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Biomarkers Of Oxidative Stress In Chronic Diseases: Clinical And Laboratory Perspectives

Sattam Khalid Alruways[1], Sultan Reda Alenazy[2], Fuad Shaker Rashad Zainy[3], Albashir Mohammed Saeed Alghamdi[4], Marwan Mushylih B. Althomali[5], Waleed Sadaqah Ismail Khairallah[6], Najd Mukhlid Zamil Al Otaibi[7], Fahad Mohammad Ageel[8], Rayan Fadhl Aldeen Kareem Jan[9], Ghaliah Alimam Muhmmad Salem Ahmed[10], Mohammed Othman karbuji[11], Ahlam Saleem A Almagnoni[12]

[1]Laboratory specialist, Aldawadmi General Hospital, Saudi Arabia.
[2]Laboratory specialist, Central Blood bank - northern border region, Saudi Arabia.
[3]Laboratory specialist, Microorganisms, Makkah Health, Saudi Arabia.
[4]Laboratory Technician, Al-Baha Health Cluster, Saudi Arabia.
[5]Laboratory specialist, King Faisal Medical Complex – Taif, Saudi Arabia.
[6]Laboratory Technician,HERA GENERAL HOSPITAL, Saudi Arabia.
[7]Laboratory specialist, Makkah Health Complex, Saudi Arabia.
[8]Aneasthesia Resident, Branch of Minstery of Health Jeddah, Saudi Arabia.
[9]Laboratory technician, Makkah Regional Laboratory, Saudi Arabia.
[10]Laboratory technician, King Fahad Hospital, Saudi Arabia.
[11]Laboratory Technician,Ohud hospital Ministry of Health Almadinah almunawwarah, Saudi Arabia.
[12]Nursing technician, Altaneem, Saudi Arabia

Abstract
Oxidative stress is a common cause of many long-term health problems, such as diabetes, cancer, heart disease, neurological disease, chronic kidney disease, and kidney disease. An excess of reactive oxygen species (ROS) can harm lipids, proteins, and nucleic acids by going beyond the body's antioxidant defenses. Measuring oxidative stress has become more important for screening, diagnosing, and evaluating treatment in the last few years. Malondialdehyde, total antioxidant capacity, 8-hydroxy-2′-deoxyguanosine, advanced oxidation protein products, and protein carbonyls are some common biomarkers. In order to test these biomarkers in a lab, it is important to carefully control all the factors that come into play before, during, and after the analysis. The integration of oxidative stress biomarkers, examined in this review alongside the challenges in their assessment, facilitates optimal disease risk classification and patient treatment.

Keywords: Oxidative stress, Reactive oxygen species, Chronic diseases, Biomarkers.

Introduction

There is a strong link between the number of people who have chronic diseases, the amount of money spent on healthcare, and the number of people who die from these diseases. Even though the causes and symptoms of different chronic diseases are different, the basic ways that they cause disease are the same. Oxidative stress is one of these that stands out as a common biological mechanism that helps diseases develop, get worse, and start. Hacker et al. (2024) say that oxidative stress happens when the body's antioxidant defense systems can't keep up with the production of reactive oxygen species (ROS), which over time hurts cells and molecules.

Reactive oxygen species are always being made in living cells as byproducts of normal metabolic processes, especially mitochondrial oxidative phosphorylation. Biologically significant ROS roles encompass immunological defense, cellular signaling, and the regulation of gene expression. Oxidative damage to proteins, nucleic acids, and lipids transpires when antioxidant capacity is insufficient or when reactive oxygen species (ROS) production is elevated. Snezhkina et al. (2019) discovered that this form of damage alters genomic stability, enzyme activity, and membrane integrity, subsequently fostering inflammation, cellular apoptosis, and tissue dysfunction.

Increasing evidence is linking the causes of many chronic diseases, such as cancer, neurological disorders, cardiovascular disease, diabetes mellitus, chronic renal disease, chronic inflammatory

conditions, and oxidative stress. Oxidative stress causes many diseases to start, makes them worse, and raises the risk of long-term effects. As a result, there is an increasing demand for precise biomarkers that can indicate the oxidative state in living organisms and provide valuable information for clinical applications (Gyurászová et al., 2020).

Oxidative stress biomarkers give us useful information about how well the body balances the production of oxidants and the defenses against them. Oxidized proteins, DNA oxidation markers, lipid peroxidation products, and other similar biomarkers are examples of oxidative damage indicators; enzymatic and non-enzymatic antioxidants are examples of antioxidant capacity indicators. Krishnamurthy et al. (2024) assert that these biomarkers can be quantified in diverse biological specimens, including blood, urine, and tissues, to facilitate early diagnosis, monitor disease progression, assess prognosis, and evaluate treatment efficacy.

There are a lot of problems to solve when you look at oxidative stress biomarkers in a lab. Their clinical utility and repeatability may be diminished due to methodological variability, non-standard reference ranges, and vulnerability to pre-analytical variables. To successfully integrate oxidative stress markers into standard laboratory procedures, it is essential to understand both their clinical significance and the technical considerations involved in their measurement. This review aims to provide a comprehensive overview of oxidative stress biomarkers in chronic diseases, emphasizing their clinical relevance and the critical laboratory variables that influence their accurate assessment (O'Callaghan et al., 2020).

Oxidative Stress: Concept and Biological Mechanisms

When pro-oxidant molecules are made faster than antioxidant defenses, the redox balance in cells is thrown off, which leads to oxidative stress, a disease state. Reactive oxygen species (ROS) like superoxide anion, hydrogen peroxide, and hydroxyl radicals are usually made as waste products of aerobic metabolism. These reactive oxygen species (ROS) are very important for many cellular functions, including signaling, controlling gene expression, protecting the immune system, and maintaining homeostasis. The mitochondrial electron transport chain is the main source of reactive oxygen species (ROS), but inflammatory cells, metabolic processes, and specialized enzymes also make ROS (Schieber and Chandel., 2014).

Cells have an antioxidant defense system that gets rid of reactive oxygen species (ROS) and keeps the redox balance in check. This system has both enzymatic and non-enzymatic antioxidants. Some examples are reduced glutathione, vitamins C and E, catalase, and superoxide dismutase. Oxidative stress, on the other hand, changes proteins and DNA, causes lipid peroxidation, and speeds up cell aging through inflammatory pathways when the body makes more ROS than it can handle. Chronic diseases are caused by oxidative stress that lasts for a long time. This makes problems like chronic inflammation, insulin resistance, and endothelial dysfunction worse. To create biomarkers and personalized treatments that bring redox balance back to chronic diseases, we need to know how oxidative stress works (Schieber and Chandel, 2014).

Classification of Oxidative Stress Biomarkers

Biomarkers of oxidative stress are very useful for figuring out how well the body's antioxidant defense systems are working. No single biomarker can completely represent oxidative stress levels due to the complexity of oxidative processes. Consequently, we can categorize them as either exhibiting antioxidant defense mechanisms or oxidative damage to biomolecules. Biomarkers of oxidative damage are useful for figuring out how bad a disease is and what chronic oxidative exposure does to macromolecules like lipids, proteins, and nucleic acids. Demirci-Çekiç et al. (2022) assert that lipid peroxidation, protein oxidation, and nucleic acid oxidation are significant indicators of cellular damage, alterations in protein structure and function, and genomic instability, respectively.

Antioxidant defense status biomarkers, on the other hand, measure how well the body can handle oxidative stress. These consist of enzymatic and non-enzymatic antioxidants, such as vitamins and glutathione. The total antioxidant capacity can give you a good idea of how well something can fight off free radicals. To enhance the comprehension of oxidative stress, it is advantageous to integrate analyses of antioxidant defense biomarkers with those of oxidative damage; this facilitates evaluation in both research and clinical contexts and simplifies risk classification for chronic diseases (Hajam et al., 2022).

Biomarkers of Lipid Peroxidation

Oxidative stress causes lipid peroxidation, which is a sign of oxidative damage to cells. It mostly affects cell membranes that are high in polyunsaturated fatty acids. This process creates a chain of oxidation products that damage the membrane's structure and function. Malondialdehyde (MDA) is a stable and easily measured by-product of lipid hydroperoxides. It is an important biomarker for lipid peroxidation. Increased malondialdehyde (MDA) levels are a sign of oxidative stress and can be found in conditions like diabetes, heart disease, and chronic inflammatory disorders (Ayala et al., 2014).

F2-isoprostanes are another important biomarker that is linked to different levels of systemic oxidative stress. They are a specific way to measure lipid damage that happens when free radicals oxidize arachidonic acid. Conjugated dienes and lipid hydroperoxides are not very useful in clinical settings because they are not stable. However, they do show the start of lipid peroxidation. It is evident that these indicators hold significant potential for monitoring and evaluating antioxidant therapies, as they elucidate oxidative membrane damage and its role in chronic diseases (Milne et al., 2005).

Biomarkers of Protein Oxidation

Oxidative stress is especially bad for proteins, and it can have a big effect on how cells work, how they stay together, and how they talk to each other. Reactive oxygen and nitrogen species can change amino acid side chains, break peptide backbones, and cause harmful changes (Zhu et al., 2024). These changes can lead to less protein function, altered enzymatic activity, impaired signaling, and more protein breakdown.

The concentration of protein carbonyls is a key sign of protein oxidation because it shows that amino acids like arginine and lysine have been oxidized directly. Because protein carbonyls build up over time, they can be used as reliable signs of oxidative damage in many types of biological material. High levels are linked to conditions like diabetes, heart disease, and diseases that cause the brain to lose function. Chlorinated oxidants are made by immune cells that have been activated during inflammation. These are a source of advanced oxidation protein products (AOPPs), which are another important biomarker. AOPPs become very important signs of oxidative stress and inflammation when someone has an autoimmune disease or chronic kidney disease. Their high levels are linked to the severity and effects of the disease (Kehm et al., 2021).

Nitrotyrosine is a specific marker of oxidative and nitrosative stress, generated when reactive nitrogen species modify tyrosine residues. Neurodegeneration and vascular dysfunction are associated with the presence of nitrotyrosine in biological samples, signifying ongoing inflammation. Bandookwala and Sengupta (2024) assert that biomarkers of protein oxidation yield significant insights into the extent of oxidative damage and inflammation. This information helps us figure out how diseases work, how bad they are, and how to keep track of how well treatments that try to lower oxidative stress are working.

Biomarkers of DNA and RNA Oxidation

Too many reactive oxygen species can damage nucleic acids, which has a big effect on how cells work, how well they stay healthy, and how diseases develop. DNA and RNA are particularly susceptible to oxidative stress due to their continuous exposure to cellular oxidants and the inadequacy of repair mechanisms in certain cellular compartments. This oxidative modification can cause changes in gene expression, base lesions, and strand breakage, which can lead to mutagenesis, cell malfunction, and cancer. 8-hydroxy-2′-deoxyguanosine (8-OHdG), which is made when DNA guanine oxidizes, can show that this kind of damage has happened. 8-OHdG is a sensitive sign of oxidative DNA damage that can be found in different body fluids and tissues. It has been linked to a higher chance of getting cancer, getting older, getting diabetes, getting heart disease, and being around harmful oxidants (Hong et al., 2024).

Recently, scientists have learned more about how oxidative changes affect RNA, which has led to more research on these changes. RNA molecules, especially messenger RNA, are more likely to be damaged by oxidative stress than DNA molecules because they are single-stranded and close to mitochondria. The presence of oxidized RNA bases, such as 8-hydroxyguanosine, in biological samples has been associated with impaired protein synthesis and cellular dysfunction. The connection between oxidative stress on RNA and metabolic diseases, neurological disorders, and other issues is strengthening (Li et al., 2020).

To understand how much oxidative damage is done to DNA and RNA and how it affects the progression of disease, biomarkers of DNA and RNA oxidation are very important. These indicators are very important in cancer research because oxidative DNA damage is known to cause genomic instability and the start of tumors. They can also be used to keep an eye on oxidative stress in the body in long-term illnesses. The assessment of preventive and therapeutic strategies aimed at oxidative stress is guided by the quantification of nucleic acid oxidation markers, which augments our comprehension of disease etiology (Chen et al., 2022).

Biomarkers of Antioxidant Defense

To understand how the organism can neutralize ROS and keep redox balance, it is important to look at antioxidant defense biomarkers. These biomarkers, which include both enzymatic and non-enzymatic parts, can help limit oxidative damage and the spread of free radicals. Catalase and glutathione peroxidase eliminate hydrogen peroxide, a byproduct generated when enzyme antioxidants such as superoxide dismutase facilitate the decomposition of superoxide anions. Cardiovascular diseases, diabetes, chronic kidney disease, and neurodegenerative disorders are chronic conditions that can impact their activities, indicating disrupted redox regulation (Jomova et al., 2024).

Antioxidants that do not involve enzymes are necessary for scavenging free radicals and preventing oxidative chain reactions; notable examples include uric acid, vitamins C and E, and reduced glutathione. A deficiency of these antioxidants is linked to chronic inflammatory and metabolic diseases, potentially exacerbating oxidative damage and hastening disease progression. Total antioxidant capacity (TAC) measures the combined antioxidant effects of both enzymatic and non-enzymatic parts. While interpretations may vary based on dietary factors and individual traits, it offers insights into the global redox status and correlates with disease severity and therapeutic responses (Pham-Huy et al., 2008).

Oxidative Stress Biomarkers in Major Chronic Diseases

It is increasingly evident that oxidative stress constitutes a prevalent pathogenic mechanism underlying various chronic diseases. An imbalance between the production of reactive oxygen species and the body's ability to fight them off affects the start, progression, and effects of diseases. Pizzino et al. (2017) discovered that assessing oxidative stress indicators in diverse chronic diseases can facilitate risk evaluation, prognosis, and treatment surveillance by elucidating disease mechanisms.

Cardiovascular Diseases

Oxidative stress has an effect on endothelial function, vascular inflammation, and lipid metabolism, which makes it an important factor in the development of cardiovascular diseases. Endothelial dysfunction is a key early step in the development of atherosclerosis. It happens when there are too many reactive oxygen species, which makes nitric oxide less available. Oxidative changes in low-density lipoproteins make foam cells and plaque unstable. Researchers have discovered that individuals with hypertension, coronary artery disease, and heart failure exhibited increased levels of lipid peroxidation markers, such as malondialdehyde and F2-isoprostanes. Diminished total antioxidant capacity and decreased antioxidant enzyme activity are additional indicators of impaired antioxidant defenses in these patients. The growing interest in oxidative stress biomarkers for cardiovascular risk assessment and prognostic evaluation is attributed to their correlation with disease severity and adverse cardiovascular outcomes (Senoner and Dichtl, 2019).

Diabetes Mellitus

Diabetes mellitus causes blood sugar levels to stay high for a long time, which greatly raises the risk of oxidative stress through a network of interconnected metabolic processes. Glucose autoxidation, advanced glycation end products generation, polyol pathway activation, and mitochondrial dysfunction are significant mechanisms that augment ROS production and diminish antioxidant activity. Malondialdehyde, protein carbonyls, and 8-hydroxy-2′-deoxyguanosine are oxidative stress biomarkers closely linked to inadequate glycemic control and the onset of chronic complications in diabetes. Endothelial dysfunction, inflammation, and microvascular injury are integral to diabetic nephropathy, neuropathy, and retinopathy, all of which initiate from oxidative damage. Ohiagu et al. (2021) assert

that oxidative stress markers can facilitate the early diagnosis of diabetes-related issues prior to the utilization of established glycemic indices.

Neurodegenerative Disorders

Neurodegenerative disorders are characterized by neuronal degeneration and synaptic dysfunction, with oxidative stress being a significant contributing factor to both. Neurons are very likely to be damaged by oxidative stress because they have a lot of lipids, don't regenerate well, and use oxygen quickly. The accumulation of reactive oxygen species leads to neuronal death and cognitive impairment by inducing lipid peroxidation of neuronal membranes, oxidative modification of proteins, and mitochondrial dysfunction. In people who are affected, their blood, CSF, and brain tissue have biomarkers that show oxidative damage. These include products of lipid peroxidation, indicators of protein oxidation, and oxidized nucleic acids. Researchers have discovered a correlation between these indicators and cognitive decline, functional impairment, and disease progression (Kim et al., 2024), indicating their potential utility in monitoring disease activity and assessing the effectiveness of neuroprotective treatments.

Chronic Kidney Disease

Patients with chronic kidney disease (CKD) experience significant oxidative stress due to diminished antioxidant defenses, chronic inflammation, and the accumulation of uremic toxins. When kidney function gets worse, it becomes harder to get rid of oxidative waste, which raises the overall oxidative stress level. In addition, factors related to dialysis may increase the production of reactive oxygen species. Research indicates that the severity of chronic kidney disease (CKD) is associated with diminished glutathione levels and elevated concentrations of advanced oxidation protein products in patients. In this cohort of patients, oxidative stress correlates with compromised endothelial function, accelerated atherosclerosis, and heightened risk of cardiovascular disease and mortality. Consequently, indicators of oxidative stress may yield valuable insights for assessing risk and monitoring the progression of renal disease in patients (Rapa et al., 2019).

Cancer

In cancer biology, oxidative stress is a double-edged sword: it can cause genomic instability and tumor initiation by breaking DNA molecule bonds, and it can also help tumors that have already formed by changing the redox balance in a way that helps cancer cells survive, multiply, and resist treatment. 8-hydroxy-2'-deoxyguanosine is one of the most important biomarkers for oxidative genomic damage and cancer risk. Changes in antioxidant enzyme activity in different types of cancer can give us information about how tumors grow, how diseases progress, and how well treatments work. Zahra et al. (2021) assert that assessing indicators of oxidative stress can enhance our understanding of tumor dynamics and the effectiveness of therapies.

Laboratory Assessment of Oxidative Stress Biomarkers

To accurately find signs of oxidative stress, you need to carefully manage things like the type of sample, the protocols for collecting it, the anticoagulants, the storage, and the exposure to the environment before, during, and after the analysis. There are many different types of analytical methods, from simple spectrophotometric tests that may not be very accurate to complicated chromatographic and immunochemical tests that need the best equipment. It is hard to compare research because there are no standard essays or reference ranges that everyone agrees on. When you think about how different people's nutrition, lifestyle, and health affect the results, it can be harder to understand them. Christenson and Duh. (2012) say that the best way to get a full picture of oxidative state is to look at many different signs.

Clinical Utility and Limitations

Oxidative stress indicators are promising for evaluating treatments, tracking disease progression, and assessing risk in chronic disorders because they reflect underlying pathophysiological processes. Nonetheless, the absence of standardization, technical challenges, biological variability, and sufficient evidence to correlate biomarker thresholds with clinical decisions constrains their clinical utility. For

greater clinical relevance and translational value, integration into clinical recommendations, assay standardization, and large-scale investigations are essential (Massaccesi and Balistreri, 2022).

Conclusion

Oxidative stress is the main cause of several long-term illnesses. When reactive oxygen species are made, the body's antioxidant defense systems get too much to handle. This is when stress happens. Antioxidant capacity indicators and biomarkers of oxidative damage to lipids, proteins, and nucleic acids provide insights into redox status and disease pathogenesis. The routine clinical use of these biomarkers is limited by methodological inconsistency, absence of standardization, and biological variability, notwithstanding their potential for risk evaluation, disease surveillance, and assessment of therapeutic responses. To make oxidative stress biomarkers more useful in the clinic and easier to use in regular lab work, we need to work on standardizing assays, creating reference ranges that are useful for the clinic, and using integrated biomarker panels.

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