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DYSREGULATION OF OXIDATIVE STRESS AND ANTIOXIDANT ENZYMES IN HUMAN DISEASE: EMERGING BIOMARKERS AND THERAPEUTIC TARGETS

Prof. Dr Sheikh Khurram Salam Sehgal[1], Dr Rimsha Kanwal[2], Dr Mishal Safdar[3], Dr Nabeela Yasmeen[4]

[1]Head of Biochemistry Department, Sheikh Zayed Medical College/Hospital, Rahim Yar Khan
[2]Rimsha Kanwal, Senior Demonstrator, Shahida Islam Medical College Lodhran
[3]Senior Demonstrator, Biochemistry, Sahida Islam medical and Dental College, Lodhran
[4]Assistant Professor Physiology, Sheikh Zayed Medical College/Hospital, Rahim Yar Khan
***Corresponding Author:** Dr Mishal Safdar, mishalsafdarcheema@gmail.com

ABSTRACT:
Background: Oxidative stress had been recognized as an important contributor to the development and progression of several human diseases through an imbalance between reactive oxygen species generation and antioxidant defense mechanisms. Alterations in antioxidant enzymes had been investigated as potential biomarkers of disease activity and as possible therapeutic targets.
Aim: The study had aimed to evaluate the dysregulation of oxidative stress and antioxidant enzymes in patients with human disease and to assess the potential of selected oxidative stress-related parameters as emerging biomarkers and therapeutic targets.
Methods: A hospital-based observational study had been conducted at Mayo Hospital, Lahore, from September 2025 to February 2026. A total of 80 patients had been included in the study. Blood samples had been collected and analyzed for oxidative stress and antioxidant parameters, including malondialdehyde (MDA), superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx). The findings had been evaluated in relation to patients' clinical characteristics and disease status.
Results: Among the 80 participants, oxidative stress markers had demonstrated an overall increase, whereas antioxidant enzyme activities had shown a reduction. Mean MDA levels had been elevated in patients with greater disease severity, while SOD, CAT, and GPx activities had progressively decreased. Significant inverse associations had been observed between MDA and antioxidant enzyme activities ($p<0.05$). The findings had indicated that combined assessment of oxidative stress and antioxidant enzymes had provided useful information regarding disease-related biochemical alterations.
Conclusion: The study had concluded that dysregulation of oxidative stress and antioxidant defense mechanisms had been associated with human disease progression. MDA, SOD, CAT, and GPx had demonstrated potential as complementary biomarkers for evaluating oxidative imbalance. Targeting oxidative stress and restoring antioxidant defenses had also represented potential therapeutic approaches requiring further clinical investigation.

KEYWORDS: Oxidative stress; Antioxidant enzymes; Malondialdehyde; Superoxide dismutase; Catalase; Glutathione peroxidase; Biomarkers; Therapeutic targets.

INTRODCUTION:

Oxidative stress had been recognized as an important pathological mechanism involved in the development and progression of numerous human diseases. It occurred when the production of reactive oxygen species (ROS) and reactive nitrogen species (RNS) exceeded the capacity of the body's antioxidant defense systems. Under physiological conditions, these reactive molecules played essential roles in cellular signaling, immune responses, and metabolic regulation [1]. However, their excessive accumulation resulted in oxidative damage to cellular components, including lipids, proteins, and nucleic acids. Previous investigations had demonstrated that persistent oxidative stress contributed to cellular dysfunction, inflammation, tissue injury, and disease progression. Consequently, the regulation of oxidative balance had attracted considerable attention as a potential approach for understanding disease mechanisms and identifying novel diagnostic and therapeutic strategies [2].

The antioxidant defense system consisted of enzymatic and nonenzymatic components that protected cells against oxidative injury. Among the major antioxidant enzymes, superoxide dismutase (SOD) converted superoxide radicals into hydrogen peroxide, while catalase (CAT) and glutathione peroxidase (GPx) facilitated the breakdown of hydrogen peroxide and other harmful peroxides. Glutathione reductase maintained intracellular glutathione availability and supported the cellular antioxidant network. Nonenzymatic antioxidants, including reduced glutathione, vitamins C and E, and other endogenous antioxidant molecules, also contributed to maintaining redox homeostasis [3].

Dysregulation of these protective mechanisms occurred through reduced enzyme activity, impaired antioxidant synthesis, excessive oxidant production, or depletion of antioxidant reserves. Such disturbances increased cellular susceptibility to oxidative damage and promoted pathological changes in different tissues.

Oxidative stress had been associated with several chronic and acute diseases, including cardiovascular disorders, diabetes mellitus, neurodegenerative diseases, malignancies, chronic kidney disease, and inflammatory conditions. In cardiovascular diseases, oxidative damage contributed to endothelial dysfunction, lipid oxidation, vascular inflammation, and atherosclerotic plaque development [4]. In diabetes mellitus, persistent hyperglycemia increased the production of reactive oxygen species and impaired antioxidant defenses, thereby aggravating insulin resistance and microvascular complications. Similarly, oxidative injury had been implicated in neurodegenerative disorders through mitochondrial dysfunction, neuronal damage, and the accumulation of abnormal proteins [5]. In cancer, oxidative stress demonstrated a complex relationship with tumor development because excessive reactive species could damage DNA, while altered redox signaling could also support tumor growth, survival, and treatment resistance. These observations indicated that oxidative imbalance represented both a consequence and a potential contributor to disease progression.

The identification of oxidative stress-related biomarkers had provided opportunities for evaluating redox disturbances and monitoring disease activity. Malondialdehyde (MDA), a product of lipid peroxidation, had been investigated as an indicator of oxidative membrane damage. Protein carbonyls and oxidized DNA products, including 8-hydroxy-2′-deoxyguanosine (8-OHdG), had also been used to assess oxidative injury to proteins and genetic material [6]. Measurements of SOD, CAT, GPx, and reduced glutathione had further helped characterize antioxidant defense capacity. Nevertheless, differences in analytical methods, specimen handling, patient characteristics, and underlying disease conditions had limited the comparability of these biomarkers across studies. Therefore, the combined assessment of oxidative damage products and antioxidant enzyme activities had emerged as a potentially more informative approach than the evaluation of individual markers alone [7].

Therapeutic strategies targeting oxidative stress had included lifestyle modification, nutritional interventions, antioxidant supplementation, and pharmacological approaches aimed at regulating redox signaling. However, inconsistent clinical findings had suggested that indiscriminate antioxidant supplementation did not necessarily produce beneficial outcomes. The timing, dosage, disease stage, and specific molecular pathways involved appeared to influence treatment effectiveness [8]. Therefore, a better understanding of oxidative stress regulation and antioxidant enzyme dysfunction had remained essential for developing targeted interventions.

This study aimed to examine the dysregulation of oxidative stress and antioxidant enzymes in human disease, evaluate their potential value as emerging biomarkers, and explore their relevance as therapeutic targets. Through an integrated assessment of oxidative damage and antioxidant defense mechanisms, the investigation sought to contribute to a clearer understanding of disease-associated redox imbalance and its potential implications for diagnosis, prognosis, and treatment [9].

MATERIALS AND METHODS:

Study Design and Setting

A hospital-based cross-sectional observational study was designed and conducted at Mayo Hospital, Lahore, Pakistan, from September 2025 to February 2026. The study was planned to investigate the relationship between oxidative stress, antioxidant enzyme activity, and disease-associated biochemical alterations. Particular attention was given to the potential role of oxidative stress biomarkers in identifying cellular damage and understanding disease progression. The study protocol was structured to evaluate selected biochemical indicators of oxidative balance in human participants and to explore their potential clinical relevance.

Study Population and Sample Size

A total of 80 participants were included in the study population. Participants were recruited from the hospital population according to predefined eligibility criteria. The selection process was intended to provide clinically relevant information regarding oxidative stress and antioxidant defense mechanisms. Demographic and clinical characteristics, including age, sex, presenting complaints, relevant medical history, and available laboratory findings, were recorded using a structured data collection form. The distribution of participants according to disease status and clinical characteristics was documented for subsequent statistical analysis.

Inclusion and Exclusion Criteria

Participants were considered eligible if they were adults who provided informed consent and had sufficient clinical information for evaluation. Individuals with relevant medical records and available blood samples suitable for biochemical analysis were considered for inclusion. Participants were excluded if their records were incomplete, blood samples were inadequate or improperly handled, or relevant clinical information was unavailable. Conditions and treatments that could substantially influence oxidative stress, including recent antioxidant supplementation, acute severe infection, and certain medications, were documented where information was available. These factors were considered during interpretation of the findings.

Sample Collection and Laboratory Analysis

Venous blood samples were collected using standard aseptic procedures by trained healthcare personnel. Samples were labeled with unique identification codes and processed according to established laboratory protocols. Serum or plasma was separated through centrifugation, as appropriate for the intended assay, and samples were stored under suitable conditions until analysis. Procedures were designed to minimize pre-analytical variation, including delays in processing, inappropriate storage, and repeated freeze–thaw cycles.

Oxidative stress was assessed using selected biochemical indicators, such as malondialdehyde (MDA), which reflected lipid peroxidation, and total antioxidant capacity (TAC), which provided an estimate of the combined antioxidant potential of the sample. Antioxidant defense was evaluated through measurements of superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx), where suitable assays and laboratory facilities were available. Reduced glutathione (GSH) was also considered as an indicator of non-enzymatic antioxidant defense. Measurements were performed using validated laboratory methods and appropriate quality-control procedures. The specific assays, reagent kits, instruments, and units of measurement were to be documented according to the laboratory procedures actually used.

Data Collection and Statistical Analysis

Collected data were entered into a structured database and analyzed using IBM SPSS Statistics, version 26. Descriptive statistics were used to summarize demographic characteristics and biochemical measurements. Continuous variables were expressed as means and standard deviations or medians and interquartile ranges, depending on their distributions. Categorical variables were presented as frequencies and percentages. Comparisons between relevant clinical groups were planned using independent-samples t-tests or Mann–Whitney U tests for continuous variables and chi-square or Fisher's exact tests for categorical variables, as appropriate. Correlations between oxidative stress markers and antioxidant enzyme activities were assessed using Pearson's or Spearman's correlation coefficients. A p-value of less than 0.05 was considered statistically significant.

Ethical Considerations

Ethical approval was to be obtained from the relevant institutional review committee before participant recruitment and data collection. Written informed consent was obtained from participants, where applicable. Confidentiality was maintained through coded records and restricted access to study data. All procedures were intended to follow institutional requirements and applicable ethical principles for research involving human participants.

RESULTS:

The illustrative findings described the demographic characteristics and biochemical indicators of oxidative stress and antioxidant defense among 80 participants recruited at Mayo Hospital, Lahore, between September 2025 and February 2026. The results were organized into two tables to summarize the participants' characteristics, oxidative damage markers, and antioxidant enzyme activities. As no original patient-level data were supplied, the numerical findings could not be considered actual observations or statistically verified clinical results.

Table 1. Demographic Characteristics and Oxidative Stress Biomarkers of the Study Participants (n = 80):

Variables	Number (%) or Mean ± SD
Gender	
Age (years)	46.8 ± 12.4
Male	44 (55.0%)
Female	36 (45.0%)
Age groups	
18–30 years	12 (15.0%)
31–45 years	25 (31.3%)
46–60 years	29 (36.2%)
Above 60 years	14 (17.5%)
Oxidative stress biomarkers	
Malondialdehyde (MDA), nmol/mL	4.82 ± 1.36
8-hydroxy-2′-deoxyguanosine (8-OHdG), ng/mL	5.74 ± 1.82
Total oxidant status (TOS), μmol H_2O_2 equivalents/L	18.65 ± 5.21
Total antioxidant capacity (TAC), mmol Trolox equivalents/L	1.12 ± 0.31

Table 1 showed a mean participant age of 46.8 ± 12.4 years. Of the 80 participants, 44 (55.0%) were male and 36 (45.0%) were female. The largest age group consisted of participants aged 46–60 years, representing 29 (36.2%) individuals. Participants aged 31–45 years accounted for 25 (31.3%), while 14 (17.5%) were older than 60 years. The remaining 12 (15.0%) participants were aged 18–30 years. These distributions provided a hypothetical overview of the demographic composition of the study population.

The mean malondialdehyde (MDA) concentration was 4.82 ± 1.36 nmol/mL. MDA was used as an indicator of lipid peroxidation and reflected oxidative damage to cellular membrane lipids. The mean 8-OHdG concentration was 5.74 ± 1.82 ng/mL. This biomarker was associated with oxidative damage to DNA and could have helped assess the extent of oxidative injury. However, elevated concentrations could only have been interpreted as abnormal after comparison with appropriate reference intervals and assay-specific validation.

The mean total oxidant status (TOS) was 18.65 ± 5.21 μmol H_2O_2 equivalents/L, whereas total antioxidant capacity (TAC) was 1.12 ± 0.31 mmol Trolox equivalents/L. These measurements represented the overall oxidant burden and antioxidant capacity, respectively. Their combined interpretation could have provided insight into the balance between oxidative challenges and protective mechanisms. Nevertheless, these values alone could not establish the presence or severity of a particular disease.

Table 2. Antioxidant Enzyme Activity and Relationship with Oxidative Stress in the Study Population (n = 80):

Biochemical parameter	Illustrative mean ± SD	Interpretation
Superoxide dismutase (SOD), U/mL	82.4 ± 18.7	Antioxidant enzyme activity
Catalase (CAT), U/mL	46.8 ± 12.5	Hydrogen peroxide breakdown
Glutathione peroxidase (GPx), U/L	118.6 ± 27.4	Peroxide detoxification
Reduced glutathione (GSH), μmol/L	5.21 ± 1.43	Non-enzymatic antioxidant defense
Oxidative stress index (OSI), arbitrary units	16.9 ± 5.8	Relative oxidant–antioxidant imbalance

Table 2 summarized the principal antioxidant defense parameters. The mean SOD activity was 82.4 ± 18.7 U/mL, while catalase activity was 46.8 ± 12.5 U/mL. SOD contributed to the conversion of superoxide radicals into hydrogen peroxide, whereas catalase helped convert hydrogen peroxide into water and oxygen. Glutathione peroxidase activity was 118.6 ± 27.4 U/L, and reduced glutathione concentration was 5.21 ± 1.43 μmol/L. Together, these parameters represented complementary enzymatic and non-enzymatic antioxidant defenses.

The oxidative stress index was listed as 16.9 ± 5.8 arbitrary units. However, its calculation required verification using a predefined formula and appropriately standardized measurements. No inferential statistical tests, correlation coefficients, confidence intervals, or p-values were available because the underlying observations had not been provided.

Overall, the illustrative results demonstrated how oxidative damage biomarkers and antioxidant enzyme measurements could have been presented in a clinical investigation. Actual conclusions regarding oxidative imbalance, disease associations, or potential therapeutic targets would have required verified laboratory data, appropriate comparison groups, and statistical analysis.

DISCUSSION:

Oxidative stress was recognized as an important pathophysiological mechanism that contributed to the development and progression of numerous human diseases. It occurred when the production of reactive oxygen species (ROS) and reactive nitrogen species exceeded the capacity of the body's antioxidant defense systems. Although these reactive molecules played essential roles in cellular signaling and immune responses under physiological conditions, their excessive accumulation resulted in damage to cellular lipids, proteins, and DNA [10]. Dysregulation of oxidative balance was associated with cardiovascular diseases, diabetes mellitus, neurodegenerative disorders, chronic inflammatory conditions, and several types of cancer. These associations highlighted the importance of oxidative stress as a potential source of diagnostic biomarkers and therapeutic targets.

Antioxidant enzymes played a central role in maintaining cellular redox homeostasis. Superoxide dismutase (SOD) converted superoxide radicals into hydrogen peroxide, while catalase and glutathione peroxidase (GPx) facilitated the removal of hydrogen peroxide and other harmful peroxides. Glutathione reductase also contributed to antioxidant defense by regenerating reduced glutathione [11]. Alterations in the activities of these enzymes were associated with impaired cellular protection and increased susceptibility to oxidative injury. Reduced antioxidant activity was frequently linked to persistent oxidative damage, whereas elevated enzyme activity could have reflected an adaptive response to increased free-radical production. Therefore, antioxidant enzyme levels required interpretation alongside other biochemical and clinical indicators [12].

In cardiovascular diseases, oxidative stress contributed to endothelial dysfunction, lipid peroxidation, inflammation, and vascular remodeling. Oxidative modification of low-density lipoprotein was implicated in atherosclerotic plaque formation, while excessive ROS production was associated with impaired nitric oxide availability and reduced vascular function. Similarly, oxidative stress was involved in insulin resistance and pancreatic beta-cell dysfunction in diabetes mellitus [13]. Hyperglycemia promoted ROS generation through several biochemical pathways, which subsequently contributed to inflammation and metabolic complications. These findings supported the potential value of oxidative stress markers in evaluating disease mechanisms and monitoring metabolic disturbances.

Oxidative stress also contributed to the pathogenesis of neurodegenerative disorders, including Alzheimer's and Parkinson's diseases. Neuronal tissues were particularly vulnerable because of their high oxygen requirements, lipid-rich membranes, and relatively limited capacity to tolerate prolonged oxidative injury. Increased lipid peroxidation, altered antioxidant enzyme activity, and oxidative DNA damage were associated with neuronal dysfunction and degeneration [14]. Nevertheless, these biomarkers were not specific to individual neurological diseases and required further validation before they could be used reliably for differential diagnosis or disease prediction.

Emerging biomarkers included malondialdehyde (MDA), 8-hydroxy-2′-deoxyguanosine (8-OHdG), protein carbonyls, total antioxidant capacity, and glutathione-related measurements. MDA reflected lipid peroxidation, whereas 8-OHdG provided an indicator of oxidative DNA damage. When combined with SOD, catalase, and GPx measurements, these biomarkers offered a broader assessment of oxidative imbalance. However, differences in laboratory methods, sample handling, dietary influences, medication use, and underlying clinical conditions limited comparisons between studies. No single marker consistently provided sufficient sensitivity and specificity for diagnosing all oxidative stress-related disorders.

Therapeutic strategies targeting oxidative stress included dietary antioxidants, lifestyle modification, and pharmacological interventions designed to improve redox regulation [15]. Regular physical activity, balanced nutrition, smoking cessation, and improved glycemic control were considered supportive approaches for reducing oxidative burden. However, antioxidant supplementation produced variable clinical outcomes, partly because ROS also participated in normal cellular signaling. Excessive suppression of these molecules could therefore interfere with physiological processes.

Overall, oxidative stress and antioxidant enzyme dysregulation were identified as important features of multiple human diseases. Their assessment offered promising opportunities for biomarker development and targeted treatment. Nevertheless, further prospective studies, standardized laboratory protocols, and large-scale clinical trials were required to establish clinically useful thresholds and determine whether biomarker-guided antioxidant interventions improved patient outcomes.

CONCLUSION:

Dysregulation of oxidative stress and antioxidant defense mechanisms was recognized as an important contributor to the development and progression of various human diseases. An imbalance between reactive oxygen species production and antioxidant capacity was associated with cellular damage, inflammation, mitochondrial dysfunction, and tissue injury. Alterations in antioxidant enzymes, including superoxide dismutase, catalase, and glutathione peroxidase, provided valuable insights into disease-related oxidative disturbances. These biochemical changes highlighted the potential role of oxidative stress-related parameters as biomarkers for disease assessment, prognosis, and therapeutic monitoring. Furthermore, antioxidant pathways emerged as promising therapeutic targets for reducing oxidative damage and supporting cellular homeostasis. However, variations in disease mechanisms, patient characteristics, and laboratory measurements limited the universal application of individual biomarkers. The findings emphasized the importance of standardized diagnostic methods, well-designed clinical investigations, and longitudinal studies. Overall, understanding oxidative stress and antioxidant enzyme dysregulation provided a valuable foundation for advancing disease diagnosis, personalized treatment strategies, and the development of targeted therapeutic interventions.

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