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# The Role of Oxidative Stress Biomarkers in Neurodegenerative Diseases: Population Based Study

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**ABSTRACT**

Neurodegenerative disorders are marked by the gradual deterioration of nerve cells, with oxidative stress being a key contributing factor. This study aims to evaluate the levels of oxidative stress biomarkers Malondialdehyde (MDA) Glutathione (GSH) and Superoxide Dismutase (SOD) in individuals with neurodegenerative diseases compared to a healthy control group. A total of 100 participants were enrolled, including patients diagnosed with Alzheimer's, Parkinson's and Multiple Sclerosis, alongside age-matched controls. Biomarker levels were measured using blood samples. Correlations between biomarker levels and disease severity, cognitive decline, and motor function were analyzed. The study found significantly higher levels of MDA and lower levels of GSH and SOD in the neurodegenerative disease group compared to controls. MDA showed a positive correlation with disease severity ($r = 0.65$) while GSH and SOD levels negatively correlated with cognitive decline ($r = -0.60$) and motor function ($r = -0.55$) respectively. Age was a significant factor, with older participants showing higher biomarker levels but no gender-based differences were observed. Specific findings for Alzheimer's and Parkinson's diseases included remarkably high MDA and low GSH levels, respectively. Statistical analyses confirmed the significance of these differences ($p<0.01$ for MDA and GSH). The study underscores the importance of oxidative stress biomarkers in understanding neurodegenerative diseases. Elevated MDA and reduced GSH and SOD levels could serve as potential indicators for disease progression and severity. Neurodegenerative diseases, oxidative stress, biomarkers, malondialdehyde, glutathione.

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**Key Words**
Neurodegenerative diseases, oxidative stress, biomarkers, malondialdehyde, glutathione

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## INTRODUCTION

Neurodegenerative diseases represent a class of conditions defined by the continual decline in both structure and functionality of the central or peripheral nervous systems[1,2]. Principal among these are Alzheimer's disease (AD) parkinson's disease (PD) and Multiple Sclerosis (MS) each presenting unique pathological features but unified by shared mechanisms of neurodegeneration. These diseases arise from a complex interplay of genetic, environmental and lifestyle influences. Within the array of underlying pathological processes, oxidative stress has been identified as a critical element influencing both the development and advancement of neurodegenerative conditions[3,4].

Oxidative stress occurs when there's an imbalance between the production of reactive oxygen species (ROS) and the body's ability to counteract or repair the damage they cause. Within neurodegenerative scenarios, an overabundance of ROS can cause various forms of cellular harm, such as the peroxidation of lipids, the oxidation of proteins and DNA damage[5]. This oxidative damage is increasingly recognized as a significant contributor to the pathogenesis of neurodegenerative diseases. ROS are primarily produced in the mitochondria and can lead to mitochondrial dysfunction, further exacerbating oxidative stress and forming a vicious cycle contributing to neuronal death[6].

A crucial aspect of studying oxidative stress in neurodegenerative diseases involves the measurement of specific biomarkers. Malondialdehyde (MDA) a byproduct of lipid peroxidation is commonly employed as a marker to indicate oxidative stress levels. Elevated levels of MDA have been associated with cell membrane damage and are observed in various neurodegenerative conditions. Conversely, Glutathione (GSH) a vital intracellular antioxidant, plays a significant role in neutralizing ROS and protecting against oxidative damage[7]. Decreased levels of GSH are indicative of a reduced antioxidant capacity, which is a characteristic feature in the pathology of neurodegenerative diseases. Similarly, Superoxide Dismutase (SOD) is an enzyme responsible for converting superoxide radicals into oxygen and hydrogen peroxide, serves as a crucial defense against oxidative stress. Alterations in SOD activity are observed in neurodegenerative diseases, reflecting an impaired oxidative stress response. The study of oxidative stress biomarkers in neurodegenerative diseases is not just of academic interest but has profound clinical implications. Firstly, these biomarkers can potentially aid in the early diagnosis of these conditions. Given that neurodegenerative diseases often progress silently over years or decades before clinical symptoms become apparent, biomarkers that can detect early pathological changes hold immense value. Secondly, understanding the role of oxidative stress in neurodegeneration can guide the development of therapeutic strategies. Antioxidant therapies aimed at reducing oxidative damage or enhancing the endogenous antioxidant defenses have shown promise in preclinical studies and offer a potential therapeutic avenue.

Furthermore the exploration of oxidative stress biomarkers in neurodegenerative diseases can shed light on disease progression and severity. There is growing evidence that the extent of oxidative damage correlates with disease severity and progression, particularly in diseases like AD and PD. Such insights are crucial not only for patient prognosis but also for tailoring individualized therapeutic approaches. In summary the investigation into oxidative stress biomarkers in neurodegenerative diseases encompasses a crucial area of research that bridges molecular pathology and clinical practice. By deepening our understanding of the role of oxidative stress in these diseases, we can pave the way for early diagnosis, innovative treatment strategies and improved patient outcomes. This study aims to contribute to this burgeoning field by providing a comprehensive analysis of oxidative stress biomarkers in a sample population afflicted with neurodegenerative diseases, offering valuable insights into their potential utility in clinical practice.

## MATERIALS AND METHOD

**Study design and setting:** This observational study was conducted at Siddhartha Medical College, Vijayawada, over a period of one year, from May-April 2022-2023. The research aimed to evaluate the levels of oxidative stress biomarkers in individuals with neurodegenerative diseases and compare them with a healthy control group.

**Participants:** The study enrolled 100 participants, divided into two groups.

**Neurodegenerative disease group:** Fifty patients diagnosed with neurodegenerative diseases (Alzheimer's disease, Parkinson's disease and Multiple Sclerosis) identified through the Neurology Department of Siddhartha Medical College.

**Control group:** Fifty healthy individuals, matched for age and gender, without any history of neurodegenerative or chronic diseases.

**Inclusion and exclusion criteria**

**Inclusion criteria:**

- Diagnosed with Alzheimer's disease, Parkinson's disease, or Multiple Sclerosis
- Age 40 years and above
- Willingness to participate in the study

Table 1: General biomarker levels in neurodegenerative diseases vs. Controls

| Biomarker | Group | Mean level | Standard deviation | Range |
|---|---|---|---|---|
| Malondialdehyde (MDA) | Neurodegenerative disease | 4.5 µmol L | 0.8 µmol L | 3.0-6.0 µmol L |
| | Control | 2.8 µmol L | 0.5 µmol L | 2.0-3.6 µmol L |
| Glutathione (GSH) | Neurodegenerative disease | 1.2 µmol L | 0.3 µmol L | 0.6-1.8 µmol L |
| | Control | 2.4 µmol L | 0.4 µmol L | 1.6-3.2 µmol L |
| Superoxide Dismutase (SOD) | Neurodegenerative Disease | 70 U mL | 15 U mL | 40-100 U mL |
| | Control | 120 U mL | 20 U mL | 80-160 U mL |

Table 2: Correlation of biomarkers with disease severity

| Biomarker | Correlation with disease aspect | Correlation coefficient |
|---|---|---|
| Malondialdehyde (MDA) | Disease severity | 0.65 |
| Glutathione (GSH) | Cognitive decline | -0.60 |
| Superoxide dismutase (SOD) | Motor function | -0.55 |

Table 3: Age and Gender Analysis of Biomarker Levels

| Factor | Description | Finding |
|---|---|---|
| Age | Increase in biomarkers after age 40 | 0.8% increase per year |
| | Biomarker levels in 65+ age group | 35% higher than younger group |
| Gender | Difference in biomarker levels | No significant difference (p>0.05) |

Table 4: Disease-specific biomarker levels

| Disease | Biomarker | Mean level | Remarks |
|---|---|---|---|
| Alzheimer's disease | Malondialdehyde (MDA) | 5.2 µmol L | Highest oxidative stress observed |
| | Glutathione (GSH) | 1.4 µmol L | Moderate antioxidant reduction |
| Parkinson's disease | Glutathione (GSH) | 0.9 µmol L | Significant antioxidant depletion |
| | Superoxide dismutase (SOD) | 65 U mL | Elevated oxidative stress |
| Multiple sclerosis | Malondialdehyde (MDA) | 4.0 µmol L | - |
| | Superoxide dismutase (SOD) | 80 U mL | Relatively stable oxidative status |

Table 5: Statistical analysis

| Biomarker | p-value | Confidence interval |
|---|---|---|
| Malondialdehyde (MDA) | < 0.01 | Alzheimer's: 95% CI = 4.9-5.5 µmol L |
| Glutathione (GSH) | < 0.01 | Parkinson's: 95% CI = 0.85-0.95 µmol L |
| Superoxide dismutase (SOD) | < 0.05 | Multiple sclerosis: 95% CI = 75-85 U mL |

**Exclusion criteria:**

- History of other chronic diseases, such as diabetes or cardiovascular diseases, which could influence oxidative stress levels
- Recent history (past 6 months) of acute illness or infection
- Current smokers or those with a history of substance abuse

**Ethical considerations:** Approval for this research was granted by the Institutional Ethics Committee at Siddhartha Medical College in Vijayawada, Andhra Pradesh, India. All participants provided informed consent before taking part in the study, which adhered to the ethical guidelines outlined in the Declaration of Helsinki.

**Data collection:** Blood samples were obtained from every participant for analysis. Using established laboratory methods, we measured the concentrations of oxidative stress markers, including Malondialdehyde (MDA) Glutathione (GSH) and Superoxide Dismutase (SOD) in these samples.

**Measurement of biomarkers**

**MDA:** Measured using the Thiobarbituric Acid Reactive Substances (TBARS) assay.

**GSH:** Quantified using the Glutathione Assay Kit.

**SOD:** Assessed via the SOD Assay Kit, which utilizes a colorimetric method.

**Statistical analysis:** Statistical software was utilized for data analysis. We employed descriptive statistical methods to outline the participant's demographic and clinical profiles. The differences in biomarker levels between the disease group and the control group were evaluated using independent t-tests or ANOVA, depending on the context. To examine the link between biomarker levels and the severity of the disease, correlation analyses were conducted. Statistical significance was established at a p-value below 0.05.

## RESULTS

Biomarker levels in neurodegenerative diseases and control groups. Our study investigated the levels of oxidative stress biomarkers-malondialdehyde (MDA) Glutathione (GSH) and Superoxide Dismutase (SOD) in individuals with neurodegenerative diseases compared to a control group. We observed a significant increase in MDA levels among the neurodegenerative disease group (Mean = 4.5 µmol L, SD = 0.8 µmol L) compared to the control group (Mean = 2.8 µmol L, SD = 0.5 µmol L). Similarly, GSH levels were lower in the disease group (Mean = 1.2 µmol L, SD = 0.3 µmol L) than in controls (Mean = 2.4 µmol L, SD = 0.4 µmol L). SOD levels also followed this trend, with the disease group showing lower levels (Mean = 70 U mL, SD = 15 U mL) compared to controls (mean = 120 U/mL, SD = 20 U mL) (Table 1).

**Correlation of biomarkers with disease severity:** The study further examined the correlation between these

biomarkers and aspects of disease severity. MDA levels showed a positive correlation (r = 0.65) with overall disease severity. Conversely, GSH and SOD levels exhibited negative correlations with cognitive decline (r = -0.60) and motor function (r = -0.55) respectively (Table 2).

**Age and gender analysis:** An age-based analysis indicated that biomarker levels increase with age, showing a 0.8% annual increase after the age of 40. Participants aged 65 and above exhibited a 35% higher level of oxidative stress biomarkers than younger groups. Gender analysis revealed no significant differences in biomarker levels between male and female participants (p>0.05) (Table 3).

**Disease-specific biomarker observations:** In Alzheimer's disease the highest oxidative stress was observed, with MDA levels at 5.2 µmol L, indicating a severe oxidative imbalance. GSH levels in Alzheimer's patients (1.4 µmol L) pointed to moderate antioxidant reduction. In Parkinson's disease, significant antioxidant depletion was noted with GSH at 0.9 µmol L and SOD at 65 U mL, indicating elevated oxidative stress. Multiple Sclerosis patients showed MDA levels at 4.0 µmol L and SOD at 80 U mL, suggesting a relatively stable oxidative status (Table 4).

**Statistical significance and confidence intervals:** Statistical analysis indicated that the differences in biomarker levels were significant. MDA levels in the neurodegenerative disease group were significantly higher than in the control group (p<0.01) with a 95% confidence interval for Alzheimer's disease at 4.9-5.5 µmol L. GSH levels were also significantly lower in the disease group (p<0.01) particularly in Parkinson's disease, with a 95% confidence interval of 0.85-0.95 µmol L. SOD levels showed a significant variation (p<0.05) with a 95% confidence interval for Multiple Sclerosis at 75-85 U mL (Table 5).

## DISCUSSIONS

This study conducted at Siddhartha Medical College, Vijayawada, has highlighted significant disparities in oxidative stress biomarkers between individuals with neurodegenerative diseases and healthy controls. Our findings, showing elevated levels of Malondialdehyde (MDA) and reduced levels of Glutathione (GSH) and Superoxide Dismutase (SOD) in neurodegenerative patients, corroborate the growing body of evidence linking oxidative stress to the pathophysiology of these diseases.

### Interpretation of key findings

**Elevated MDA levels:** The increased MDA levels observed in our study, particularly in Alzheimer's patients, are in line with the findings of Kim *et al*. and Sidorova and Domanskyi, who noted MDA as a critical marker of oxidative damage in neurodegenerative pathologies[8-12]. This points to the role of lipid peroxidation and membrane damage as significant factors in neurodegenerative conditions.

**Reduced GSH and SOD levels:** Our observation of decreased GSH and SOD levels aligns with the work of Huang *et al*[9-15]. and Chang and Chen, who also reported impaired antioxidant defense systems in neurodegenerative diseases, particularly Alzheimer's and Parkinson's. This supports the hypothesis that neurodegenerative diseases are marked by a compromised ability to counteract oxidative stress, thereby accelerating neuronal damage and disease progression.

**Correlation with disease severity:** The correlations we observed between MDA levels and disease severity and the inverse correlations of GSH and SOD levels with cognitive and motor functions, resonate with the findings of Rekatsina *et al*. and Puspita *et al*.[10,11] suggesting these biomarkers as potential indicators of disease progression and severity.

**Implications for clinical practice:** Our findings underscore the importance of early detection of neurodegenerative diseases using biomarkers like MDA, GSH and SOD, even before the onset of clinical symptoms. Echoing the perspectives of Domanskyi and Parlato, our study advocates for therapeutic strategies focused on modulating oxidative stress, potentially through antioxidant supplementation or enhancement of endogenous antioxidant defenses[13].

**Comparison with existing literature:** Consistent with the broader research landscape, our results substantiate the notion posited by Zhang *et al*. that oxidative stress is not merely a consequence but a driving factor in the pathogenesis of neurodegenerative diseases[14].

**Study limitations:** Our study, while insightful, has limitations. The sample size of 100 participants may affect the generalizability of our findings. The cross sectional design limits our ability to establish causality, and being a single-center study, our results may be influenced by local demographic and environmental factors.

**Future research directions:** In line with the suggestions by Rekatsina *et al*. future research should aim to establish a causal relationship between oxidative stress and neurodegenerative diseases[10]. Longitudinal studies with larger, more diverse populations and

multi-center collaborations are essential for more comprehensive insights. Investigating targeted antioxidant therapies in the management of these diseases, as indicated by Domanskyi and Parlato, is a promising direction[13].

## CONCLUSION

our study reinforces the pivotal role of oxidative stress in neurodegenerative diseases, evidenced by altered biomarker levels. These biomarkers, notably MDA, GSH and SOD, show promise as potential diagnostic and prognostic indicators. Continued research is vital for advancing therapeutic approaches targeting oxidative stress, offering hope for more effective management of these challenging conditions.

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