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# Oxidative Stress and Anemia.

# Review Article: Oxidative Stress in Anemia: An Update

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## Abstract
Anemia is a condition in which you lack enough healthy red blood cells to carry adequate oxygen to your body's tissues. Low haemoglobin, a synonym name for anemia, can leave you feeling lethargic and weak. The increased generation of reactive oxygen species under hypoxic conditions usually seems contradictory. A prooxidant shift is brought on by modifications in cellular metabolism, particularly energy metabolism, higher flux rates in catecholamine metabolism, and persistent leukocyte activation. Following this increased production of free radicals, an anemic body's depleted antioxidant defences fight. We discussed the function of oxidative stress and its potential connection to anemia in this review.

## 1. Introduction

The "5.5 billion individuals" that in the world are anemic or around one-third of them. Around the world, "35% of women, 51% of pregnant women, 40% of children (0 to12 years), and 18% of males" are anemic. [1] Because the diagnosis of anemia is based on the World Health Organization definition of anemia—hemoglobin less than 11 g/dL for children under the age of four and pregnant women, "less than 12 g/dL for children between the ages of five and twelve and non-pregnant women"—these numbers are likely conservative estimates. [2]

Particularly among mothers and small children, the scope of the issue in underdeveloped nations is huge. Also impacted are developed nations. Approximately 3% of women and 0.5% of males were anaemic in the United States in 1995, according to data based on household interviews. [3] A little bit larger percentages, 6.6% for males and

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12.4% for women, are provided by the Mayo Clinic for Olmsted County, Minnesota citizens.[4]

Anemia is a sign of underlying disorders, some of which are common and others of which are uncommon or incredibly uncommon. Globally, “iron deficiency, thalassemia and hemoglobinopathies, folate deficiencies, and parasite infections” are the most common causes of anaemia. [5] Chronic diseases, thalassemia, and a lack of iron with each accounting for over one third of occurrences, anaemia has three primary causes in the United States. [6] A small but considerable fraction is due to “folic acid and vitamin B12 deficiency”. The remaining anemias are caused by a variety of “hematologic disorders”, primarily “hemoglobinopathies and diseases” that affect the “bone marrow”. Only a little is spoken about maternal anaemia when it comes to anaemia in newborns and children.

An exhaustive and detailed history of “blood loss, drug and chemical exposure, nutrition, family history”, and everything else that might point to an underlying problem is taken before evaluating a patient with anemia. In moderate anemia, there are no distinctive physical features. Mucous membrane pallor is hardly ever noticeable. In this overview, we'll talk about oxidative stress in both hemolytic anemia and iron deficiency anemia.

Under hypoxic conditions, the increased reactive oxygen species production frequently seems paradoxical. Changes in cellular metabolism, particularly energy metabolism, increased flux rates in catecholamine metabolism and persistent leukocyte activation lead to a prooxidant shift. This increased creation of free radicals is subsequently met with resistance from an anemic body's significantly compromised antioxidant defences.

This increased production of free radicals is subsequently met with resistance from an anemic body's significantly compromised antioxidant defences. The glutathione systems as well as intracellular enzymes like superoxide dismutase and catalase are found in the erythrocytes, which are a significant element of the blood's antioxidant capacity. Thus, it is probable that oxidative stress is at least partially to blame for some uremia-related problems. Cardiovascular disorders, early biological ageing, and increased infection susceptibility are just a few of these. Thus, it is anticipated that long-term benefits will result from strategies to boost the intricate endogenous free radical responses. [7]

An imbalance between “free radicals and antioxidant molecules” known as “oxidative stress” can have a significant impact on the pathophysiology of “iron deficient anemia (IDA)”. “Reactive oxygen species (ROS)” generation and antioxidant defence might be viewed as being out of balance, which is what is meant by oxidative stress. This imbalance may cause molecules to oxidize, causing tissue injury. The "oxidant state" is primarily influenced by the oxidative actions taking place within the organism [8]. Because the mitochondria are responsible for metabolizing 90% of the oxygen in a human body, changes in the “mitochondrial enzyme complex cytochrome oxidase account” for a significant portion of oxidative processes. A portion of the oxygen that is processed in the “mitochondria” may leak through the “electron transport chain”, creating “oxygen free radicals like superoxide anions and hydrogen peroxide” as well as “reactive oxygen intermediates”.

These ROS are key contributors to oxidative stress because they can diffuse from the mitochondria [8, 9]. On the other hand, a variety of enzyme functions, including “superoxide dismutase, catalase”, “glutathione (GSH) reductase (GRed), and GSH peroxidase (GPx)”, determine antioxidant defence, resulting in “ROS” elimination and buffering [8,10,11].

Primary antioxidant reduced GSH has been suggested as a significant ROS scavenger. The GPx/GRed system maintains GSH levels in the cells. The “oxidation of GSH” to its disulfide form, GSSG, is associated with the reduction of H2O2 to H2O, which is catalyzed by GPx. Through GRed, the oxidation of “NADPH to NADP” is connected with the reduction of GSSG to GSH. Because they may recycle GSH formation via the GPx/GRed pathway, erythrocytes are essential for maintaining “both systemic and local redox equilibrium”. As a result, evaluating the erythrocyte's GSH system characteristics is seen to be a trustworthy way to learn about redox status. [11].

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"The decrease in deformability, increase in cytosolic calcium and increase in membrane stiffness of RBCs can be attributed to oxidative stress" [12,13]. Increased lipid peroxidation, a reduction in antioxidant defence enzymes such glutathione peroxidase, and a higher susceptibility to the addition of pro-oxidants are all indicators of increased oxidative stress during anaemia [15–17]. However, it has not always been proven that oxidative stress occurs in RBCs during anaemia [18,19]. Given its impact on DNA damage and lipid peroxidation, oxidative stress is recognised as a beneficial contributor to anaemia. Aerobic metabolism results in the production of reactive oxygen species such as hydroxyl radicals, superoxide, and hydrogen peroxide [20]. Oxygen reactive species Mammalian cells may experience oxidative stress that results in the breakdown of macromolecules and aberrant functioning if it is not promptly cleared by an antioxidant system ("neurotransmission function and altered immunologic and inflammatory defenses"). Normal blood cells have demonstrated iron-mediated oxidative damage in vivo. [21]. Superoxide radicals are produced by the continuous auto-oxidation of haemoglobin, and they can be produced by spontaneous or enzymatic dismutation to produce hydrogen peroxide [20, 21].

"Many disorders, including hemolytic anemia, are thought to have symptoms that are made worse by oxidative stress. The hemoglobinopathies (thalassemia and sickle cell anemia), glucose6phosphate dehydrogenase deficiency, hereditary spherocytosis, congenital dyserythropoietic anemias, and paroxysmal nocturnal Hemoglobinuria were all linked to oxidative stress. Although oxidative stress is not the primary cause of these disorders, oxidative damage to their erythroid cells is a major factor in hemolysis because erythropoiesis is inefficient in the bone marrow and red blood cells (RBC) have a short shelf life in the bloodstream. Moreover, oxidative stress affects platelets and polymorphonuclear (PMN) white cells. As a result, in addition to chronic anemia, some patients may experience thromboembolic symptoms and recurring bacterial infections". [22]

The early oxidation of red blood cells occurs in hemolytic anemias. While oxidative stress does not cause most hemolytic anemias, it does mediate a number of their diseases, including hemolysis. It is produced by a number of factors, most frequently iron overload, in red blood cells and other blood cells. [23]

Here in we present an overview of anemic diseases that are closely related to oxidative damage.

## 2. Discussion

Under hypoxic environments, the increased production of reactive oxygen species frequently seems paradoxical. Changes in cellular metabolism, particularly energy metabolism, increased flux rates in catecholamine metabolism and persistent leukocyte activation lead to a prooxidant shift. This increased creation of free radicals is subsequently met with resistance from an anemic body's significantly compromised antioxidant deficiency. The glutathione system and intracellular enzymes like superoxide dismutase and catalase are found in the erythrocytes, which are a significant element of the blood's antioxidant capacity. Thus, it is probable that oxidative stress is at least partly responsible for some uremia complications.

Anemia is a condition in which the number of red blood cells becomes insufficient to meet the body's physiologic needs. Anemia is one of the major public health problems around the world.

Chronic anaemia results in a reduction in the amount of oxygen delivered to peripheral tissues, which in turn results in decreased energy generation and systemic diseases. In fact, a number of genetic disorders are linked to anaemia. Many genes are involved in the development of erythroid cells and the physiological action of RBC. Recently, the epidemiological perspective was used to review the research on common inherited RBC-related illnesses [24].

Lahera V. et.al (2006) stated in their study that "Consecutive or combined treatment with intravenous iron and erythropoiesis stimulating oxidative agents clearly is beneficial for patients with CKD and iron deficiency, and anemia and could contribute to prevent the risk for cardiovascular events in these patients" [25]

Aslan et al. came to the conclusion that IDA (iron deficiency anemia) patients have higher levels of

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oxidative stress and DNA damage in 2007. Increased oxidative stress appears to be a significant component in these IDA patients' development of DNA damage. Given the relationships between oxidative stress and DNA damage and the severity of anemia, it is likely that both of these factors contribute to the pathogenesis of IDA..[26]

A nine Week study by Nagababu E. (2008) Increased haemoglobin autoxidation and subsequent generation of ROS can account for the shorter RBC lifespan and other pathological changes associated with iron-deficiency anemia.[27]

"Fibach, E. (2014) used flow cytometry for measuring oxidative stress parameters, which enables the evaluation of the patient's status with respect to oxidative stress as well as monitoring of the effect of treatment" [23]

A study by Madhikarmi L. (2014) revealed "higher oxidative stress before vitamin supplementation in iron deficiency anemic patients and after supplementation, lowers lipid peroxidation and increased antioxidant vitamins were achieved".[28]

Out of 770 individuals in a cross-sectional study by Payang R. (2018), 19.7% had severe anemia. The investigation only found two haemoglobin types: Hb S and -thalassemia. In this investigation, the key factors influencing anemia were haemoglobin type, mean corpuscular volume, TIBC, and serum ferritin level. [29] Sharma R. study (2020) Oxidative stress is evident in IDA, but it affects women more severely and with less compensation than it does men. [30]

High incidence of anemia (53%) and high frequency of underweight girls (45%) hint to inappropriate food consumption compromising both general health and micronutrient status, according to a 2018 study by Singhal P. and Agarwal.V. The majority of participants had unhealthy eating habits, which highlights the value of sound dietary guidance in battling nutritional anemia. [31]

## 3. Conclusion

The absence of protein-regenerating mechanisms in differentiated cells makes RBC cellular homeostasis particularly sensitive to mutations in a range of genes and environmental factors. When in the proper shape, haemoglobin interacts with oxygen molecules but is normally safe because of the abundance of antioxidative and redox mechanisms. It's possible that red cell degeneration is the cause of the decreased red cell life span associated with anaemia. Reactive oxygen species on the membrane surface have been shown to alter deformability and expose phosphatidyl serine, which has been linked to a reduction in RBC longevity during anaemia. Oxidative stress brought on by anaemia can be seen as an increase in both oxidants and antioxidants.

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