SUMMARY

Antioxidants like glutathione, superoxide dismutase, Vitamin C, and E are crucial to all stages of pregnancy i.e. From pre-conception to fetal growth and development, to labor and post-natal development. They help to protect the fetus from the damaging effects of pollutants, carcinogens and teratogens, and provide protection against the oxidative stress that is known to cause congenital malformations, abortion and miscarriage. These antioxidants are crucial in preventing oxidative stress in pregnant women with inflammation or disease conditions like diabetes and pre-eclampsia, or in fetuses at risk for developing cystic fibrosis.

Antioxidant supplementation can decrease the incidence of birth defects and protect both mothers and the fetuses from the damaging and possibly fatal consequences of pregnancy complications.

In the present study, the first group consist of 100 healthy non-pregnant women was studied. Second group was age and socio-economic status matched 100 healthy normal pregnant women. The third group was included 100 pregnant women with Iron Deficiency Anemia. Fourth group was 100 pregnant women with Gestational Diabetes Mellitus and last study group included 75 pregnant women with mild preeclampsia & 25 women with severe preeclampsia. All the study groups were assessed for serum MDA, Vitamin C, E, Uric acid, lipid profile and Erythrocytic SOD, Catalase.
In the non pregnant women serum MDA level was 2.39±0.63 nmoles/ml, while in normal pregnant women it was 2.85±0.46 nmoles/ml. This change was less significant with p value of <0.05. Erythrocytic SOD and Catalase in non pregnant women was 767.9±49.8 U/gm Hb and 7.12±0.89 U/mg Hb respectively. While in normal pregnant women SOD was 689.4±37.5 U/gm Hb & Catalase was 6.28±0.95 U/mg Hb. Change in SOD was with p value of <0.001 & in Catalase with p value of <0.05. Serum Ascorbate, α-Tocopherol and Uric acid in non pregnant was 0.99±0.13 mg/dl, 1.42±0.27 mg/dl and 3.92±0.86 mg/dl respectively. This level in normal pregnant women was 0.89±0.08 mg/dl, 0.87±0.09 mg/dl and 3.74±0.82 mg/dl respectively. Change in ascorbate level in normal pregnant women was non significant with p value of <0.05, in α-tocopherol highly significant with p value of <0.001 and in Uric acid less significant (p>0.05). Significant increase in MDA and significant decrease in enzymatic and non enzymatic antioxidant shows oxidative stress environment in normal pregnancy. Serum total Cholesterol, Triglyceride, HDL-C, LDL-C, VLDL-C were 169.9±14.2 mg%, 101.9±13.7 mg%, 57.9±8.41 mg%, 90.1±15.5 mg%, 20.38±2.99 mg% in non pregnant control group, respectively. Value of these parameters in normal pregnant women were 232.4±43.1 mg%, 175.2±15.6 mg%, 65.2±12.0 mg%, 126.7±14.2 mg%, 35.06±5.63 mg%, respectively. Highly significant increase (p<0.001) was observed in Total Cholesterol, Triglyceride, LDL-C and VLDL-C in normal pregnant women compared to non pregnant women. In HDL-C, non significant (p>0.05) change was observed.

In conclusion, results of present study have shown higher oxygen free radical production and decreased antioxidant activity, which supports the higher oxidative stress hypothesis in pregnancy.
One of the common short term control of Iron deficiency anemia is oral iron supplementation (Srigiridhar, Nair KM 2000). Iron Deficiency anemia ranks 9th among 26 diseases with highest burden. Asia bears 71% of this global burden. Adverse maternal and birth outcome associated with hemoglobin status renders the issue worth attention. Indian scenario has worsened over the period despite continuous international and national efforts. This indicates some lacunae in the approach and strategies applied. Various reports state that even with maximum effort to increase outreach and monitoring for adherence to Iron schedule, consumer’s compliance remains abysmally low. Recent studies has pointed out biological basis of side effects (gastrointestinal complains and systemic events) as raised oxidative stress for which iron is the key catalyst. Up till now the only target of research has been to raise hemoglobin of pregnant women above 11gm/dl. With the reports of pregnancy specific morbidities i.e. hemorrhage and septicemia with low hemoglobin, eclampsia, small for gestation age, gestational diabetes with higher ranges of hemoglobin, alarm is raised to define optimum range. Use of oxidative stress as biochemical marker with different doses and schedules has been defined because India lack information for its own population upon oxidative stress status when iron is supplemented as per current guidelines. Studies done in India and abroad have defined that too much and too less, both may raise oxidative stress and studies of this sort may provide biochemical scale for optimization. (Neeta kumar et al, 2009)

In the Iron Deficiency Anemia study group MDA was 3.54±0.72 nmoles/ml, which increased higly significantly (p<0.001), compared to normal pregnant women. SOD and Catalase were
645.3±22.9 U/gm Hb, 5.90±0.73 U/mg Hb respectively, showed significant decrease \( p<0.001 \), compared to normal pregnant control group. Serum Ascorbate was 0.70±0.08 mg%, α-tocopherol was 0.68±0.06 mg%, showed significant decrease with \( p \) value of <0.001. Uric acid showed non significant change \( p>0.05 \), compared to normal pregnant women. Total Cholesterol was 259.1±27.0 mg%, TG was 230.8±42.1 mg%, HDL-C was 60.21±9.57 mg%, LDL-C was 152.6±12.5 mg% and VLDL-C was 46.27±2.93 mg%. Highly significant increase \( p<0.001 \) observed in TG, LDL-C, VLDL-C and less significant \( p<0.05 \) increase in Total Cholesterol while decrease \( p<0.05 \) in HDL-C, compared to normal pregnant women.

On the basis of the results of the present study, it may be concluded that iron deficiency anemia is associated with free radical generation; abnormalities and peroxidation of vital body molecules which implies increased risk for pregnant women as well as for fetous. However, further in-depth studies are needed to assess the status of antioxidant in pregnancy related abnormality. Gestational diabetes induces a condition of oxidative stress leading to an easier membrane lipoperoxidability and consequently easier membrane damage during diabetic gestation.

The magnitude of GDM varies according to the country and their ethnical groups. The lifestyle, educational status, history of diabetes in family and many other factors play an important role (Harlass 1991; Lavin et al 1981). In developing country like India, early detection and prevention will be more cost-effective.

In the Gestational Diabetes Mellitus study group MDA was 3.47±0.62 nmoles/ml, which increased highly significantly \( p<0.001 \), compared to normal pregnant women. SOD and Catalase were
425.7±37.7 U/gm Hb, 6.11±0.89 U/mg Hb, respectively, showed significant decrease (p<0.001), in SOD and less significant (p<0.05) decrease in catalase compared to normal pregnant control group. Serum Ascorbate was 0.73±0.08 mg%, α-tocopherol was 0.77±0.1 mg%, showed significant decrease with p value of <0.001 in Ascorbate and less significant decrease (p<0.05) in α-Tocopherol. Uric acid showed significant increase (p<0.001), with serum value of 5.26±0.66 mg% compared to normal pregnant women. Total Cholesterol was 237.0±57.1 mg%, TG was 249.1±22.4 mg%, HDL-C was 66.3±11.2 mg%, LDL-C was 115.6±12.3 mg% and VLDL-C was 49.85±3.69 mg%. Highly significant increase (p<0.001) observed in TG, VLDL-C and non significant (p>0.05) change in Total Cholesterol, HDL-C and LDL-C compared to normal pregnant women.

The increased oxidative stress is demonstrated in pregnant women with GDM in present study. There is decrease in antioxidant activity and increased free radical generation indicate antioxidants are consumed by enhanced levels of free radicals produced during glucose induced oxidative stress.

It is interesting that women with diabetes mellitus are at increased risk for preeclampsia (Chappel LC et al, 2002a). There is evidence that this disease is associated with endothelial cell compromise and elevated plasma and/or artery tissue lipid peroxides (Yagi K, 1982 et al; Nishigaki I et al, 1981). If future work confirms an etiologic role for lipid peroxidation in preeclampsia, antioxidant therapy, perhaps in combination with dietary omega-3 fatty acids, might be of value in shifting the thromboxance-prostacyclin balance toward a less thrombogenic state and preserving the overall integrity of the vascular endothelium (Walsh SW et al 1985, et al)
In the mild preeclampsia study group MDA was $5.15 \pm 0.68$ nmoles/ml, and in severe preeclampsia it was $5.87 \pm 0.74$ nmoles/ml which increased highly significantly $(p<0.001)$ compared to normal pregnant women. SOD was $419.0 \pm 35.1$ U/gm Hb, in mild preeclampsia and in severe preeclampsia it was $435.5 \pm 12.3$ U/gm Hb showed significant decrease $(p<0.001)$, compared to normal pregnant control group. Erythrocytic Catalase was $5.39 \pm 0.59$ U/mg Hb in mild preeclampsia and $5.56 \pm 0.55$ U/mgHb in severe preeclampsia, which decreased significantly $(p<0.01)$ compared to normal pregnant women. Serum Ascorbate was $0.78 \pm 0.07$ mg% in mild preeclampsia & $0.75 \pm 0.05$ mg% in severe preeclampsia, α-tocopherol was $0.52 \pm 0.08$ mg% in mild preeclampsia & $0.50 \pm 0.06$ mg% in severe preeclampsia, showed significant decrease with $p$ value of $<0.001$ compared to normal pregnant women. Uric acid showed significant increase $(p<0.001)$, with serum value of $6.25 \pm 0.63$ mg% in mild preeclampsia & $6.34 \pm 0.5$ mg% in severe preeclampsia compared to normal pregnant women. Total Cholesterol was $310.6 \pm 25.9$ mg%, TG was $271.31 \pm 19.2$ mg%, HDL-C was $68.9 \pm 11.7$ mg%, LDL-C was $187.3 \pm 13.7$ mg% and VLDL-C was $54.35 \pm 7.68$ mg%. In mild preeclampsia, highly significant increase $(p<0.001)$ observed in TC, TG, LDL-C, VLDL-C and non significant $(p>0.05)$ increase in HDL-C compared to normal pregnant women. Total Cholesterol was $315.9 \pm 13.1$ mg%, TG was $275.7 \pm 20.4$ mg%, HDL-C was $69.24 \pm 7.84$ mg%, LDL-C was $190.6 \pm 16.5$ mg% and VLDL-C was $55.02 \pm 7.20$ mg% in severe preeclampsia. Highly significant increase $(p<0.001)$ observed in TC, TG, LDL-C, VLDL-C and non significant $(p>0.05)$ increase in HDL-C compared to normal pregnant women.
Lipid peroxides could be a part of the cytotoxic mechanisms leading to the endothelial injury. The decreased concentrations of the antioxidant supports the hypothesis that lipid peroxidation is an important causative factor in the pathogenesis of preeclampsia. Present study supported by the studies of Wickens D. et al (1981) who found lipid peroxidation as an important causative factor in the pathogenesis of PIH. Therefore, the treatment with antioxidants in the initial stages of the disease may be useful as secondary therapy to prevent the Oxidative damage.

Human defense mechanisms against oxidative stress and free radical damage primarily consist of antioxidant enzymes and antioxidants nutrients. The antioxidant enzymes (superoxide dismutase, catalase, and glutathione peroxidase) are synthesized in the body, and their concentrations cannot be easily influenced. In contrast, antioxidant nutrient levels can be simply manipulated by dietary or pharmacologic supplementation. The concept of increased utilization of reduced ascorbic acid α-tocopherol, and beta-carotene in normal and abnormal pregnancy raises the possibility of a potential protective role for antioxidant nutrients. It is tempting to speculate that adequate plasma or placental tissue concentrations of antioxidants in women destined to develop GDM and preeclampsia may inhibit the initiation or propagation of free radical-mediated lipid peroxidation and thereby protect against endothelial cell damage.

Further work is needed to support the preliminary findings of the present study to elucidate the mechanism(s) involved in the disorders associated with pregnancy.