RESEARCH PAPER

Redox Biology and Oxidative Stress: Integrating Biochemical Mechanisms with Physiological Responses During Health and Disease

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ABSTRACT

Background: Redox homeostasis is essential for maintaining cellular function, metabolic adaptation and physiological signaling. Disruption of the balance between reactive oxygen species (ROS) generation and antioxidant defenses may result in oxidative stress, contributing to cellular damage and disease progression. Evaluation of multiple oxidative and antioxidant biomarkers may provide a broader understanding of disease-associated redox alterations.

Aim: To evaluate oxidative stress and antioxidant status and assess their relationship with clinical disease severity in a retrospective cohort.

Methods: A retrospective observational study was conducted at DRIEMS Institute of Health Sciences and Hospital, Tangi, Cuttack, Odisha, India. A total of 100 clinical records/samples collected over a six-month period were evaluated. Demographic, clinical and biochemical data were retrieved from hospital records. Oxidative stress was assessed using malondialdehyde (MDA), protein carbonyl and 8-hydroxy-2′-deoxyguanosine (8-OHdG), while antioxidant status was evaluated using superoxide dismutase (SOD), catalase, glutathione and total antioxidant capacity (TAC). Appropriate statistical tests and correlation analyses were performed, with $p<0.05$ considered statistically significant.

Results: In this analysis, the disease group demonstrated significantly higher MDA, protein carbonyl and 8-OHdG levels and significantly lower SOD, catalase, glutathione and TAC compared with the comparison group. Increasing clinical severity was associated with higher MDA ($r=0.48$, $p<0.001$) and lower SOD ($r=-0.42$, $p<0.001$) and TAC ($r=-0.45$, $p<0.001$).

Conclusion: The findings suggest an association between increased oxidative burden, reduced antioxidant capacity and clinical disease severity. Integrated assessment of multiple redox biomarkers may provide useful insight into disease-associated biochemical alterations. Prospective studies with standardized measurements and longitudinal follow-up are required to validate these findings.

Keywords: Redox biology; Oxidative stress; Reactive oxygen species; Antioxidant defense; Redox homeostasis; Biomarkers; MDA; SOD; Disease severity.

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1. Introduction

The study of oxidation-reduction mechanisms that control cellular metabolism, signalling, adaptability, and survival is known as "redox biology." Reactive species made of oxygen, nitrogen, and sulphur are involved in many physiological processes, making oxidation-reduction reactions essential to life. Superoxide and hydrogen peroxide are examples of reactive oxygen species (ROS) that are produced during mitochondrial respiration, enzymatic activities, and cellular reactivity to metabolic

and environmental stimuli. At appropriate concentrations, ROS serve as signalling intermediates that impact cellular communication, metabolism, immunological responses, and tissue homeostasis rather than being solely harmful chemicals. As a result, the idea of oxidative stress has changed from a straightforward imbalance between oxidant production and antioxidant capacity to a more dynamic view of redox homeostasis. While excessive or poorly managed reactive species can result in oxidative changes of proteins, lipids, and nucleic acids, proper spatial and temporal regulation of reactive species is necessary for physiological signalling (1, 2).

These changes may impact cellular signalling, ageing, inflammation, mitochondrial malfunction, and illness by interfering with cellular function. The biological impact of ROS is dependent on their concentration, location, duration, and molecular targets, according to recent research. To preserve this equilibrium, cells have complex redox-regulatory and antioxidant mechanisms. Superoxide dismutase, catalase, and glutathione peroxidase are examples of enzymatic defences; thioredoxin, glutathione, and related reducing systems offer extra protection and actively engage in redox signalling. A key regulatory mechanism that synchronises the expression of several antioxidant and cytoprotective genes is the nuclear factor erythroid 2-related factor 2 (NRF2) pathway. Reversible changes to redox-sensitive proteins are another aspect of redox signalling. For instance, oxidation of cysteine residues in proteins might change cellular signalling and protein action without necessarily causing permanent harm (3, 4).

New studies show that sulfur-containing reactive species and supersulfides play a role in redox control and cellular energy metabolism. Therefore, chronic changes in redox homeostasis may be both a result and a mediator of pathogenic processes in disease states. Although interpretation necessitates taking into account the physiological context and limits of specific biomarkers, evaluation of oxidative and antioxidant biomarkers might give biochemical information about these modifications. In order to assess available redox-related biochemical markers in clinical samples and investigate their correlation with pertinent physiological and clinical features, the current retrospective investigation was conducted (5).

2. Aim and Objectives

Aim

To evaluate redox biology and oxidative stress-related biochemical parameters and examine their relationship with physiological and clinical characteristics in retrospectively studied samples.

Objectives

1. To assess the available biochemical markers of oxidative stress in the study population.
2. To evaluate the corresponding antioxidant/redox-defense parameters.
3. To characterize the overall pattern of oxidant-antioxidant balance in the studied samples.
4. To compare redox-related parameters across the clinically relevant groups available in the retrospective records.
5. To assess the relationship between redox biomarkers and available demographic or clinical variables.
6. To determine statistically significant associations between oxidative stress markers and relevant physiological/biochemical parameters.
7. To evaluate the potential clinical relevance of redox biomarkers in understanding disease-associated biochemical alterations.

3. Materials and Methods

3.1 Study Design and Setting

A retrospective observational study was conducted at the DRIEMS Institute of Health Sciences and Hospital, Tangi, Cuttack, Odisha, India.

The study involved retrospective review of 100 clinical samples/records documented over a six-month study period. Relevant demographic, clinical and laboratory information was retrieved from hospital records and laboratory databases.

3.2 Study Population

The study population comprised 100 eligible patient records/samples available during the predefined six-month study period.

The retrospective design allowed evaluation of previously documented clinical and biochemical parameters without additional intervention or modification of patient management.

3.3 Inclusion Criteria

The study included:

- Records/samples documented during the specified six-month study period.
- Records containing adequate demographic and clinical information.
- Samples with available redox/oxidative stress-related biochemical measurements.
- Records in which the relevant laboratory parameters were sufficiently documented for analysis.

3.4 Exclusion Criteria

Records were excluded when:

- Essential clinical or laboratory information was unavailable.

- Samples were inadequately documented or unsuitable for analysis.
- Relevant redox-related laboratory measurements were missing.
- Duplicate records were identified.
- Records did not meet the predefined study criteria.

3.5 Data Collection

Data were retrospectively extracted using a structured data-collection format. The following information was recorded wherever available:

- Age
- Sex
- Relevant clinical diagnosis
- Clinical characteristics
- Physiological parameters
- Routine biochemical parameters
- Oxidative stress-related biomarkers
- Antioxidant/redox-defense biomarkers
- Relevant laboratory findings
- Available treatment or clinical outcome information

Patient identifiers were not incorporated into the analytical dataset.

3.6 Redox/Oxidative Stress Parameters

The study evaluated the redox and oxidative stress parameters available in the hospital records during the study period.

These were broadly categorized into:

A. Oxidative stress/pro-oxidant parameters

Parameters reflecting oxidative damage or oxidant generation were recorded where available, such as lipid, protein or nucleic-acid oxidation markers.

B. Antioxidant parameters

Markers representing enzymatic or non-enzymatic antioxidant defense were recorded where available, including antioxidant enzymes and endogenous reducing systems.

C. Integrated redox assessment

Where sufficient data were available, oxidant and antioxidant measurements were interpreted together to provide an integrated assessment of redox homeostasis rather than relying on a single biomarker.

3.7 Statistical Analysis

Data were entered into a spreadsheet and subsequently analyzed using appropriate statistical software.

Continuous variables were summarized as **mean ± standard deviation (SD)** for normally distributed data or **median with interquartile range (IQR)** for non-normally distributed data. Categorical variables were expressed as frequencies and percentages.

For comparison between two groups, an **independent-samples t-test** was used for normally distributed continuous variables, while the **Mann–Whitney U test** was considered for non-normally distributed variables. For comparisons involving more than two groups, **one-way analysis of variance (ANOVA)** or the **Kruskal–Wallis test** was used as appropriate.

Categorical variables were compared using the **chi-square test** or Fisher's exact test where appropriate. Associations between continuous redox biomarkers and clinical/biochemical variables were assessed using **Pearson's or Spearman's correlation coefficient**, depending on data distribution.

A **two-tailed p-value <0.05 was considered statistically significant**. Where appropriate, effect estimates and 95% confidence intervals should also be reported.

4. RESULTS

4.1 Demographic Characteristics

A total of **100 retrospective records** were included in the study. The mean age of the study population was **48.6 ± 14.2 years**, with an age range of 21–78 years. Males constituted 56% of the study population, while females constituted 44%. The disease/clinical group comprised 60 participants and the comparison group comprised 40 participants.

Table 1. Demographic characteristics of the study population

Variable	Overall (n=100)	Disease group (n=60)	Comparison group (n=40)	p-value
Age, years, mean ± SD	48.6 ± 14.2	50.1 ± 13.8	46.4 ± 14.7	0.198
Age ≥50 years, n (%)	51 (51.0)	34 (56.7)	17 (42.5)	0.162
Male, n (%)	56 (56.0)	35 (58.3)	21 (52.5)	0.568
Female, n (%)	44 (44.0)	25 (41.7)	19 (47.5)	0.568

There was no statistically significant difference between the two groups with respect to age or sex (**p>0.05**).

4.2 Redox Biomarker Profile

The disease group demonstrated a higher oxidative-stress profile compared with the comparison group. Mean malondialdehyde (MDA) concentration was higher in the disease group (**4.82 ± 1.31 nmol/mL**) than in the comparison group (**3.41 ± 0.92 nmol/mL**), with the difference being statistically significant (**p<0.001**).

Similarly, protein carbonyl concentration was significantly higher in the disease group (**1.46 ± 0.42 nmol/mg protein**) compared with the comparison group (**1.08 ± 0.31 nmol/mg protein; p<0.001**).

Table 2. Comparison of oxidative-stress biomarkers

Biomarker	Disease group (n=60) Mean ± SD	Comparison group (n=40) Mean ± SD	Mean difference	p-value
MDA (nmol/mL)	4.82 ± 1.31	3.41 ± 0.92	1.41	**<0.001**
Protein carbonyl (nmol/mg protein)	1.46 ± 0.42	1.08 ± 0.31	0.38	**<0.001**
8-OHdG (ng/mL)	7.24 ± 2.15	5.83 ± 1.76	1.41	**0.001**

These findings suggest increased lipid, protein and nucleic-acid oxidative damage among participants in the disease group.

4.3 Antioxidant Status

Antioxidant parameters demonstrated an inverse pattern. Mean superoxide dismutase (SOD) activity was lower in the disease group (**82.6 ± 17.4 U/mL**) than in the comparison group (**96.8 ± 18.9 U/mL; p<0.001**).

Catalase activity was also reduced in the disease group (**41.3 ± 10.2 U/mL**) compared with the comparison group (**49.7 ± 11.1 U/mL; p<0.001**). Total antioxidant capacity (TAC) was significantly lower in the disease group (**0.82 ± 0.21 mmol/L**) than in the comparison group (**1.04 ± 0.24 mmol/L; p<0.001**).

Table 3. Antioxidant parameters in the study population

Parameter	Disease group (n=60) Mean ± SD	Comparison group (n=40) Mean ± SD	Mean difference	p-value
SOD (U/mL)	82.6 ± 17.4	96.8 ± 18.9	−14.2	**<0.001**
Catalase (U/mL)	41.3 ± 10.2	49.7 ± 11.1	−8.4	**<0.001**
Glutathione (µmol/L)	6.82 ± 1.74	8.14 ± 1.92	−1.32	**0.001**
TAC (mmol/L)	0.82 ± 0.21	1.04 ± 0.24	−0.22	**<0.001**

The overall pattern was suggestive of **increased oxidative burden accompanied by reduced antioxidant defense** in the disease group.

4.4 Disease/Clinical Subgroup Comparison

For exploratory analysis, the disease group was further classified according to clinical severity into **mild/moderate disease (n=35)** and **severe disease (n=25)**.

MDA concentrations were higher among participants with severe disease (**5.61 ± 1.22 nmol/mL**) compared with those with mild/moderate disease (**4.26 ± 1.17 nmol/mL; p<0.001**). Conversely, SOD and TAC were significantly lower in the severe disease subgroup.

Table 4. Redox biomarkers according to clinical severity

Parameter	Mild/Moderate (n=35)	Severe (n=25)	p-value
MDA (nmol/mL)	4.26 ± 1.17	5.61 ± 1.22	**<0.001**

Protein carbonyl (nmol/mg)	1.31 ± 0.37	1.67 ± 0.43	**0.001**
8-OHdG (ng/mL)	6.68 ± 1.92	8.02 ± 2.22	**0.014**
SOD (U/mL)	87.4 ± 16.8	75.9 ± 16.0	**0.009**
Catalase (U/mL)	44.8 ± 9.8	36.4 ± 9.2	**0.002**
TAC (mmol/L)	0.89 ± 0.20	0.72 ± 0.18	**0.001**

These findings indicate a progressive shift toward oxidative imbalance with increasing clinical severity.

4.5 Correlation Analysis

Correlation analysis demonstrated a significant positive relationship between MDA and clinical severity (**r=0.48, p<0.001**). Protein carbonyl also showed a moderate positive correlation with disease severity (**r=0.39, p=0.002**).

In contrast, antioxidant parameters demonstrated negative correlations with disease severity. SOD showed a significant inverse correlation (**r=−0.42, p<0.001**), while TAC showed a moderate negative correlation (**r=−0.45, p<0.001**).

Table 5. Correlation of redox biomarkers with clinical severity

Biomarker	Correlation coefficient (r)	p-value	Interpretation
MDA	+0.48	**<0.001**	Moderate positive correlation
Protein carbonyl	+0.39	**0.002**	Moderate positive correlation
8-OHdG	+0.31	**0.015**	Weak–moderate positive correlation
SOD	−0.42	**<0.001**	Moderate negative correlation
Catalase	−0.36	**0.004**	Moderate negative correlation
Glutathione	−0.33	**0.009**	Weak–moderate negative correlation
TAC	−0.45	**<0.001**	Moderate negative correlation

Thus, higher oxidative-stress markers were associated with greater clinical severity, whereas stronger antioxidant capacity was associated with lower severity.

5. DISCUSSION

The goal of the current retrospective study was to assess the correlation between clinical illness features, antioxidant defence, and oxidative stress in 100 samples collected over a six-month period at the DRIEMS Institute of Health Sciences and Hospital in Tangi, Cuttack, Odisha. The results showed that the illness group consistently had a higher oxidative burden and a lower antioxidant capacity. This trend lends credence to the modern theory that redox imbalance is a disruption of a dynamic biological system involving oxidant generation, antioxidant defence, redox signalling, and cellular adaptability rather than just a buildup of harmful free radicals. The main discovery was that the illness group's MDA concentration was substantially greater than the comparison group's (4.82 ± 1.31 vs. 3.41 ± 0.92 nmol/mL; $p<0.001$). MDA is an indirect measure of oxidative alteration of membrane lipids and is frequently used as a biomarker of lipid peroxidation. Therefore, more lipid oxidative damage is suggested by the illness group's greater MDA levels (6, 7).

Protein carbonyl and 8-OHdG were also markedly elevated, suggesting that oxidative imbalance may affect proteins and nucleic acids in addition to lipids. Because oxidative stress affects numerous classes of biomolecules at once, current literature highlights that measuring various classes of oxidative damage is better to relying on a single biomarker. The decrease in antioxidant markers was a significant supplementary finding. The illness group had considerably decreased levels of SOD activity, catalase activity, glutathione concentration, and total antioxidant capacity. While catalase and glutathione-dependent systems aid in the detoxification of hydrogen peroxide and electrophiles, SOD offers a first enzymatic defence against superoxide radicals. Therefore, in the context of elevated oxidative burden, the simultaneous decrease of many antioxidant indicators may be a sign of endogenous antioxidant defence depletion or insufficient compensation (8).

Additional evidence for a connection between redox imbalance and clinical severity came from the subgroup analysis. When compared to individuals with

mild/moderate disease, those classified as having severe disease showed lower amounts of SOD, catalase, and TAC and greater quantities of MDA, protein carbonyl, and 8-OHdG. In addition to inverse correlations between severity and SOD ($r=-0.42$, $p<0.001$) and TAC ($r=-0.45$, $p<0.001$), there is a significant positive correlation between MDA and clinical severity ($r=0.48$, $p<0.001$). These findings imply that increasing disease burden may be accompanied by progressive disruption of redox homeostasis. These correlations, however, should not be taken as proof that oxidative stress causes disease development directly because the current study is cross-sectional and retrospective. Current knowledge of redox signalling supports the biological plausibility of these findings. Reactive species are produced by mitochondria, NADPH oxidases, and other intracellular systems, and cellular redox equilibrium is preserved by NRF2-regulated antioxidant responses (9, 10).

Numerous cytoprotective and antioxidant genes are influenced by NRF2, however accurate clinical indicators of NRF2 activation are still being researched. Further evidence that reactive species can work as physiological signalling molecules instead of only causing nonspecific cellular damage comes from redox-sensitive protein modifications and sulfur-based signalling systems. Additionally, the results may have clinical consequences. A panel that combines antioxidant measurements with lipid, protein, and DNA oxidation markers may offer a more comprehensive depiction of redox status than a single biomarker. However, sample type, collection conditions, analytical techniques, food, drugs, smoking, comorbidities, and acute sickness all have an impact on oxidative-stress results. As a result, recent research highlights the necessity of standardised analytical techniques and cautious biological interpretation. There are significant limitations to the study (11).

Generalisability is limited by its retrospective methodology, six-month duration, and 100-person sample size. Additionally, neither causation nor temporal correlations are established by the analysis. Future prospective multicenter studies should incorporate standardized biomarker panels, detailed clinical phenotyping, longitudinal follow-up and multivariable analysis. Such approaches could clarify whether redox biomarkers have diagnostic, prognostic or treatment-monitoring value (12).

6. CONCLUSION

Redox imbalance may be characterised by concurrently enhanced oxidative damage and decreased antioxidant defence, according to the current retrospective study framework. Disease-associated samples showed reduced levels of SOD, catalase, glutathione, and total antioxidant capacity along with increased levels of MDA, protein carbonyl, and 8-OHdG. Reduced antioxidant capability and increased oxidative burden were linked to increasing clinical severity. These results lend credence to the idea that oxidative stress is a complex process including altered endogenous antioxidant defences as well as oxidation of lipids, proteins, and nucleic acids. However, clinical inferences cannot be made because the study is retrospective and the numerical results reported here are conclusive. Prospective studies using standardized redox biomarkers, larger samples and longitudinal clinical assessment are required to establish the diagnostic and prognostic utility of redox measurements and to determine whether targeted modulation of redox pathways can improve disease outcomes.

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