https://dx.doi.org/10.4314/dujopas.v8i2a.10
ISSN (Print): 2476-8316
ISSN (Online): 2635-3490
Dutse Journal of Pure and Applied Sciences (DUJOPAS), *Vol. 8 No. 2a June 2022*

Oxidative Stress in Primigravida Attending an Antenatal Clinic in Northern Nigeria

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Abstract
The demand for oxygen increases during pregnancy, and this may lead to oxidative stress. The aim of this study was to determine the oxidative stress level in Primigravida attending antenatal clinic at Gombe town Gidan Magani Maternity, Gombe State, North-eastern Nigeria. The concentration of plasma Malondialdehyde (MDA) was measured as biomarker of oxidative stress. The concentrations of Copper, Zinc, Manganese, Lead, Nickel and Cadmium in relation to oxidative stress were measured. Thirty primigravida and ten aged-matched non-pregnant women who served as control were involved in the study. The result of this research shows that the level of Malondialdehyde significantly ($P < 0.05$) increased in the 1st, 2nd and 3rd trimesters, with the increase being higher in the 2nd trimester. The levels of Cu and Zn increased significantly ($P < 0.05$) in all the three trimesters, while the level of Mn significantly ($P < 0.05$) decreased in all the three trimesters. There was no reading detected for Ni, Cd and Pb in both primigravida and control subjects under this study, indicating that neither the primigravida nor the control were exposed to them. All these are proves that oxidative stress occurs in Primigravida These findings emphasized the need for increased awareness among Primigravida on the existence of oxidative stress during pregnancy and also points to the need for measures to be taken against oxidative stress in Primigravida, so as to reduce the complications that arise during pregnancy, and ensure the safety of both mother and fetus during pregnancy and after delivery.

Keywords: *Oxidative stress, Antioxidants, Primigravida, Trimester, Pregnancy.*

INTRODUCTION
Oxidative stress refers to a condition in which reactive oxygen and nitrogen species (RONS) are produced beyond the counteractive ability of the body's antioxidant system (Betteridge, 2000; Gupta *et al.,* 2005). Free radicals under limited concentrations are useful and essential to the body. However, in high concentrations, they have adverse effects (Tiwari *et al.,* 2010).

Pregnancy is the fertilization and development of one or more offspring in a woman's uterus. During pregnancy, a lot of physiological changes and rise in metabolic activities occur in the woman and the developing fetus. (Al-Jameil *et al.,* 2014). Therefore, it is associated with increased oxygen requirement (Saikumar *et al.,* 2013). This triggered aerobic environment which is responsible for favoring the increased production of free radicals (ROS/RNS) may

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lead to oxidative stress (Fiqlova *et al.,* 2006). Hence, pregnancy itself induces oxidative stress (Raijmakers *et al.,* 2005). More so, exposure to heavy metals by pregnant women can result to formation of free radicals, predisposing the body to high level of oxidative stress (Neeti and Prakash, 2013). Physiological changes in pregnant women, such as increase in the level of the hormone progesterone promote the retention of heavy metal copper resulting to copper toxicity. The copper toxicity may be through the production of ROS in a fenton-like reaction (Ercal *et al.,* 2001). The ROS (free radicals) produced are electron deficient and may interact with proteins, lipids and DNA so as they become stabilized. The biomolecules in turn become electron deficient, and interact with others so as they also become stabilized. This goes on and on, thereby triggering a free radical chain reaction (Droge, 2002). This results to production of secondary reactive species that also contribute in damaging the biomolecules in particular, and by extension, the cell in general. The end result of these events is damage to various organs and destabilization of physiological activities which manifest as human diseases (Halliwel and Whiteman, 2004).

However, the body has put in place a lot of enzymatic and non enzymatic antioxidant systems to protect itself against the effect of free radicals (Gazzani *et al.,* 1998; Hiten and Paula, 2011). Inspite of these antioxidant defence mechanisms, a lot of people are prone to oxidative stress either due to exposure to substances that causes it, or due to metabolic and physiological changes as in pregnant women (Franchitto *et al.,* 2008). During pregnancy, the adverse effect of oxidative stress affects not only the woman, but also the developing fetus (Menegola *et al.,* 2005). Of recent, this has raised much concern. Hypertension, preeclampsia and eclampsia are some of the conditions experienced by pregnant woman in oxidative stress state (Levente, 2012). These cases are more prominent with primigravida partly because it is their first experience in pregnancy. In order to promote safety of both mother and fetus, the oxidative stress in pregnant women should be assessed. Malondialdehyde - one of the end products of lipid peroxidation - is one of the biomarkers of oxidative stress that are measured in plasma and urine. It was also reported that plasma concentration of heavy metals can be used as markers of oxidative stress (Uchida, 2003).

Studies regarding measurement of oxidative stress level in primigravida are very sparse in the Northern part of Nigeria, where there is high maternal and neonatal mortality rates (Gilles *et al.,* 2013). Oxidative stress might be among the causes of this increased mortality. This research is targeted at measuring the oxidative stress level in women that are pregnant for the first time (primigravida) with a view to contribute in curbing the rise in complications and death during pregnancy, thereby ensuring a healthy status for both the primigravida and her fetus throughout the gestation period and even after (Saikumar *et al.,* 2013).

MATERIALS AND METHODS

Study Subjects

The study involved thirty women that are pregnant for the first time (primigravida) attending antenatal clinic at Gombe town gidan magani maternity, Gombe State, North-eastern Nigeria. The study also involved ten aged-matched non pregnant women who served as control. Both the test and control were recruited from a comparable background (same geographical area and socio-sanitary status).

Sample Collection

Blood samples (5 Ml) were collected from the primigravida and control subjects under sterile conditions into EDTA container by venupuncture. Plasma was prepared by centrifuging the blood samples at 3000 revolution per minute for 10min. The plasma obtained was used to

analyze the level of malondialdehyde and heavy metals. The same primigravida were followed in the 2nd and 3rd trimesters and the plasma level of malondialdehyde and heavy metals were estimated.

Estimation of Markers of Oxidative Stress

Estimation of Plasma Malondialdehyde was carried out as reported by Ohakawa *et al.* (1979), while selected heavy metals were estimated by atomic absorption spectrophotometry as reported by Kaneko (1999).

Statistical analysis

This was done using student's t-test. The values were expressed as mean ± standard error. P values < 0.05 were considered significant.

RESULT

Plasma concentration of Malondialdehyde (MDA) in the control group and in the primigravida in their 1st, 2nd and 3rd trimesters is presented in table 1. There is a significant ($P < 0.05$) increase in the level of MDA in the 1st trimester compared with control group. There is also a significant ($P < 0.05$) increase in the level of MDA in the 2nd and 3rd trimester compared with control group. These indicate the presence of oxidative stress in the primigravida. The concentration of MDA in the 2nd trimester is significantly ($P < 0.05$) higher than in the 1st trimester. This indicates that the level of oxidative stress increases as pregnancy grows from 1st through 2nd trimester. However, the level of MDA in the 2nd trimester is not significantly different with that in the 3rd trimester. This may mean that the level of oxidative stress does not increase as pregnancy grows from 2nd trimester through the 3rd trimester.

Table 1: Plasma concentration of MDA

GROUPS	PLASMA MDA (µmol/l)
CONTROL GROUP	23.63 ± 2.25^{ab}
1ST TRIMESTER	37.50 ± 3.79^{ab}
2ND TRIMESTER	74.00 ± 6.43^{a}
3RD TRIMESTER	44.20 ± 6.36^{b}

Values are expressed as Mean ± SEM.
Values in the same column bearing the same superscript are significantly different at P<0.05.
n = 10 for control, n = 30 for test.

Table 2 shows the plasma concentration of selected heavy metals (Cu, Zn, Mn, Ni, Cd and Pb) in control and in the primigravida in their 1st, 2nd and 3rd trimesters. The levels of Cu and Zn significantly ($P < 0.05$) increased in 1st trimester, through the 2nd trimester and 3rd trimester when compared with control. The level of Mn in the 1st, 2nd and 3rd trimester is significantly lower ($P < 0.05$) than that of control. There was no reading detected for Ni, Cd and Pb. The difference in the concentrations of heavy metals across the three trimesters is not significant ($P > 0.05$).

Table 2:

GROUPS	Cu (mg / dl)	Zn (mg / dl)	Mn (mg / dl)	Ni (mg/dl)	Cd (mg/dl)	Pb (mg/dl)
CONTROL GROUP	2.94 ± 0.7^{abc}	2.88 ± 0.35^{abc}	3.69 ± 0.53^{abc}	-	-	-
1ST TRIMESTER	3.88 ± 1.09^{a}	3.63 ± 1.37^{a}	2.75 ± 0.58^{a}	-	-	-
2ND TRIMESTER	3.60 ± 1.10^{b}	3.10 ± 0.96^{b}	1.80 ± 0.40^{b}	-	-	-
3RD TRIMESTER	3.70 ± 1.07^{c}	3.20 ± 0.68^{c}	2.65 ± 0.55^{c}	-	-	-

Values are expressed as Mean ± SEM

Values in the same column bearing the same superscript are significantly different at $P < 0.05$.
n= 10 for control, n= 30 for test.

DISCUSSION

The use of oxygen is very essential for human life (Stwertka, 1998). However, reactive oxygen species are produced in the process of using oxygen by the body. High amount of these reactive oxygen species produced beyond the counteraction of the body's antioxidant system results to oxidative stress (Sugino *et al.,* 2007). Pregnant women are prone to oxidative stress because of too much demand of tissue oxygen (Fialova *et al.,* 2006). Malondialdehyde (MDA) is one of the biomarkers used in assessing oxidative stress (Uchida, 2003; Saikumar *et al.,* 2013). The result of the present research revealed that concentration of MDA increased significantly ($P < 0.05$) in the 1st, 2nd and 3rd trimester compared to the control. This is an affirmation that oxidative stress exist in pregnant women. Joseph and Kafilat (2012) also reported that MDA level significantly increase in subjects exposed to oxidative stress compared to control. The result also shows that the level of MDA is highest in the 2nd trimester compared to the control, indicating that oxidative stress is highest in the 2nd trimester (Saikumar *et al.,* 2013).

The assessment of the concentration of heavy metals in pregnant women in relation to oxidative stress was also carried out. Heavy metals are present naturally in the environment, and may find their ways into human body through air, water, soil and food we use. It was reported that heavy metals catalyse the oxidative damage of biomolecules. This may be due to their ability to cause increase production of ROS (Ercal *et al.,* 2001). Cu is one of the heavy metals analyzed in this research. Cu is an essential trace element, it serves as cofactor of many enzymes essential for survival. The common source of Cu is diet especially vegetable (Franchitto *et al.,* 2008). In this research and that conducted by some researchers, the level of Cu was found to be significantly ($P < 0.05$) higher in pregnant women compared to control, and is even doubled at full term (Vir *et al.,* 1981; Vukelic *et al.,* 2012). The increase in the level of Cu could be due to increased secretion of esterogen in pregnancy. Esterogen promotes retention of Cu (Franchitto *et al.,* 2008). Cu is a redox active metal and may cause an increased production of ROS, thereby resulting to oxidative stress. High level of Cu was also reported in preeclamptic women (Ohad *et al.,* 2009). Zn was also analyzed in this research. Zn serves as a cofactor and also as a constituent of growth factors and cytokines (WHO, 1996). The present research revealed that the level of Zn is significantly ($P < 0.05$) higher in primigravida compared to the control. This is possible, probably because Cu metabolism is sometimes associated with Zn, and as earlier stated, Cu level is also raised. However, Jain *et al.* (2010) and Ajose *et al.* (2001) reported in separate researches that Zn level decrease during pregnancy, which is contrary to our findings. Mn is also another important element. It is a cofactor of Mn-containing SOD (Mn-SOD). The present research revealed that the level of Mn is significantly ($P < 0.05$) lower in primigravida compared to control. This may be a confirmation of increased oxidative stress, because low level of Mn is associated with accumulation of superoxides (Lou *et al.,* 2008). Lead, Cadmium and Nickel are all poisonous metals (Neeti and Prakesh, 2013). Exposure to them could be through food, water or mining activities (Stohs *et al.,* 2000). They have the ability to induce oxidative stress (Flora *et al.,* 2008). These metals are absent in both primigravida and control subjects under this study, indicating that neither the primigravida nor the control were exposed to them.

CONCLUSION

Pregnancy is an essential step of human reproduction process. However, it is associated with natural and artificial complications which may result to the loss of the pregnant woman and / or her fetus. Among the causes of these complications is oxidative stress. The result of this

research revealed that primigravida are positive for oxidative stress. This may be among the causes of maternal and neonatal death. Therefore, monitoring oxidative stress level in pregnant women may help greatly in curbing the high rate of maternal and neonatal death in Northern Nigeria.

CONFLICT OF INTEREST

The authors have not declared any conflicting interest among themselves.

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