INTRODUCTION

Stress, undoubtedly, is the most popular medical term used by people all over the world today. It is fashionable for people to complain that they are stressed. Unfortunately, while most of us associate stress with negativity, many of us don’t know that stress can be used to our advantage too, i.e. ‘eustress’, which arises out of happy occasions. It is an exciting experience even though it evokes the same physiological changes in the body as bad stress. However in this situation, the body experiences pleasure rather than any discomfort & it actually encourages more efficient body functioning. Stress in a moment of jest, has been termed as the "mother of all illness".

The term stress describes a state of threatened "homeostasis" or "loss of balance". The disturbing forces are defined as "stressors" which can be work related, family related, social or individual and counteracting forces are called "adaptive responses". The adaptive response to stress depends upon the quality (psychological or physical), strength & duration (chronic & acute) of the stressor. During stress, plasma level of cortisol rises sharply, which is a steroid hormone synthesized by suprarenal cortex and have role in generating hyperglycemia, acts as immunosuppressor, help in the development of CNS in fetus. Regulation of cortisol secretion is done by HPA axis (Hypothalamus-Pitutary-Adrenal Axis). Stress stimuli activate the entire system to cause rapid release of cortisol, and the cortisol in turn initiates a series of metabolic effects directed toward relieving the damaging nature of the stressful state. There is also direct feedback control of the cortisol to both the hypothalamus and the anterior pituitary gland to decrease the concentration of cortisol in the plasma at times when the body is not experiencing stress (Chaudhari S.K. 2008). This is shown in
FIGURE NO. 1: REGULATION OF GLUCOCORTICOID SECRETION
Pregnancy stress situation manifest itself by constant hyperfunction of adrenal cortex. The rate of adrenocortical secretion of the glucocorticoids is moderately increased throughout pregnancy. It is possible that these glucocorticoids help in mobilizing amino acids from the mother's tissues so that these can be used for synthesis of tissues in the foetus. Pregnant women usually have about a two fold increase in the secretion of aldosterone, reaching a peak at the end of gestation. This, along with the actions of estrogens, causes a tendency for even a normal pregnant woman to reabsorb excess sodium from her renal tubules and, therefore, to retain fluid, occasionally leading to pregnancy-induced hypertension (Guyton A, 2006). The nine months of pregnancy, although physiologically normal, is seen as a period of stress, during which the nutritional need of the developing fetuses is dependent on the mother. It is more stressful to primiparous women, who face the challenges of pregnancy. Thus pregnancy stress is due to endocrine, metabolic & psychological changes.

Pregnancy is mostly because of the mitochondria-rich placenta, a condition that favours oxidative stress, defined here as a disturbance in the pro-oxidant & antioxidant balance in favour of the former, leading to potential damage. Oxidative stress peaks by the second trimester of pregnancy. It is characterized by dynamic changes in multiple body systems resulting in increased basal oxygen consumption and changes in energy substrate use by different organs including the fetoplacental unit. From early pregnancy the human placenta influences maternal homeostasis; it is rich in mitochondria and when fully developed consumes about 1% of the basal metabolic rate of the pregnant women. It is highly vascular and is exposed to high maternal oxygen partial pressure. These characteristics explain, in part, the generation of superoxide
and other free radicals, because about 5% of all electrons in the mitochondrial respiratory chain leak out of the mitochondria (Sies H. et al., 1991). The human placenta is hemomonochorial, meaning that only one chorionic cell layer exists between maternal and fetal bloods, favouring exchanges of gases, nutrients and metabolic products. Initially the placenta, has a hypoxic environment, as it matures and its vascularization develops, it changes to an oxygen-rich environment and its abundant mitochondrial mass favours the production of reactive oxygen species (ROS) (Page K.R et al., 1993).

Now-a-days lipid peroxidation has become an acceptable trend in medicine to consider it at molecular level. Lipid peroxidation is an oxidative process which occurs at low levels in all cells and tissues. Under normal conditions a variety of antioxidant mechanisms serve to control this peroxidative process.

Oxidative stress and free radical formation can cause birth defects, abortion and miscarriages in pregnancy, more and more stress is being laid on the biochemical changes, which occur in the blood during normal pregnancy which is becomes exaggerated in complications of pregnancy like pre-eclampsia, gestational diabetes mellitus etc. The supplementation with antioxidants protects the fetus and mother from the harmful effect of oxidant stress in fertility (D. Wickens et al., 1981).

Hypertensive medical disorder are the most common medical complications of pregnancy causing mobidity and mortality to both mother and child, with a reported incidence ranging between 5%-10% (Sibai BM, 1992). Pre-eclampsia is a common problem during pregnancy, affecting upto one in seven pregnant women around the world (Dutta DC et al, 2004). In India the national incidence of PIH
is 15.2% and the incidence of pre-eclampsia is reported to be 8-10% of the pregnancies (Krishna menon et al, 1994).

**Pregnancy Induced Hypertension (PIH)** is a syndrome of hypertension in pregnancy with or without proteinuria and oedema. If associated with proteinuria then the condition is known as pre-eclampsia, which may occur as early as 20 weeks of pregnancy and more common in nulliparous women.

Oxidative stress increases during pre-eclampsia and results in increased production of lipid peroxides, reactive oxygen species and free radicals to cause endothelial injury and dysfunction (Vascular endothelial dysfunction may be caused by uncontrolled lipid peroxidation), platelet and neutrophil activation abnormal placentation, (Dutta DC et al, 2004 and Riza M et al, 1999). These observations in pre-eclampsia have given rise to increased interest in antioxidants such as Ascorbic acid (Vitamin C), Vitamin E and Uric acid. Although Pre-eclampsia contributes significantly to maternal and fetal morbidity and mortality, the etiology of which is described as increased thromboxane and decreased prostacyclin production (Walsh SW et al, 1985; Friedman SA et al, 1991). The imbalance between thromboxane and prostacyclin is probably caused by the increase in oxidative stress because oxidative stress increases the synthesis of thromboxane, but decreases the synthesis of prostacyclin.

Vascular endothelial damage is known to play a role in the pathophysiologic mechanisms of preeclampsia. Endothelial cell injury is thought to decrease prostacyclin synthesis, resulting in an increase in peripheral vascular resistance and platelet aggregation (Rodger GM et al, 1998 and Roberts JM et al, 1989). The pathogenesis of such endothelial cell injury, however remains
unclear. It has been suggested that free radical cell-mediated lipid peroxidation may be involved. The several reports support this concept, that is increase in lipid peroxidation products (Maseki M et al, 1989) and a decrease in antioxidant activity (Davidge ST et al, 1992) in pre-eclampsia compared with normal pregnancy. In addition, lipid peroxidation of the platelet lipid membrane has recently been shown to occur in pre-eclampsia (Garzetti GG et al, 1993), which may predispose to platelet membrane damage and increased platelet aggregation. Antioxidant nutrients counteract free radical disturbances and thereby protect cell membranes against free radical-mediated lipid peroxidation (Piyor WA et al, 1984; Wisdom SJ et al, 1991). Excess free radical disturbances are typically accompanied by increased utilization of antioxidants, resulting in their decrease concentrations (Freeman B. et al, 1982). Normal pregnancy favours the actions of prostacyclin, but preeclamptic pregnancy favours the actions of thromboxane.

Pregnancy is a potentially diabetogenic condition due to numerous hormonal and metabolic changes that occur. An inherent genetic predisposition to insulin resistance and/or insulin deficiency can get unmasked, though temporarily, in the pregnant woman. This then needs to be identified speedily as otherwise, both maternal and fetal outcomes can be adversely affected. Therefore, screening tests for the condition are warranted. (Neeta Deshpande, 2010).

A study done in India reported the prevalence of known diabetes and Gestational Diabetes Mellitus (GDM) to be 1.19 and 0.56%, respectively (Ramachandran et al, 1994). Based on the National Diabetes Data Group criteria, the percentage of pregnant diabetic women who had GDM was 4%. (National Diabetes Data group, 1979). However, the fourth international Workshop-Conference on
Gestational Diabetes showed that the percentage of non diabetic pregnant women having GDM increased to 7% resulting in more than 200,000 cases annually (Naylor CD et al,1996). Similar study done in Australia in 2005-06, diagnosed GDM in 4.6% of women aged 15 to 49 years (GDM in Australia, 2005-6).

The risk of GDM increases with age, from 1% among 15 to 19 year to 13% among women aged 44 to 49 years. Women aged 30 to 34 years accounted for more than one-third of GDM cases in 2005-06 (GDM in Australia, 2005-6).

GDM may develop at any stage of pregnancy, but most commonly appears after the middle of the second trimester i.e. between 24 to 28 weeks of gestation, which is defined as glucose intolerance of variable severity with onset or first recognition during pregnancy (Metzer BE et al, 1997), irrespective of whether the condition persist or not after pregnancy. This is regardless of the therapy uses and the reclassified status after pregnancy. For example, it could be unrecognized type 1 or type 2 diabetes.

It is one of the common medical condition during pregnancy, some of them are overt and others are gestational diabetes. It is detected first time during pregnancy and becomes normoglycemic in postpartum period. Due to increased level of human placental lactogen, steroid hormones there is marked insulin resistance during pregnancy and some of these ladies will come in the boundary of gestational diabetes.

Glucose tolerance deteriorates in human pregnancy, but about 97% to 98% of all pregnant women retain a normal glucose tolerance and only 2% to 3% develop GDM (Kuhl C.et al, 1991). Although the blood sugar level comes to normal level during
postpartum, these ladies have high chance of developing overt diabetes in their future life.

Diabetes is associated with a greater incidence of congenital anomalies in comparison with non diabetic pregnancy. Frequency of congenital malformation among infants of diabetic is estimated to be 6%-10% (Hagay ZJ, 1995; Reece EA et al, 1998). Factors responsible for these abnormalities are not fully understood but there are reports suggesting that increased free radical production and antioxidant depletion in diabetic pregnant female may contribute to this risk (Eriksson UJ et al, 1991).

**Anemia** during pregnancy is a commonest medical disorder that have deleterious effects on mother and as well as on fetus in the form of maternal morbidity and mortality, intrauterine growth retardation, poor weight gain, premature labor, preterm delivery and perinatal morbidity and mortality (Bothwell TH et al, 2000). Among pregnant women at least half of all anemia cases have been attributed to iron deficiency. In India about 90% of anemia cases are reported to be due to iron deficiency, because high iron requirements during pregnancy are not easily fulfilled by dietary intake alone, especially when iron bioavailability is poor (Galan P et al, 1990), because of religious reasons, poverty, or both. Indian population observes dietary patterns that are largely vegetarian (Sharma JB et al, 2003). There are also reports that iron deficiency can lead not only to anemia but it may also impair work performance, lead to an abnormal neurotransmitter function and result in altered immunological and inflammatory defences. In severe anemia hemoglobin is less than 80 g/l in the first half of pregnancy is proved to be associated with preterm delivery and small-for-gestational-age fetus (Scanlon KS et al, 2000; Schumann K et al, 2001). In contrast, the values of borderline anemia (95-
105g/l of Hb) appear to be related to the minimum incidence level of preterm delivery (Steer PJ et al, 2000).

The prevalence of iron deficiency anemia in pregnancy is still on the high in developing countries like India though a lot is known about it and many treatment strategies are available. The increasing prevalence could be due to poor compliance which is attributed to the side effects that arise during oral iron supplementation.

Oxidative stress as shown to play an important role in pathogenesis of Iron Deficiency Anemia [IDA] (Vives et al, 1995). Furthermore, it has been shown that the addition of synthetic antioxidants in the treatment of IDA results in decrease of lipid peroxidation, prevention of pathologic progression and rapid improvement of clinical manifestations (Shved et al, 1995). This confirms iron deficiency anemia is a state of oxidative stress.

The effects of antioxidants with oral iron to combat the stress and side effects have been tried in both human subjects (Carrier et al 2002) and animals (Srigiridhar, Madhavan Nair 2000).