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Birth Weight and Third-trimester Maternal Vitamins A, C, and E Levels

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Authors' contributions

This work was carried out in collaboration among all authors. Author GUJ helped in concept, design, literature search, clinical studies, experimental studies, data acquisition, data analysis, statistical analysis, and manuscript review. Author OTO did experimental studies, data acquisition, statistical analysis, and manuscript review. Author RAO did literature search, experimental studies, data acquisition, and manuscript review. Author AAI helped in concept, design, the definition of intellectual content, literature search and prepared, reviewed and edited the manuscript. All authors read and approved the final manuscript.

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ABSTRACT

Background: Deficiencies of micronutrients (especially vitamins C, A, and E) during intra-uterine life have been linked with the possibility of increased risk of some diseases (e.g. cardiovascular disease and type 2 diabetes) in adulthood.
Aims: Therefore, it becomes expedient that persistent and vigorous attention be paid to maternal vitamin status during gestation.

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Methodology: This is a cross-sectional comparative study carried out at maternity centres in Osogbo Local Government. Forty women who were at least 29 weeks of gestation and 40 apparently healthy women, age-matched, non-pregnant constituted the test and control groups respectively. Blood was obtained through an ante-cubital vein, centrifuged and used for vitamin estimations (High-Performance Liquid Chromatography). Birth weight and neonatal mortality ratio were the birth outcomes that were obtained. Data analysis was by Student's t-test and Pearson's correlation coefficient. P≤0.05 was considered significant.

Results: Serum status of vitamins A (2.68±3.88 µg/dL); C (0.95±0.44 mg/dL); and E (0.67±0.04 mg/dL) were significantly lower at third trimester compared with the corresponding values of 6.98±1.26 µg/dL; 2.99±0.11 mg/dL; and 1.66±0.08 mg/dL among non-pregnant control. There were significant adverse pregnancy outcomes as signified by 10% stillbirths. In addition, low birth weight (1.5-2.4 kg) was observed among approximately 50% of the babies but no correlation was observed except between vitamins C and E.

Conclusions: The results of this study revealed that among Nigerian pregnant women, there are risks of abnormal birth outcomes and low levels of vitamin A, C, and E. Aside depletions in vitamin C and E, the results of the study (r= .376; p= .020) suggest possible metabolic interaction between both.

Keywords: Ascorbic acid; vitamin E; vitamin A; gepstation.

1. INTRODUCTION

Extensive efforts have been and are being currently exerted to understand the dynamics involved in micronutrient status during gestation [1]. This is not limited to the developing world where scientific communities continue to study how and why micronutrient depletion occurs during gestation but also its impact on maternal and fetal health [2,3]. Moreover, it has also been reported- that there are socio-economic implications of intra-uterine vitamin depletions not only on the growing fetus but on the health of the child later in life, especially during adulthood [4]. Of note is the observation of Mendes *et al*. [5]; they reported a higher incidence of certain metabolic diseases during adulthood among individuals who suffered micronutrient depletion during intra-uterine life as evidenced by low serum maternal vitamin concentrations. According to them the intrauterine environment in gestation has effects on the level of gene expression which sometimes continues until adulthood and initiates multifactorial diseases such as type 2 diabetes and obesity [4]. Additionally, micronutrient deficiencies during embryonic, fetal and early life have been reported to result in type 2 diabetes and cardiovascular diseases. Low maternal vitamin levels that give rise to or impact and altered vasculature, distort organ growth and function as well as create an imbalance in metabolic processes (such as abnormal lipid profile, markers of cardiometabolic disorder and renal dysfunction) seem to initiate the occurrence of these 2 categories of disorders.

Aside from the relationship between vitamin deficiencies during intra-uterine life and increased risk of some diseases in adulthood, also it becomes expedient to carry out this study among pregnant women in South Western Nigeria as data obtained from Nwagha and Ejezie [6] as well as Shu and Ogbodo [7] from studies carried out in South-Eastern Nigeria revealed that there was significant reduction of vitamin C in pregnant women. With the present endeavor, attempts will be made to ascertain whether micronutrient deficiency among Nigerian pregnant women is limited to vitamin C or it extends to 2 other vitamins with antioxidant potential. Especially as micronutrient status in pregnancy has been hypothesized as a determinant factor of fetal growth and survival [8].

2. MATERIALS AND METHODS

2.1 Study Participants/Study Site

All those that partook in the study were apparently healthy women. They consisted of 80 females- 40 pregnant women in the third trimester (29 weeks to term) and 40 age-matched non-pregnant women served as the control group. Recruitment of pregnant participants took place at Fiwasaye Clinic & Maternity Hospital, Oke-Baale Maternity Center and Akepe Maternity Center in Osogbo Local Government when the women presented for their regular antenatal clinics.

2.2 Study Plan/Sampling Method

Cross-sectional study. Simple random sampling technique.

2.3 Exclusion Bench Marks

All factors capable of influencing or modulating vitamin levels were taken into consideration before the sampling of participants took place. Indices such as income, education and occupation- factors capable of influencing dietary choices on which vitamin availability is based were considered for inclusion and exclusion criteria. Additionally, other factors like acute or chronic diseases (e.g. diabetes, hypertension and human immunodeficiency virus infection, malaria infections or any other disease) and lifestyles (e.g. smoking, alcohol consumption) capable of influencing body contents of vitamins were taken into consideration to prevent their confounding effects. Patients in the first or second trimester as well as those unsure of the trimester of pregnancy were not recruited. Those with obstetrical abnormalities were also excluded.

2.4 Collection of Blood Samples/ Analyses of Vitamins and Trace Elements

Five millimeters (5 mL) of venous blood from the antecubital fosa was collected with minimum stasis using pyrogen free needles and syringes. This was carefully dispensed into dry, plain (anti-coagulant-free) bottles. The blood samples were allowed to clot, retracted and centrifuged at 2000 revolutions per minute (rpm) for 10 minutes after which the sera were separated and stored at a temperature of -20^{o}C until required for analytical processes. Analyses of vitamins A, C and E were carried out using High Performance Liquid Chromatography (Waters 616/626 HPLC, USA).

2.5 Statistical Analysis

Results are presented as mean± standard error of means (SEM). Data were analysed using Statistical Package for the Social Sciences (SPSS) version 16.0. [IBM, SPSS Inc., Chicago IL]. Comparison between subjects (third-trimester pregnant women) and control was performed using Student's t-test. Pearson's correlation coefficient was used to establish relationship between parameters. The statistical significance was set at $p<0.05$.

3. RESULTS

The results of serum concentrations of vitamins A, C and E are shown in Table 1. Serum levels of vitamins A, C and E were significantly lower in pregnant women compared with control. The use of Pearson's correlation study to understand the relationship between one vitamin and another revealed there was no significant relationship between vitamins A and E as well as between vitamins A and C but there was a significant positive correlation between vitamins C and E (Table 2). Ten percent stillbirth was observed among the neonates. Another important adverse birth outcome was the low birth weight (1.5-2.4 kg) which more than half of the babies born to the test group presented with at birth. The correlation study revealed no correlation except between vitamins C and E.

Table 1. Concentrations of serum vitamins A, E and C of third-trimester pregnant women and non-pregnant control

Vitamins	Third-trimester pregnant women	Non-pregnant women (control)	P value
Vitamin A	2.68±3.88 µg/dL	6.98±1.26 µg/dL	< .001
Vitamin E	0.67±0.04 mg/dL	1.66±0.08 mg/dL	0.010
Vitamin C	0.95±0.44 mg/dL	2.99±0.11 mg/dL	0.010

P significant at 0.05

Table 2. Correlations study of the serum vitamins of third-trimester pregnant women

	Vitamin A	Vitamin E	Vitamin C
Vitamin A	1	R= -.036 P= .828	R= -.093 P= .568
Vitamin E	R= -.036 P= .828	1	R= .376 P= .020*
Vitamin C	R= -.093 P= .568	R= .376 P= .020*	1

**P significant at 0.05*

4. DISCUSSION

The mean serum vitamin A concentration showed significantly lower levels in the third trimester when compared with the control. This is not consistent with earlier observation from a study carried out in Enugu state, South-east, Nigeria. It can be hypothesized that the significantly lower levels may be due to limited intake of vitamin A-rich food, (a common occurrence in developing countries) and fetal demand. An estimated 15 out of 100 pregnant women in low-income countries experience vitamin A deficiency according to the World Health Organization [9, 10], sometimes a severe enough to cause 8% of pregnant women to suffer severe form of the ocular consequence of vitamin A deficiency i.e. night blindness [9].

Congenital ocular defects, compromise in growth (low birth weight), night blindness, premature birth, intrauterine growth retardation, and antepartum hemorrhage due to abruption placentae and insufficient vitamin A stores of the fetus have been implicated in infants born to pregnant mothers who were vitamin A deficient. The results of the study suggest depletion during gestation. Maternal vitamin A deficiency has also been linked with an increased risk of maternal and infant mortality. An observation that is in accord with the results of this study in which four stillbirths were recorded from a total of forty. Vitamin A deficiency reduces leukocyte numbers, lymphoid tissue weights, complement, T cell functions, tumors resistance, natural killer cell numbers, antigen-specific immunoglobulin G and E, and increases interferon-γ synthesis [11-13]. Fetal weight gain and accumulation of vitamin A are strongly associated in animals and humans (that is, smaller fetuses have lower vitamin A stores) [14], which supports the low birthweight among many neonates. Fetal growth gain has been linked also with the availability of vitamin C, yet there was no correlation (r= -.093; p= .568) between vitamins A and C, both vitamins that play an important role in foetal growth.

The mean serum of vitamin C showed a significantly lower concentration in the third trimester compared with the control. This is consistent with earlier studies in which low vitamin C levels were reported in pregnancy [15]. The reason for the significantly lower levels during pregnancy compared with the non-pregnant state is not clear but is consistent with the postulation that uteroplacental perfusion [16] induces oxidative stress and ascorbate consumption [17,18]. However, the depletion in vitamin C levels may not be unexpected because sources of vitamin C are not adequately supplied or available as reported in literature among male and female Nigerians [19]. When present as part of the routine diets of Nigerians they are mostly subjected to various types of food processing methods which are capable of greatly reducing the vitamin C content of food items by as much as 90% [20]. Meanwhile, poor eating habits occasionally associated with pregnancy in some individuals or prevailing harsh economic conditions in a developing country like Nigeria can result in the inability of these pregnant women to meet fetal and maternal demands as reflected in the study results.

In pregnancy vitamin C plays significant role in metabolism within the body including the prevention of iron-deficiency anemia [21]. This vitamin also affects several components of the human immune system, particularly the stimulation of both the production and functions of leukocytes, especially neutrophils, lymphocytes and phagocytes [13]. Leukocytes help the mother and the baby to fight infections. In addition, the intake of adequate vitamin C from the 20th week of pregnancy was found to reduce the risk of rupturing the chorio-amniotic membrane, thereby reducing infection and premature delivery [22]. As an antioxidant, vitamin C is capable of regenerating other antioxidants, especially vitamin E [23,24]. Even though both vitamins C and E were depleted, the results of the study (r= .376; p= .020) suggest such metabolic interaction between the two. Results of the study of significantly low concentrations of vitamin C observed in this population portray great risk to both expectant mothers and their unborn infants as it may hamper many of these important physiologic functions. However it has also been reported that maternal vitamin C deficiency without clinical symptoms is sometimes common in some categories of pregnant subjects [25].

Furthermore, mean serum concentration of vitamin E from the controls was significantly lower during pregnancy as compared with control. This result is not in agreement with earlier reports of higher level of vitamin E concentration during pregnancy [26]. The functions of vitamin E in human reproduction cannot be over-emphasized. It has been proven to be involved in several biological processes including immune functions, growth and cell differentiation, and early embryogenesis [27].

Moreover, its deficiency in pregnant rats was found to have caused pregnancy termination due to fetal death and resorption of uterine contents.

Vitamin E, as phosphorylated α-tocopherol, stimulates vascularization of the placenta, from amplified expression of angiogenic factors like vascular endothelial growth factor (VEGF) [28]. Vitamin E also affects the expression and activities of molecules and enzymes in immune and inflammatory cells, implying that it has vital immune functions. In addition, vitamin E is nature's most potent fat-soluble antioxidant and also plays a significant role in the metabolism of another antioxidant – selenium in the prevention of oxidative stress. Therefore, it implies that these pregnant mothers and their fetuses face an increased risk of many other medical problems associated with vitamin E deficiency. Aside from the risk in the uterine life, the fetus may also be at risk in the early stages of neonatal life. For example, vitamin E plays an important role in maintaining the membrane integrity of erythrocytes and insufficient vitamin E has been linked with neonatal hemolytic anemia. Sometimes the consequences of vitamin E extend beyond the early period, there is also the possibility of increased risk of chronic diseases during adulthood. Such a claim was made by Kemkem et al. [29] and Brenseke et al. [30] and supported by a few others, meaning it cuts across races, geographic locations, and socio-economic differences. Therefore, there is a need for follow-up of the study participants and their infants to verify the role intra-uterine vitamin depletions play as an etiologic factor of chronic diseases at the adult stage of life. Vitamins A and E are both fat-soluble with overlapping roles from embryonic to fetal development [31-33], yet not one but both were depleted at the third trimester. Furthermore, that these results should be of concern are several factors and deleterious situations that cut across age groups already mitigating against the health and well-being of individuals in the different communities where the participants were recruited [34-37].

5. CONCLUSION

The low birth weight of babies born to the women who exhibited significantly low levels of vitamins compared with others in non-pregnant conditions revealed there is need that urgent attention to be paid to vitamin status of women within the reproductive stage especially pregnant ones more so as 10% of the gestations resulted in stillbirths.

6. RECOMMENDATION

The study indicates vitamins A, C, and E imbalance during gestation. It behooves the government through its various organs such as the Ministries of Health, Information and Education to educate females of all ages on the benefits of adequate micronutrient intake (food fortification, supplementation). This can be achieved by using every available forum e.g. media campaigns. This type of education should commence early in life. Therefore, inculcating nutrition education programs into primary and secondary school curricula will also help in no small measure.

7. LIMITATION OF STUDY

The study is limited by the small number of participants recruited for the study as well as time constraints. Administration of a food frequency questionnaire to the study participants as well as the inclusion of neonatal outcomes would have enriched the study.

CONSENT AND ETHICAL APPROVAL

Before to the commencement of the study, ethical clearance for the human study involving the assessment of serum vitamins in the third trimester was obtained from the Health Research Ethics Committee of the Hospital Management Board Asubiaro, Osogbo Osun state. Additionally, from each participant informed consent was obtained and confidentiality of information obtained was observed.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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