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# Intermittent Preventive Treatment with Sulphadoxine-Pyrimethamine's Modifications of Plasma Glutathione Peroxidase (GPX) Levels in Parturients and their Controls.

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***Abstract***
***Background:*** *Successful pregnancy continuation in malaria endemic areas may not be without adequate malaria prevention. Prevention of malaria infections during pregnancy is a sinequanon for reducing its problems to humans as well as the consequent burdens that malaria places on pregnancy. Pregnancy associated miscarriages, anaemias, preterm labours and births, small for gestational age feotuses, intrauterine fetal malformations and in utero deaths etc are some of these burdens. Worthy of note is that optimal antioxidant status, like that of Glutathione Peroxidase has been noted as important partakers in ensuring that pregnant women enjoy uneventful pregnancies, have better pregnancy outcomes as well as to prevent other problems of pregnancy which may include intrauterine growth retardations (IUGR), maternal and neonatal anaemias, increased admissions into special care baby units and even maternal and neonatal deaths.*
***Objectives:*** *To study the modifications of plasma Glutathione Peroxidase (GPX) levels in parturients by intermittent preventive treatment with sulphadoxine-pyrimethamine.*

***Method:*** *This study held at the Federal Medical Centre (FMC), Owerri, a town where malaria menace is at its optimum and remains a major problem to the pregnant state. Longitudinal participant recruitment duly followed ethical clearance and certification obtained from the ethics committee of the health facility. This was done in conjunction with adequate counseling and informed consent involving both groups. A total of 296 participants finally completed the laboratory based, cross-sectional descriptive study. All recruited participants successfully satisfied the inclusion criteria as stipulated for either the study or control groups. Following final recruitment, participants were followed up through the entire antenatal period till delivery. The follow up was to enable a meticulous collection of blood samples for plasma Glutathione peroxidase estimation. This was done using the method of* ***Rotruck, Pope, Ganther, Hofeman & Hoekstro, 1973.*** *The principle is based on the scientific basis that GPx in the presence of hydrogen peroxide ($H_2O_2$) oxidizes reduced glutathione (GSH) to form $H_2O$. The amount of GSH consumed is directly proportional to the activity of GPx and it is expressed as U/ml (µmol of GSH consumed/minute). The GSH remaining after the reaction is allowed to react with 5'-5' dithiobis-2-nitrobenzoic acid (DTNB) to form a yellow complex that absorbs maximally at 412 nm.* ***Data analysis:*** *Analysis of the obtained data was done using the computer Software Package for Social Science (SPSS) version 20.0 (SPSS, Inc, 2007, Chicago). Additionally, descriptive statistics (mean, standard deviation, range, percentages etc) were determined for continuous variables. For the purpose of this study, p-value less than* ***<0.05 at 95%*** *confidence interval was considered statistically significant.* ***Result:*** *The mean serum level of Glutathione Peroxidase (GPX) in the study group was 0.899 U/ml ± 0.199 while the minimum and maximum serum Glutathione Peroxidase were 0.016 and 1.587 U/ml respectively. For their controls, the mean serum level of Glutathione Peroxidase was 0.856 U/ml ±*

*0.310. However, the minimum and maximum serum Glutathione Peroxidase were 0.101 and 1.923 U/ml respectively. The difference was not statistically significant (p= 0.153) with odds ratio 1.92 (CI of 95% 0.785-4.680).*

***Keywords:*** *Anaemia in pregnancy, Antenatal Course, Glutathione, Hydrogen peroxide, Malaria endemicity, and Sulphadoxine Pyrimethamine.*

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## I. Introduction

Medicine net defined malaria as a serious, life-threatening and sometimes fatal disease spread by mosquitoes and caused by a parasite, plasmodium. Malaria used to be responsible for a significant health risk in the United States of America until it was successfully eliminated by multiple disease-control programs in the late 1940s. It is an infectious disease caused by a protozoan parasite from the Plasmodium family that can be transmitted by the bite of the female Anopheles mosquito or by contaminated needles and syringes or transfusion. Falciparum malaria is the most deadly type (Chukwu LC, PhD Thesis, 2019; https://www.medicinenet.com on malaria definition).

According to the world malaria report 2011, estimated 216 million cases of clinical malaria occurred in 2010 resulting in about 655,000 deaths across the globe. It was regrettable that 91% of these deaths occurred in Africa (Chukwu, Agbasi, Unekwe, Oguwike, 2019; UN Inter-Agency for Child Mortality Estimation, 2012). About 2.2 billion people are exposed to malaria and its menace annually, and out of which 300-500 million cases of the disease are developed. In 2006, unfortunately 247 million cases of malaria were estimated with about one (1) million deaths, mostly among African children (Chukwu, Agbasi, Unekwe, Oguwike, 2019; Byakika-Kibwika, P., et al, 2010).

Malaria disease remains a major public health problem in Nigeria and unfortunately, children under the age of five (5) and pregnant women are the most vulnerable groups. Prevalent studies show that more than **60% of** outpatient visits to Nigerian hospitals are due to malaria disease and its complications. The disease has impacted negatively on our economy with about **132 billion Naira** lost to the disease as cost of treatment and loss of man hours (Salwa et al., 2016; Federal Republic of Nigeria, 2015; Kathryn et al., 2014; FMOH Nigeria, 2011; Uzochukwu et al. 2010).

During pregnancy, deranged foetal blood and other nutrient supply may ensue from the invasion of the placental bed by inflammatory cells and cytokines characteristic of malaria disease. As a result, the foetus may be of low weight at birth or even small-for date or may suffer from prematurity with its attendant consequences. Babies born small-for date are at high risks of neonatal or infantile morbidity and mortalities (Falade et al, 2007; van Geetruyden, Thomas, Erhart & D' Alessandro, 2004).

Malaria hyperpyrexia has been implicated in the causation of pregnancy loses due to abortion or premature labours. It may also lead to small-for date neonates, intra-uterine fetal death with attendant macerated fetuses. Malaria parasites have the capacity of destroying both maternal and foetal red blood cells which subsequently can lead to red cell haemolysis and anaemia of folic acid deficiency. **Parasitization of the placenta is a condition caused by the malaria parasite invasion of the pregnant placenta.** This condition causes placental insufficiency leading to the delivery of low-birth-weight babies even at term, that is if born alive (Chukwu, LC., an MSc Dissertation, 2009).

For these reasons, intermittent preventive treatment, usually with sulfadoxine-pyrimethamine was introduced by the WHO to help curb the menace of malaria in pregnancy. IPT-SP has been shown to prevent pregnancy-related malaria and its complications (Brentlinger, Behrens & Micek, 2006). Anaemia in pregnancy is also a major cause of maternal and fetal mortality in Africa and Asia. It is a reduction below normal in the number of red blood cells per cubic millimetre, the quantity of haemoglobin and the volume of packed red cells per 100ml of blood. Usually, it is a common complication of pregnancy especially in the tropics where it is usually of the severe type (Chukwu, LC., an MSc Dissertation, 2009). The World Health Organization (WHO) defined anaemia as a haematologic condition and a sign of an underlying disorder characterized by a reduction in the number of red blood cells, or a reduction in the concentration of haemoglobin in the blood stream to a level below 10.5g/Dl (Ejiofor; Ozokono; Ugwu, 2019; WHO, 2007).

Anaemia from malaria, remains a major global public health problem especially in the developing countries of the Sub Saharan Africa. It is often noticed among primigravids who are more susceptible to malaria infection mainly due to Plasmodium falciparum species (Savage, Msyamboza, Gies, D' Alessandro & Brabin, 2007).

Generally, malaria is a common public health problem affecting both the mother and her unborn child. In the less developed countries of the world, it is seen as a major public health problem that is said to affect 41%

of pregnant women worldwide. Africa has the largest share with 17.2 million women representing 57.1% of cases. This estimate may be highly conservative (Lealam, Asrat, Yaregal & Andualem, 2015).

In Africa, malaria accounts for up to a third of all hospital admissions, and up to a quarter of all deaths of children under the age of five (FMOH Nigeria, 2005).

There are up to 800,000 infantile mortalities and a substantial number of miscarriages and very low birth weight (VLBW) babies per year due to the disease (WHO malaria guideline, 2006).

It is said that a bout of malaria typically costs 10 working days, adding to the economic burden. In Africa it is estimated that an individual receives 40-120 infective mosquito bites per year, compared to only 2 in India (Nwani & Unekwe, 2005).

In Africa, malaria accounts for up to a third of all hospital admissions, and up to a quarter of all deaths of children under the age of five. Malaria is responsible for 30% childhood mortality, 11 % maternal mortality as well as account for more than 60% outpatient visits that is due to malaria making it a major public health problem in Nigeria. The disease has impacted negatively on the economy with about 132 billion naira lost to malaria as cost of treatment and loss in man-hours (Chukwu, LC., an MSc Dissertation, 2009; National antimalarial guidelines, 2005).

It has also been noted that falciparum malaria ensues reactive oxygen species (ROS) leading to noticeable alterations in the levels of antioxidant status. This happens especially in the pregnant state where it can have the capacity to overwhelm the body's antioxidant defenses leading to oxidative stress. An imbalance between reactive oxygen species and antioxidant defense mechanisms of a cell amounts to **oxidative stress.** The relationships between IPT-SP ingestion and antioxidant status during pregnancy remains a virgin area with key research interests. It is worthy of note that very major attention has always been invested while trying to prevent malaria in pregnancy in the past, currently and in the future as expected. This is not unconnected with the problems that an episode of untreated malaria infection (in pregnancy) can met out to the trio of the mother, the foetus and the neonate. Owing to this, strategies for the prevention of malaria in pregnancy has evolved through several protocols from the past to the present day.

Many studies have reported that the pathophysiology of malaria infection involves oxidative stress. This is especially so with malaria in pregnancy where the natural body defense mechanisms are markedly reduced especially in first pregnancies. In Cameroon, Tiyong and co prospectively studied the activities of oxidants and antioxidants. From their study outcome, they suggested the existence of an imbalance between oxidants and antioxidants in pregnant women suffering from malaria. This situation that could cause severe damage to the mother, the fetus or both. (Tiyong et al., 2009).

In another study, the antioxidant status of newborns analyzed showed low concentrations of glutathione peroxidase, superoxide dismutase, ß-carotene, riboflavin, α-proteinase, vitamin E, selenium, copper, zinc, transferrin and other plasmatic factors (Buonocore and Groenendaal, 2007), while immediately after birth, values of oxidative stress markers in mothers and newborns were elevated and increased further during the first few days of neonatal life. Breast milk was the only nutritional substance with high antioxidant activity. At the same time, TBARS levels in breast milk decreased, which might indicate its protective role in reducing oxidative stress in newborns (Wilinska, Borszewska-Kornacka, Niemiec & Jakiel, 2015).

Oxidative stress (OS) is majorly caused by reactive oxygen species (ROS), which principally are derivatives of molecular oxygen. Aerobic organisms in response to both external and internal stimuli constantly generate small amounts of ROS namely: hydroxyl radicals (•OH), superoxide anions ($O_2^-$), and hydrogen peroxide ($H_2O_2$). Due to their high chemical reactivity, they are highly transient and can lead to lipid peroxidation, oxidation of some enzymes, and massive protein oxidation and degradation (Claudio et al., 2011).

While we acknowledge the various studies already done on the problems of malaria in pregnancy, its treatment in various regions, it is noteworthy to categorically state here that a lot still needs to be done especially on the effects of sulphadoxine-pyrimethamine on malaria in pregnant women. Further studies may also be necessary to compare the Glutathione peroxidase levels of parturients who received intermittent preventive treatment with sulfadoxine-pyrimethamine (IPT-SP) at varying trimesters during their concurrent confinements with those of parturients who did not receive any IPT at Owerri, a malaria endemic area in Imo State, South East Nigeria.

Presently, there is dearth of scholarly works assessing glutathione peroxidase levels and their interactions with Intermittent Preventive Treatment with Sulphadoxine Pyrimethamine in pregnant women who received Intermittent Preventive Treatment with Sulphadoxine Pyrimethamine and their controls during current confinements. In order to fill the above research gaps, this study was conducted to ascertain a comparative assessment of the plasma Glutathione peroxidase levels in Parturients who Received Intermittent Preventive Treatment with Sulphadoxine Pyrimethamine (IPT-SP), and their controls during their current confinements. The outcome of this study, we believe will help policy makers and obstetrics practice practitioners adopt strategies that will ensure better pregnancy courses for our pregnant women. The research question is: does the ingestion of IPT-SP for malaria prophylaxis affect glutathione peroxidase levels in malaria endemic areas?

**MALARIA, GLUTATHIONE PEROXIDASEAND ANTIOXIDATION**

"Free radicals are a necessary waste product of cellular energy production, but our cells must rid themselves of this waste or succumb to the ravaging effects of oxidative damage. Glutathione acts in every cellular compartment— the cytosol, the nucleus, and the mitochondria, to quell these free radicals. Adequate glutathione is not just desirable, it is essential for the survival of each cell, making it essential to life itself". Tina Kaczor, ND, Fabno (www.RoundTableCancerCare.com); Sarah, 2017).

Glutathione (GSH) is a tripeptide and the most abundant free radical scavenger synthesized endogenously in humans. Increasing mechanistic, clinical, and epidemiological evidence demonstrated that GSH status is significant in acute and chronic diseases. Despite its ease of delivery, limited or no research data exist that has evaluated the activities GSH during malaria infection in the background of on intermittent preventive treatment for malaria infection (Jason and Ryan, 2011).

Superoxide and hydrogen peroxide are reactive oxygen species generated in all cells by mitochondrial and enzymatic sources. These reactive species if left unchecked can cause oxidative damage to DNA, proteins, and membrane lipids. As an intracellular antioxidant enzyme, Glutathione peroxidase-1 (GPx-1) can enzymatically reduce hydrogen peroxide to water limiting its harmful effects. Certain reactive oxygen species like hydrogen peroxide, are also essential for mitochondrial functions, growth factor-mediated signal transduction, and maintenance of normal thiol redox-balance. Thus, by limiting the accumulation of hydrogen peroxide, GPx-1 also modulates these processes (Edith, Joseph & Diane, 2011).

Wdowaik and co studied the activities of SOD and GPx in the blood and placental tissues of pregnant women with diabetes (study group), women with physiological pregnancy (healthy pregnant group), and non-pregnant women (control group). They found that GPx activity in erythrocytes was considerably higher in the group of patients with diabetes, compared to the other 2 groups and the differences was statistically significant, $p<0.001$. Also, between the control group (CG), and the group of healthy pregnant women (HP) and the group of pregnant women with diabetes (PD) the differences in GPx activity were statistically significant (Wdowiak, Brzozowski & Bojar, 2015).

Jason and Ryan conducted a randomized, double-blind, placebo-controlled clinical trial aimed at determining the effect of oral GSH supplementation on biomarkers of systemic oxidative stress in human volunteers. In their own study they found no differences in oxidative stress biomarkers between treatment groups at baseline. Total reduced, oxidized, and ratio measures of GSH status were also unchanged (Jason and Ryan, 2011).

In conclusion, Wdowaik and co posited that in pregnancies complicated by diabetes, the GPx activity in blood was higher than those for women with physiological pregnancies and the control group. The same GPx activity was also noticed to be increased in the placental tissues of diabetic women than their physiological pregnant counterparts (Wdowiak et al. 2015). On the contrary, Jason and Ryan in their own study concluded that no significant changes were observed in biomarkers of oxidative stress, including glutathione status, in their clinical trial of oral glutathione supplementation in healthy adults (Jason and Ryan, 2011). It is worthy of note that this very research was carried out in healthy adults.

An increase in the antioxidant activity following increased production of free radicals is common. This may result in antioxidant insufficiency or exhaustion. The increased production of free radicals is considered as one of the key factors leading to damage in the course of uncontrolled diabetes. This was emphasized by Agarwal and colleagues in their report. They considered free radicals produced during pregnancy as one of the most important factors affecting the development of the foetus (Wdowiak et al. 2015, Agarwal, Gupta & Sikka, 2006). This may be same for malaria in pregnancy.

The unfavorable effect of oxidative stress in pregnancy has been emphasized by many researchers. Numerous important pathologies which develop in the course of oxidative stress may include: miscarriages, premature deliveries, preeclampsia, intra uterine growth retardation, pregnancy induced hypertension, as well as metabolic disorders, such as gestational diabetes (Wdowiak et al. 2015; Clapés, Fernandez & Susrez, 2013; Hong et al., 2007; Mier et al., 2007). Malaria and Anaemia in Pregnancy may also be affected by these processes. The forgoing exposes very important research gaps which this study aims at filling.

Also, there are abridged to minimal works assessing Glutathione Peroxidase levels and their interactions with Intermittent Preventive Treatment with Sulphadoxine Pyrimethamine in Parturients who Received Intermittent Preventive Treatment with Sulphadoxine Pyrimethamine in pregnancy. Hence, we conducted this study to ascertain a comparative assessment of the Plasma Glutathione Peroxidase Levels in Parturients who Received Intermittent Preventive Treatment with Sulphadoxine Pyrimethamine (IPT-SP), and their controls during their current confinements.

## II. MATERIALS AND METHODS:

**STUDY CENTER:**

This study was carried out at the Federal Medical Center Owerri (FMC) which is a tertiary health center offering most of the specialist medical services available in Nigeria. Such services include Obstetric care, Gynaecological services, Paediatric care, Ear, Nose and Throat care, Dermatology, Specialist Laboratory services to mention but a few.

**STUDY SETTING:**

The hospital is located at the heart of Owerri town enabling easy access to the inhabitants of Owerri and its environs. Owerri is the capital city of Imo State in Nigeria, situated in the heart of Igboland. It is also the largest city in the State and is followed by Orlu, Okigwe and Ohaji / Egbema. Owerri consists of three Local Government Areas including Owerri Municipal (where the study was actually carried out), Owerri North and Owerri West. In 2016, Owerri had an estimated population of about 1,401,873 with an approximate area of 100 square kilometers (40 square meters). The Otamiri River borders Owerri to the east, while the Nworie River borders it to the south. (Acholonu, 2008; Encyclopaedia Britannica, 2007). The Owerri Slogan is Heartland.

**STUDY DESIGN:**

The present Prospective cohort study was conducted among pregnant women receiving Antenatal care at the Federal Medical Center Owerri. The study protocol was intensively reviewed by the ethics committee of the hospital enabling them to grant us an ethical certificate **No. FMC/OW/HREC/55: May 12, 2016.** All enrolled women provided a written informed consent for study participation. However, the women were recruited using the Purposive sampling technique. The pregnant women in the study group received two (2) doses of IPT-SP, given one month apart for as early as possible in the second trimester and were compared with the group of pregnant women who did not receive any IPT-SP.

The inclusion criteria were pregnant women without any symptom nor signs of malaria; no parasitological nor other diagnosis of malaria; had an ancillary body temperature of less than or equal to $37.4^0$ centigrade; no co-existing medical disorder nor comorbidities; no ingestion of any form of antimalarial two weeks prior to recruitment. The recruited women were to be resident in Owerri or its suburb to enable them deliver at FMC Owerri so as to enable timely collection of blood samples for the estimation of serum Glutathione Peroxidase.

For the control group women recruited included those presenting at very late pregnancy for delivery or those booking that late for antenatal care (last month of pregnancy) or having obvious allergies for Sulphadoxine-Pyrimethamine (SP). These women were to have met other criteria for inclusion as stated above.

Exclusion criteria did include women with body temperature more than $37.5^0$C, those suffering from malaria or having co-existing medical disorders / comorbidities. Equally excluded were those pregnant women that had ingested any form of antimalarial at about two weeks prior to recruitment or those with any form of allergy to any component of SP. From history, those women who were adjudged not to able to deliver at FMC, Owerri were also excluded from the study. This ensured that we were able to collect blood samples from the participating women for the estimation of Glutathione Peroxidase.

**ESTIMATION OF GLUTATHIONE PEROXIDASE [GPX]**

The activity of glutathione peroxidase was determined the method of Rotruck et al. (1973).

GPx in the presence of H2O2 oxidizes reduced glutathione (GSH) to for H2O. The amount of GSH consumed is directly proportional to the activity of GPx and it is expressed as U/ml (µmol of GSH consumed/minute). The GSH remaining after the reaction is allowed to react with 5'-5' dithiobis-2-nitrobenzoic acid (DTNB) to form a yellow complex that absorbs maximally at 412 nm.

$$2GSH + H2O2 \xrightarrow{GPx} GSSG + 2\,H_2O$$

**Procedure**

The reaction mixture contained 0.4 ml of phosphate buffer (pH 7.0), 0.1 ml sodium azide and 0.2 ml of the plasma or standard or blank, 0.2 ml of glutathione and 0.1 ml of $H_2O_2$. The resulting solution was thoroughly mixed and incubated at 37°C for 10 minute. The reaction was arrested by the addition of 0.4 ml of 10% trichloroacetic acid (TCA). The tubes were centrifuged at 4000 rpm for 5 minutes. Thereafter, 0.5 ml of the supernatant was added into a cleaned test tube followed by the addition of 2 ml of phosphate buffer (pH 7.0) and 0.5 ml of 40 mM DTNB. The solution was thoroughly mixed and the resulting yellow colour was read at 412 nm. A blank was treated the same way except that it contained 0.2 ml of Dist. water instead of sample. 20 mg/100 ml of GSH standard (0.651 µmol/ml) was also used.

The activity of glutathione peroxidase was expressed as U/mL of plasma (µmoles of GSH utilized / minute).
Calculation:
Actual Test OD = OD Blank – OD Test
Actual Std OD = OD Std – OD Blank.
GPx activity = Actual OD Test/Actual OD Std X Std Concentration, U/mL (Rotruck et al 1973).

**STASTISTICAL ANALYSIS**

The results from the study were presented as mean±std deviation. Computer Software Package for Social Science (SPSS) version 20.0 (SPSS, Inc, 2007, Chicago) was used for computations and analysis. Descriptive statistics (mean, standard deviation, range, percentages etc) were determined for continuous variables. The results obtained were presented as tables, histograms and box plots in the next section. P-value less than **(<0.05) at 95%** confidence interval was considered to be statistically significant.

## III. RESULTS:

In the course of participant recruitment, a total of 330 pregnant women were assessed for eligibility. Out of this number, 310 were recruited (enrolled). 14 women were excluded from the study leaving a total of 296 that were analyzed. This comprised of 148 pregnant women that received the IPT-SP and served as the study / case group and 148 pregnant women in the control group that did not receive the IPT-SP.

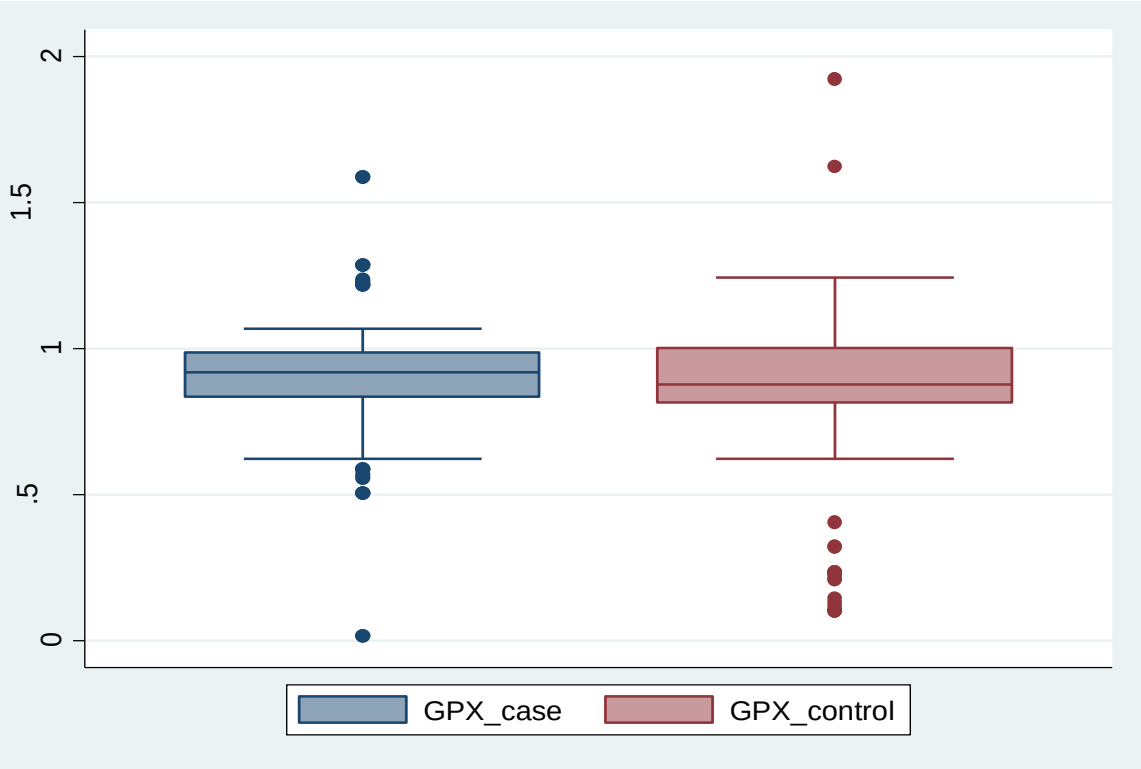


**Figure 1 (Box plot 1): Serum levels of Glutathione Peroxidase (GPx) in the study (case) and control groups.**

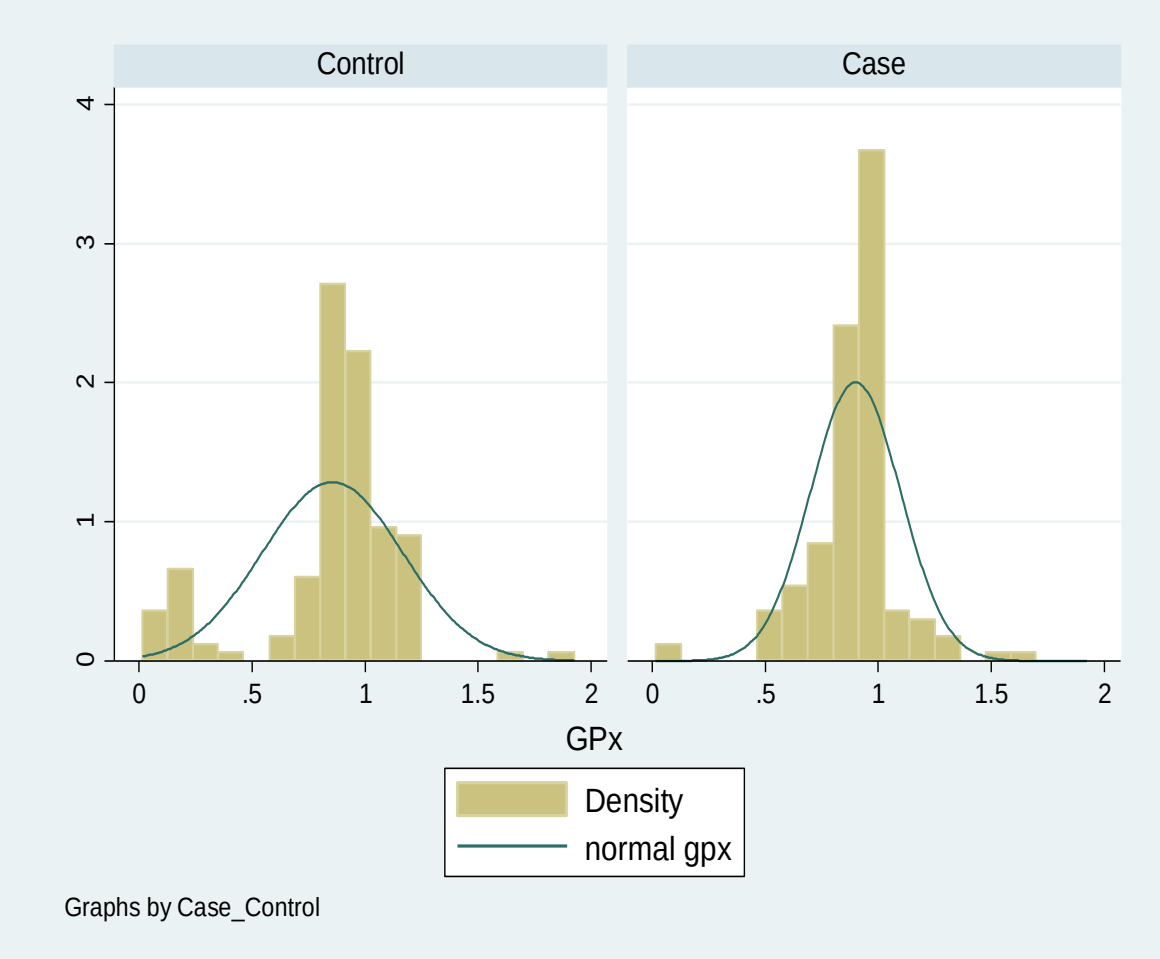


**Figure 2 (Histogram 1): The serum levels of Glutathione Peroxidase (GPX) in both the study (case) and control groups.**

**Table 1: The Effects of the serum levels Glutathione Peroxidase in both the** study **and control groups.**

| Variable | n | min | max | Mean | Std. dev | coef | S.e. | p-value | OR | 95% C.I.for OR Lower | Upper |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Case | 148 | 0.016 | 1.587 | 0.899 | 0.199 | | | | | | |
| Control | 148 | 0.101 | 1.923 | 0.856 | 0.310 | 0.650 | 0.455 | 0.153 | 1.92 | 0.785 | 4.680 |

From the table above, the average Glutathione Peroxidase (GPx) of the mothers was 0.899 ± 0.20 for the study and 0.856 ± 0.31 for the control.

**Influence of GPX serum levels in both the study and control groups**

The average Glutathione Peroxidase (GPx) was slightly higher (0.899) U/ml among women that took IPT (study) compared to the average level for the control group (0.856) U/ml. This can be clearly observed in a comparative Box plot (Figure 4.4) above. The analysis indicates that the observed difference was not statistically significant (p= 0.153, 95% CI =0.785 – 4.680) and thus may have occurred by chance (see table 1 above).

## IV. DISCUSSION

The results of this study demonstrated that the mean serum level of Glutathione Peroxidase among the study group was 0.899 U/ml while in the control, it was 0.856. The difference was not statistically significant (p= 0.153) with odds ratio 1.92 (CI of 95% 0.785-4.680). The high levels of serum Glutathione Peroxidase, an antioxidant enzyme may have been conferred by the administered IPT-SP among the treatment group.

Adisa and co investigated the effects of treatment with SP on the antioxidant defense system using a model. Ten male rabbits were divided into two groups of five animals each. The first group received normal saline

and served as control while the second received a single dose of 26.25mg/kg body weight of SP. Blood samples were collected before and at 6, 12 and 24 h after drug administration. Activity of cellular enzymatic antioxidants, SOD, catalase (CAT), and level of reduced glutathione (GSH) were assayed using standard spectrophotometric methods. They reported that, the level of GSH decreased by 41.9% at 6 h and remained so up till the 12 h, but by 24 h after drug administration, the level of the thiol substance had increased considerably up to 48.4% above the baseline level. Their conclusion was that SP treatment alters the antioxidant defense system in blood and may therefore induce oxidative stress by generating reactive oxygen species (ROS). This might play significant roles in the therapeutic and adverse effects associated with the drug (Adisa, Ogunbayo, Olorunsogo & Ademowo, 2011). This finding did not clearly compare with the results of this study though some association can be deduced.

In the study by Atiba and co on pre-eclamptic women, serum Glutathione peroxidase level was significantly higher in the third trimester (2804.11±1573.00U/L) as compared to the second trimester (2655.00±1751.30U/L), p= 0.0001. Glutathione peroxidase activity in the third trimester of normal pregnancy (3339.50±1733.80U/L) was also found to be higher than in the second trimester (3023.50±1115.90U/L) and p= 0.131 (Atiba et al., 2014). A finding which compared with the findings of this study.

Recent studies have further suggested that oxidative stress can partake in the pathogenesis of thrombocytopenia associated with malaria. This was evidenced by the fact that the number of platelets and the activities of antioxidant enzymes, SOD and GSH-Px in patients with vivax malaria were reduced while lipid peroxidation of platelets (estimated by measuring the MDA), was elevated in infected individuals, suggesting a negative correlation between platelet count and platelet level of lipid peroxidation. These results suggested that oxidative stress occupied an important role in the pathogenesis of thrombocytopenia in malaria. This is envisaged to occur through loss of elasticity of membranes and by increasing brittleness which causes dysfunction in receptors, resulting in considerable functional impairment of thrombocytes (Sandro et al., 2012; Erel, Vural, Aksoy, Aslan & Ulukanligil, 2001).

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**DECLARATION FOR CONFLICTS:** There was and has been no conflict of interest.
**ETHICAL APPROVAL:** For the conduct of this research, Ethical permission was gotten from the Federal Medical Center, Owerri ethics committee. This was after a thorough review and consideration of the study proposal.

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