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Assessment of oxidative and cardiovascular changes in pregnant women attending antenatal clinic at Federal Medical Centre, Owerri Nigeria

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Abstract

Background: In pregnancy which is a physiological state that is accompanied by high energy demand, there is an increased intake and utilization of oxygen, hence augmented levels of oxidative changes that are associated with a lot of risks, one of which is cardiovascular diseases. This research aims to investigate the oxidative changes that occur among pregnant women by determining the levels of High Sensitivity c-Reactive Protein (hs-CRP) and Oxidized Low-Density Lipoprotein (OxLDL) in first, second and third trimesters.

Materials and Methodology: A total of 60 pregnant women were recruited for the study. Twenty (20) pregnant women each from the three trimesters while Twenty (20) non-pregnant pubertal women without any chronic disease were used as control. 5ml of venous blood was collected from all subjects and analyzed for OxLDL and hs-CRP using an Enzyme-Linked Immunosorbent Assay (ELISA) technique. The data were analyzed using Statistical Package for the Social Sciences (SPSS) version 18.

Results: Oxidized Low-Density Lipoprotein (OxLDL) showed mean variations across the groups but was not significant ($P>0.05$) but Pregnant women in their second trimester showed significant mean variation ($P<0.05$) (3716.11±599.86) in when compared to non-pregnant women (control) (4305.33±68.90) respectively. Pregnant women in the second trimester showed significantly decreased mean variation ($P<0.05$) in High sensitivity C-reactive protein (85.09 ±12.38) when compared to non-pregnant women (control) (219.45 ±64.61) respectively.

Conclusions: This study shows that there are increases in levels of OxLDL and a decrease in plasma concentration of hs-CRP which are more significant in the second trimester.

Keywords: Oxidative stress, Trimester; Cardiovascular; Oxidized Low-Density Lipoprotein; Pregnancy; High sensitive C-reactive protein

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1. Introduction

Changes that occur during pregnancy range from hematological, hormonal, nutritional, and systemic to even emotional changes. Hence, physiologically, the mother becomes almost a new person during pregnancy. Pregnancy is a state characterized by many physiological changes, which would be pathological in the non-pregnant state [1]. Campolong, *et al.*, [2] agrees that there are three stages of pregnancy, known as trimesters. In pregnancy, lipid metabolism undergoes complicated changes; lipid levels such as Low-density Lipoprotein (LDL), High-density Lipoprotein (HDL), Total Cholesterol (TC), and Triglyceride, above or below the normal range can lead to pregnancy complications that may end up to preterm delivery [3].

Oxidized low-density lipoprotein (OxLDL) is highly associated with the development of atherosclerosis, hence a risk factor for cardiovascular disease [4]. Also, increased level of progesterone, hypercholesterolemia, and hyperglycemia which occur during gestational diabetes mellitus (GDM) accelerates the rate of oxidation of LDL [5].

Oxidative stress, also known as oxidative changes, is defined as an imbalance between antioxidants and pro-oxidants in favor of oxidants [6] The principal causes of oxidative stress (OS) are reactive oxygen species (ROS), which may be broadly defined as derivatives of molecular oxygen [7]. Every molecule of ROS contains an atom of oxygen with an unpaired electron, this seems to be the basis of its high reactivity. In pregnancy, a physiological state accompanied by high energy demand, there is an increased intake and utilization of oxygen, hence an augmented level of oxidative changes [8].

Oxidative stress is a mediator of endothelial dysfunction and contributes to preeclampsia, eclampsia, and cardiovascular complications. Hence in pregnancy, oxidative changes, if not diagnosed and properly treated can degenerate into preeclampsia, Low Birth Weight, Small-for-Gestation Age, and in severe cases, stillbirth [9].

In the serum of healthy individuals, the High Sensitivity c-Reactive Protein level is low, while it is shown to be elevated drastically in non-infectious inflammation [10]. High sensitivity c-reactive protein is a sensitive marker of systemic inflammation and is primarily synthesized in hepatocytes in response to infection and tissue injury [11]. It has also been reported to be increased in disease conditions like hypertension [12]. High Sensitivity c-Reactive Protein is an indicator of atherosclerosis and is also one of the risk factors for hypertension, which normally occurs in Pregnancy Induced Hypertension (PIH) [10]. Production of High Sensitivity C-reactive protein is stimulated by the release of pro-inflammatory cytokines such as interleukin-1, interleukin-6, and Tumor Necrosis Factor-α (TNF-α) [11]. hs-CRP is synonymously also sometimes called an acute phase reactant and it is mostly associated with most inflammatory diseases [13]. In his work, "Plasma c-Reactive Protein in Early Pregnancy and Preterm Delivery", Pitiphat, *et al.,* [13] suggested that very high levels of High Sensitivity c-Reactive Protein in early pregnancy are associated with preterm delivery.

The assessment of oxidative and cardiovascular changes in pregnant women within Imo State Nigeria using oxidized Low-Density Lipoprotein (OxLDL) and High Sensitivity C-reactive protein (hsCRP) have not been fully understood. An understanding of the changes in High Sensitivity C-reactive Protein and Oxidized Low-Density Lipoprotein across the trimesters will contribute to the knowledge of their predisposition to pre-eclampsia, and cardiovascular conditions.

This research aims to investigate the oxidative changes and cardiovascular changes among pregnant women attending the antenatal clinic at Federal Medical Centre Owerri Imo State by measuring OxLDL and hs-CRP during the first, second, and third trimesters in pregnant women.

2. Material and methods

2.1. Subjects

Sixty pregnant women registered with the antenatal clinic at Federal Medical Centre Owerri were used for this study. Working in collaboration with doctors and nurses in the unit, the pregnant women were divided into twenty in the first trimester (Group one), twenty in the second trimester (Group two), and twenty in the third trimester (Group three).

2.2. Ethical Consideration and Informed Consent

An ethical clearance certificate was obtained from the University of Nigeria Teaching Hospital Research and Ethical Committee with registration number: NHREC/05/01/2008B-FWA00002458-1RB0002323. Informed consent was as well obtained from each of the participants before the commencement of the study.

2.3. Pregnant Women in the First Trimester

The study was carried out on twenty pregnant women in the first trimester who have been registered and attending the outpatient department of gynaecology and Obstetrics Department, Federal Medical Center, Owerri, Imo State.

2.3.1. Inclusion Criteria

- Age: 18-45years old
- Pregnant women in the first trimester

2.3.2. Exclusion Criteria

Pregnant women in the first trimester but with uncontrolled chronic disease such as diabetes mellitus, high blood pressure, pelvic inflammatory disease, tuberculosis etc.

2.4. Pregnant Women in the Second Trimester

The study was carried out on twenty pregnant women in the second trimester who have been registered attending the outpatient department of gynaecology and Obstetrics department, Federal Medical Center Owerri, Imo State.

2.4.1. Inclusion Criteria

- Age: 18-45years old
- Pregnant women in the second trimester.

2.4.2. Exclusion Criteria

Pregnant women in the second trimester but with uncontrolled chronic disease such as diabetes mellitus, high blood pressure, pelvic inflammatory disease, tuberculosis etc.

2.5. Pregnant Women in the Third Trimester

The study was carried out on twenty pregnant women in the third trimester who have been registered attending the outpatient department of gynaecology and Obstetrics department, Federal Medical Center, Owerri, Imo State.

2.5.1. Inclusion Criteria

- Age: 18-45years old
- Pregnant women at third trimester

2.5.2. Exclusion Criteria

Pregnant women in the third trimester but with uncontrolled chronic disease such as diabetes mellitus, high blood pressure, pelvic inflammatory disease, tuberculosis etc.

2.6. Controls

The control subjects are apparently healthy women without chronic disease e.g. diabetes mellitus, tuberculosis, pelvic inflammatory disease, Lassa fever, Corona virus.

2.7. Sample Collection

Five milliliters of venous blood were collected from the subjects. All samples for Oxidized Low Density Lipoprotein and High Sensitivity c-Reactive Protein was collected into plain venoject bottle and transported to the laboratory within 30 minutes and store in refrigerator until analysis.

2.8. Biochemical Estimation

The following parameters was estimated on each sample collected:

- Oxidized Low-Density Lipoprotein (oxLDL)
- High sensitivity c-Reactive Protein (hsCRP)

2.9. Assay method and procedure

Generally, the method used in both parameter assay involved Enzyme Linked Immunosorbent Assay (ELISA) principle. All reagents, standard solutions and samples were prepared as instructed in the Elabscience kit. All reagents are brought to room temperature before use and the assay was performed at room temperature.

OxLDL and hs-CRP were both measured and calculated using the Elabscience kit procedure as instructed by the manufacturer. The concentration of Human OxLDL and hs-CRP in the samples were calculated by comparing the optical density (OD) of the test samples to the standard curve.

2.10. Data Analysis

Statistical analysis difference was estimated using ANOVA and correlation. Values were reported as Mean±SEM. The statistical package for social sciences(SPSS) version 18 was used. A value of $P<0.05$ is considered significant.

3. Results

Table 1 Oxidized Low Density Lipoprotein and High sensitivity C-reactive protein values in pregnant women and control group

	Control n=20	1st Trimester n=20	2nd Trimester n=20	3rd Trimester n=20	P-value
Ox-LDL (pg/ml)	3716.11±599.86	3876.47±153.43	4305.33±68.90	4031.98±103.50	0.149
Hs-CRP (pg/ml)	219.45 ±64.61	183.01±33.46	85.09 ±12.38	163.01±48.18	0.092

Data expressed in mean ±SEM, n=number of subjects and P<0.05 is taken to be significant. Legends: hs-CRP = High sensitive C-reactive protein; OxLDL = Oxidized Low-Density Lipoprotein

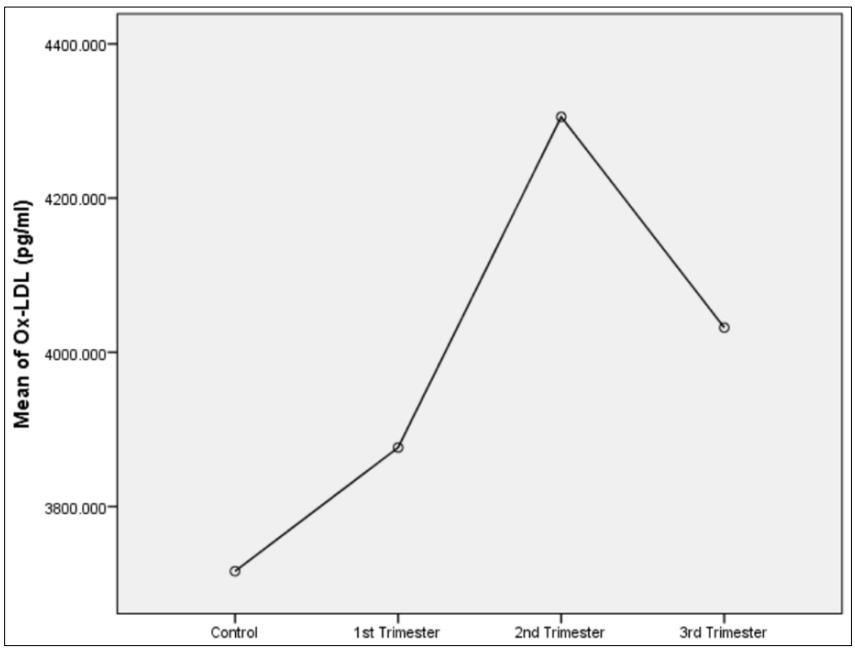

Figure 1a Line graph representation of Oxidized Low Density Lipoprotein values variation in pregnant women and the control group

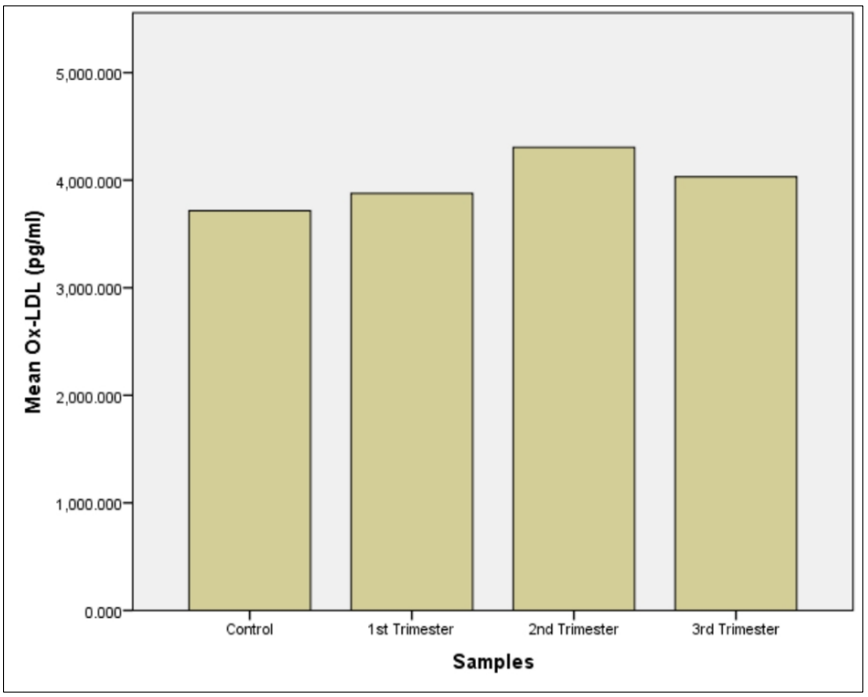

Figure 1b Bar graph representation of Oxidized Low Density Lipoprotein values variation in pregnant women and the control group

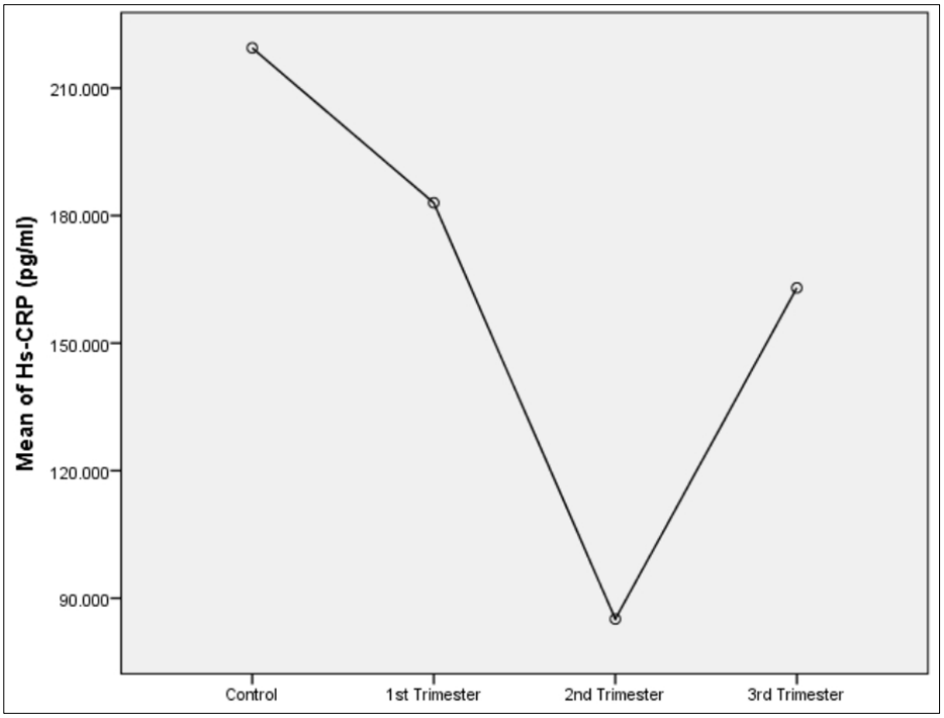

Figure 2a Line graph representation of High sensitivity C-reactive protein values variation in pregnant women and the control group

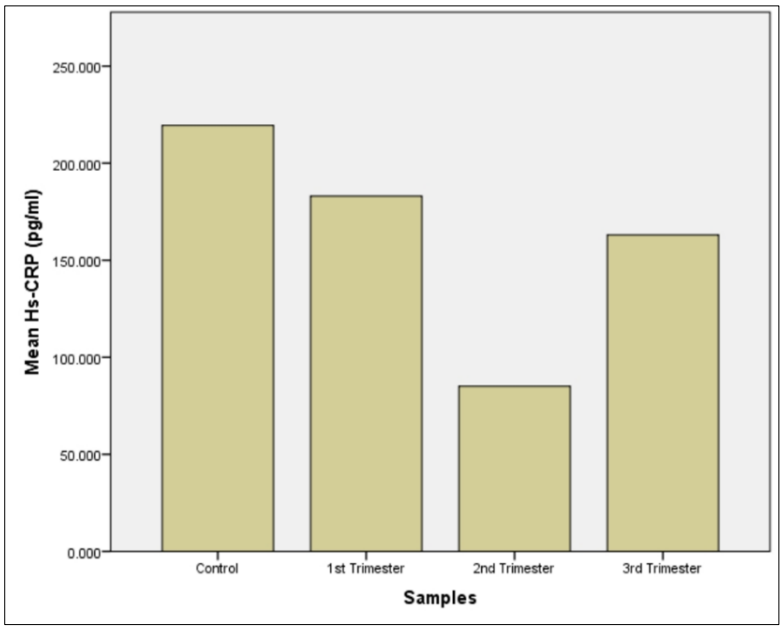

Figure 2b Bar graph representation of High sensitivity C-reactive protein values variation in pregnant women and the control group

4. Discussion

Assessment of oxidative stress in pregnancy using High Sensitivity c-Reactive Protein and Oxidized Low Density Lipoprotein as measuring parameters helps to monitor and prevent possible symptoms of pregnancy complications during or after pregnancy.

Placental oxidative stress is clearly associated with multiple adverse pregnancy outcomes and conversion of maternal spiral arteries appears to be mechanistically linked. If the pro-oxidant state during pregnancy is pushed further there may be increased risks of miscarriage, preterm birth, pre-eclampsia, eclampsia, gestational diabetes, etc. Further, these insults may impair fertility to some extent as well [14-16].

In this study, the results of oxidative changes in pregnant women were obtained using twenty non-pregnant pubertal women as control and twenty pregnant women each from the three trimesters. The findings show that the level of oxidized low-density lipoprotein in the second trimester increased significantly when compared to non-pregnant women. This could be attributed to underlying pregnancy complications such as preeclampsia. Preeclampsia is a pregnancy-specific complication characterized by an onset of hypertension, and proteinuria edema in the late second trimester, after twenty weeks of gestation [17]. It complicates five to six percent of all pregnancies and remains a major cause of maternal and perinatal morbidity and mortality worldwide according to the national institute of child health and human development network of maternal-fetal medicine units.

Our findings are in agreement with the studies of Makedou et al., [18] and Tesfa et al., [19] who reported that pregnant women presented higher oxidized low-density lipoprotein levels than non-pregnant control hence, predisposing them to preeclampsia and other pregnancy complications. Also, the level of oxidized low-density lipoprotein in the first and third trimester (3716±599.86pg/ml and 4031.98±103.50 respectively) was higher in the pregnant women than in the control. This is also, in accordance to the study of Qiu et al., [20] who in his report, recorded elevated level of oxidized low-density lipoprotein among pregnant women and agreed that women with both elevated low-density lipoprotein and low vitamin C concentration experienced a 9.8% fold increased risk of pre-eclampsia [20].

Furthermore, this study shows that pregnant women in the second trimester (85.09±12.38pg/ml) had a decrease in the level of high sensitivity c-Reactive protein when compared to non-pregnant control (219.45±64.61pg/ml). The concentrations of the high sensitivity c-reactive protein in the first and third trimester (183.01±33.46 and 163.01±48.18) was higher than that of the second trimester, though the values across the three trimesters were still lower than the control value. This may be due to the intake of anti-oxidants that these pregnant women are exposed to during pregnancy such as copper, Vitamin C, Vitamin E, and zinc. These antioxidants convert the oxidants such as

superoxide to hydrogen peroxide which is then rapidly removed from the body [21]. Regular exercise or physical activities can also play a role in the reduction of the level of high sensitivity c-reactive protein during pregnancy [22].

5. Conclusion

This study shows that there are increases in levels of oxidized low-density lipoprotein in pregnant women attending the antenatal clinic of Federal Medical Centre Owerri Imo state; the increase being more significant in the second trimester with respect to non-pregnant controls. The study also indicates that there are decreases in plasma concentration of high sensitive C-reactive protein in pregnant women attending the same clinic, also the second trimester has a more significant decrease as compared to non-pregnant controls. Again the result finds out that the concentration of oxidized low-density lipoprotein when compared with first and third trimesters was not significant($P>0.05$). The same applies to the results obtained in high-sensitivity C-reactive protein.

Recommendations

These findings are crucial to the safety of the mother and child during and after pregnancy. We recommend that this work be replicated in a larger number of subjects. We also recommend that these parameters be estimated after parturition and among breastfeeding mothers to understand if these markers are increased or decreased.

Compliance with ethical standards

Acknowledgments

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Disclosure of conflict of interest

We declare no conflict of interest.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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