



Physiological Impact of Stress on Women Health

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ABSTRACT

One can experience various amplitude of stress depending on the frequency and duration of of the stressors. The short-term stress can be balanced by body's own homeostatic mechanisms but the long-term stress has a negative impact on both the physiological and psychological well-being of an individual. The chronic stress is associated with increased emotional feeding, visceral fat accumulation, change in glucose uptake and metabolism, altered sleep cycle, anxiety and depression. In physiological conditions stress is manifested by the generation and accumulation of free radicals in the body. Some of the health hazards of stress are experienced equally both by men and women like weaker immune systems, sleeping disorder and digestive symptoms. But there are other ways stress can affect women's health like problems in conception across the fertile window, hormonal changes through the Hypothalamus-Pituitary-Ovary axis causing more susceptible to menstrual disorders. Women also face an increase level of anxiety, depression, emotional eating and obesity in exposure to long-term stressors. Antioxidants can terminate the chain reaction initiated by free radicals preventing oxidative stress-related damage. A woman needs to manage the stressors with proper food and lifestyle modifications. Among different stress management strategies diet can be one of them.

Keywords: stressors, chronic stress, Hypothalamus-Pituitary-Ovary axis, anxiety, depression, emotional eating, free radicals, antioxidants

INTRODUCTION

Women are always in action whether in or out of the family. Some works are exclusively the domain of women like baby care and nursing. Being a mother or wife, a good deal of work has been performed by a woman within the family. With the progress of societal thoughts and women's education nowadays women are not restricted in household activities only rather are engaged in a vast range and different dimensions of work starting from informal to formal work (Penny,1863). So apart from the works done exclusively by woman being the female sex no other works can be categorized as women work (Borck, 2019). Stress is any type of body's reaction to a change or challenge. It can be physical, mental or

emotional. Sometimes stress is a cause of conflict and conflict influences stress in a negative way. Each person responds to stress differently. Studies show that women more likely experience stress than men because of different levels of stress hormones (Verma *et al.* 2011, Bangasser, 2013). Women facing disagreement between peers, groups, organizations are more likely to be stressed. The mental wellbeing of women is worsened by stress and in a long-term state it leads to depression and anxiety (Hammen *et al.* 2009).

Stress Types

One can experience different degrees of stress depending on the duration and frequency of the stressors. The short-term stress can be managed with a low or no impact. Body's own homeostatic mechanisms can beat these stressors. But problems arise with persistent recurrent stressors making an altered hormonal interplay in the body. The long-term stress induces hyperactivation of stress hormones and influences other behavioural and physiological alterations like increased emotional feeding, visceral fat accumulation, change in glucose uptake and metabolism, altered sleep cycle, anxiety and depression.

Free radicals and Stress

In physiological conditions stress is manifested by the generation and accumulation of free radicals in the body. A free radical is any molecule capable of independent existence due to the unpaired electron in the outer orbital. They can either donate an electron to or accept electrons from other molecules thus serving as oxidants or reductants. Many radicals are unstable and highly reactive.

Free radicals play an important role in destroying the internalized bacteria by phagocytosis, maintaining body homeostasis and a wide range of cellular functions (Finkel and Holbrook, 2000; Bhattacharyya *et al.*, 2014). They are also involved in some signaling processes like redox signaling (Finkel and Holbrook, 2000). Excessive production and accumulation of free radicals cause lipid, protein and DNA damage. In particular they induce structural modification of proteins, fragmentation of peptide chain, enzymatic inactivation, increased membrane fluidity by lipid peroxidation, modification of bases of DNA thus leading to disruption of vital cellular processes (Finkel and Holbrook, 2000; Kaminski *et al.*, 2002, Sharma *et al.*, 2012; Cadet and Wagner, 2013; Cadet *et al.*, 2017). The free radical accumulation in the body contributes to many diseases

like cancer, stroke, myocardial infarction, diabetes (Tsatsakis *et al.*, 2019, Padureanu *et al.*, 2019).

Characteristics features of free radicals:

1) Free radicals are highly reactive and unstable. The reactivity of these radicals is due to the presence of one unpaired electron which tends to donate it or to obtain another electron to attain stability. Hence they are short-lived (of the order of 10^{-9} to 10^{-12} seconds) (Phaniendra *et al.* 2015)

2) Free radicals have a beneficial role in several biological processes. They perform intracellular destruction of bacteria by phagocytes, especially by granulocytes and macrophages. Free radicals are involved in the redox signaling process. ROS plays a beneficial role in maintenance of homeostasis as well as a wide variety of cellular functions.

3) Excessive free radicals production leads to cellular dysfunctions and disruptions of vital cellular processes which cause apoptosis, contributing to many diseases such as cancer, stroke, diabetes, cardiovascular disease, asthma, neurodegenerative diseases etc. High ROS levels cause lipid, protein and DNA damage.

4) In pathological or stress conditions, ROS overwhelms antioxidant systems leading to an imbalance, which, in turn, causes oxidative stress and irreversible changes in cell compounds in addition to being able to disrupt normal cellular-signaling mechanisms.

5) In autoimmune diseases, free radicals lead to the chemical modification of amino acids in proteins, so the generated proteins are recognized as nonself by the immune system. Free radicals can change the expression of self-antigen-type proteins, increasing their immune response or changing their antigenic profile.

6) Free radicals are classified in two groups -radicals and non-radicals.

Radicals are less stable than non-radical species, although their reactivity is generally stronger. The examples for the radicals include Superoxide ($O_2^{\bullet-}$), Hydroxyl (OH^{\bullet}), peroxy radical (ROO^{\bullet}), nitric oxide (NO^{\bullet}), nitrogen dioxide (NO_2^{\bullet}) etc.

Non-radical species are not free radicals but can easily lead to free radical reactions in living organisms. The examples of non-radical species include hydrogen

peroxide (H₂O₂), hypo-chlorous acid (HOCl), (HNO₂), nitrosyl cation (NO⁺), nitroxyl anion(NO⁻) etc. hypobromous acid (HOBr), ozone(O₃), nitrous acid (Phaniendra *et al.*2015), Figure 1, Table 1.

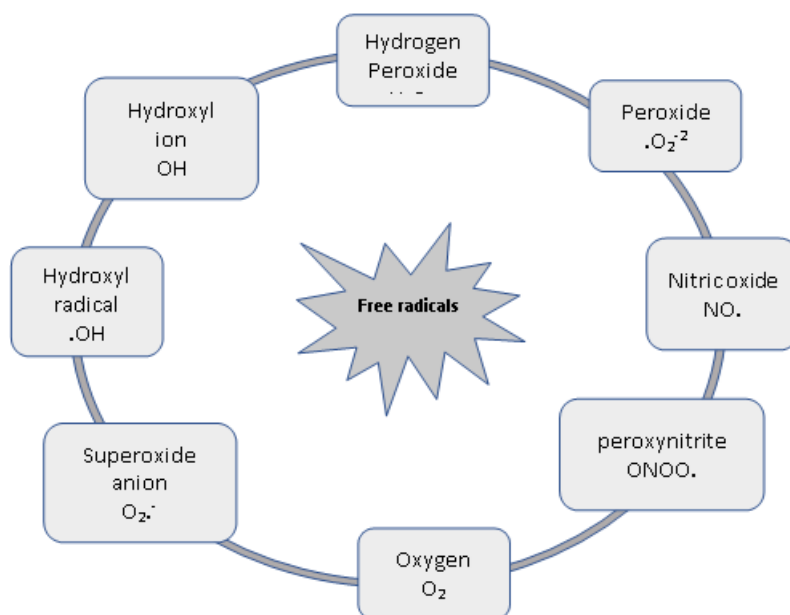


Figure1: Free radicals (ROS and RNS)

Table 1: Different types of reactive oxygen species (ROS) and reactive nitrogen species (RNS)

Reactive Oxygen Species (ROS)	Reactive Nitrogen Species (RNS):
<p>Radicals: O₂⁻ Superoxide .OH Hydroxyl RO₂ Peroxyl RO Alkoxy HO₂ Hydroperoxyl</p> <p>Non-Radicals: H₂O₂ Hydrogen peroxide HOCl Hypochlorous acid O₃ Ozone ¹O₂ Singlet oxygen ONOO- Peroxynitrite</p>	<p>Non-Radicals: ONOO- Peroxynitrite ROONO Alkyl peroxy nitrites N₂O₃ Dinitrogen trioxide N₂O₄ Dinitrogen tetroxide HNO₂ Nitrous acid NO₂⁺ Nitronium anion NO⁻ Nitroxyl anion NO⁺ Nitrosyl cation NO₂Cl Nitryl chloride</p> <p>Radicals: NO Nitric Oxide NO₂ Nitrogen dioxide</p>

Impact of Stress on Women Health

Some of the health hazards of stress are experienced equally both by men and women like weaker immune systems, sleeping disorder and digestive symptoms. But there are other ways stress can affect women's health (Figure 2).

A stressed condition leads to Tension Type Headache (TTH) also known as muscle contraction headache and

stress headache. It is more prevalent in women (88%). Long term tension leads to headache, migraine and body aches (Farooq 2008). Women experience depression twice as likely as men (SAMHSA, 2018). Both acute and chronic stress contribute to the major depressive episodes (MDE) in women with no history of dysthymic disorder (Hammen *et al.* 2009). This can raise their risk of depression and anxiety.

Young women with ischemic heart disease are disproportionately affected by emotional stress (Vaccarino,2014). Women 50 years or younger showed a more adverse psychological profile compared to age-matched men (Vaccarino,2014). Younger women with heart problems are vulnerable to negative effects of stress on the heart (Vaccarino,2014). Short term stressors cause non serious stomach issues but chronic digestive disorders like irritable bowel syndrome (IBS) is twice as common in women as in men in long term stress conditions (Grundmann,2010).

There are various stressors which can interfere with growth and development. In mammals the endocrine stress response system is called limbic-hypothalamic-pituitary-adrenal axis (LHPA). It helps the body remain stable under physiological and psychological stress. Both rapid activation and inhibition of stress response are important for maintaining stress responsiveness. Failure of those places the organism in a fragile state of mind or interferes with growth and development of different systems like the central nervous system. Studies show that women are at greater risk than men for stress induced disorders like emotional eating and obesity in a dietary environment wherein calorically dense diets (i.e., high in fats and sugars; CDD) are available leading to increased body weight (Michopoulos, 2016). The relation between stress and weight gain is stronger in women than men (Michopoulos, 2016). The increased activity of the LHPA axis results in an obese phenotype due to excess glucocorticoids secretion promoting food intake and accumulation of visceral fat (Bjorntorp, 2001). Women are likely more vulnerable to obesity than men because exposure to stress and dysregulation of LHPA alter the behavioral and psychological sensitivity of gonadal hormones (estradiol) and increase anxiety, depression, emotional eating and obesity (Beery,2011).

Women with higher levels of stress are facing problems in conception across the fertile window than women with lower stress levels (Louis,2011). Among different biomarkers for assessing psychological stressors alpha amylase acts as a good biomarker for its secretion from the parotid gland is regulated by the sympathetic medullary system in response to sympathetic stimuli (physical and/or emotional stressors) resulting in increased blood catecholamines (Harmon ,2008). Women with higher concentrations

of alpha amylase were less likely to conceive than women with lower concentrations (Louis,2011).

Long term stress interferes with hormonal changes through the Hypothalamus-Pituitary-Ovary axis in women. Alteration of ovarian hormones render a woman more susceptible to menstrual disorders (Gollenberg, 2010). Stress-induced cortisol rise develops PMS in women through the activation of the hypothalamic-pituitary-adrenal (HPA) axis (Rabin *et al.* 1988). Increased level of cortisol is associated with increased fluid retention and symptoms like bloating, breast tenderness, body aches (Woods *et al.* 1998). Women with PMS are also having altered levels of the neurotransmitters epinephrine, norepinephrine, and serotonin leading to anxiety and mood disorders in women (Woods *et al.* 1998).

Women with long term stress require longer time to get aroused and have a lower sex drive due to increased level of cortisol than women with lower levels of stress (Hamilton and Meston, 2013). The chronic stressors make women distracted during sex (Hamilton and Meston, 2013).

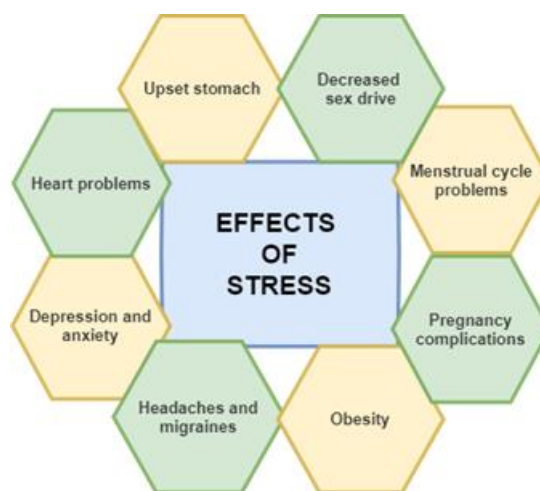


Figure2: Effects of stress on Women health

Antioxidants and Dietary Stress Management

An antioxidant is a molecule capable of neutralizing the damaging potential of free radicals by donating an electron to the rampaging free radical. Antioxidants can terminate the chain reaction initiated by free radicals. During normal metabolic processes some antioxidants like glutathione, ubiquinol, and uric acid are produced. Several enzymatic antioxidants are occurring in our body that prevent the formation of free radicals and neutralize or repair the damage

caused by them (Clark *et al.*, 1985). The principal micronutrients with antioxidant properties are vitamin E (α -tocopherol), vitamin C (ascorbic acid) and vitamin A (β -carotene). Body cannot manufacture these micronutrients, so a dietary supplement is needed.

Enzymatic Antioxidants:

Three groups of enzymes play significant roles in protecting cells from oxidant stress:

Superoxide dismutases (SOD) are enzymes that catalyze the conversion of two superoxides into hydrogen peroxide and oxygen. The benefit here is that hydrogen peroxide is substantially less toxic than superoxide. SOD accelerates this detoxifying reaction roughly 10,000-fold over the non-catalyzed reaction.

SODs are metal-containing enzymes that depend on a bound manganese, copper or zinc for their antioxidant activity. In mammals, the manganese-containing enzyme is most abundant in mitochondria, while the zinc or copper forms predominant in cytoplasm. Interestingly, SODs are inducible enzymes - exposure of bacteria or vertebrate cells to higher concentrations of oxygen results in rapid increases in the concentration of SOD.

Catalase is found in peroxisomes in eucaryotic cells. It degrades hydrogen peroxide to water and oxygen, and hence finishes the detoxification reaction started by SOD.

Glutathione peroxidase is a group of enzymes, the most abundant of which contain selenium. These enzymes, like catalase, degrade hydrogen peroxide. They also reduce organic peroxides to alcohols, providing another route for eliminating toxic oxidants.

In addition to these enzymes, glutathione transferase, ceruloplasmin, hemoxygenase and possibly several other enzymes may participate in enzymatic control of oxygen radicals and their products.

Non-enzymatic Antioxidants

Three non-enzymatic antioxidants of particular importance are:

Vitamin E (α -tocopherol) is a lipid soluble antioxidant (Lazzarino *et al.*, 2019) that provides protection against membrane lipid damage (Nimse *et al.* 2015). Food rich in vitamin E like nuts (almonds, hazelnuts,

peanuts, pistachios), seeds (sunflower, pumpkin), fatty fish, spinach, avocados provide better protection against the oxidative damage caused by different stressors at cellular level.

Vitamin C (ascorbic acid) is a water soluble free radical scavenger (Lazzarino *et al.*, 2019). It changes to ascorbate radicals by donating an electron to the lipid radical and terminating lipid peroxidation. Ascorbic acid cannot be synthesized in our body and must be ingested by food (or supplements) like tomatoes, pineapples, watermelons and all citrus fruits (Banafsheh and Sirous, 2016).

Vitamin A (β -carotene) is a lipid soluble antioxidant that protects lipids against rancidity (Monaghan and Schmitt, 1932). Food rich in vitamin A protects human LDL against copper stimulated oxidation (Livrea, 1995).

CONCLUSION

A society cannot flourish unless a healthy youth persists. A healthy youth cannot sustain itself unless a happy mother survives. To be happy in and out a woman needs to manage the stressors with proper food and lifestyle modifications. Among different stress management strategies diet can be one of them. Foods can either boost the level of serotonin, a soothing brain chemical, or can cut down the levels of stress hormones like adrenaline and cortisol. To overcome any stress and related physiological damage and associated emotional hygiene a balanced diet rich in vitamins and fibers can serve the best.

Antioxidants break radical chain reactions, preventing oxidative stress-related damage. The first class comprises all antioxidants that cells can synthesize from smaller building blocks. Accordingly, all enzymatic antioxidants are endogenous, as well as some non-enzymatic ones (i.e., thiols antioxidants and coenzyme Q10). Primary enzymes (SOD or peroxidases) act directly in scavenging ROS. Secondary enzymes, such as glutathione reductase and glucose-6-phosphate dehydrogenase, support the action of primary enzymes regenerating NADPH and reduced glutathione. On the contrary, exogenous antioxidants have to be ingested through the diet, since their synthesis is impossible in eukaryotic cells. So, particular attention should be paid on this latter class,

since this is the most unpredictable component in cellular redox balance.

Conflict of interest

The author declares that there is no conflict of interest.

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