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Biochemical Changes in Lipid Profile and Antioxidant Status in Pregnancy

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ABSTRACT

Pregnancy represents a multifaceted physiological phenomenon influenced by a variety of interrelated factors. The causes of abortion or pregnancy disruption are diverse, encompassing genetic, hormonal, environmental, and immunological elements. A comprehensive understanding of the factors contributing to pregnancy loss is crucial for enhancing both maternal and fetal health outcomes. The progression of fetal development during pregnancy, along with the implications of childbirth, is closely associated with the maternal lipid profile and antioxidant levels. This investigation was prompted by an observed increase in pregnancy loss (abortion), pregnancy-induced hypertension, preeclampsia, and gestational diabetes, particularly among women in their second and third trimesters. A total of 50 women were recruited from two Primary Healthcare facilities in Akure, comprising 25 pregnant women (subjects) with normal pregnancies and 25 non-pregnant women of reproductive age (controls). The lipid profile (including Low-Density Lipoprotein-LDL, High-Density Lipoprotein-HDL, Total Cholesterol-TC, and Triacylglycerol-TAG), antioxidant status (measured by Glutathione Peroxidase activity-GPx), and lipid peroxidation (assessed through Malondialdehyde-MDA) were evaluated using analytical test kits on blood samples collected from participants. The findings revealed a statistically significant increase ($p < 0.05$) in lipid parameters—LDL, TAG, TC, and HDL—in the subjects compared to the control group. Additionally, GPx activity was significantly elevated ($p < 0.05$) in the subjects

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relative to the controls. MDA levels were also significantly higher in the subjects than in the control group. Furthermore, fasting blood sugar (FBS) levels were significantly ($p < 0.05$) elevated in the non-pregnant control group compared to the pregnant group. This study indicates the necessity of assessing the lipid profile and antioxidant levels in pregnant women to enhance pregnancy outcomes and decrease the rates of pregnancy loss.

Key words: - Lipid profile, Pregnancy, Antioxidant, Peroxidation, miscarriage, abortion

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INTRODUCTION

Pregnancy is defined as a physiological condition characterized by the implantation of products of conception, which may occur within the uterus or in other locations within the body. The completion of pregnancy can occur through spontaneous or elective abortion, or via delivery. Throughout the process of conception, the maternal organism experiences a series of physiological changes that affect all organ systems, facilitating the sustenance of the developing fetus [1]. This state can be described as a multifaceted physiological phenomenon that relies on the complex interaction of various factors. Notably, pregnancy duration is typically calculated from the first day of the last menstrual period, averaging approximately 280 days [1]. During pregnancy, significant alterations occur in the maternal body, alongside fetal development, which are closely linked to the maternal lipid profile and antioxidant status [2,3]. Generally, there is an observed increase in total cholesterol, low-density lipoprotein (LDL) cholesterol, and triglyceride levels, while high-density lipoprotein (HDL) cholesterol levels may experience a slight decrease. Specifically, total cholesterol levels can rise by about 50%, LDL cholesterol by 30-40%, HDL cholesterol by 25%, and triglycerides may increase two- to threefold. These lipid changes are considered normal physiological adaptations that meet the heightened energy and nutritional requirements of the growing fetus and establish energy reserves for lactation post-delivery [2,4]. The rise in plasma lipid concentrations during pregnancy is significantly influenced by insulin resistance and estrogen stimulation. Numerous studies have demonstrated that levels of total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and

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triglycerides (TG) are markedly elevated during this period.

The extent of lipid alterations during pregnancy can exhibit significant variability among individuals, influenced by factors such as baseline lipid levels prior to pregnancy, weight gain throughout gestation, and the stage of pregnancy [1]. It is crucial to recognize that while a certain increase in lipid levels is typically regarded as normal during pregnancy, elevated maternal total cholesterol and/or triglyceride levels have been linked to adverse outcomes such as preterm birth (PTB) [5,6], pregnancy-induced hypertension (PIH), preeclampsia [7,8], and even pregnancy loss. Furthermore, it has been observed that pregnancy induces oxidative stress, primarily as a result of a normal systemic inflammatory response, which can lead to heightened levels of circulating reactive oxygen species (ROS) [3]. Oxidative stress arises from an imbalance between the production and accumulation of reactive oxygen species (ROS) in cells and tissues and the biological system's capacity to detoxify these reactive products [9]. Given that indicators of oxidative stress are known to be elevated during a typical pregnancy, it is anticipated that pregnancy may exacerbate oxidative stress, potentially resulting in increased oxidant levels and a corresponding decrease in total antioxidant capacity (TAC).

Dyslipidemia and the abnormal generation of reactive oxygen species (ROS) during pregnancy can significantly impact both maternal and fetal health. The potential consequences of these conditions include developmental delays, preterm birth, low birth weight, respiratory complications, compromised maternal and placental functions, gestational diabetes mellitus, and even miscarriage [10,11]. While oxidative stress is a common occurrence during pregnancy, it is crucial to maintain a balance between

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oxidant and antioxidant production throughout various stages of gestation. This study aims to assess the biochemical alterations in lipid profiles (including total cholesterol, high-density lipoprotein, low-density lipoprotein, and triglycerides), antioxidant levels (specifically glutathione peroxidase), and lipid peroxidation (measured by malondialdehyde, MDA) during pregnancy, comparing these findings with those from women of reproductive age who will serve as a control group.

METHODOLOGY

A total of fifty (50) healthy female participants were enlisted for this study. Among them, twenty-five (25) pregnant women were selected from antenatal clinics at primary health centers in Akure, Ondo State, serving as the case (test) group. The remaining twenty-five (25) participants were non-pregnant women of reproductive age, who constituted the control group.

Inclusion criteria

1. Subjects were declared pregnant (in second/third trimester) by certified and qualified

doctor/midwife

2. Subjects were only be on routine drugs/medication provided by the antenatal clinic.

Exclusion criteria

1. Subjects with history or current abuse of substance (drug)

2. Subjects with diagnosis or on treatment for certain diseases like diabetes, HIV/AIDS,

hypertension, etc.

3. Subjects with history of miscarriage.

Data Collection

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A questionnaire designed for data collection was utilized, encompassing information regarding demographic characteristics, anthropometric measurements, medical history (including obesity and any familial hyperlipidemia), as well as dietary habits and physical activity levels. Recruitment of subjects was conducted through personal interviews, during which informed consent was secured from all participants after they were informed about the study's benefits and significance. Ethical approval for the study was granted by the ethics committee of the University of Medical Sciences.

Biochemical Analysis

Fasting blood samples were collected via venipuncture, and various parameters were assessed in both the case and control groups. The lipid profile parameters were determined using Randox test kits, following the manufacturer's guidelines.

I. Total Serum Cholesterol (CHOD-PAP Method) [12].
II. Serum triglycerides (GPO-Trinder Method) [13].
III. Serum High density lipoproteins (HDL) (Phosphotungstic Acid Method) [14].
IV. Serum Low density lipoproteins (LDL) (Freidwald equation) [15].
V. Serum Very low- density lipoproteins (VLDL) (Freidwald equation) [15].
VI. Antioxidant activity: Glutathione peroxidase [16].
VII. Lipid peroxidation: Malondialdehyde (MDA) [17].
VIII. Fasting blood sugar**:** Using FBS test strips

Statistical analysis

Statistical analysis was conducted on the collected data utilizing one-way analysis of variance (ANOVA), followed by the

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Tukey test, employing GraphPad Prism version 9.0.0. The findings are expressed as mean ± standard error of the mean (SEM). A significance level of $p < 0.05$ at a 95% confidence interval was established to determine differences between the means of the pregnant subjects and the non-pregnant control group.

RESULT

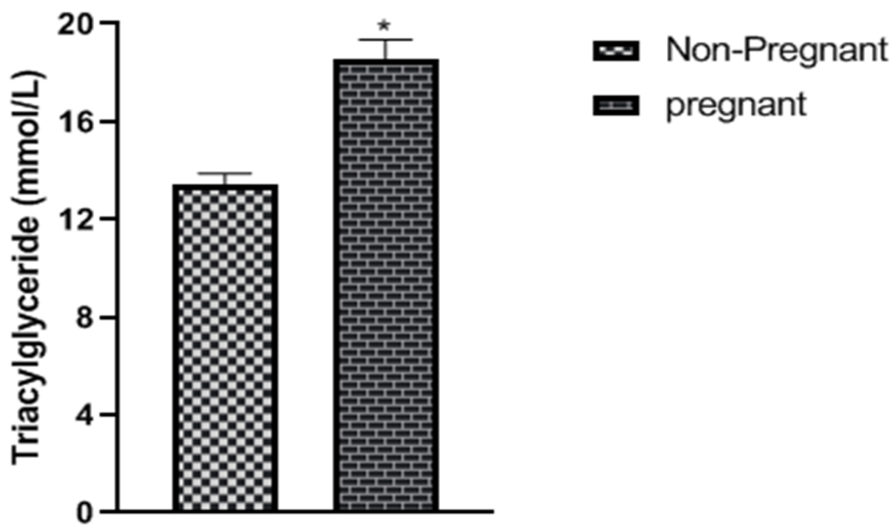

Figure I: The levels of triglycerides in pregnant women (PP) and non-pregnant women (NPP) exhibit a statistically significant difference, with ($P < 0.05$)

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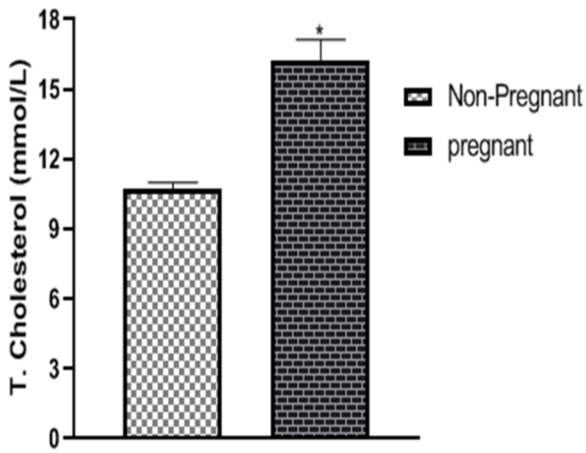

Figure II: The total cholesterol levels in pregnant women (PP) and non-pregnant women (NPP) exhibit a significant difference, with (P < 0.05)

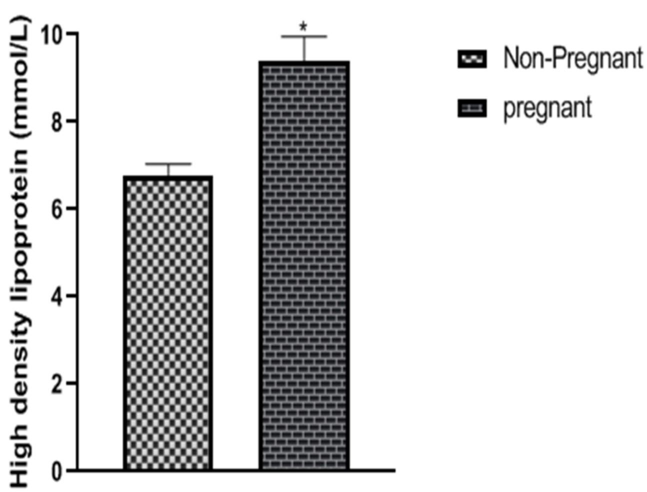

Figure III: The concentration of high-density lipoprotein (HDL) in pregnant women (PP) is significantly different from that in non-pregnant women (NPP) with (P < 0.05)

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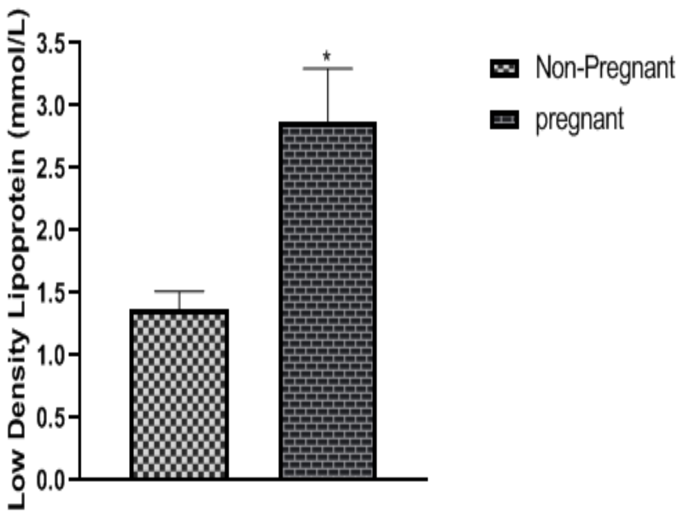

Figure IV: The levels of low-density lipoprotein in pregnant women (PP) and non-pregnant women (NPP) exhibit a statistically significant difference, with (P < 0.05)

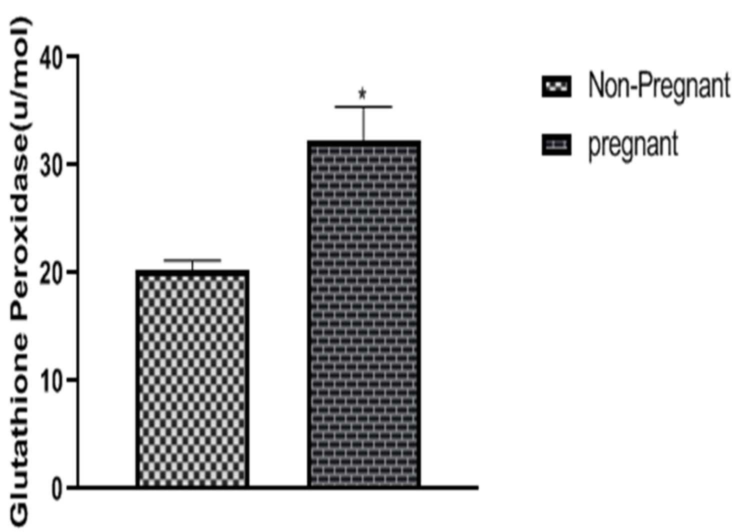

Figure V: The levels of glutathione peroxidase in pregnant women (PP) and non-pregnant women (NPP) were found to be significantly different, with a statistical significance of (P < 0.05)

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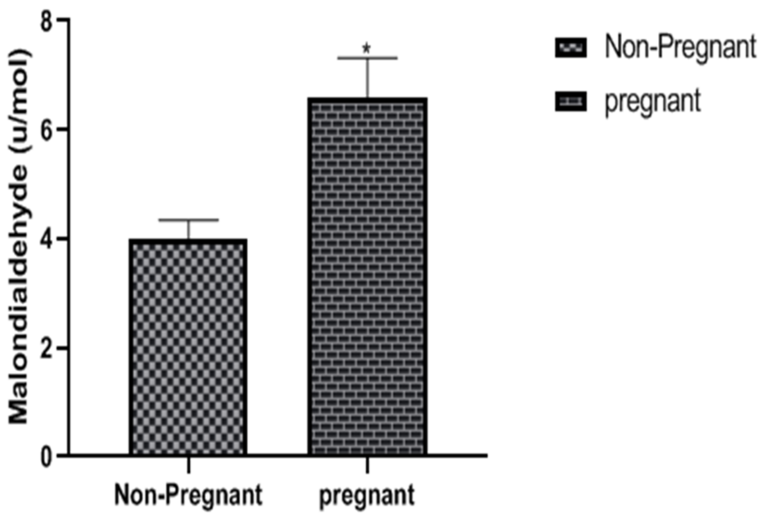

FIGURE VI: The levels of Malondialdehyde in pregnant women (PP) and non-pregnant women (NPP) exhibit a statistically significant difference, with (P < 0.05)

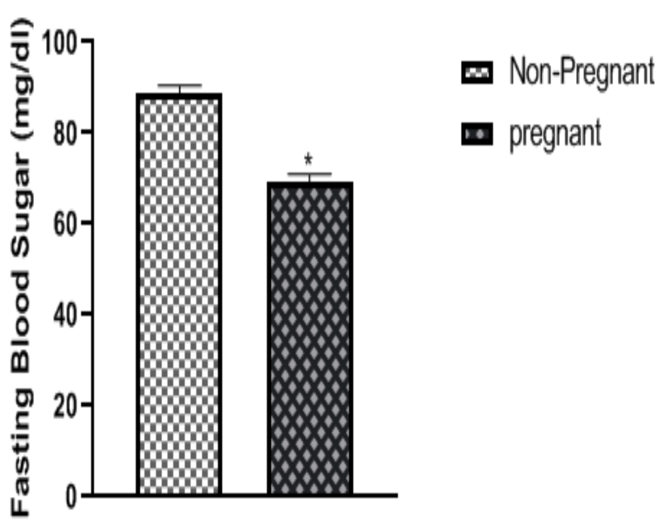

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Figure VII: The levels of fasting blood glucose in pregnant women (PP) and non-pregnant women (NPP) exhibit a significant difference, with ($P < 0.05$)

DISCUSSION

Pregnancy represents a complex physiological state characterized by numerous hormonal and metabolic alterations that facilitate fetal development and survival. Nevertheless, disruptions in biochemical profiles can result in unintended miscarriages and various complications during pregnancy. Consequently, it is essential to assess the biochemical profiles of pregnant women. In the present study, pregnant participants exhibited a notable reduction in fasting blood glucose levels compared to the control group. This phenomenon may be attributed to metabolic factors, particularly the heightened demand for glucose by the developing fetus. This finding aligns with the research conducted by Milana *et al.* [18]., which documented a decrease in fasting glucose levels among pregnant women relative to their non-pregnant counterparts, with a reduction of 0.34 (0.18, 0.51) mmol/l ($p < 0.0001$) during early pregnancy and 0.45 (0.29, 0.61) mmol/l ($p < 0.0001$) in mid to late pregnancy. The maternal metabolic landscape undergoes significant changes in the first trimester, driven by elevated levels of estrogen and progesterone, which subsequently stimulate pancreatic beta-cell hyperplasia, resulting in increased insulin secretion and a corresponding decline in fasting blood glucose levels [19]. However, a contrasting study by Afolayan *et al.* [20]. reported no significant difference in fasting blood glucose levels between pregnant and non-pregnant women.

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This research demonstrated that pregnant women exhibited significantly elevated ($p < 0.05$) levels of serum total cholesterol, triglycerides, and low-density lipoprotein (LDL) compared to their non-pregnant counterparts. Supporting this finding, studies by Mankuta *et al.* [21]., Giomisi *et al.* [22]., Shilpa *et al.* [23]., and Begum *et al.* [24]. also reported notable increases in total cholesterol (TC), LDL, and triglyceride (TAG) levels, respectively. The heightened triglyceride levels during gestation can largely be attributed to diminished lipoprotein lipase activity in adipose tissue, a consequence of insulin resistance [25]. Furthermore, prenatal insulin resistance, which typically peaks in the third trimester, enhances hormone-sensitive lipase activity in maternal adipocytes, leading to the hydrolysis of triglycerides. Consequently, the released glycerol and free fatty acids become available for very-low-density lipoprotein (VLDL) synthesis, resulting in an increase in plasma triglycerides as pregnancy progresses. In this investigation, a significant rise ($p < 0.05$) in serum cholesterol and LDL-C levels was noted among pregnant women when compared to non-pregnant women. This observation aligns with findings from Pusukuru *et al.* [26], Alemu *et al.* [27]., and Ghio et al. [28], who reported significant elevations ($p < 0.05$) in cholesterol and LDL-C levels (211.9±40.88 and 172.40±29.64 mg/dl, respectively) in pregnant women relative to non-pregnant women. Such changes may result from physiological and homeostatic adaptations in the body to support fetal growth and survival. Maternal hypercholesterolemia has been associated with adverse effects on fetal development and pregnancy outcomes [5,29]. Throughout the course of pregnancy, there is a progressive increase in progesterone and estrogen levels, which suppresses the hypothalamic axis [30].

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The biochemical profiles of most organ systems reflect these adaptive changes, resulting in significant differences from the non-pregnant state. The increase in LDL-C is primarily driven by progesterone, which serves as the main substrate for subsequent placental progesterone production.

A notable increase ($p < 0.05$) in HDL-C levels was identified among pregnant women in this study. This finding aligns with the research conducted by Roopan *et al.* [31], which reported higher HDL levels in pregnant women compared to their non-pregnant counterparts. The rise in HDL cholesterol during pregnancy is attributed to elevated estrogen and progesterone levels, with estrogen playing a particularly influential role in modulating HDL concentrations [32]. Additionally, LDL-C levels also had significant alterations throughout pregnancy, driven by hormonal fluctuations and metabolic adjustments, likely serving as an adaptive response to ensure adequate cholesterol supply for placental and fetal development [33]. Furthermore, the study revealed that the level of MDA in pregnant women was significantly elevated ($p < 0.05$) compared to non-pregnant women. This observation is consistent with findings from a series of cross-sectional comparative studies by Gohil *et al.* [34]. Padmini and Uthra [35], Kaur et al. [36], also reported increased MDA levels in pregnant women. MDA is recognized as a significant marker of lipid peroxidation, and the consistently higher levels observed in pregnant women can be attributed to the distinct physiological requirements of pregnancy. Factors contributing to elevated MDA levels include increased metabolic demands, hormonal fluctuations, and placental development, all of which play a role in inducing oxidative stress during this period [35]. The heightened MDA levels

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observed during pregnancy are likely a consequence of the physiological adaptations and metabolic requirements associated with this state.

Glutathione peroxidase (GPx) activity exhibited a notable increase ($p < 0.05$) in pregnant women compared to their non-pregnant counterparts. This finding aligns with the research conducted by Roopam *et al.* [31] and Zych *et al.* [37], which also documented a significant rise in superoxide dismutase (SOD) and GPx levels among pregnant women relative to non-pregnant women. The elevation of antioxidant enzymes activity, including GPx and SOD, is typically associated with the presence of oxidative stress. While oxidative stress is an inherent aspect of pregnancy, excessive levels of reactive species may lead to adverse conditions such as preeclampsia, premature birth, and spontaneous abortion [35].

Recommendation

It is crucial to monitor lipid profile parameters and antioxidant status throughout pregnancy to ensure the health of both the mother and the developing fetus, thereby mitigating the risk of complications and preventing unintended pregnancy loss. These parameters serve as vital indicators for assessing the overall effects of oxidative stress, dyslipidemia, and lipid peroxidation on maternal and fetal health. Their interpretation should take into account pregnancy-related factors, and strategies aimed at reducing oxidative stress, including the use of antioxidant supplements and lifestyle modifications, should be actively considered.

Declaration by Authors

Ethical Approval: Approved

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Conflict of Interest: The authors declare no conflict of interest.

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