ORIGINAL ARTICLE

COMPARISON OF OXIDATIVE STRESS LEVELS DURING THE THIRD TRIMESTER IN NORMAL PREGNANCY AND PREECLAMPSIA

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Background: The placenta is a complex transiently formed organ which plays a crucial role in the development of the foetus. As the placenta is responsible for maintaining pregnancy placental defects are mainly responsible for pregnancy-related issues. Preeclampsia is a pregnancy-related disorder due to uteroplacental insufficiency resulting from deficient remodelling of spiral arteries causing ischemic reperfusion injury which is finally responsible for the generation of reactive oxygen species and oxidative stress by the placenta. So, this study was planned to determine and compare serum levels of oxidative stress markers (ischemia-modified albumin and malondialdehyde) in preeclampsia and normal pregnancy in the third trimester. **Methods**: Study design: Cross-sectional comparative study Settings Gynae/Obs Department and Pathology Laboratory, Lahore General Hospital, Lahore. Study population: 42 Pregnant females at 34–36 weeks of gestation were selected. Group 1 compromised 21 normal healthy pregnant females and group 2 included 21 preeclamptic patients. Sampling technique: non-probability purposive sampling. Blood samples were taken at 34–36 weeks of gestation. Serum was stored for ischemia-modified albumin and malondialdehyde. Data was analyzed using SPSS version 20. An Independent t-test was used to compare values between the groups during the third trimester. A *p*-value of ≤0.05 was considered significant. **Results:** Comparison of ischemia-modified albumin and malondialdehyde values between group I and group 2 showed a highly significant difference of *p*-value of <0.001. **Conclusion:** Oxidative stress markers were higher in preeclamptic patients as compared to normal pregnant females during the third trimester suggesting the role of the placenta in oxidative stress.

Keywords: Oxidative stress; Placenta; Preeclampsia

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INTRODUCTION

Pregnancy is a state of physiological stress to the mother in which many biochemical alterations occur in the milieu interior of the body from the period of fertilization to the delivery of the baby. The intense physical changes related mainly to maternal adaption to pregnancy, and adaptations related to structural, metabolic & endocrine functions in the body. These modifications may lead few pregnant women at serious health issues.[1] The development, replication, differentiation, and maturation of the developing cells of foetal tissues and organs during normal gestation needs an adequate supply of oxygen and nutrients. Oxygen consumption during biological processes results in the production of reactive oxygen species.[2] Normally there is a balance between the generation and degradation of reactive oxygen species and the actions of antioxidants. This balance is crucial for maintaining these oxidants at optimal levels within the human body for the signalling of various cellular pathways and normal development and functioning of the body.[3] The last trimester of pregnancy is a special period of increased production of hydrogen peroxide, fat catabolism, increasing insulin resistance, and the release of free fatty acids.[4] ROS in excess can lead to cellular destruction and dysfunction and can produce harmful impacts on tissue functions due to lipid peroxidation, deoxyribonucleic acid (DNA) oxidation and modification of proteins and amino acids.[5]

Oxidative stress is defined as an imbalance between oxidant and antioxidant production and degradation. It has a central role in the development of placental-related diseases.[6] The placental barrier formed by the trophoblast and endothelial cells that separates the maternal and foetal circulation is disrupted by tissue damage and oxidative stress and results in leakage of placental-derived factors into maternal circulation leading to maternal endothelial cell damage and systemic manifestations of preeclampsia.[7]

MATERIAL AND METHODS

A cross-sectional comparative study was conducted on 42 pregnant females, 20–35 years of age. The study setting was Lahore General Hospital, Lahore. The sampling technique was non-probability purposive

sampling. Inclusion criteria: Group 1 consisted of 21 normal healthy pregnant and group 2 included 21 preeclamptic females. Diagnostic criteria for preeclampsia was new-onset hypertension with systolic blood pressure (SBP) ≥140 mmHg or diastolic blood pressure (DBP) ≥90 mmHg on two separate occasions at least 4 hours apart after 20 weeks of pregnancy with or without proteinuria (≥300 mg/24h urine collection or dipstick reading of 1+ or protein/creatinine ratio ≥0.3). Exclusion criteria: gestational diabetes, any recent ischemic attack, subjects suffering from major systemic illnesses, myocardial infarction, acute coronary syndrome, metabolic syndrome, peripheral arterial disease. Blood samples were taken at 34–36 weeks of gestation. Serum was stored for malondialdehyde and ischaemia-modified albumin. Serum malondialdehyde was measured by Elisa kit and ischemia-modified albumin was measured by colourimetric assay. Human serum albumin can bind transition metals like cobalt at its N terminus. The ischemic tissue causes a change in the structure of the N terminus and changes its binding capacity. So that it can no longer bind cobalt. This unbound cobalt is measured by this colourimetric assay. Absorbance levels are increased due to unbound cobalt.[8] Data was analyzed using SPSS version 20. Independent t-test was used to compare values between the groups during pregnancy. A *p*-value of ≤0.05 was considered significant.

RESULTS

The majority of the subjects (52.4%) in group 1 and (57.1%) in group 2 were in the 20–25 years of age. Body mass index showed that 71.4% of participants in group 1 and 85.7% in group 2 were obese according to the WPRO criteria (BMI range 25–29.9 Kg/m^2).

During the third trimester of gestation in group 1, 85.7% of the female had IMA levels <0.40 ABSU, while 14.3% of the female had IMA levels ≥0.40 ABSU. In group 2, 14.3% of the females had IMA levels <0.40 ABSU, while 85.7% of the females had IMA levels ≥0.40 ABSU. The mean IMA level in group 1 and group 2 during the third trimester of pregnancy was 0.33±0.07 and 0.50±0.09 respectively, as shown in Table 1. IMA values in both groups showed a highly significant difference (p<0.001) when compared during the third trimester of gestation by applying an independent t-test, as shown in Table 2.

The mean MDA level during the third trimester in group 1 was 1.07±0.37 and the mean MDA value in group 2 was 1.79±0.63. MDA values between group I and group 2 showed a highly significant difference (p<0.001) during pregnancy when compared by independent t-test, as shown in Table 2.

Table-1: Frequency distribution of IMA levels during the third trimester of delivery in groups 1 and 2

IMA (ABSU)	Group-1 Normal pregnant (n=21)	Group-2 Preeclamptic n=21
	Frequency (%)	Frequency (%)
	Third trimester	Third trimester
<0.400	17 (85.7)	3 (14.3)
>0.400	4 (14.3)	18 (85.7)
Mean±SD	0.336±0.077	0.502±0.094

Table-2: Comparison of biochemical markers between group 1 and group 2 during third trimester of pregnancy

Biochemical markers	During third trimester		*p*-value
	Group 1 n=21	Group 2 n=21	
IMA (ABSU)▲	0.33±0.07	0.50±0.09	<0.001***
MDA mmol/L)▲	1.07±0.37	1.79±0.63	<0.001***

▲Comparison by independent t-test. *** *p*-value <0.001 considered highly significant

DISCUSSION

In the present study oxidative stress markers, serum malondialdehyde and IMA have been measured and compared in 42 pregnant females divided into two groups, group 1 comprising normal healthy pregnant females and group 2 of preeclamptic patients. The results of this study show a raised MDA value in preeclamptic patients as compared to normal healthy pregnant females during the third trimester with a statistically significant difference of p<0.001. These findings are from a study conducted by Atiba AS[9] on 98 preeclamptic patients, 115 normal pregnant and 90 non-pregnant females. They observed higher MDA values during pregnancy in the preeclamptic group as compared to normal pregnant and non-pregnant females. This is also analogous to the study conducted by Shilpa AV[10] on 30 preeclamptic, 30 normal pregnant and 30 non-pregnant females. They found raised serum MDA levels in preeclampsia as compared to the other two groups during the third trimester of pregnancy. The placenta is the main site for oxidative stress in pregnancy. Deficient perfusion of the fetoplacental unit initiates peroxidation of lipids in the cell membranes, transferring fatty acids to lipids peroxides and raising MDA levels.[11]

Ischemia-modified albumin (IMA) is another marker of oxidative stress. Human serum albumin has an N terminal region particular for binding with transition metals like nickel, cobalt and copper and is also the most vulnerable site for degradation. Ischemia and reperfusion reduce albumin binding capacity with transition metals. This lately transformed albumin is now known as ischemia-modified albumin.[12]

When serum levels of ischemia-modified albumin are compared between both groups during the third trimester, elevated values are observed in preeclamptic patients as compared to normal pregnant females with a statistically significant difference

$p<0.001$. Similar results of increased serum IMA levels in preeclampsia during the third trimester have been reported in the literature. The research conducted by Gafsou B[13] found elevated serum IMA in normal pregnant and preeclamptic patients as compared to non-pregnant females. In another study carried out by Kaushik and Satwika[14] IMA levels were reported higher in preeclamptic females as compared to normal pregnant females during the third trimester.

However, in a contrary study of oxidative stress markers, serum IMA levels were found elevated in normal pregnant controls as compared to the non-pregnant controls (p=0.01) but the IMA levels in preeclampsia were similar to those of normal pregnant controls (p=0.65) and they have attributed this to a small sample size of 12 in each group of non-pregnant, normal pregnant, and preeclamptic females.[15]

In the normal placental development plugging of spiral arteries occurs with the endovascular trophoblast. Imperfect invasion of endovascular trophoblast causes deficient refurbishing of uterine spiral arteries which results in vasoconstriction in the placenta causing hypoxic surroundings and production of reactive oxygen species (ROS), leading to oxidative stress, which is thought to play a role in the pathophysiology of preeclampsia.[16] The results of the present study show that preeclamptic patients have more elevated oxidative stress in comparison to healthy pregnant women, which is the leading cause of endothelial dysfunction, which in turn is the main source behind hypertension, proteinuria and hypoalbuminemia in preeclampsia. These results show that oxidative stress markers are very reliable and sensitive indices to evidence the biochemical changes in normal pregnant and preeclamptic females.

CONCLUSION

Oxidative stress was significantly higher in preeclamptic females as compared to normal healthy pregnant females during the third trimester.

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AUTHORS' CONTRIBUTION

MT: Literature search, conceptualization of the study design, data analysis, data interpretation, and write-up. NS: Proofreading. MT: Data collection. Fawad: Literature search. FR, Durrira: Write-up.

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