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**| RESEARCH ARTICLE**

## **Mental Health Disorders Due to Oxidant and Antioxidants Imbalance: A Literature Review Study**

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**| ABSTRACT**

Health is a significant thing in human life because it is one of the supports for human activity. By living a healthy life, everyone can be productive socially and economically to achieve their desired life goals. Oxidative stress is an imbalance between the cellular production of Reactive Oxygen Species (ROS) and antioxidant countermeasures. The high oxygen consumption and lipid-rich environment in the brain are thought to be highly susceptible to oxidative stress or redox imbalance. Various kinds of literature show accumulating evidence of implications for free radical-mediated pathology, altered antioxidant capacity, neurotoxicity, and inflammation in neuropsychiatric disorders. Oxidative stress contributes to the specific clinical symptomatology of complex and debilitating psychiatric illnesses. This complex and heterogeneous oxidative stress disorder negatively impacts the quality of life, morbidity or mortality, and cognitive function, known as depression. Oxidative stress has received much attention concerning psychiatric illness and has also been suggested as a contributing factor to depression.

**| KEYWORDS**

Health Disorders, Mental, Oxidative Stress

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**1. Introduction**

Health is a significant thing in human life because it is one of the supports for human activity. By living a healthy life, everyone can be productive socially and economically to achieve their desired life goals. Mental health disorders with various symptoms, pathogenesis, prognosis, and resource allocation are some of the significant public health problems worldwide. The Global Burden of Disease, Injuries, and Risk Study in 2020 confirms that mental and substance use disorders, as indicated by the presence of depressive disorders, are the leading causes of public health problems that have a significant impact on individuals and society (Abbafatiet al., 2020). Studies on mental health disorders' causes, etiology, and pathogenesis are still not clearly understood. In general, the causes of mental health disorders are the result of dysfunction of dopaminergic neurotransmission, serotonergic, and glutamatergic. However, several other factors that cause mental disorders are neurotrophic factors, the immune system, the neuroendocrine system, and epigenetics. Even in the last few decades, many studies have explained the role of oxidative stress in the pathophysiology of mental health disorders (Sutkowyet al.,2021).

Balanced oxidative stress is essential for the normal functioning of the body. High oxidation levels can cause oxidative protein changes, which are essential in many human diseases (Surguchevaet al., 2020). Excessive peroxide levels cause damaging oxidation and chemical modification of biomacromolecules, consequently contributing to various pathological mechanisms of the disease. The brain is a lipid-rich organ with enormous oxygen consumption and a lack of an adequate antioxidant barrier, which makes the brain especially vulnerable to oxidative stress imbalances. Therefore, unbalanced oxidative stress is related to the pathophysiology of various mental health disorders, including schizophrenia, depressive disorders, bipolar disorders, and so on (Poljsaket al., 2019). Various observational studies have shown a link between oxidative stress and mental health disorders. Causality studies suggest a

suggestive causal association was found between gout and the risk of disorders bipolar and attention deficit hyperactivity disorder, between catalase and the risk of eating disorders, and between albumin and the risk of autism spectrum disorders (Firth et al., 2019). This association points to an imbalance of peroxide and antioxidant defenses as potential causes of mental health disorders. In addition, the antioxidative effects of antipsychotics, antidepressants, and mood stabilizers and the symptom improvement effect of supplementation with antioxidants also emphasize the findings, namely, that the oxidative stress system plays a role in the pathogenesis of mental health disorders (Ribbaud et al., 2020).

Oxidative stress is a condition where there is an imbalance between the number of oxidants (free radicals) and the number of antioxidants in the body, causing damage to a chain starting from cells to a higher level. Oxidative stress can cause cell damage and is the basis of pathogenesis for chronic disease processes such as cardiovascular, autoimmune, pulmonary, and metabolic disorders. Oxidative stress status can be identified from the degree of oxidative damage to lipids, proteins, and DNA, which can be measured with specific biomarkers. Increased production of Reactive Oxygen Species (ROS) induces tissue damage through a mechanism that activates several cellular signaling pathways, which causes depression (Niki, 2019). Major depression represents 12 percent of all diseases, and the percentage is growing so that by 2020 it is said to reach more than 15 percent and occupy second place after cardiovascular disease (Janssen & Mossman, 2021). Among adults, 15 percent of those diagnosed with depression die due to suicide (Saran & Bors, 2018).

## 2. Research Methods

The research design used is a Literature review. A literature study is a research conducted by researchers by collecting several articles or journals related to the problem and research objectives. This technique is carried out to disclose theories relevant to the problems being faced/researched as reference material in discussing research results. Data analysis is used by using thematic analysis. Analysis Thematic is one way to get results by conducting data analysis which aims to identify patterns or determine themes through data that has been collected by research (Braun & Clarke, 2006 in Heriyanto, 2018), while the stages of data analysis include (1) Compare, finding similarities among several kinds of literature; (2) Contrast, find the differences between some literature and conclude and (3) Criticize, give your own opinion based on the source read.

## 3. Results and Discussion

Mental health disorders are thought to have a close relationship with diet and food consumption (Farhangiet al., 2018). A diet high in calories and fat and a lack of variety of foods is associated with inflammation and the possibility of stress and anxiety. A healthy diet has a protective effect on depressive symptoms and can reduce the risk of developing depression by up to 25%. et al., 2020). Stress increases the desire to eat. Hyperpalatable food intake becomes higher because it is considered comfort food. Anxiety and mental health disorders are also related to the emergence of eating disorders in a person, such as binge eating and high consumption of foods high in calories and saturated fat. Mental health disorders are often associated with changes in appetite, which can be in the form of decreased appetite (melancholic depression) or increased appetite (depression with atypical features) (Privateer et al., 2020).

Mental health disorders are closely related to oxidative stress according to a study conducted by Luet et al. (2022) showed that there was no significant causal effect of biomarkers of oxidative stress (OSIB) injury on mental health disorders, while the findings indicated that part of stress is oxidative nominally associated with risk of mental health disorders as a cause namely gout, bipolar disorder, and attention deficit hyperactivity disorder; catalase causes happening anorexia nervosa and albumin are the causes of autism. Studies also show that depressive disorders are significantly associated with decreased bilirubin, attention deficit hyperactivity disorder is significantly affected by decreased ascorbate, as well as some causal effects of mental health disorders on oxidative stress (disturbance bipolar on decreased uric acid and increased retinol; depressive disorders in increased uric acid and decreased ascorbate; schizophrenia in decreased uric acid, increased retinol and albumin; attention deficit disorder or hyperactivity on increased uric acid, and decreased catalase, albumin, and bilirubin as well as anorexia disorders on decreased uric acid. This study provides evidence of a potential causal link between oxidative stress and mental health disorders.

Oxidative stress is an imbalance between the cellular production of Reactive Oxygen Species (ROS) and antioxidant countermeasures. The high oxygen consumption and lipid-rich environment in the brain are thought to be highly susceptible to oxidative stress or redox imbalance. The fact that oxidative stress has implications for several mental disorders, including depression, anxiety disorders, schizophrenia, and bipolar disorder, is not surprising (Matsumoto, 2021). Various studies have established a relationship between oxidative stress and mental health disorders. This is because, in mitochondria, oxidative phosphorylation occurs and is the primary source of ATP in aerobic organisms. These conditions generate free radicals as by-products, including Reactive Oxygen Species (ROS), reactive nitrogen species (RNS), carbon-centered, and sulfur-centered radicals. The number of unpaired electrons, free radicals, are atoms or groups of atoms which are highly reactive substances that produce chain reactions with each step of their formation. The main ROS generated in humans are hydrogen peroxide, superoxide radicals, and hydroxyl radicals. During the auto-oxidation of hemoglobin and photolysis, superoxide radicals are generated. This superoxide

is not particularly reactive by itself. However, it can be catalytically converted by superoxide dismutase (SOD) into H<sub>2</sub>O<sub>2</sub>, which decomposes to give hydroxyl radicals which are highly reactive in the presence of iron. Oxidative stress is considered a state of cellular imbalance in which the production of ROS outweighs the antioxidant response mechanisms supporting DNA, RNA, and lipids resulting in various pathophysiological consequences.

ROS can exist in O<sub>2</sub>, hydroxyl radicals (OH), hypochlorous acid (HOCL), and peroxy radicals. ROS can damage cells by damaging lipid membranes through several chemical peroxidation reactions. This happens because the cell membrane contains high amounts of polyunsaturated fatty acids (PUFA). Lipid membrane peroxidation will cause cell changes, such as increased membrane permeability, decreased calcium transport in the sarcoplasmic reticulum, and impaired mitochondrial function. Halliwell and Gutteridge, (2017). Oxidative DNA damage results from oxidative stress generally occurring in nucleobase guanine because it is more easily oxidized than the others. Excess ROS will hydrolyze the guanine base and form 8-hydroxylamine (8-OH-Gua), generating 8-hydroxy-2'-deoxyguanosine (8-OHdG) via electron abstraction or 8-oxo-7,8-dihydro-2'-deoxy-guanosine (8-oxodG) through in tautomerism keto-enol of 8-OHdG. Most literature usually uses the terms 8-OHdG and 8-oxodG as the same compound. This production results in oxidative DNA damage, one of the primary forms of DNA damage that leads to DNA modification with altered function (Raza et al., 2018). Because this mutagenic deoxyguanosine can cross cell membranes easily, it is more commonly referred to as an indicator of oxidative damage. It is further classified as a biomarker in the early detection of various diseases (Korkmaz et al., 2018).

Weakness of the antioxidant defense system, including depletion of antioxidant and antioxidant-enhancing enzymes, is implicated in developing mental illness. The association between higher levels of oxidative stress markers and mental illness further suggests the involvement of oxidative stress in the pathophysiology of mental illness. Increases in oxidants and decreases in antioxidants have been reported in patients' brains and peripheral tissues. Oxidative damage is strongly associated with mental illness. Genetic and environmental factors can cause damage to the DNA repair system, thus causing accumulation of DNA damage which in turn will cause changes in the structure and function of neurons. This relationship is also shown by a study conducted by Christensen et al. (2018), where the level of 8-oxodG was significantly higher in the urine and cerebrospinal fluid of patients who died from severe mental illness, thus indicating that oxidative DNA damage is the significant oxidative damage.

Mental disorders can be caused by both genetic and environmental factors, according to a study by Gohet et al. (2020) revealed that oxidative DNA damage was significantly higher in patients with schizophrenia and bipolar disorder. Levels of oxidative DNA damage were significantly higher in the lymphocytes and urine of patients with schizophrenia and bipolar disorder. Larger effect sizes were observed in hospitalized patients and patients with longer disease duration and treatment history. Significantly higher ROS were also observed in schizophrenic patients but not in depressed patients, suggesting that mental health disorders are caused by oxidative stress. There are different types of anxiety disorders, including post-traumatic stress disorder, panic disorder and obsessive-compulsive disorder, and generalized anxiety disorder. Multiple signaling pathways involving antioxidant, anti-inflammatory, or anti-apoptotic mechanisms may regulate anxiety-like behavior.

Further evidence suggests that the NOX-derived ROS hypothesis is involved in the pathophysiology of anxiety and bipolar disorder. A complex and heterogeneous disorder that negatively impacts the quality of life, morbidity and mortality, and cognitive function is known as depression. Oxidative stress has received much attention concerning psychiatric illness and has been suggested as a causative factor for depression (Kim et al., 2021). Some evidence determines the involvement of oxidative stress and nitrosative in the pathophysiology of major depression. Therefore, for new antidepressants and oxidative mechanisms, nitrosative has been proposed as a target. It has been studied that individuals suffering from depression have been shown to have lower serum or plasma antioxidant potency and reduced brain GSH levels. In depressed patients, circulating levels of F<sub>2</sub>-isoprostanes are increased and correlate with the severity of depressive symptoms and urinary excretion. Hydroxydeoxyguanosine appears to be higher when compared to healthy controls (Matsumoto, 2021).

Bipolar disorder is characterized by intermittent episodes of mania or hypomania that are usually associated with episodes of depression. It is also a severe mood disorder clinically presented as unusual mood, energy, and cognitive changes, with or without depressive episodes. The symptoms are different from the regular ups and downs, and this disorder can be very damaging to relationships, work life, or school performance and even lead to suicide. In several studies, it has been reported that patients with bipolar disorder experience significant changes in lipid peroxidation, antioxidant enzymes, and nitric oxide levels, such as increased lipid peroxidation and increased levels of Nitric Oxide (Rahsepar & Mohammadpour, 2021). Accordingly, accumulating evidence has implications for free radical-mediated pathology, altered antioxidant capacity, neurotoxicity, and inflammation in neuropsychiatric disorders. Also stated is the extent to which oxidative stress contributes to specific symptomatology clinical presentation of complex and debilitating psychiatric illness.

#### 4. Conclusion

Mental health disorders are thought to have a close relationship with diet and food consumption. A diet high in calories and fat and a lack of variety of foods is associated with inflammation and the possibility of stress and anxiety. Balanced oxidative stress is essential for the normal functioning of the body. High oxidation levels can cause oxidative protein changes, which are essential in many human diseases. Oxidative stress is an imbalance between the cellular production of Reactive Oxygen Species (ROS) and antioxidant countermeasures. The high oxygen consumption and lipid-rich environment in the brain are thought to be highly susceptible to oxidative stress or redox imbalance. Various literature show accumulating evidence of implications for free radical-mediated pathology, altered antioxidant capacity, neurotoxicity, and inflammation in neuropsychiatric disorders. Oxidative stress contributes to specific symptomatology clinical presentation of complex and debilitating psychiatric illnesses. Complex and heterogeneous oxidative stress disorders negatively impact the quality of life, morbidity and mortality, and cognitive function, known as depression. Oxidative stress has received much attention concerning psychiatric illness and has also been suggested as a contributing factor to depression.

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