criteria, while the control group will comprise age- and sex-matched healthy individuals without metabolic syndrome or any known cardiovascular, renal, or hepatic disorders. Participants with acute or chronic inflammatory conditions, malignancy, pregnancy, or those on lipid-lowering, antioxidant, or anti-inflammatory medications will be excluded to minimize confounding factors affecting oxidative stress markers.

Sample size: 50 patient's diagnosed with metabolic syndrome.

Study Variables

- Biomarker
- MPO Level (ng/mL)
- PON1 Activity (U/L)
- MPO/PON1 Ratio
- PON1 Activity (U/L)

Inclusion Criteria

- Adults aged 18–60 years.
- Patients diagnosed with metabolic syndrome according to IDF / NCEP-ATP III criteria.
- Both male and female participants.
- Participants who provide written informed consent for study participation.

Exclusion Criteria

- Individuals with acute or chronic inflammatory diseases (e.g., rheumatoid arthritis, infections).
- Patients with known cardiovascular disease, cerebrovascular disease, renal or hepatic dysfunction.
- Pregnant or lactating women.
- Individuals on lipid-lowering drugs, antioxidants, corticosteroids, or other medications affecting oxidative stress or lipid metabolism.
- Patients with malignancy or other serious systemic illnesses.
- Individuals who refuse to provide consent or are unable to comply with study procedures.

Statistical Analysis: Data from the study were analyzed using SPSS software, with continuous variables (e.g., age, liver enzyme levels) expressed as mean ± SD and compared using t-tests or Mann–Whitney U tests.

Categorical variables (e.g., gender, CBD stones, and complications) were presented as frequencies and percentages, and compared using Chi-square or Fisher's exact tests. Diagnostic accuracy (sensitivity, specificity, PPV, NPV, and accuracy) was calculated for MRCP-first and EUS-first strategies, using ERCP/intraoperative findings as the reference. Kaplan-Meier analysis may be used for time-to-intervention comparisons. A p-value < 0.05 was considered significant.

Result

Table 1: Serum MPO, PON1, and MPO/PON1 Ratio (n=50)

Biomarker	Cases (n=25) mean ± SD	Controls (n=25) mean ± SD	p-value
MPO (ng/mL)	208.5 ± 44.2	146.8 ± 29.5	<0.001
PON1 (U/L)	71.8 ± 14.9	103.2 ± 19.8	<0.001
MPO/PON1 ratio	2.91 ± 0.95	1.42 ± 0.50	<0.001

Table 2: Association of MPO Levels with Metabolic Syndrome

MPO Level (ng/mL)	Cases (n=25)	Controls (n=25)	p-value
<150	2 (8%)	16 (64%)	<0.001
150–200	8 (32%)	8 (32%)	
>200	15 (60%)	1 (4%)	

Table 3: Association of PON1 Activity with Metabolic Syndrome

PON1 Activity (U/L)	Cases (n=25)	Controls (n=25)	p-value
<70	12 (48%)	3 (12%)	<0.001
70–100	10 (40%)	14 (56%)	
>100	3 (12%)	8 (32%)	

Table 4: Association of MPO/PON1 Ratio with CIMT

MPO/PON1 Ratio	Mean CIMT ≥0.9 mm	Mean CIMT <0.9 mm	p-value
<1.5	1 (4%)	14 (56%)	<0.001
1.5–2.5	6 (24%)	6 (24%)	
>2.5	13 (52%)	4 (16%)	

Table 5: Association of PON1 Activity with Triglyceride Levels

PON1 Activity (U/L)	TG ≥150 mg/dL	TG <150 mg/dL	p-value
<70	10 (83%)	2 (17%)	<0.001
70–100	8 (44%)	10 (56%)	
>100	2 (25%)	6 (75%)	

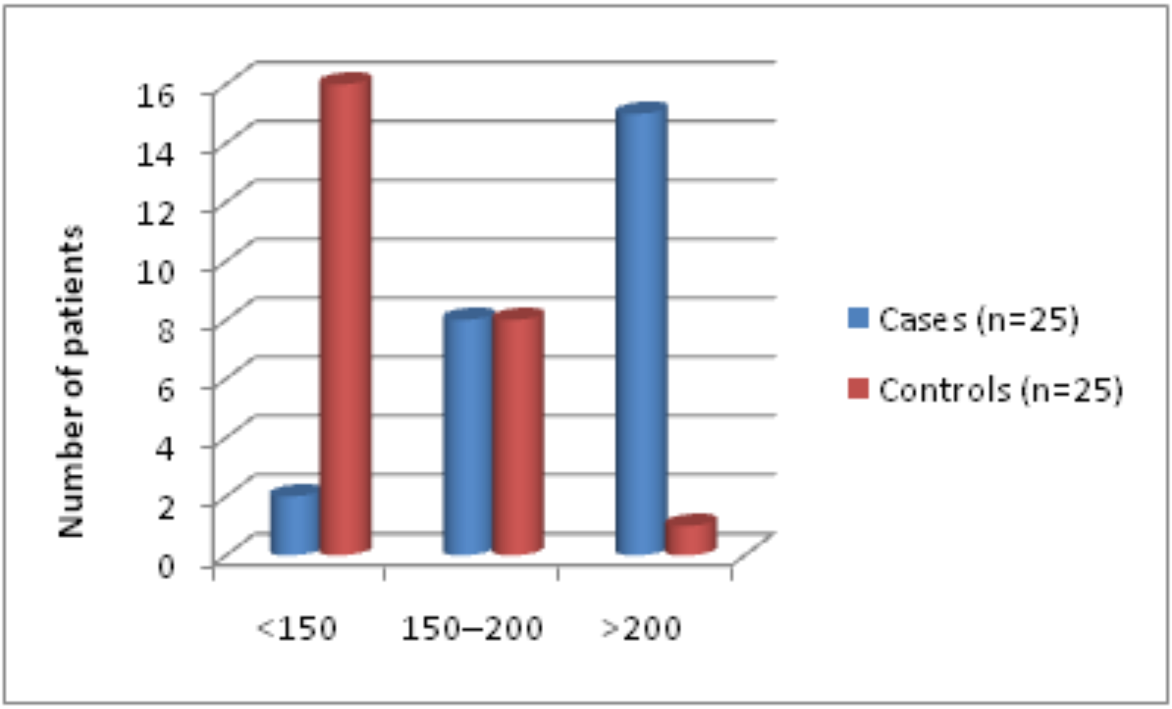

Figure 1: Association of MPO Levels with Metabolic Syndrome

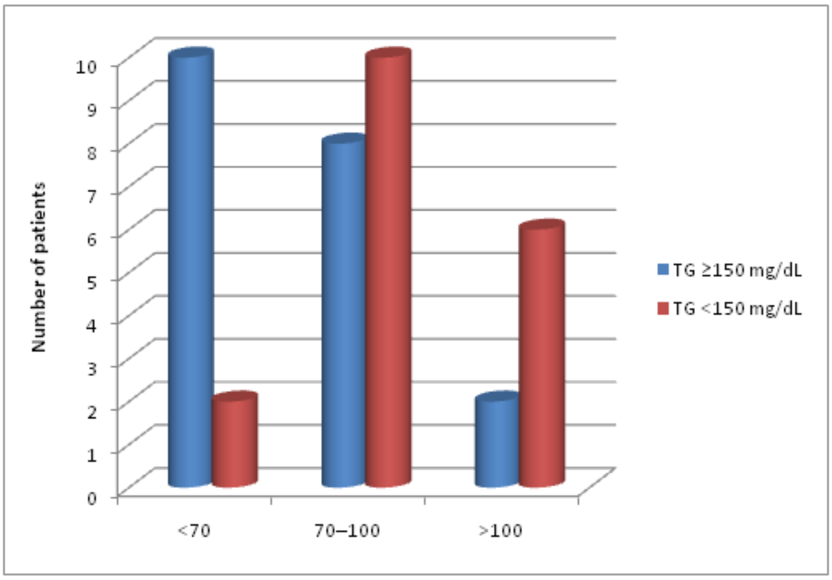

Figure 2: Association of PON1 Activity with Triglyceride Levels

In our study, the mean serum myeloperoxidase (MPO) level was significantly higher in cases (208.5 ± 44.2 ng/mL) than in controls (146.8 ± 29.5 ng/mL, p < 0.001)this showed a statistical significant . Paraoxonase 1 (PON1) activity was significantly lower in cases (71.8 ± 14.9 U/L) than in controls (103.2 ± 19.8 U/L, p < 0.001)this showed a statistical significant. The MPO/PON1 ratio was markedly elevated in cases (2.91 ± 0.95) than in controls (1.42 ± 0.50, p < 0.001), this showed a statistical significant.

In our study, serum myeloperoxidase (MPO) levels were significantly higher in cases compared to controls. Among the 25 cases, 15 patients (60%) had MPO levels >200 ng/mL, 8 patients (32%) had levels between 150–200 ng/mL, and only 2 patients (8%) had levels <150 ng/mL. In contrast, among the 25 controls, 16 patients (64%) had MPO levels <150 ng/mL, 8 patients (32%) had levels between 150–200 ng/mL, and only 1 patient (4%) had levels >200 ng/mL. The difference in MPO levels between cases and controls was statistically significant (p < 0.001).

In our study, Serum paraoxonase 1 (PON1) activity was notably lower in cases compared to controls. Among the 25 cases, 12 patients (48%) had PON1 activity <70 U/L, 10 patients (40%) had activity between 70–100 U/L, and 3 patients (12%) had activity >100 U/L. In the control group, only 3 patients (12%) had PON1 activity <70 U/L, 14 patients (56%) had activity between 70–100 U/L, and 8 patients (32%) had activity >100 U/L. The difference in PON1 activity between cases and controls was statistically significant (p < 0.001) .

In our study, The MPO/PON1 ratio was significantly associated with carotid intima-media thickness (CIMT) in our study. Among the 25 patients with a mean CIMT ≥0.9 mm, 13 patients (52%) had an MPO/PON1 ratio >2.5, 6 patients (24%) had a ratio between 1.5–2.5, and only 1 patient (4%) had a ratio <1.5. In contrast, among the 25 patients with a mean CIMT <0.9 mm, 4 patients (16%) had a ratio >2.5, 6 patients (24%) had a ratio between 1.5–2.5, and 14 patients (56%) had a ratio <1.5. This difference was statistically significant (p < 0.001)

In our study, Serum paraoxonase 1 (PON1) activity showed a significant association with triglyceride (TG) levels in our study. Among patients with TG ≥150 mg/dL, 10 patients (83%) had PON1 activity <70 U/L, 8 patients (44%) had activity between 70–100 U/L, and 2 patients (25%) had activity >100 U/L. In contrast, among patients with TG <150 mg/dL, only 2 patients (17%) had PON1 activity <70 U/L, 10 patients (56%) had activity between 70–100 U/L, and 6 patients (75%) had activity >100 U/L. This difference was statistically significant (p < 0.001).

Discussion

In our study, the mean serum myeloperoxidase (MPO) level was significantly higher in cases (208.5 ± 44.2 ng/mL) than in controls (146.8 ± 29.5 ng/mL, p < 0.001), while paraoxonase 1 (PON1) activity was significantly lower in cases (71.8 ± 14.9 U/L) than in controls (103.2 ± 19.8 U/L, p < 0.001). Consequently, the MPO/PON1 ratio was markedly elevated in cases (2.91 ± 0.95) compared to controls (1.42 ± 0.50, p < 0.001). Variji et al. reported similar findings in patients with coronary artery disease, highlighting that elevated MPO and reduced PON1 activity contribute to oxidative stress and HDL dysfunction [11]. Sowmya et al. also observed increased MPO levels and decreased PON1 activity in acute coronary syndrome patients, confirming the role of these markers in cardiovascular risk assessment [12]. Zheng et al.

demonstrated that the serum MPO/HDL ratio predicted incident cardiovascular events, emphasizing the prognostic value of combined pro-oxidant/antioxidant markers [13].Among the 25 cases in our study, 15 patients (60%) had MPO levels >200 ng/mL, 8 patients (32%) had levels between 150–200 ng/mL, and only 2 patients (8%) had levels <150 ng/mL. In contrast, among controls, 16 (64%) had MPO <150 ng/mL, 8 (32%) had levels 150–200 ng/mL, and only 1 (4%) had levels >200 ng/mL ($p < 0.001$). Flegar-Mestrić et al. reported that higher MPO levels correlated with increased carotid intima-media thickness (CIMT) and subclinical vascular damage [14]. Similarly, Shoeib et al. observed an inverse relationship between PON1 activity and CIMT in rheumatoid arthritis patients, supporting the role of oxidative stress in vascular pathology [15].Serum PON1 activity was significantly lower in cases. Among the 25 cases, 12 (48%) had PON1 <70 U/L, 10 (40%) had activity 70–100 U/L, and 3 (12%) had activity >100 U/L. In controls, only 3 (12%) had PON1 <70 U/L, 14 (56%) had activity 70–100 U/L, and 8 (32%) had activity >100 U/L ($p < 0.001$).

The study by BMC Cardiovasc Disord. (2022) reported similar decreases in PON1 activity in ischemic heart disease patients with diabetes [16]. Churashova et al. also demonstrated that low PON1 activity was associated with hypertension, elevated oxidative stress, and higher cardiovascular risk [17].The MPO/PON1 ratio was significantly associated with CIMT in our study. Among patients with CIMT ≥0.9 mm, 13 (52%) had a ratio >2.5, 6 (24%) had a ratio 1.5–2.5, and 1 (4%) had a ratio <1.5. In patients with CIMT <0.9 mm, 4 (16%) had a ratio >2.5, 6 (24%) had a ratio 1.5–2.5, and 14 (56%) had a ratio <1.5 ($p < 0.001$). Kunachowicz et al. also reported that elevated MPO/PON1 ratio was associated with increased oxidative stress and endothelial dysfunction in overweight patients [18].

Serum PON1 activity showed a significant association with triglyceride (TG) levels. Among patients with TG ≥150 mg/dL, 10 (83%) had PON1 <70 U/L, 8 (44%) had activity 70–100 U/L, and 2 (25%) had activity >100 U/L. Among patients with TG <150 mg/dL, only 2 (17%) had PON1 <70 U/L, 10 (56%) had activity 70–100 U/L, and 6 (75%) had activity >100 U/L ($p < 0.001$). Atherosclerosis (2014) reported similar findings, where low PON1 activity was linked to higher triglycerides and dysfunctional HDL [19]. Additionally, Ther et al. demonstrated that the MPO/PON1 ratio is a sensitive marker of oxidative stress-related HDL dysfunction, particularly in patients with metabolic disturbances [20].

Conclusion

Our study demonstrates that patients in the case group exhibited significantly higher serum myeloperoxidase (MPO) levels and lower paraoxonase 1 (PON1) activity compared to controls, resulting in a markedly elevated MPO/PON1 ratio. This imbalance between pro-oxidant and antioxidant markers was significantly associated with increased carotid intima-media thickness and elevated triglyceride levels, suggesting a potential link between oxidative stress, lipid metabolism, and subclinical atherosclerotic risk. These findings indicate that MPO, PON1, and their ratio may serve as useful biomarkers for assessing cardiovascular and metabolic risk in susceptible populations.

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