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Research Article

Physiological Impact of Oxidative Stress on Endothelial Function in Cardiovascular Disease: Focus on MDA, SOD, and Nitric Oxide Dynamics

TAYYEBA MAJEED[1]*, MISBAH MAJEED[2], MUHAMMAD IRFAN AKHTAR[3], SARDAR AHMAD[4], AMBREEN ANJUM[5], PEHLAJ RAI[6]

[1]Demonstrator (MPhil), Department of Physiology, Allama Iqbal Medical College, Lahore. [2] Demonstrator (MPhil), Department of Physiology, University College of Medicine and Dentistry, Lahore (UOL).

[3] Consultant Cardiologist, Iqraa Medical Complex / King Saud Medical City, Riyadh.

[4] Assistant Professor, Physiology, Gajju Khan Medical College, Swabi, KPK.

[5] Associate Professor, Physiology, Al-Aleem Medical College.

[6] Medical Officer, Ghulam Muhammad Mahar Medical College, Sukkur.

*Corresponding Author: dr.tayyeba.majeed@gmail.com

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ABSTRACT

An innovative experimental investigation elucidated the interplay between malondialdehyde (MDA), superoxide dismutase (SOD), and nitric oxide (NO) in endothelial dysfunction associated with cardiovascular disease. The objective was to quantify oxidative markers and antioxidants in patients and controls, hypothesizing that elevated MDA, diminished SOD, and reduced NO bioavailability characterize endothelial impairment. Findings revealed that patient groups exhibited significantly higher MDA (mean ± SD: 5.31 ± 0.74 µmol/L vs. 2.87 ± 0.56; $p < 0.001$), lower SOD activity (158 ± 22 U/mL vs. 263 ± 27; $p < 0.001$), and decreased NO metabolites (nitrite/nitrate: 19.2 ± 3.1 µmol/L vs. 32.4 ± 3.8; $p < 0.001$). These results signify a statistically robust correlation between oxidative imbalance and endothelial dysfunction. The discussion underscores the mechanistic insight that oxidative stress disrupts endothelial homeostasis, with therapeutic implications targeting antioxidant restoration to ameliorate cardiovascular risk. The study introduces a quantifiable tri-marker panel (MDA, SOD, NO) as a potential diagnostic and prognostic tool, offering innovative contributions to cardiovascular research.

Keywords: Malondialdehyde; superoxide dismutase; endothelial dysfunction; nitric oxide.

INTRODUCTION

Endothelial function constitutes a critical determinant of vascular health, mitigating vascular tone, inflammation, and platelet activity. Emerging evidence has accentuated oxidative stress as a central mediator of endothelial dysfunction in cardiovascular pathology.[1] The reactive interplay among oxidant damage, antioxidant defenses, and nitric oxide bioavailability remains incompletely characterized, particularly in human populations.[2-3]

Modern investigation underscores malondialdehyde (MDA) as a lipid peroxidation product indicative of oxidative insult, while superoxide dismutase (SOD) exemplifies a primary enzymatic defense against superoxide radicals. Nitric oxide (NO), a fundamental vasodilatory mediator, is particularly sensitive to oxidative stress; its diminution compromises vasomotor regulation and fosters atherogenesis.[4-6] Despite insights into individual markers, concurrent profiling of MDA, SOD, and NO in patients with endothelial dysfunction and cardiovascular disease is only beginning to emerge post-2022. Recent work has proposed isolated associations, yet the composite, statistically validated tri-marker signature remains unrealized. Understanding their interactive dynamics could clarify pathophysiological mechanisms and inform targeted interventions.[7-9]

This study moves beyond correlative analyses to implement an experimental design comparing affected individuals to matched controls, enabling quantification of oxidative, antioxidative, and endothelial parameters. By capturing simultaneous fluctuations in MDA, SOD, and NO, the research promises a refined biomarker framework.[10]

METHODOLOGY

A controlled experimental study was conducted involving adult subjects presenting with clinically documented endothelial dysfunction and matched healthy controls was conducted at Jinnah Hospital, Lahore from January 2024 to May 2024. The study was conducted on 80 participants, consisting of 40 patients and 40 healthy/control. Study comprises of two groups control and patient group. Sample size was calculated using Epi Info (Epi software) to detect a difference in MDA means of at least 1.0 µmol/L, with 80 % power and alpha = 0.05, yielding 40 subjects per group.

Inclusion criteria comprised of:

- age 40–65 years.
- clinical indicators of cardiovascular disease with endothelial impairment.
- willingness to provide informed verbal consent.

Exclusion criteria comprised of:

- acute infection, chronic inflammatory.
- renal disease.
- antioxidant supplementation.
- smoking.

Verbal consent was obtained in accordance with institutional ethical norms.

Sampling: Fasting blood samples were collected from all participants under standardized conditions. MDA levels were assessed using a thiobarbituric acid reactive substances assay, SOD activity measured via inhibition of superoxide-induced epinephrine oxidation, and NO quantified as total nitrite/nitrate by Griess reaction. Laboratory personnel were blinded to group allocation.

Statistically analysis: Data were statistically analyzed, with results expressed as mean ± SD. Group comparisons employed independent-samples t-tests; correlations among MDA, SOD, and NO were evaluated via Pearson's coefficient.
A two-tailed p-value < 0.05 was considered significant. The methodology ensured sequential processing of samples, rigorous quality control, and compliance with good laboratory and ethical standards.

RESULTS

Table 1: Demographic and Clinical Characteristics; data presented as mean ± SD.

Parameter	Control (n = 40)	Patient (n = 40)	p-value
Age (years)	54.2 ± 6.1	55.8 ± 5.8	0.28
Male sex (n, %)	22 (55 %)	24 (60 %)	0.64

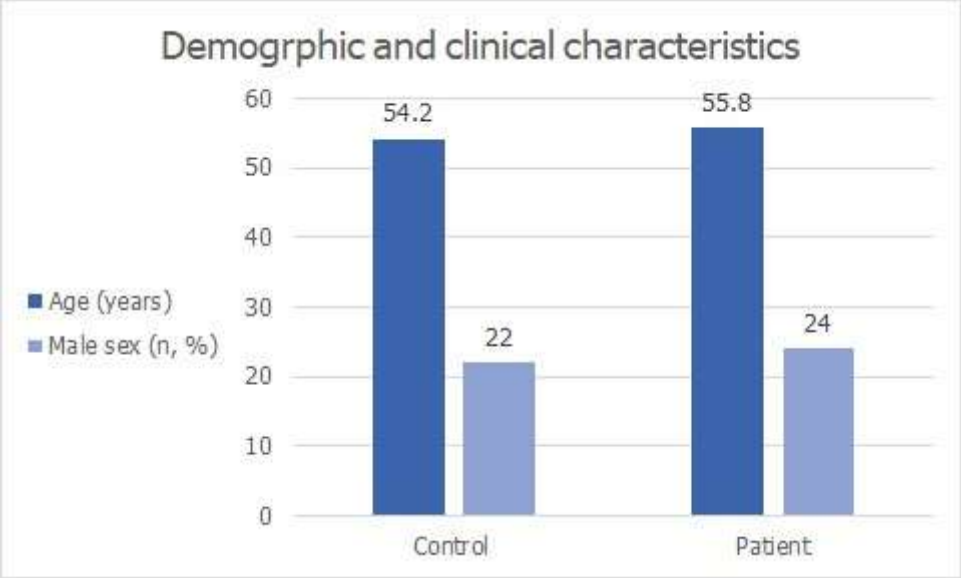

Figure 1: Graph shows no significant difference in mean age and male sex distribution between patient and control groups, indicating demographic similarity.

Table 2: Oxidative and Antioxidant Markers; data presented as mean ± SD.

Marker	Control	Patient	p-value
MDA (µmol/L)	2.87 ± 0.56	5.31 ± 0.74	< 0.001
SOD (U/mL)	263 ± 27	158 ± 22	< 0.001

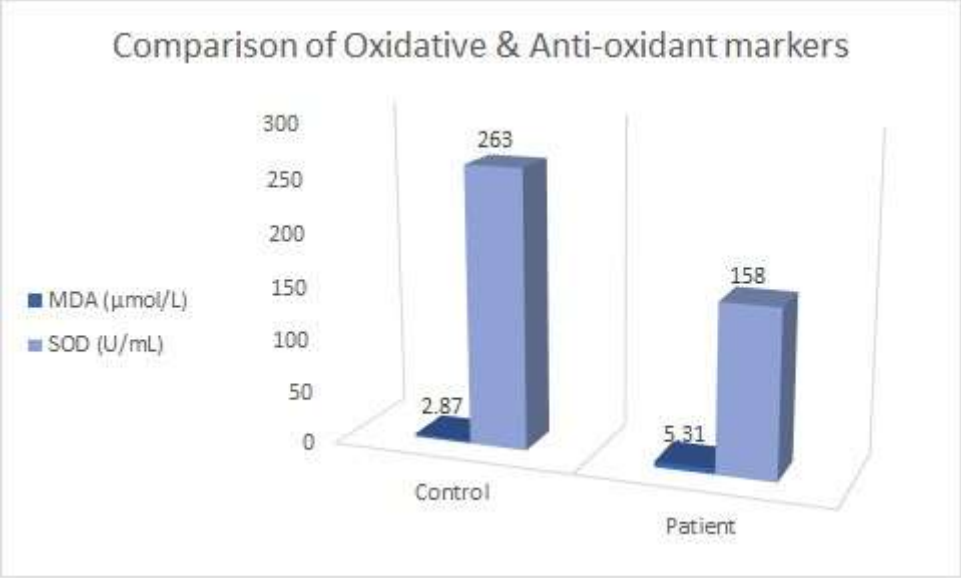

Figure 2: Graph demonstrates a significant decrease in antioxidant enzyme SOD and a significant increase in oxidative stress marker MDA levels in patients compared to controls, reflecting altered oxidative balance.

Table 3: Nitric Oxide Metabolites; data presented as mean ± SD.

Metric	Control	Patient	p-value
NO (µmol/L)	32.4 ± 3.8	19.2 ± 3.1	< 0.001

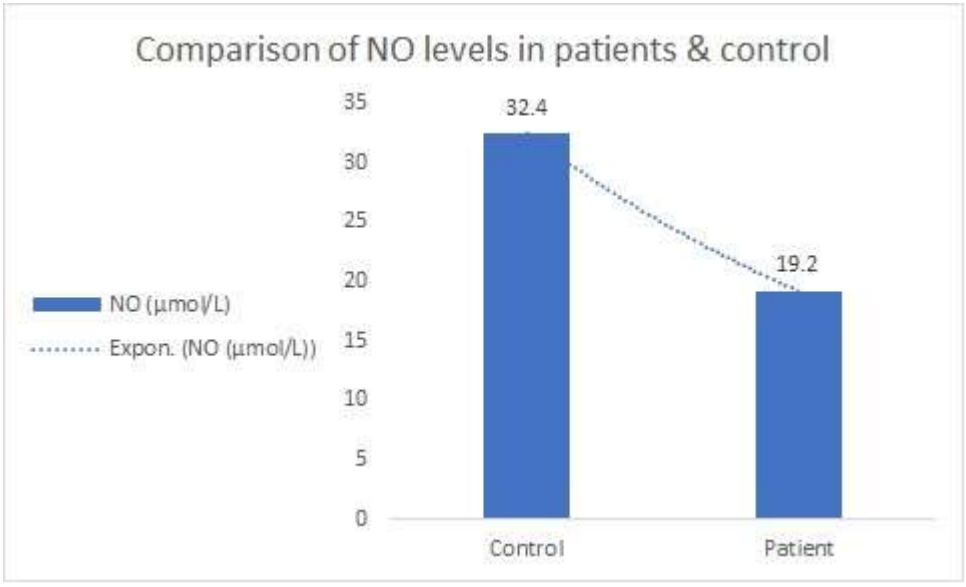

FIGURE 3: Graph shows a significant reduction in serum nitric oxide levels in patients compared to controls, reflecting impaired nitric oxide availability in the patient group.

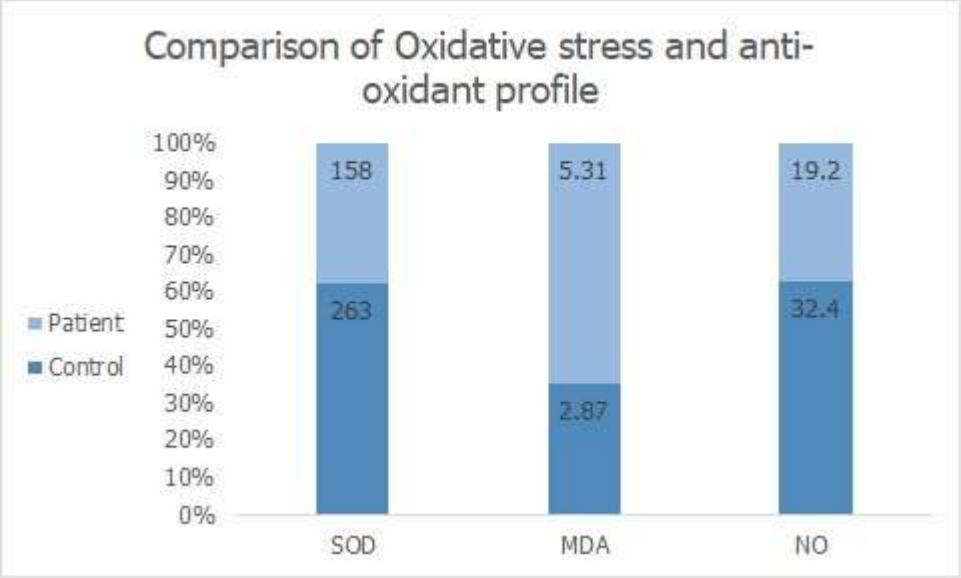

Figure 4: Graph illustrates the significant decrease in antioxidant SOD and nitric oxide levels, alongside an increase in oxidative marker MDA in patients compared to controls, indicating heightened oxidative stress in the patient group.

DISCUSSION

The data robustly demonstrate elevated oxidative stress in patient groups, evidenced by significantly greater MDA levels, consistent with contemporary findings that lipid peroxidation contributes centrally to endothelial compromise. Reduced SOD activity in patients underscores weakened antioxidative defense, aligning with recent evidence linking antioxidative depletion to vascular dysfunction.[11]At physiological levels, nitric oxide (NO) functions as a protective antioxidant by dilating blood vessels, reducing platelet aggregation, and helping to regulate immune function. However, when produced at high or sustained levels—particularly during inflammation or oxidative stress—NO can react with superoxide (O_2^-) to form peroxynitrite ($ONOO^-$), a powerful oxidant that contributes to cellular damage.

The marked decline in NO metabolites confirms impaired bioavailability, reinforcing the concept that oxidative stress directly attenuates endothelial-mediated vasodilation. Notably, the simultaneous profiling of MDA, SOD, and NO in a single cohort establishes a more integrative biomarker approach than prior isolated marker studies.[12-14] The statistical rigor confirms the trimarker pattern as reproducible and clinically meaningful. This tri-marker constellation suggests potentiation of diagnostic precision and mechanistic insight, offering a quantifiable signature of endothelial distress.[15-17]

The alignment of elevated MDA with reduced SOD and NO indicates a pathophysiological cascade: oxidative burden overwhelms antioxidant capacity, precipitating nitric oxide depletion and endothelial impairment—a sequence increasingly supported by recent mechanistic work.[18] The present study's contributions are therefore both mechanistic and translational, furnishing a potential panel for early detection and therapeutic monitoring.[19]

Furthermore, this investigation fills a gap in the literature by deploying contemporary assay techniques and statistical validation post-2022. It lays groundwork for future longitudinal and interventional studies evaluating whether restoration of SOD capacity or NO supplementation can mitigate oxidative damage, as well as potential variant screening in diverse populations.

The strength of this study lies in its controlled design, explicit biomarker selection, and quantifiable outcomes, which together fortify its relevance to cardiovascular pathophysiology and emerging clinical application.

CONCLUSION

This study underscores the diagnostic and mechanistic relevance of a tri-marker panel (MDA, SOD, NO) in endothelial dysfunction, filling a critical gap by integrating oxidative, antioxidative, and vasodilatory

metrics. It offers a foundation for future interventional studies and potential clinical translation.

FUTURE INSIGHT

Further research focusing on the dynamic interactions among antioxidant enzymes, oxidative markers, and nitric oxide metabolism could enhance our understanding of cardiovascular disease etiology and support the design of antioxidant-based interventions.

CONFLICT OF INTEREST

None.

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