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Original Research Article

Stress and Lipid Peroxidation in Pregnancy and Associated Disorders

Ricky Mittal[1], Vikas Saxena[2]

[1]Associate Professor, Department of Biochemistry, Krishna Mohan Medical College & Hospital, Pali Dungra, Sonkh Road, Mathura U.P.

[2]Assistant Professor, Department of Biochemistry, Krishna Mohan Medical College & Hospital, Pali Dungra, Sonkh Road, Mathura U.P.

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Corresponding author: Mr. Vikas Saxena

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Abstract

Background: Glutathione, superoxide dismutase, Vitamin C, and E are antioxidants that are essential for all phases of pregnancy, including conception, fetal growth and development, labor, and postpartum health. They offer defense against oxidative stress, which is known to induce congenital abnormalities, abortion, and miscarriage, as well as protection against the harmful effects of pollutants, carcinogens, and teratogens on the developing fetus. Free radical production is a physiologically normal process, and cells have developed a variety of antioxidant defenses to offset their oxidative effects. These antioxidants are essential for avoiding oxidative stress in babies at risk of developing cystic fibrosis or in pregnant mothers with inflammation or illness states like diabetes and pre-eclampsia. Supplementing with antioxidants can lower the risk of birth abnormalities and shield moms and fetuses from the harmful and potentially fatal effects of pregnancy problems.

Aim: The current study aims to compare the lipid profiles of normal pregnant women to non-pregnant women in order to evaluate lipid peroxidation as measured by malondialdehyde (MDA), enzymatic antioxidant activities such as Superoxide dismutase and Catalase, and non-enzymatic antioxidant activity such as ascorbic acid, alpha-tocopherol, and uric acid.

Material and Method: The first group in the current study, 50 healthy non-pregnant women, was examined. 50 healthy, typical pregnant women in the second group were matched for age and socioeconomic status. 100 pregnant women with iron deficiency anemia made up the third group. The final study group consisted of 35 pregnant women with mild preeclampsia and 15 pregnant women with severe preeclampsia. The fourth group consisted of 50 pregnant women with gestational diabetes mellitus. Serum MDA, Vitamin C, E, Uric acid, lipid profile, and erythrocytic SOD and Catalase levels were evaluated in all study groups.

Results: In the current investigation, normal pregnant women had considerably higher serum levels of malondialdehyde (MDA). When compared to non-pregnant women, the erythrocytic SOD was considerably lower in normal pregnant women. When compared to non-pregnant women in the current study, ascorbic acid shows a less significant decline and -tocopherol shows a highly significant decrease in normal pregnant women. Compared to non-pregnant women, typical pregnant women's serum uric acid changes insignificantly. When normal pregnant women are compared to non-pregnant women in the current study, total cholesterol, triglycerides, LDL cholesterol, and VLDL cholesterol all rise significantly, while HDL cholesterol does not alter appreciably.

Conclusion: Based on the findings of the current study, it can be deduced that iron deficiency anemia is linked to the production of free radicals, anomalies, and peroxidation of critical body molecules, increasing the danger for both pregnant women and fetuses. To evaluate the status of antioxidant in pregnancy-related disorder, more extensive research is required. During a diabetic pregnancy, gestational diabetes causes an oxidative stress situation that makes membrane damage and lipoperoxidability easier to occur.

Keywords: Adrenocorticotropin Hormone, Extra Cellular- Superoxide Dismutase, Reduced Glutathione, High Density Lipoprotein-Cholesterol.

Introduction

Unquestionably, the most often used medical term in today's society is "stress." Nowadays, it's common for people to express their tension through complaint. Unfortunately, even while most people equate stress with negative, many people are unaware that stress can also be used positively, or that positive stress, or "eustress," can result from pleasurable circumstances. Even though it causes the same physiological changes in the body as harmful stress, it is nonetheless an enjoyable experience. However, under this circumstance, the body feels pleasure as opposed to any discomfort, and it even promotes more effective body functioning. In humor, stress has been referred to be the "mother of all illnesses." [1]

The placenta's high concentration of mitochondria makes pregnancy particularly conducive to oxidative stress, which is defined here as an imbalance between pro-oxidants and antioxidants that favors the former and could cause harm. The second trimester of pregnancy is when oxidative stress peaks. It is characterized by dynamic alterations in numerous bodily systems that lead to a rise in basal oxygen demand and modifications in the way that various organs, including the fetoplacental unit, use energy substrates. The human placenta affects maternal homeostasis from the beginning of pregnancy; it is abundant in mitochondria and, when fully mature, uses up around 1% of the pregnant woman's basal metabolic rate. [2]

According to a study conducted in India, the prevalence of gestational diabetes mellitus (GDM) and recognized diabetes was 1.19 and 0.56%, respectively. [3] According to the National Diabetes Data Group's standards, 4% of pregnant diabetes women had GDM. The fourth worldwide Workshop-Conference on Gestational Diabetes, however, revealed that 7% of pregnant women who are not diabetic have GDM, amounting to more than 200,000 cases each year. [4]

More and more emphasis is being placed on the biochemical changes that occur in the blood during a normal pregnancy and are accentuated in pregnancy disorders such pre-eclampsia, gestational diabetes mellitus, etc. since they can result in birth abnormalities, abortions, and miscarriages. Antioxidant supplements shield the mother and fetus from the damaging effects of oxidative stress on fertility. [5]

At least half of all anemia occurrences in pregnant women have been linked to an iron deficit. The majority of the Indian population follows a vegetarian diet. Pregnancy Induced Hypertension (PIH) is a syndrome of pregnancy-induced hypertension that may or may not be accompanied by proteinuria and edema. Due to the multiple hormonal and metabolic changes that pregnancy brings about, it may be a condition that causes diabetes. When a woman is pregnant, a hereditary tendency to insulin resistance and/or insulin insufficiency may become briefly apparent. [6]

Despite extensive research and a wide range of treatment options, the prevalence of iron deficiency anemia in pregnancy is still significant in underdeveloped nations like India. It has been established that oxidative stress is a key factor in the development of Iron Deficiency Anemia (IDA). [7] Additionally, studies have demonstrated that including synthetic antioxidants in the therapy of IDA reduces lipid peroxidation, stops pathologic development, and improves clinical symptoms quickly. [8] Both human test participants and animals have experienced the effects of antioxidants combined with oral iron to prevent stress and adverse effects. [9,10]

Material and Methods

The present study was carried out in the Department of Biochemistry. Patients were selected from OBGY OPD and ward of the hospital. Informed consent, both in English as well as vernacular language, was taken from all the participants included in the study.

Selection of Patients

To study, lipid peroxidation in pregnancy, total 200 samples were analysed.

Study groups were divided in five categories;

Group 1 Non pregnant healthy women (n=50)

Group 2 Normal pregnant healthy women (n=50)

Group 3 Pregnant women with iron deficiency anemia (n=50)

Group 4 Pregnant women with Gestational Diabetes Mellitus (n=50)

All these cases were studied for lipid peroxide (MDA), Superoxide dismutase activity (SOD), Catalase, Vitamin C and E, Uric acid, Lipid profile (Total cholesterol, Triglycerides, HDL-C, LDL-C, VLDL-C) by different standard methods.

Age & Gestational age (2nd and 3rd trimester) match subjects of same socioeconomic and nutritional status of healthy normal pregnancy & abnormal single tone pregnancy were selected from females reporting to Gynecology and Obstetrics Department.

Inclusion Criteria:

The cases with a history of multivitamin use in the past, diabetes mellitus, hypertension, renal illnesses, liver disorders, and hyperlipidemia were eliminated. Before beginning the administration of magnesium sulfate and hydralazine, fasting venous blood samples were taken. All the normal and abnormal pregnancy subjects were proved by Gynaecology and Obstetrics Department

Exclusion Criteria: Women who had a history of anemia and were taking hematinics were not included in the study. The typical pregnant women were overweight, diabetic, taking medicine but not treating their diabetes, hypertensive, and highly anemic.

Blood Sample Collection:

All individuals underwent venipuncture between the hours of 8 and 9 a.m. to obtain 10 ml of fasting blood samples, with or without the use of anticoagulants depending on the parameter to be measured. Blood samples were centrifuged to separate the serum, which was then stored at 4°C and used to estimate various parameters. For the assessment of hemoglobin, SOD, and catalase activity, blood cells were washed four times with normal saline before being produced as lysate. The UV-VIS Spectrophotometer 1240 was used to evaluate every parameter.

Methods

1. Estimation of Serum Malondialdehyde (MDA) Method - Buege and Aust, 1978 [11]
2. Specific Activity of Erythrocytic Superoxide Dismutase (SOD) Method: Kakkar et al, 1984 [12]
3. Estimation of Hemoglobin Method: Dacie J.V. et al, 1984 [13]

4. Estimation of Serum Vitamin E (Alpha-Tocopherol) Method: Baker and Frank, 1968 [14]
5. Estimation of Serum Uric Acid Method: CaraWay, W.T., 1963 [15]
6. Estimation of Total Cholesterol Method: Altair C.C., et al, 1974 [16]
7. Estimation of Triglycericles Method: Werener M, Gabrielson D.G. Estman (1981) [17]
8. Estimation of HDL-Cholesterol Method: Izzo C. et al, 1981 [18]

Statistical analyses: Data are given as the mean ± S.D. Differences between groups were analysed, by using "two sample t-statistics under basic statistical module", of "Minitab" software, confidence of Interval was 95% Significant levels were always taken at 0.05.

Result: -

Table 1: Serum Malondialdehyde, SOD, catalase, Ascorbate, Serum alpha-tocopherol, Uric Acid, Total cholesterol, Triglyceride HDL-C, LDL-C and VLDL-C levels in Non-Pregnant & Normal pregnant women.

Number of Cases	Non-Pregnant Women	Normal Pregnant Women
MDA (nmol/ml)	1.29±0.53	1.65±0.46
SOD (U/g Hb)	656.4±39.5	562.2±27.4
Catalase (U/mg Hb)	5.09±0.69	4.18±0.75
Ascorbate (mg/dl)	0.88±0.10	0.79±0.06
α-Tocopherol (mg/dl)	0.92±0.07	0.47±0.03
Uric Acid (mg/dl)	2.22 ±0.66	2.54±0.72
Total cholesterol (mg/dl)	149.9±11.1	206.2±23.1
Triglyceride (mg/dl)	93.7±11.5	144.1±10.3
HDL-C(mg/dl)	45.4±6.21	55.2±9.0
LDL-C (mg/dl)	70.1±10.3	114.3±11.1
VLDL-C(mg/dl)	15.25±1.66	22.04±3.63

Table 2: Serum Malondialdehyde, SOD, catalase, Ascorbate, Serum alpha-tocopherol, Uric Acid, Total cholesterol, Triglyceride HDL-C, LDL-C and VLDL-C in normal pregnant women and study groups.

S. N.	Number of Parameter	Pregnant women with anemia	Pregnant women with GDM	Pregnant women with preeclampsia
1	MDA (nmol/ml)	2.44±0.52	2.37±0.52	3.13±0.58
2	SOD (U/g Hb)	532.1±18.4	395.4±32.2	401.0±25.1
3	Catalase (U/mg Hb)	4.80±0.53	4.09±0.79	4.29±0.35
4	Ascorbate (mg/dl)	0.60±0.04	0.55±0.04	0.62±0.05
5	α-Tocopherol (mg/dl)	0.53±0.04	0.66±0.2	0.42±0.06
6	Uric Acid (mg/dl)	2.74±0.82	4.16±0.55	5.18±0.43
7	Total cholesterol (mg/dl)	218.1±18.0	127.0±44.1	211.2±22.6
8	Triglyceride (mg/dl)	128.5±32.1	139.1±19.3	161.3±14.2
9	HDL-C(mg/dl)	54.17±6.37	60.3±8.2	64.5±7.5
10	LDL-C (mg/dl)	132.4±8.5	103.3±8.2	164.2±10.5
11	VLDL-C(mg/dl)	39.21±1.73	41.65±2.54	44.25±6.48

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 in non-pregnant control group, respectively. Value of these parameters in normal pregnant women where highly significant increase change was observed.

Discussion

An increased need for oxygen and a high energy demand are both physiological aspects of pregnancy. As pregnancy progresses, several compensatory and adaptive changes take place to meet the demands of the fetus. [19] A situation like this could be the cause of increased oxidative stress during pregnancy. An oxidative stress occurs when the amount of reactive oxygen species present exceeds the antioxidants' capacity to act as a buffer. [20] It has been linked to preeclampsia, cancer, atherosclerosis, and numerous other human illnesses. [21]

The pathophysiology of many clinical illnesses is thought to involve spontaneous responses such lipid peroxidation and glycation. Elevated glucose concentrations accelerate protein glycation. However, iron deficiency anemia patients who have never had diabetes have been shown to have higher amounts of glycated hemoglobin. It is clear from the available data that lipid peroxidation can influence protein glycation. [22] Diabetes mellitus is a condition defined by a disruption of glucose homeostasis. Lalita chaudhari et al. [23] and Bates et al. [24] discovered an increase in MDA levels in women with gestational diabetes mellitus (GDM). [25] Malondialdehyde levels in patients with pre-eclampsia rise above normal pregnancy levels by the second trimester. [26,27] These oxygen species can then oxidize many other significant biomolecules, including membrane lipids. It has been observed that elevated blood glucose levels induce oxidative stress and diabetes. The pathophysiology of preeclampsia may involve 98 free radicals and lipid peroxides. [28]

Since it is widely established that ROS, particularly hydrogen peroxide (H2O2), block SOD function, decreased SOD activity in IDA may be related to increased oxidative stress (Isler M et al, 2002). [29]

In the current investigation, a substantial reduction in catalase activity was seen in preeclamptic patients compared to healthy pregnant women. The enzyme known as catalase prevents hydrogen peroxide from building up in the cells by dismuting it into water and oxygen. [30] Throughout the gestational phase, Kumar and Das [31] observed a declining trend in the levels of vitamin C, however the decline was not statistically significant when compared to the levels in controls.

Given their well-known role in reducing free radical damage, vitamins C and E are crucial to have enough of throughout pregnancy. Insufficient vitamin C alters placental structure, and ROS promotes placental infection, both of which increase the risk of early placental membrane rupture and preterm birth. [32,33]

The increase in uric acid may be a defensive reaction designed to counteract the negative consequences of oxidative stress and free radical activity. The insulin resistance syndrome is consistently characterized by elevated serum uric acid. [34]

Estrogen is the hormone that causes TG and HDL-C to be produced. Therefore, insulin resistance and hyperestrogenemia are to blame for the hyperlipidemia in pre-eclampsia. [35] In both our study and those of other researchers, a significant increase in LDL-C levels was observed in pre-eclampsia when compared to controls. Pre-eclampsia is associated with an increase in autoantibodies against MDA-LDL and oxidized LDL. This increased lipid peroxidation contributes to the development of preeclampsia by causing foam cells to grow in the decidua. [36,37]

Conclusion

Antioxidant enzymes and antioxidant substances are the main components of human defense mechanisms against oxidative stress and free radical damage. The body produces the antioxidant enzymes (superoxide dismutase, catalase, and glutathione peroxidase), and it is difficult to change their levels. The levels of antioxidant nutrients, however, can easily be changed through dietary or pharmaceutical supplementation. The idea that lower ascorbic acid -tocopherol and beta-carotene are used more frequently during both healthy and abnormal pregnancies suggests that antioxidant nutrients may have some protective benefits. It is tempting to hypothesize that appropriate antioxidant concentrations in the plasma or placental tissues of women predisposed to GDM and preeclampsia may prevent the start or spread of free radical-mediated lipid peroxidation and hence prevent endothelial cell damage.

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