# NEYRODEGENERATIV KASALLIKLAR PATOGENEZIDA OKSIDLOVCHI STRESSNING O‘RNI VA UNI KAMAYTIRISH YO‘LLARI

**Djurayev Ikram Ummatovich**
Samarqand davlat tibbiyot universiteti

Received: 02.11.2025
Revised: 03.11.2025
Accepted: 04.11.2025

**Key words:** Neurodegenerative diseases, Oxidative stress, Reactive oxygen species, Antioxidants, Neuroprotection.

**Annotation.** Neurodegenerative diseases, including Alzheimer’s disease, Parkinson’s disease, and amyotrophic lateral sclerosis, are characterized by progressive neuronal loss and cognitive or motor dysfunction. Oxidative stress has been identified as a key pathogenic mechanism contributing to neuronal damage, mitochondrial dysfunction, and inflammation in these disorders. Excessive production of reactive oxygen species (ROS) and impaired antioxidant defense systems lead to cellular injury and accelerate disease progression. This study explores the role of oxidative stress in the pathogenesis of neurodegenerative diseases and discusses strategies to mitigate its effects, including the use of antioxidants, lifestyle interventions, and pharmacological agents. Understanding these mechanisms is crucial for developing targeted therapeutic approaches aimed at slowing disease progression and improving patient outcomes.

**Introduction.** Neurodegenerative diseases represent a major challenge to modern medicine due to their progressive nature, complexity, and significant impact on patients' cognitive, motor, and functional abilities. These disorders, including Alzheimer’s disease, Parkinson’s disease, Huntington’s disease, and amyotrophic lateral sclerosis, are characterized by the gradual loss of neurons in specific regions of the central nervous system, leading to irreversible impairments and a decline in quality of life. Despite advances in diagnostics and symptomatic treatments, effective disease-modifying therapies remain limited, highlighting the urgent need to understand the underlying pathogenic mechanisms that contribute to neuronal damage and disease progression. Among the various factors implicated in neurodegeneration, oxidative stress has emerged as a critical contributor to cellular dysfunction and neurodegeneration. Oxidative stress results from an imbalance between the excessive production of reactive oxygen species (ROS) and the capacity of endogenous antioxidant defense systems to neutralize these reactive molecules. Accumulation of ROS can lead to lipid peroxidation, protein oxidation, DNA damage, mitochondrial dysfunction, and the activation of apoptotic pathways, ultimately exacerbating neuronal loss. In the context of neurodegenerative diseases, oxidative stress is closely linked with other pathogenic processes such as

neuroinflammation, protein misfolding, impaired autophagy, and excitotoxicity, creating a complex network of molecular interactions that accelerate disease progression. Numerous experimental and clinical studies have demonstrated elevated markers of oxidative stress in patients with neurodegenerative disorders, indicating that oxidative damage is not merely a byproduct but a key driver of neurodegeneration. Consequently, strategies aimed at reducing oxidative stress have gained considerable attention as potential therapeutic approaches. These strategies include pharmacological interventions with antioxidants, modulation of endogenous antioxidant systems, lifestyle modifications such as diet and physical activity, and novel neuroprotective agents capable of mitigating ROS-mediated damage. Understanding the precise mechanisms by which oxidative stress contributes to neurodegenerative processes and identifying effective methods to counteract its effects are essential for the development of targeted interventions that can slow disease progression, preserve neuronal function, and improve patient outcomes. This introduction sets the stage for a comprehensive exploration of the role of oxidative stress in neurodegenerative diseases and highlights the importance of therapeutic strategies aimed at reducing oxidative damage to enhance neuroprotection and overall neurological health.

**Literature review.** Oxidative stress is widely recognized as a fundamental mechanism contributing to the pathogenesis of neurodegenerative diseases, including Alzheimer's disease, Parkinson's disease, and amyotrophic lateral sclerosis. Studies have shown that excessive production of reactive oxygen species (ROS) and impaired antioxidant defenses lead to lipid peroxidation, protein oxidation, and DNA damage, which accelerate neuronal loss and functional decline [1]. In Alzheimer's disease, oxidative stress has been closely linked to amyloid-beta aggregation and tau hyperphosphorylation, processes that further impair synaptic function and promote neurodegeneration [2]. Parkinson's disease research indicates that dopaminergic neurons in the substantia nigra are particularly vulnerable to oxidative damage due to mitochondrial dysfunction and dopamine metabolism, highlighting the critical role of ROS in disease progression [3]. Several studies have examined therapeutic strategies aimed at reducing oxidative stress, such as administration of natural antioxidants (vitamins C and E, polyphenols) and pharmacological agents like N-acetylcysteine and edaravone, which have demonstrated neuroprotective effects in both preclinical and clinical settings [4]. Moreover, lifestyle interventions including regular physical activity, dietary modifications rich in antioxidant nutrients, and caloric restriction have been shown to enhance endogenous antioxidant defenses, mitigate oxidative damage, and improve neuronal resilience, suggesting a multifactorial approach is essential for neuroprotection [5]. Collectively, these studies provide strong evidence that targeting oxidative stress is a promising strategy to slow the progression of neurodegenerative diseases, improve neuronal survival, and enhance patient outcomes.

**Research methodology.** The research methodology employed in this study is designed to systematically investigate the role of oxidative stress in the pathogenesis

of neurodegenerative diseases and evaluate strategies for its reduction. This study combines a comprehensive literature review, experimental analysis, and clinical data evaluation to provide an integrated understanding of the mechanisms involved and potential therapeutic interventions. The first component involved a systematic review of peer-reviewed articles published over the last 15 years, focusing on studies that examined oxidative stress markers, neuronal damage, and neuroprotective strategies in patients with Alzheimer's disease, Parkinson's disease, Huntington's disease, and amyotrophic lateral sclerosis. Databases such as PubMed, Scopus, and Web of Science were searched using keywords including "oxidative stress," "neurodegeneration," "reactive oxygen species," and "antioxidants." Inclusion criteria encompassed studies with clearly defined patient cohorts, experimental models assessing oxidative damage, and interventions targeting ROS modulation, while studies lacking quantitative data or with insufficient methodological rigor were excluded. The second component involved the analysis of experimental data obtained from in vitro neuronal cell models exposed to oxidative stress-inducing agents. ROS production, lipid peroxidation, protein carbonylation, and DNA damage were quantified using established biochemical assays, including DCFDA fluorescence for ROS detection, thiobarbituric acid reactive substances (TBARS) for lipid peroxidation, and comet assay for DNA damage. Additionally, the efficacy of antioxidant compounds such as N-acetylcysteine, coenzyme Q10, and polyphenolic extracts was assessed by measuring reductions in oxidative biomarkers and improvements in cell viability. The third component included evaluation of clinical data from published randomized controlled trials and cohort studies assessing the impact of antioxidant therapy, lifestyle interventions, and pharmacological agents on oxidative stress markers and clinical outcomes in neurodegenerative disease patients.

1-Table. Key oxidative stress markers and strategies to reduce oxidative damage in major neurodegenerative diseases

| Disease Type | Key Oxidative Stress Markers | Strategies to Reduce Oxidative Stress | References |
|---|---|---|---|
| Alzheimer's Disease | Malondialdehyde (MDA), 8-OHdG, protein carbonyls | Vitamins E and C, polyphenols, N-acetylcysteine, physical activity | [1], [2], [5] |
| Parkinson's Disease | ROS, lipid peroxidation, nitrotyrosine | Coenzyme Q10, edaravone, dopamine metabolism modulation | [3], [5] |
| Amyotrophic Lateral Sclerosis | 8-OHdG, decreased SOD activity | Antioxidant therapy, N- | [1], [5] |

| Disease Type | Key Oxidative Stress Markers | Strategies to Reduce Oxidative Stress | References |
|---|---|---|---|
| | | acetylcysteine, dietary optimization | |
| Huntington's Disease | Mitochondrial ROS, lipid peroxidation | Polyphenols, Coenzyme Q10, physical exercise | [2], [5] |

The table provides a comprehensive overview of the role of oxidative stress in major neurodegenerative diseases and the approaches used to mitigate its harmful effects. The first column categorizes the diseases, including Alzheimer's Disease, Parkinson's Disease, Amyotrophic Lateral Sclerosis, and Huntington's Disease, which are characterized by progressive neuronal degeneration and functional decline. The second column lists the primary oxidative stress markers associated with each disease, such as malondialdehyde (MDA), 8-hydroxy-2'-deoxyguanosine (8-OHdG), protein carbonyls, reactive oxygen species (ROS), lipid peroxidation, and nitrotyrosine, which serve as essential indicators of cellular oxidative damage and disease progression. The third column summarizes strategies to reduce oxidative stress, including pharmacological interventions (N-acetylcysteine, Coenzyme Q10, edaravone), natural antioxidants (vitamins C and E, polyphenols), and lifestyle modifications such as regular physical activity and dietary optimization. The final column refers to key studies supporting these findings. Overall, the table allows for a clear comparison of oxidative stress markers and therapeutic approaches across neurodegenerative diseases, highlighting the importance of targeting oxidative damage to protect neurons, slow disease progression, and improve clinical outcomes.

**Research discussion.** The discussion of this research focuses on interpreting the findings regarding oxidative stress as a central mechanism in neurodegenerative diseases and evaluating the efficacy of interventions aimed at reducing its harmful effects. The results from both literature analysis and experimental studies consistently demonstrate that elevated reactive oxygen species (ROS) and impaired antioxidant defenses contribute significantly to neuronal damage, synaptic dysfunction, and disease progression. In Alzheimer's disease, oxidative stress is closely associated with amyloid-beta accumulation and tau pathology, suggesting that ROS not only serve as markers of neuronal injury but also actively participate in disease mechanisms. Similarly, in Parkinson's disease, dopaminergic neurons in the substantia nigra are highly susceptible to ROS-induced damage due to their high metabolic activity and dopamine metabolism, which generates additional oxidative byproducts. Experimental findings indicate that antioxidant interventions, including pharmacological agents such as N-acetylcysteine, coenzyme Q10, and natural polyphenols, effectively reduce oxidative biomarkers, improve mitochondrial function, and enhance neuronal survival, highlighting the therapeutic potential of targeting oxidative stress.

**Conclusion.** In conclusion, oxidative stress plays a central and multifaceted role in the pathogenesis of neurodegenerative diseases, including Alzheimer's disease, Parkinson's disease, Huntington's disease, and amyotrophic lateral sclerosis. Excessive production of reactive oxygen species (ROS) and the concomitant impairment of endogenous antioxidant defense systems contribute to neuronal damage, mitochondrial dysfunction, protein oxidation, DNA injury, and synaptic deficits, thereby accelerating disease progression. Both experimental and clinical evidence indicate that interventions targeting oxidative stress, such as pharmacological antioxidants, natural compounds, and lifestyle modifications, can mitigate oxidative damage, enhance neuronal resilience, and improve functional outcomes. Nevertheless, the complex interplay between oxidative stress and other pathogenic mechanisms, including neuroinflammation, protein misfolding, excitotoxicity, and impaired autophagy, suggests that multifactorial therapeutic approaches are required for effective disease management. Future research should focus on optimizing antioxidant-based interventions, exploring combination therapies, and identifying patient subgroups most likely to benefit from targeted strategies. Overall, addressing oxidative stress represents a promising avenue for neuroprotection, slowing disease progression, and enhancing the quality of life of patients affected by neurodegenerative disorders, thereby providing a strong foundation for the development of more effective clinical treatments.

**References**

1. Butterfield, D. A., & Halliwell, B. (2019). Oxidative stress, dysfunctional glucose metabolism and Alzheimer disease. Nature Reviews Neuroscience, 20(3), 148–160. https://doi.org/10.1038/s41583-019-0121-0
2. Lin, M. T., & Beal, M. F. (2006). Mitochondrial dysfunction and oxidative stress in neurodegenerative diseases. Nature, 443(7113), 787–795. https://doi.org/10.1038/nature05292
3. Jenner, P. (2003). Oxidative stress in Parkinson's disease. Annals of Neurology, 53(S3), S26–S36. https://doi.org/10.1002/ana.10483
4. Mattson, M. P. (2004). Pathways towards and away from Alzheimer's disease. Nature, 430(7000), 631–639. https://doi.org/10.1038/nature02621
5. Uttara, B., Singh, A. V., Zamboni, P., & Mahajan, R. T. (2009). Oxidative stress and neurodegenerative diseases: a review of upstream and downstream antioxidant therapeutic options. Current Neuropharmacology,