ISSN No. 2454-6194 | DOI: 10.51584/IJRIAS | Volume VIII Issue IV April 2023

Interactions of Ascorbic Acid with Intermittent Preventive Treatment with Sulphadoxine Pyrimethamine in Parturients and their Controls

Chukwu Leo Clinton[1*]; Ekenjoku Azubuike John[2]; Olisa Chinedu Lawrence[3]; Ogabido Chukwudi Anthony[4]; Ramalan Aliyu Mansur[5]; Okoye Innocent Chukwuemeka[6]; Nwankwo Malarchy Ekwunife[4]; Ezeigwe Chijioke Ogomegbunam[4]; Chukwuka Benjamin Uzodinma[7], Nweze Sylvester Onuegbunam[8]

[1]College of Medicine, Chukwuemeka Odumegwu Ojukwu University, Awka Nigeria
[2]Dept. of Pharmacology & Therapeutics. Coll. of Medicine & Health Sciences, Abia State University Uturu, Nigeria
[3]Dept. of Pharmacology & Therapeutics, Nnamdi Azikiwe University, Nnewi, Nigeria
[4]Dept. of Obstetrics & Gynecology, Nnamdi Azikiwe University, Nnewi Campus, Nigeria
[5]Dept. of Internal Medicine, Aminu Kano Teaching Hospital / Bayero University Kano, Nigeria
[6]Dept. of Medicine, Chukwuemeka Odumegwu Ojukwu University, Awka Campus Nigeria
[7]Dept. of Pharmacology. Faculty of Pharmaceutical Sciences, Nnamdi Azikiwe University Awka, Nigeria
[8]Department of Obstetrics and Gynaecology, Enugu State University College of Medicine (ESUCOM), Enugu Nigeria

Correspondence: Chukwu, Leo Clinton*

DOI: **https://doi.org/10.51584/IJRIAS.2023.8415**

Received: 17 March 2023; Accepted: 24 March 2023; Published: 04 May 2023

Abstract.

Background: Malaria deaths in the world have remained worrisome for many decades to centuries now. The issue of its prevention pre pregnancy, during pregnancy and post pregnancy periods needs continuous emphasis especially in our endemic areas. This will help us achieve the desired goals of eliminating malaria menace in Sub-Saharan Africa. The benefits of malaria prevention in helping to reduce the problems of malaria in pregnancy though proven needs continuous emphasis. The problems of prolonged maternal malaria illnesses especially if left untreated during pregnancy may include but not limited to preterm labours / births, pregnancy anaemias, small for date babies, high rates of admissions into special care baby units (SCBU) and intrauterine deaths. The above have been greatly reduced by concurrent practice of preventive measures like the now in use, Intermittent Preventive Treatment with Sulphadoxine Pyrimethamine (IPT-SP). It has also been noted that optimal levels of antioxidant status like Ascorbic acid (Vitamin C), Superoxide Dismutase, Glutathione Peroxidase have shown great promises in assisting our pregnant women enjoy uneventful pregnancies as well as avert most other pregnancy associated problems. Top on the list of which are maternal and neonatal anaemias, preterm labours and births, intrauterine growth restrictions (IUGR), increased admissions into special care baby units and even neonatal deaths to mention but a few.

Objectives: This study made a comparative assessment of the plasma Ascorbic acid levels in parturients who judiciously received IPT-SP during their current confinements and their controls.

Method: We carried out this study at the Federal Medical Centre (FMC) which is located in Owerri, the state capital of Imo state Nigeria. Owerri is noted to have a typical malaria endemic setting as with most parts of our African sub rejoin. Ethical certification was sought for and obtained from the ethics committee of the hospital enabling the commencement of a longitudinal participant recruitment after adequate counseling and informed consent. This involved both groups. The study was a laboratory based, cross-sectional descriptive study that involving 296 participants that satisfied set out inclusion criteria for one of the groups as allotted. Participants were followed up following recruitment throughout their antenatal course till delivery. This enabled a dutiful collection of blood samples for the estimation of Ascorbic acid. Vitamin C estimation was done using the Omaye, Turabull & Sanberlish method, 1979. The methodology principle is based on the fact that Ascorbic acid is oxidized by copper to form dehydroascorbic acid. The product when treated with 2, 4 dinitrophenyl hydrazine forms tris 2, 4 dinitrophenyl hydrazone which undergoes rearrangement to form a product with the absorption maximum at 520 nm in spectrophotometer.

Data analysis: Computer Software Package for Social Science (SPSS) version 20.0 (SPSS, Chicago) was used to analyze obtained data. The descriptive statistics (mean, standard deviation, range, percentages etc) were determined for continuous variables, while a P-value less than (<0.05) at 95% confidence interval was considered statistically significant.

ISSN No. 2454-6194 | DOI: 10.51584/IJRIAS | Volume VIII Issue IV April 2023

Result: The mean ascorbic acid value was lower among the study group than the control. Mean ascorbic acid value for the study group was 1.75 ± 0.67 while the minimum and maximum serum ascorbic acid levels were 0.064 and 3.29 respectively. From the control group, the mean ascorbic acid level was 2.03 ± 0.68 while the minimum and maximum serum ascorbic acid levels were 0.056 and 3.75 respectively. From the results above, **the mean difference of 0.28 was found to be statistically significant with (p value= 0.001) with an odds ratio of 0.54 (95% CI =0.380 – 0.771).**

Keywords: Anaemia in pregnancy, Antenatal course, Ascorbic acid, Copper, Dehydroascorbic Acid, Dinitrophenyl Hydrazine, Malaria Endeminicity, Sulphadoxine-Pyrimethamine.

I. Introduction

Malaria infection is of major public health importance having afflicted several humans the world over. The malaria endemic areas of the world like the Sub-Saharan Africa (SSA), feels the menace of its infection the more. Malaria is a significant cause of morbidity and mortality especially among our pregnant mothers, their fetuses, neonates as well as young children and the elderly. Malaria is known to constitute enormous social and economic burdens. Although it may be relatively uncommon in developed countries, it occurs among travelers on return from endemic regions and remains one of the most prevalent infections of humans worldwide (Chukwu LC, Ph.D Thesis, 2019; WHO International Travel and Health, 2018; Kathrine et al, 2014).

Approximately 30 million pregnant women at risk for malaria in SSA. With a prevalence of about 28%, malaria in pregnancy is associated with placental parasitaemia, severe maternal anaemia, low birth weight (LBW), and increased perinatal morbidity and mortality. The World Health Organization (WHO) recommended intermittent preventive treatment of malaria in pregnancy, specifically with sulphadoxine-pyrimethamine to help reduce the risk of poor pregnancy outcomes. Sulphadoxine-pyrimethamine which is given without determining parasitaemia status is aimed at either treating patients with parasites or providing a prophylactic effect to non-infected patients (Kathrine et al, 20I4, Dellicour et al, 2010; Desai et al, 2007; World Health Organization Strategic Framework (WHO), 2004).

Malaria in pregnancy remains a major public health problem to families and health authorities especially in Asia and Sub Saharan Africa. These are areas where malaria is endemic especially the later. Pregnancy is known to lower the acquired immunity that is meant to protect against malaria during cyesis especially in first pregnancies. In subsequent pregnancies, malaria may not have a great deal of influence on the patient's acquired immunity to protect against malaria infection (Ojo & Briggs, 2006).

Worse still, the pregnant mother is a higher risk of contacting malaria than her non-pregnant counterpart. This ease to surfer malaria infection in pregnancy is as stated above, due to a transiently depressed state of immunity of the pregnant mother, allowing for an increased susceptibility of the pregnant state to malaria. Although malaria in pregnancy is often asymptomatic, in the immune or the semi-immune woman, it may be one of the most likely causes of unfavorable pregnancy outcomes both for the mother and her baby, giving rising cases of miscarriages, premature / preterm labours, small for date neonates, low birth weights babies as well as neonatal / maternal deaths (Chukwu LC, Ph.D Thesis, 2019; Falade et al., 2007; Bray & Anderson, 1979).

Worthy of note is the issue of malaria hyperpyrexia. This has been implicated in the causation of abortion or premature labour. It may also lead to small-for date neonates, intra-uterine fetal death giving macerated fetuses. Malaria parasites have the capacity of destroying both maternal and foetal red blood cells which subsequently leads to red cell haemolysis and anaemia of folic acid deficiency variety. Placental invasion by these malaria parasites gives rise to a condition known as ***parasitization of the placenta.*** This condition causes placental insufficiency leading to the delivery of low-birth-weight babies even at term, if born alive (Chukwu LC, Ph.D Thesis, 2019; Chukwu LC, MSc Dissertation, 2009).

In areas of high malaria endemicity, it is known that fetal abortions, premature labor, small-for-date babies and fetal or even maternal deaths remain some of the consequences of malaria parasite invasion of the pregnant placenta. In the course of these invasions, cytokines and some inflammatory cells are released which also aid to further complicate the unfavorable pregnancy outcomes classically associated with malaria parasite sequestration in the placental intervillous spaces around the chondroitin sulphate, A (Chukwu LC, Ph.D Thesis, 2019; Falade et al, 2007; Williams, 1996).

Worthy of note is the fact that this fight against malaria in pregnancy led to the launching of the Roll Back Malaria initiative in **April 25, 2000.** Quite a reliable, remarkable and commendable commitment of the African leaders. The initiative was aimed at fighting this disease which is estimated to kill over one million sufferers (especially children and pregnant women) virtually every year. The Roll Back Malaria is noteworthy, and a highly commendable approach (FMOH Nigeria, 2011). Later in the fight against malaria in pregnancy, intermittent preventive treatment for malaria (IPT-SP) was introduced. The World Health Organization (WHO) policy on IPT-SP did stipulate that "all pregnant women residing in stable malaria transmission areas should receive at least two doses of the recommended antimalarial drug preferably at the first and second regularly scheduled antenatal

ISSN No. 2454-6194 | DOI: 10.51584/IJRIAS | Volume VIII Issue IV April 2023

clinic (ANC) visits after quickening". Quickening is said to be the first noted foetal movement / kick during pregnancy **(WHO, 2002a).**

The delivery of IPT-SP at each scheduled visit after 'quickening' would help ensure that a proportion of pregnant women received the minimum two doses of IPT. **WHO antenatal care randomized trial: manual for the implementation of the new model [WHO/RHR/01.30) WHO, Geneva] (WHO, (2002a).**

The most dangerous form malaria disease is severe malaria. It is said to be a less common form (less prevalent) than the uncomplicated variety and is difficult to define precisely, especially in regions where malaria is endemic. It is acute malaria with major signs of organ dysfunction or high levels of parasitaemia (Chen, Wilson & Schlagenhauf, 2007; Freedman, Weld & Korzarsky, 2006).

Young children are at a higher risk of severe malaria in areas where malaria is endemic. Older children and adults usually develops partial immunity against malaria infection. This is after repeated infections (Rosenthal, 2008; Ladhani, Aibara, Riordan &, Shingadia 2007). These repeated infections coupled with the accrued partial immunity reduces the chances of severe or complicated malaria in the adults residing in endemic areas and hence makes it far less common than the uncomplicated variety (Chukwu LC, Ph.D Thesis, 2019.

It is equally posited that Reactive oxygen species (ROS), can develop due to malaria infection. Antioxidant enzymes in the body functions among other things to remove these reactive oxygen species. It is noted that catalase (CAT), glutathione peroxidase, glutathione transferase, glutathione reductase, superoxide dismutase (SOD), and antioxidant molecules, such as glutathione are among the antioxidants. They are helpful in clearing these reactive oxygen species. They work in concert within the cell to metabolize and transform these noxious forms of oxygen into innocuous substances (Ademuyiwa, Odusoja, Adebawo & Ugbaja, 2007). Till date it is not very clear to what extent if any, differences exist regarding the serum levels of various antioxidants in pregnant women on IPT-SP and those of their counterparts who did not take the medication (IPT-SP) and how the levels of these antioxidants affect the course of pregnancy. This represents an important research gap for the research world and serves as a major drive for this study.

The principal causes of oxidative stress (OS) are reactive oxygen species (ROS), which may be broadly defined as derivatives of molecular oxygen (Gupta, Wen & Garg, 2009). In aerobic organisms, small amounts of ROS, including hydroxyl radicals (•OH), superoxide anions (O_2^-), and hydrogen peroxide (H_2O_2), are constantly been generated in response to both external and internal stimuli (Jornot, Petersen & Junod, 1998). Vitamin C (Ascorbic Acid) is a water-soluble vitamin that acts as an important antioxidant, especially protecting the cells of the immune system from the free radicals generated during their activities in humans (Nicholas, Manish, Terrence & Joshua, 2016).

Some researchers have suggested that vitamin C supplementation may have a role in the case management of malaria (Nicholas, Manish, Terrence & Joshua, 2016; Marva et al., 1992). It has also been demonstrated that the plasma concentration of this antioxidant, Vitamin C is usually significantly decreased in chronic and acute malaria infections (Nicholas, Manish, Terrence & Joshua, 2016; Mohammad, 2012; D'Souza V and D'Souza B et al, 2006). Part of our duty in this research was establishing whether vitamin C supplementation during malaria infection and case management is necessary as well as sustain its recommendation. This supplementation is usually done in pregnancy especially during the antenatal and postnatal course. It is part of the routine haematinics given to pregnant women during antenatal and postnatal visits.

In a study of oxidative stress and antioxidant defenses in pregnant women, the exogenous antioxidant showed a statistically significant difference between the study and control groups. The plasma vitamin C (ascorbic acid) was decreased in the study groups with $p = <0.05$ when compared with the control group (Claudio et al., 2011).

The body uses small molecules that reduces the reactivity of various reactive radicals as an auxiliary antioxidant defense system. They include large number of molecules, such as vitamins A, C and E, beta-carotene, uric acid and reduced glutathione molecule (GSH). In addition, the body has proteins that bind to transition metals preventing them from catalyzing the Fenton and Haber-Weiss reactions, important sources of reactive species production. These metal chelators include ferritin, transferrin and lactoferrin (chelating iron), ceruloplasmin and albumin (copper chelators) and metallothioneins having thiol groups capable of binding several heavy metals (Halliwell and Gutteride, 2007).

It could be recalled that the concept that highly reactive hydroxyl radical (HO) could be generated from an interaction between superoxide (O(2)(-)) and hydrogen peroxide (H(2)O(2)) was proposed (with Joseph Weiss) in Professor Haber's final paper published in 1934 (Kehrer, 2000).

The role of oxidative stress in malaria pathophysiology is a multifactorial phenomenon and represents an important aspect of the intricate and complex host-parasite relationship. The sources of oxygen and nitrogen reactive species generation implicated

ISSN No. 2454-6194 | DOI: 10.51584/IJRIAS | Volume VIII Issue IV April 2023

in the malaria disease are: (1) The host's inflammatory response, (2) catalysis of Haber-Weiss and Fenton reactions due to high availability of free iron, (3) the occurrence of ischemia and reperfusion syndrome, the fluctuating result in the ability of red blood cells being able to transport oxygen during malarial paroxysm and of cytoadherence, (4) direct production by parasites and (5) the action of certain pro-oxidants antimalaria drugs (Sandro et al, 2012).

Investigations on synergistic antimalarial effect of some ketones and vitamin C have been equivocal. While an earlier study on vitamin C posited that it can augment the antimalarial effects of a ketone, exofone, against P. falciparumin in-vitro, with a possible pro-oxidant activity (Winter et al., 1997), another study reported the possibility of poor synergism **(5%)** against P. berghei in mice as was observed between certain ketones and vitamin C at a dose of 80 mg/kg body weight each (Mahajan, Kamath & Ghatpande, 2005). From the above, the authors concluded that the lower doses of the ketones used in the combined therapy may be the reason for the observed poor synergism.

A large randomized trial on Malian school-aged demonstrated that, IPT with either Sulphadoxine Pyrimethamine plus Artesunate (SP/AS) or Amodiaquine plus Artesunate (AQ/AS) was superior to vitamin C in reducing malaria incidence, all-cause clinic visits, anaemia and asymptomatic parasitaemia. This study assessed the efficacy of intermittent preventive treatment (IPT) using Artemisinin based Combination Therapy/ACT (the current standard of care for the treatment of clinical malaria infection) against malaria infection in school aged children. There was no clear difference between the ACT arms with respect to parasitemia or anaemia though fewer episodes of clinical malaria were observed with SP/AS than with AQ/AS (Breanna et al., 2009 [available 2011]). Another study also demonstrated that a co-administration of the vitamin with Chloroquine at a dose of 25 mg/kg body weight each restored oxidative stress in female P. berghei-infected mice (Iyawe, Onigbinde & Aina, 2006). Another study investigated the effects of vitamins C and E supplementation on oxidative stress resulting from the use of oral contraceptives in which one hundred and twenty (120) healthy women participated. Participants who used oral contraceptives had decreased plasma glutathione levels (Glutathione peroxidase and reductase) compared to the group of women who did not use them. Vitamins C and E significantly increased glutathione activity. This study concluded that low-dose oral contraceptives, by enhancing the oxidative stress and lipid peroxidation, may represent a potential cardiovascular risk factor, and the use of vitamins E and C may be beneficial in reducing this side effect of oral contraceptives (Zal, Mostafari-Pour, Aina & Heindari, 2012). These varying reports further exposes major research gaps with respect to the inconsistent findings concerning the effects of Vitamin C on malaria and anti malaria outcomes especially with respect to malaria in pregnancy as well as the vitamin C interactions with IPT-SP in pregnancy, and hence we study.

There are also negligible to minimal research works assessing Ascorbic Acid levels and their interactions with Intermittent Preventive Treatment with Sulphadoxine Pyrimethamine (IPT-SP) in Parturients who Received Intermittent Preventive Treatment with Sulphadoxine Pyrimethamine in pregnancy. For the above and other reasons, we chose to conduct this study to ascertain a comparative assessment of the Plasma Ascorbic Acid Levels in Parturients who Received Intermittent Preventive Treatment with Sulphadoxine Pyrimethamine (IPT-SP), and their Controls during pregnancy. It is believed that the results of this study will in no small measures assist stakeholders and policy makers in obstetrics and gynecological practice to adopt strategies that will ensure better pregnancy outcomes for our women.

The research question is: Does the levels of Ascorbic Acid affect pregnancy outcomes in malaria endemic areas of the world?

II. Study Setting and Study Center

Federal Medical Centre (FMC) Owerri was the center for this study. It is located in the center of Owerri town. Owerri metrological synoptic station is located between Lat. $05^{0}29^{'}$ and Long. $07^{0}02'$ within the study area, Owerri metropolis in Imo State, South Eastern Nigeria which is urban in nature (Echebima, Ndukwu and Obafemi, 2019). Owerri has an estimated population of about 1,401,873 as at the year 2016. It has approximately 100 square kilometers (40 sqm) in area. The town is bounded by the 'Otamiri River to the East and the Nworie River to the South. A disposition that aids malaria transmission. Malaria transmission and infection is witnessed all the year round in Owerri with its peak during the rainy season months of May to October and a nadir during in the dry season months of November to April. Owerri environment especially the suburbs areas have lots of forests, bushes, slumps etcetera. These factors help to encourage mosquito breeding and consequently malaria transmission. The Owerri slogan is Heartland (Wikipedia.org; on Owerri population).

Located in the state capital of Imo, FMC Owerri is a tertiary health institution offering specialist medical services. Their service includes specialist emergency obstetric care, safe motherhood, and comprehensive maternity care amongst others. Its exact address is at No. 105 Hospital / Orlu Road, 460281, Owerri, Imo State Nigeria.

Study Design

ISSN No. 2454-6194 | DOI: 10.51584/IJRIAS | Volume VIII Issue IV April 2023

The study is a **Prospective Comparative Cohort study.** All participating women in the case (study) group received 2 doses of the recommended antimalarial drug IPT-SP while those in the control arm did not. Also home visitations in the form of follow up visits were carried out as necessary to encourage compliance. The IPT-SP was administered at the recommended dose of three tablets of sulphadoxine-pyrimethamine (each tablet containing 500mg/25mg of SP) giving the total required dosage of 1500mg/75mg of SP per study group participant and twice in the course of the study.

As a way of encouraging the women, all the drugs (IPT-SP) administered to these pregnant women were procured by the principal researcher and given to the selected pregnant women in the study group free.

Study Population and Recruitment

The population were made up of pregnant women who used FMC, Owerri for their antenatal care programs within the stated study period. They were either booked antenatal gravid women or those unbooked women that presented in only labour who actually constituted majority of the control women. All recruited women had no clinical signs of malaria infection nor any parasitological or any other form of malaria diagnosis.

These pregnant women having witnessed quickening (first fetal kicks or movement) and satisfied the inclusion criteria were longitudinally recruited. It is usually noticed from about 16-18 weeks but can occur as late as 20 weeks. Participant selection did employ a **Purposive Sampling technique**. In the course of every antenatal visit, an interval history was taken coupled with physical examination. These were done to ascertain the state of health of the participant during the period from the last visit. Laboratory investigations done included Haemoglobin estimation and Urinalysis. They are part of routine antenatal investigations. Malaria Parasite test (MP test) was done for suspected cases of malaria in the women with a view to discard those that had malaria from the study. Such women were then sent to the appropriate clinics for proper treatment.

Inclusion Criteria: they included: (i). Recruited participants were booked antenatal patients with ancillary body temperature of < 37.5 ^{o}C and without any symptoms nor signs as well as no laboratory diagnosis of malaria, for both the study and control groups. (ii). Pregnant women resident in Owerri or any of its neighbouring towns. This helped the women to effectively afford antenatal follow up as well as readiness to deliver at FMC, Owerri. This criterion equally sufficed for both the study and control groups. (iii). None ingestion of antimalarial drug at about the time of presentation (at least ≥ 2 weeks) for both the study and control groups.

Specific Inclusion Criteria for The Control Group

The control group specifically consisted of unbooked mothers who presented for delivery **(unbooked)** but meeting other criteria for inclusion or those who presented late for antenatal care **(late booking)** and also met other criteria for inclusion. Established allergies to SP was also another criterion for women who met other criteria for inclusion. A good history helped to exclude ingestion of SP prior to presentation.

Exclusion Criteria: Some pregnant mothers were excluded from the study: i). mothers with coexisting medical conditions (known diabetics, hypertensive or those with cases of congestive heart failure, HIV/AIDS, SCD women, nephrosis, or other co-morbidities that may to affect the results of the study). ii). mothers with allergies to any component of the drug combination (SP). These parturient were then included among those who did not receive any IPT-SP (control group) during their current pregnancies provided they met other criteria for inclusion. iii). pregnant women with symptoms and signs of severe malaria. iv). mothers with Haemoglobin AS were also excluded from the study. v). Others excluded were women who had used any antimalarial drug in the past 2 weeks prior to recruitment as well as women who lived far away from study base that may discourage effective follow-up.

vi). Those women from history, that were not likely to deliver at FMC, Owerri. Such will discourage the estimation of plasma ascorbic acid and hence, were politely excluded from the study.

Sampling Size Determination:

Sample size was calculated with the following formula: $n = \frac{z^2pq}{d^2}$

Where: n= the desired sample size.

z= the standard normal deviate, usually set at 1.96 (or more simply 2.0).

This corresponds to the 95% confidence level.

p= incidence of malaria in pregnancy in Owerri, reported as **11%** (Ogbusu, Nwoke, Njoku, Anosike, & Uwaezuoke, 2004).

ISSN No. 2454-6194 | DOI: 10.51584/IJRIAS | Volume VIII Issue IV April 2023

$$n = \frac{(1.96)^2 (0.11) (1-0.11)}{(0.05)^2}$$

= 148. (Araoye, 2004; Ogbusu, et al 2004).

The value gotten was approximated to 150 to account for minimal attrition. A sample size of 150 subjects for each group. These are women who meet the inclusion criteria and consented to the study (both verbally and in writing) as well as used the above hospital for antenatal care and delivery. ***They were recruited longitudinally using a Purposive Sampling method***. However, only 148 participants for each group completed the study.

III. Results

In the course of participant recruitment, more than 456 antenatal women were assessed for eligibility. Fifty-six (56) of these women were excluded from the study leaving us with four hundred (400) participants on whom questionnaires were administered. Equal numbers, each of study/case (148) and control (148) groups completed the study giving a total of 296 mothers that were fully studied eventually.

Table 1.0: Summary of mothers Biochemical Parameters studied

Variable	n	min	max	mean	Std.dev	coef	S.e.	p-value	OR	95% C.I.for OR Lower	Upper
Case	148	0.064	3.29	1.75	0.67						
Control	148	0.056	3.75	2.03	0.68	-0.614	0.180	<0.0001	0.54	0.380	0.771

Table 1.0: showed the summary of the mothers' plasms Vitamin C levels studied. The average serum Vitamin C level for the mothers were 1.746 ± 0.67 for the study/cases and 2.025 ± 0.68 for the control.

Influence of Serum levels of vitamin C in both the study group and the control population.

The average serum vitamin C level appeared to be lower in the study group compared to what was observed on the control. The table indicated that the average serum vitamin C levels were found to be 1.75 mg/dl and 2.03 mg/dl respectively for the study and control groups. This mean difference was statistically significant with p= < 0.0001; 95% CI =0.380 – 0.771.

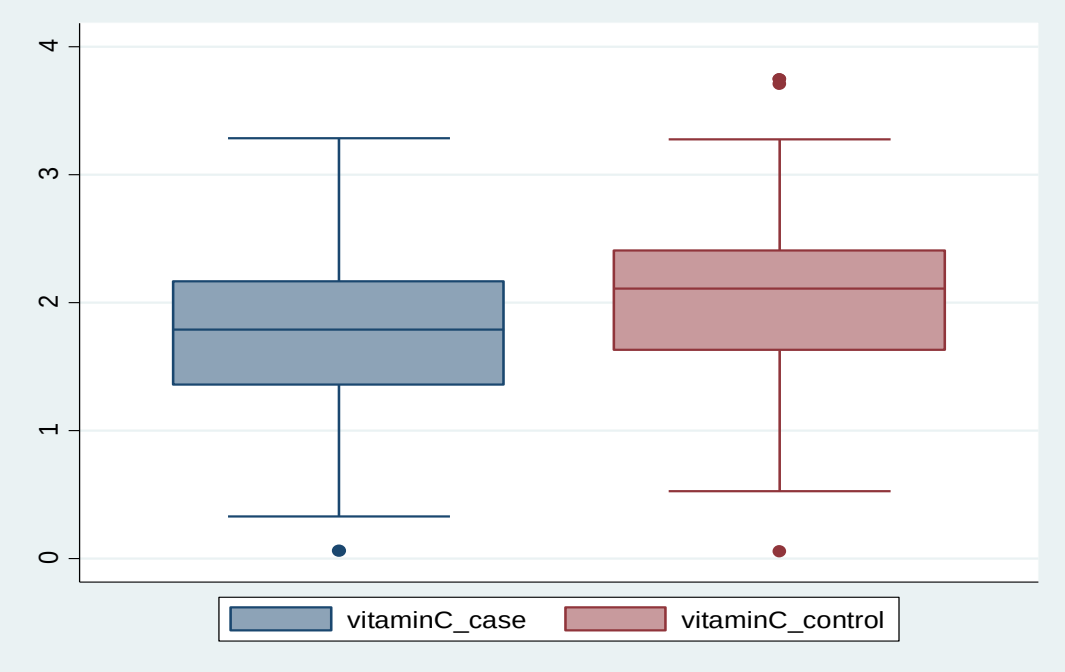

Figure 1. (Box plot 1.0): Showing serum levels of Vitamin C (Vit C) level in both the study/treatment and control groups

ISSN No. 2454-6194 | DOI: 10.51584/IJRIAS | Volume VIII Issue IV April 2023

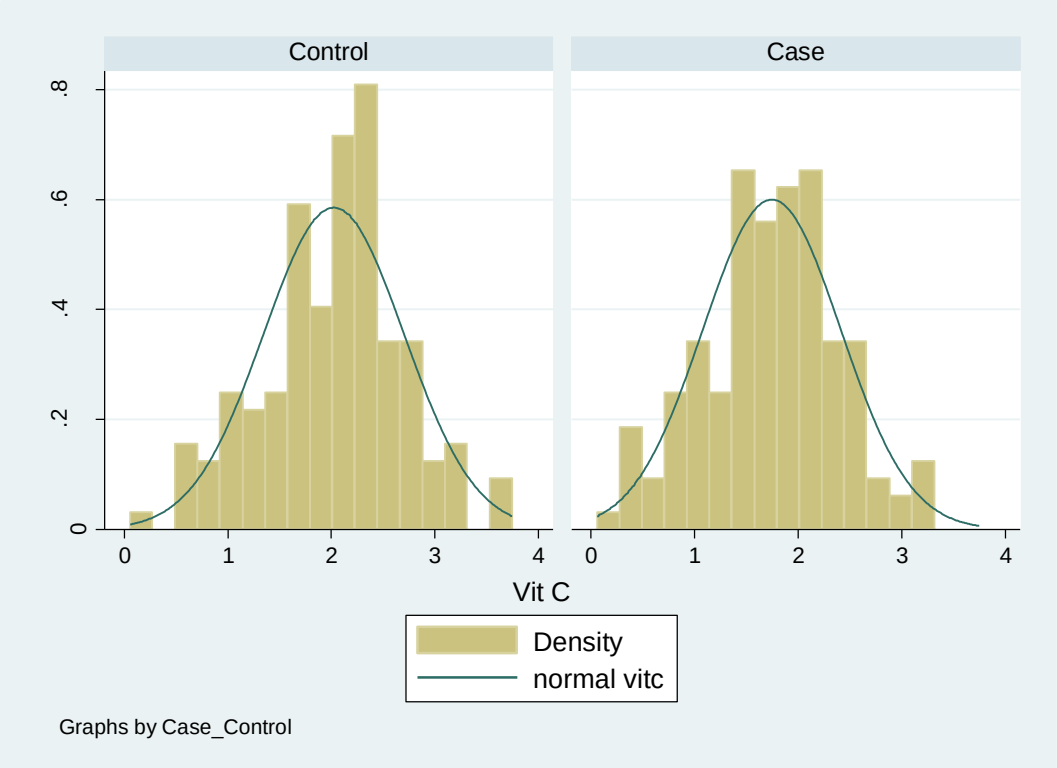

Figure 2 (Histogram 1.0): shows serum levels of Vit C (Vit C) in both the study/treatment and control groups

IV. Discussion

From this study, the mean serum level of Vitamin C in the case group was 1.75 mg/dl while in the control, it was 2.03 mg/dl. The difference was found to be statistically significant (p= <0.001) with an odds ratio 0.54 (CI of 95% 0.380-0.771). This was also illustrated in the corresponding histogram in the result section above. The reason for reduced Vitamin C levels might not be unconnected to the fact that most women in developing countries might have low Vit. C levels even before getting pregnant and pregnancy may worsen this. While this reason does not entirely explain the difference noted between the study and control groups, a comparable report has been documented in another study where the plasma vitamin C (ascorbic acid) was decreased in the study groups with P< 0.05 when compared with the control group. This was equally significant and compared with the findings of this very our study (Claudio et al., 2011). In a study of oxidative stress and antioxidant defenses in pregnant women, the exogenous antioxidant showed a statistically significant difference between the study (IPT-SP) and control groups. The plasma vitamin C (ascorbic acid) was significantly decreased in the study group [and compared with the results of this study]; P< 0.05 when compared with the control group (Claudio et al., 2011).

Some Nigerian studies had demonstrated low serum vitamin C levels among cohorts (groups) of pregnant women. This was not the same in developed countries where vitamin C deficiency among pregnant women was uncommon and hence does not support vitamin C supplementation in pregnancy. The existing widespread maternal malnutrition in developing countries may support the need for vitamin C supplementation in pregnancy and it was thought to help reduce the incidence of some complications of pregnancy (Ugwa, 2015).

V. Conclusion / Precommendation

1. From the results of this study, we hereby sustain and as well as recommend that vitamin C supplementation during malaria infection and case management be made a necessity.
2. Equally, we suggest that it's use as a routine drug in pregnancy be continued. This supplementation is usually done in pregnancy especially during the antenatal and postnatal courses. It is part of the routine haematinics given to pregnant women during antenatal and postnatal visits. This should be continued to help eradicate vitamin C deficiency during pregnancy.
3. We also recommend that this study be repeated with a larger sample size and in a multi-center setting.

ISSN No. 2454-6194 | DOI: 10.51584/IJRIAS | Volume VIII Issue IV April 2023

Research funding:

No form of funding was received in the course of this study. However, the authors will be very grateful to receive grants in the future.

Conflict of interest:

The authors hereby declare that there was no conflict of interest in the course of this study till this time of publication.

Ethical approval:

Ethical approval and subsequent certification were obtained from the ethics committee of the Federal Medical Center Owerri (FMC). The study protocol was then approved by their Ethics Committee with Ref. No. FMC/OW/HREC/55; May 12, 2016. However, a written informed consent prior to study participation was willingly signed by all enrolled mothers. These were dutifully adhered to all done before the commencement of participant recruitment

Acknowledgment:

It is our good intentions to acknowledge the efforts of my teachers and mentors. The assistance of the medical and other staff of the Federal Medical Center, Owerri is also hereby acknowledged. Permit me to also acknowledge the co-operation of my family members especially my dear children. May the good Lord bless them all.

References

1. Chukwu LC, Ph.D Thesis. 2019. Pharmacodynamic Effects of Sulphadoxine-Pyrimethamine on Pregnancy Outcome in Women Attending Antenatal Clinic and Their Knowledge, Attitude and Practice of Intermittent Preventive Treatment. Abia State University, Uturu Nigeria
2. World Health Organization. (2018). *WHO International Travel and Health*, (2018)
3. Kathrine, R. T., Bonnie, L. K., Kimberly, E. M., Michael, N., Steve, M. T., Steven, R. M., Ryan, E. W., Victor, C., Scott, J. F., Mulakwa, K., Allen, S. C. (2014). Efficacy of Sulphadoxine-Pyrimethamine for intermittent preventive treatment of malaria in pregnancy, Mansa, Zambia. *Malaria Journal* **13**:227. https://doi.org/10.1186/1475-2875-13-227. Tan et al.; licensee BioMed Central Ltd. 2014
4. Dellicour S, Tatem AJ, Guerra CA, Snow RW, ter Kuile FO. Quantifying the number of pregnancies at risk of malaria in 2007: a demographic study. PLoS Med. 2010;7:e1000221. doi: 10.1371/journal.pmed.1000221.
5. Desai M, ter Kuile FO, Nosten F, McGready R, Asamoa K, Brabin B, Newman RD. Epidemiology and burden of malaria in pregnancy. Lancet Infect Dis. 2007;7:93–104. doi: 10.1016/S1473-3099(07)70021-X.
6. World Health Organization. A Strategic Framework for Malaria Prevention and Control during Pregnancy in the African Region. Brazzaville: Regional Office for Africa; 2004. AFR/MAL/04/01.
7. Ojo, A. O., Briggs, E. B. (2006). *Malaria and anaemia in pregnancy. A Textbook For Midwives in the Tropics*. *Jaypee Brothers Medical Publishers (P) Ltd, Nodder Arnold*; New Delhi. 2nd Edition
8. Falade, C. O., Yusuf, B. O, Fadero, F. F., Mokuolu, O. A., Hamer, D. H., Salako, L. A. (2007). Intermittent Preventive Treatment with Sulphadoxine-Pyrimethamine is effective in preventing maternal and placental malaria in Ibadan, South-Western Nigeria. *Malaria Journal*,6(88).doi:10.1186/1475-2875-6-88. http://www.malariajournal.com/content/6/1/88
9. Bray, R. S., Anderson, M. J. (1979). Falciparum malaria and pregnancy. *Trans R Soc Trop Med Hyg*, 73, 427-431
10. Chukwu, L. C. (2009). Evaluation of the effectiveness of Arthemether/Lumefantrine combination in the treatment of uncomplicated malaria in Elele, a malaria endemic area in Rivers State, Nigeria. MS.c Dissertation, *Dept of Pharmacology. Nnamdi Azikiwe University, Awka, Nigeria*
11. Williams, N. (1996). Malaria hideout found in new mothers. *Science*, 272, 1416-1417
12. Federal Ministry of Health [FOH Nigeria]; National guidelines for diagnosis and treatment of malarial. (2011). National Malaria and Vector Control 33 Division, Abuja Nigeria
13. WHO (2002a). WHO antenatal care randomized trial: manual for the implementation of the new model. Trans R Soc Trop Med Hyg 2000;94:Suppl 1:S1-S90. (WHO/RHR/01.30) WHO, Geneva
14. Chen, L. H, Wilson, M. E., Schlagenhauf, P. (2007). Controversies and misconceptions in malaria chemoprophylaxis for travelers. *JAMA*, 297, 2251-2263
15. Freedman, D. O., Weld, L. H., Kozarsky, P. E. (2006). Spectrum of disease and relation to place of exposure among ill returned travelers. *N Engl J Med,* 354(119-130). Erratum, N Engl J Med 2006;355:967
16. Rosenthal, P. J. (Ed) (2008). Artesunate for the Treatment of Severe Malaria. *The new England Journal of Medicine*, 358(17), 1829 – 1836,

ISSN No. 2454-6194 | DOI: 10.51584/IJRIAS | Volume VIII Issue IV April 2023

17. Ladhani, S., Aibara, R. J., Riordan, F. A., Shingadia, D. (2007). Imported malaria in children: a review of clinical studies. *Lancet Infect D*is, 7, 349-357
18. Ademuyiwa, O., Odusoga, O. L., Adebawo, O. O., Ugbaja, R. N. (2007). Endogenous antioxidants defences in plasma and erythrocytes of pregnant women during different trimesters of pregnancy. *Acta Obst et Gynec*, *86*,1175–80
19. Gupta, S., Wen, J. J., Garg, N. J. (2009). Oxidative stress in chagas` disease. *Hindawi Publishing Corporation: Interdiscip Perspect on Infect Dis*, Volume 2009, 8 pages doi:10.1155/2009/190354
20. Jornot, L., Petersen, H., Junod, A. F. (1998). Hydrogen Peroxide induced dna damage is independent of nuclear calcium but dependent on redox-active ions. *Biochem J*, 335:85–94
21. Nicholas, F. N., Manish, M., Terrence, M., Joshua, B. O. (2016). Effects of vitamins in augmentation of malaria treatment: *A review*. DOI: 10.21276/apjhs.2016.3.4.6
22. Marva, E., Golenser, J., Cohen, A., Kitrossky, N., Har- El, R., Chevion, M. (1992). The effects of Ascorbate-induced free radicals on Plasmodium falciparum. *Trop Med Parasitol*, 43, 17–23
23. Mohammad, A. (2012). Effect of serum antioxidant Ascorbic acid concentration by malarial infection in man. *The Experiment*, 3(4): 214-215
24. D'Souza, V., D'Souza, B. (2006). Comparative study on lipid peroxidation and antioxidant vitamins E and C in falciparum and vivax malaria. *Indian J Clin Biochem*, 21(2),103–106
25. Claudio, A. M. Leal., Maria, R. C. Schetinger., Daniela, B. R. Leal., Vera, M. Morsch., Aleksandro, Schafer da Silva., João, F. P. Rezer.,… Jeandre Augusto dos Santos Jaques. (2011). Oxidative stress and antioxidant defenses in pregnant women. *Communications in Free Radical Research*, 16(6), pp 230-236 https://doi.org/10.1179/1351000211Y.0000000013
26. Halliwell, B., Gutteridge, J. M. C. (2007). Free radicals in biology and medicine. 3rd ed. *Oxford University Press; New York*, NY, USA
27. Kehrer, J. P. (2000). The Haber-Weiss reaction and mechanisms of toxicity. Toxicology 14;149(1):43-50. PMID: 10963860. *Division of Pharmacology and Toxicology, College of Pharmacy*, The University of Texas at Austin, Austin, TX 78712-1074, USA. keherjim@mail.utexas.edu
28. Sandro, Pecario., Danilo, R. Moreira., Bruno, A. Q. Gomes., Michelli, E. S. Ferreira., Ana, C. M. Goncalves., Paula, S. O. C. Laurindo.,… Micheal, D. Green. (2012). Oxidative stress in malaria. *Int J Mol Sci*, 13(12), 16346-16372. Doi: 10.3390/131216346. PMCID: PMC 3546694
29. Winter, R. W., Ignatushchenko, M., Ogundahunsi, O. A., Cornell, K. A., Oduola, A. M., Hinrichs, D. J., Riscoe, M. K. (1997). Potentiation of an Antimalarial Oxidant drug. *Antimicrob Agents Chemother*, *41*(7):1449–1454
30. Mahajan, S. S., Kamath, V. R. and Ghatpande, S, S. (2005). Synergistic antimalarial activity of Ketones with Rufigallol and vitamin C. *Parasitol*, 131, 459–466
31. Breanna, B., Hamma, M., Oumar, B. T,. Mamadou, T., Intimbeye, T., Antoine, D.,… Abdoulaye, A. D. (2009). Intermittent preventive treatment using Artemisinin-based combination therapy reduces malaria morbidity among school-aged children in Mali. *Trop Med Int Health*. 14(7), 784-791. doi: 10.111/j.1365-3156.2009.02294.x: available in PMC 2011 Feb 14. PMCID: PMC3038653; NIHMSID: NIHMS267870; PMID: 19497079
32. Iyawe, H. O. T., Onigbinde, A. O., and Aina, O. O. (2006). Effect of Chloroquine and Ascorbic Acid interaction on the oxidative stress status of Plasmodium berghei infected mice. *Int J Pharmacol*, 2(1),1–4
33. Zal, F., Mostafavi-Pour Z., Amina, F., Heindari, A. (2012). Effect of vitamin E and C supplements on lipid peroxidation and GSH-Dependent antioxidant enzyme status in the blood of women consuming oral contraceptives. Contraception. 2012 Jul;86(1):62-6. doi: 10.1016/j.contraception.2011.11.006. Epub 2012 Apr 9
34. Echebima, S., Ndukwu, B., Obafemi, A. (2019) Climate Study of Owerri and Comparative Analysis of Different Methods of Base Factor Computation. Atmospheric and Climate Sciences, 9, 310-322. Doi:10.4236/acs2019.93022
35. Araoye, M. O. (2004). Research methodology with statistics for health and social sciences. subject selection, sample size determination. *Nathadex Publishers*, ISBN 978-36450-8-0: p 115-121
36. Ogbusu, P. I., Nwoke, B. E., Njoku, A. J., Anosike, J. C. Uwaezuoke, J. C. (2004). Prevalence of malaria among pregnant women in Owerri Municipality, Imo State, Nigeria. *African Journal of Applied Zoology and Environmental Biology*. ISSN: 111 9-023X. AJAZEB 6, pp 31-35
37. https://en.mwikipedia.org > wiki (Wikipedia.org; on Owerri population).
38. Ugwa, E. A. (2015). Vitamin C Supplementation in Pregnancy: A review of current literature. *Nigerian Journal of Basic and Clinical Sciences*, 12(1) Pp: 1-5. doi: 10.4103/0331-8540.156660. http://www.njbcs.net/text.asp?2015/12/1/1/156660