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Maternal to fetal transfer of vitamin C and vitamin E: effect on birth outcome in a Nigerian population

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ABSTRACT

Background: New evidence suggests that excessive production of reactive oxygen species give rise to oxidative stress which could impair fetal growth. Antioxidant vitamin C and vitamin E have vital role in physiological process of pregnancy and health of the developing fetus. **Aims and Objectives:** To determine the concentrations of vitamin C and vitamin E in pair-matched maternal and cord serum of newborns and to determine the relationship between maternal/cord serum vitamin C and vitamin E at delivery and birth outcomes. **Materials and Methods:** A total of 209 maternal and cord blood samples were collected during delivery for serum vitamin C and E determination. Birth outcomes; birth weight, birth length, head circumference, and Apgar score were determined. **Results:** Newborns had significantly higher levels of vitamin C as compared to their mothers, but had non-significant lower level of vitamin E. Levels of vitamin C and E in both maternal and cord serum were positively correlated to birth weight, birth length, head circumference and Apgar score. **Conclusion:** Maternal vitamin C and E had significant effects on birth outcomes. A positive correlation of vitamin C and E indicates that their status in mother does influence newborns status.

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Key words: Vitamin C, Vitamin E, Antioxidant, Maternal, Newborn, Birth outcome, Nigeria

INTRODUCTION

Numerous evidence abound confirming the excessive production of reactive oxygen species and other reactive species causing oxidative stress during both normal and abnormal pregnancies.[1,2] Maternal stress during pregnancy plays vital role in pathogenesis of chronic diseases in adulthood.[3,4] Maternal and fetal nutritional alterations in pregnancy may affect the fetal development/growth and may facilitate the incidence of chronic disorders in adulthood.[5,6] Several micronutrients are important for the health of the developing fetus, and ingestion of particular micronutrients may cause a shift in oxidative status. The micronutrients most relevant to this include fat-soluble carotenoids, vitamin E and water soluble vitamin C.[7,8] Vitamin E is a potent chain breaking antioxidant, scavenging oxygen radicals and terminating free radical chain reactions.[9] Vitamin E is well recognized for its role in maintaining membrane integrity and protection from reactive oxygen species.[8] Vitamin C has been shown to scavenge aqueous superoxide and hydroxyl radicals and act as a chain- breaking antioxidant in lipid peroxidations. Vitamin C appears to be important in antioxidant protection in the plasma, as well as in other extracellular/intracellular fluids and membranes.[7] Besides vitamin C is a hydrophilic antioxidant capable of protecting the fetus against insults resulting from oxygen free radicals by scavenging hydroxyl free radicals.[10]

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Some investigators[11,12] reported that maternal oxidative stress during pregnancy contributes to low birth outcomes and that antioxidant vitamin A, E and C may have important role in fetal development, while others reports were conflicting.[13] Recently Wang et al.,[14] reported that maternal vitamin A, but not E and C during pregnancy had a significant effect on birth outcome. It has been previously reported that serum contents of vitamin E is lower[15] while vitamin C is higher[16] in maternal than in cord blood. The relationship between the serum vitamin E and C contents of mother and newborn remains unknown particularly in tropical African environment like Nigeria. Besides the effect of antioxidant vitamins in birth outcomes remain controversial. Therefore the aims of this present study were to determine the concentrations of antioxidant vitamin E and C in Maternal and cord blood and their relationship with birth outcomes in Nigeria.

MATERIALS AND METHODS

Sample size determination

Sample size was calculated based on 95% Confident interval, desired accuracy of 0.05 with an assumed 40% prevalence of vitamin E and C deficiency in pregnancy in this environment, using the formula of Araoye.[17]

Study design

Pregnant women who attended ante-natal clinic at Irrua Specialist Teaching Hospital, Irrua, Edo state Nigeria were recruited for this study. This Hospital located at Irrua is the only tertiary health institution which covers patients from Auchi, Ehor, Ekpoma, Ewu, Irrua, Sabongida Ora, Uromi, Uruekpen and other environs. The study period lasted from November 2006 to September 2009.

Ethical consideration

The Research protocol was reviewed and approved by the Institutional Ethics Committee of Irrua Specialist Teaching Hospital Irrua, Edo state. The informed consent and approval of all the subjects were obtained. Each participant signed a consent form after the procedure and implications have been explained to the subject in English Language or Special English or local dialect she understands. Participation was voluntary and each participant could withdraw from the study at any time.

Subjects

A total of 283 pregnant women were enrolled initially for this study. Of these, 46 withdraw from the study while 28 did not finally deliver in the selected hospital of study, so that the final number of the subjects was pair matched 209 pregnant women and 209 newborns. The inclusion criteria for the pregnant women were age range of 20 to 35 years. While the exclusion criteria were history of any chronic disease.

Blood sample collection and data abstraction

Paired maternal venous blood and newborn's cord blood was collected from each participant at delivery and dispensed into plain container to obtain serum for vitamin E and vitamin C determination within 24hours of collection. Trained Midwives and resident Doctors measured the birth weight, head circumference and birth length immediately after delivery and recorded this information on medical charts. Medical and obstetrics histories as well as delivery data were obtained from each participant's file and the medical charts by two resident Doctors who were blinded to the goal of the study. To ensure consistent data abstraction and handling, they filled-in a printed form for each participant, which was handed to the principal investigator for data processing. Body mass index (BMI) was calculated from the weight and height of each participant. Gestational age was calculated based on maternal report for the last menstrual period and on ultrasound measurement by Obstetricians. Additional demographic data were obtained using the study questionnaires administered to subjects during a structured interview by trained interviewer. This included basic socioeconomic information, educational level and intake of vitamins.

Determination of vitamin C and vitamin E

Vitamin C was determined by the colorimetric method of Aye kyaw,[18] with very little modifications. Acid phosphotungstate was used to precipitate out proteins in fresh serum and also reacts with ascorbic acid in the serum to form a bluish colour whose absorption was measured at 700nm. The intensity of the colouration is proportional to the concentration of the ascorbic acid. Vitamin E was determined by the colorimetric method of Quaife and Dju.[19] Fresh serum vitamin E was extracted into xylene layer and reacts with α,α–dipyridyl to form a reddish brown complex, which is measured at 520 nm. The intensity correlates the concentration of vitamin E.

Statistical analysis

Data generated were analyzed using 'SPSS 16.0 software for windows' and Microsoft Excel. Correlations between maternal and cord serum vitamin E and vitamin C, and also between maternal/cord serum vitamins and pregnancy outcomes were measured by Pearson correlation coefficient which describes the simple correlation between dependent variable and independent variable. Student t-test was used to compare means of maternal and cord serum vitamins, and means between vitamins E and C respectively in normal and low birth weight newborns.

RESULTS

Demographic/clinical characteristics of mothers and birth outcomes of newborns

The mean age and BMI of the mothers were 26.9±3.5 years and 28.2 ± 4.1 respectively. A lower percentage (12.5%) of the mothers had educational status up to tertiary level, while higher percentage had =secondary school level (68.8%) and ≤primary (18.7%) respectively. The main source of vitamin C and E intake were through fruits and vegetables. Only 6.7% of all the mothers took vitamin C supplements during pregnancy, while none (0%) took vitamin E supplements. The mean gestational age was 38.1± 2.4 weeks (Table 1).

Serum vitamins C and E levels in maternal and cord blood

Serum vitamin C level was significantly higher in cord blood than in maternal blood (p<0.01).There was non significant higher maternal serum vitamin E compared to newborn cord serum (p>0.05). Maternal serum vitamin C and vitamin E were positively correlated with cord serum vitamin C and vitamin E (r = 0.930 and r = 0.955 respectively (Table 2).

Table 1: Demographic/clinical characteristics of mothers and birth outcomes of newborns

Variables	Mothers (n=209)	Newborn (n=209)
Age (year)		
Mean±SD	26.9±3.5	
BMI (kg/m²)		
Mean±SD	28.2±4.1	
Educational level (%)		
≥Tertiary	26 (12.5)	
=Secondary	144 (68.8)	
≤Primary	39 (18.7)	
Dietary intake (%)		
Vit. C supplement	14 (6.7)	
Vit. E supplement	0 (0)	
Fruits (citrus) (%)	209 (100)	
Vegetabes (%)	209 (100)	
Vaginal delivery n (%)	167 (80)	
Caesarean section n (%)	42 (20)	
Gestational age (weeks)		
Mean±SD		38.1±2.4
Birth weight (kg)		2.99±0.49
Birth length (cm)		47.49±3.41
Head circumference (cm)		34.38±2.07
Apgar score		9.17±1.06

Correlation of maternal serum vitamin C with pregnancy outcomes in newborns

Maternal serum vitamin C was significantly positively correlated with all the pregnancy outcomes in this study (for birth weight r = 0.622, for birth length r = 0.482, for head circumference r = 0.556 and for Apgar score r = 0.546) (Table 3).

Correlations of cord serum vitamin C with pregnancy outcomes in newborns

Cord serum vitamin C was significantly positively correlated with all the pregnancy outcomes (for birth weight r = 0.634, for birth length r = 0.479, for head circumference r = 0.586 and for Apgar score r = 0.569) (Table 3).

Correlations of maternal serum vitamin E with pregnancy outcomes in newborns

Maternal serum vitamin E was significantly positively correlated with all the pregnancy outcomes in this study (for birth weight r = 0.607, for birth length r = 0.473, for head circumference r = 0.546 and for Apgar score r = 0.511) (Table 4).

Correlations of cord serum vitamin E with pregnancy outcomes in newborns

Cord serum vitamin E was significantly positively correlated with all the pregnancy outcomes (for birth weight r = 0.652, for birth length r = 0.475, for head circumference r = 0.560 and for Apgar score r = 0.545) (Table 4).

Serum vitamin C and E in mothers of newborns with birth weight ≥2.5KG and <2.5KG

Mothers that delivered low birth weight newborns had significantly lower serum vitamin C and vitamin E levels than mothers that delivered normal birth weight newborns (p<0.001) (Table 5).

Cord serum vitamin C and E in newborns with birth weight ≥2.5KG and <2.5KG

Low birth weight newborns had lower serum vitamin E level compared to normal birth weight newborns. There was no significant difference in serum vitamin C level between the two groups (Table 5).

DISCUSSION

Man and primates have an inborn error in metabolism which renders them incapable of synthesizing ascorbic

Table 2: Serum vitamin C and vitamin E levels in maternal and cord blood

Variables (mean±SD)	Mother (maternal) (n=209)	Newborn (cord blood) (n=209)	t-value	p-value	Correlation (r)
Vitamin C (mg/dl)	3.3±0.6	4.0±0.7	2.8154	0.01(S)	0.930**
Vitamin E (mg/dl)	0.86±0.17	0.72±0.15	1.2710	>0.05 (NS)	0.955**

acid.[20] Findings from this study shows that the newborn had a lower serum vitamin E level, which is not significantly different from their mother's level, while newborns were found to have significantly higher levels of vitamin C (ascorbic acid) and there is a strong positive correlation between maternal and cord serum vitamin E and vitamin C respectively. The high placental transfer of vitamin C most probably relates placental transferable function. It has been reported that placenta is permeable to dehydroascorbic acid, but not to ascorbic acid.[21] Ascorbic acid is selectively transferred across the placenta from the maternal circulation as dehydro ascorbic acid and is selectively retained by the fetus after reduction to ascorbic acid, which gives rise to elevated level of vitamin C in cord blood.[22,21] In contrast, limited permeability of lipid soluble antioxidants (like vitamin E) across the placenta lowers their concentration in cord blood.[23,24,15] However the mechanism of vitamin E transportation from mother to fetus has not been clarified.[14]

Table 3: Correlation of maternal/cord serum vitamin C with birth outcomes in newborns

Dependent Variables in newborn	N	r-value (maternal)	r-value (cord)
Birth weight	209	0.622	0.634
Birth length	209	0.482	0.479
Head circumference	209	0.556	0.586
Apgar score	209	0.546	0.569
Gestational age	209	0.520	0.552

Table 4: Correlations of maternal/cord serum vitamin E with birth outcomes in newborns

Dependent Variables in newborn	N	r-value (maternal)	r-value (cord)
Birth weight	209	0.607	0.652
Birth length	209	0.473	0.475
Head circumference	209	0.546	0.560
Apgar score	209	0.511	0.545
Gestational age	209	0.550	0.574

A positive correlation between mother and newborn levels of vitamin C and vitamin E shows that the nutritional status of mother influence antioxidant vitamin status of the newborn.[25] This is further clear from the finding in this study that mothers deficient in antioxidant vitamin E and vitamin C tends to produce newborn with relatively low levels of these antioxidants vitamins. Gómez et al.,[26] nearly two decades ago reported that plasma levels of vitamin E in the newborn infants are significantly lower than that of their mother's and that there is a close correlation between umbilical cord vitamin E concentration and vitamin E levels in the mother's plasma.[26] And recently other researchers reported that newborn had significantly higher levels of vitamin C as compared to their mother but had significantly lower levels of vitamin E, with positive correlation between mother and newborn vitamin C and vitamin respectively.[14,27] These observations were almost consistent with the present report. However Scaife et al.,[28] had earlier reported that maternal diet influences cord plasma levels of vitamin C, but not vitamin E.

In addition, in the present study, cord serum vitamin C level was increased with gestational age, which is consistent with the report of Wang et al.,[14] but not consistent with the report of Das and Powers.[29] However it was noted that the serum vitamin C levels observed for the subjects were higher than levels reported from other geopolitical zones in this country. The study area; Edo state in the south –south zone of Nigeria has in abundant numerous plant food very rich in antioxidant vitamin C.[30] However this present finding is consistent with report of Ihemeje et al.,[31], who had previously reported higher plasma values of antioxidant vitamin C and E in normotentives in Edo state, Nigeria, compared to values published elsewhere in this country.

It is shown from this study that maternal and cord serum vitamin C and vitamin E were positively correlated with

Table 5: Serum vitamin C and E in mothers of newborns with birth weight ≥2.5 kg vs <2.5 kg and in newborns with birth weight ≥2.5 kg vs <2.5 kg

Variables (mean±SD)	Mothers of newborn ≥2.5kg (n=165)	Mothers of newborn <2.5kg (n=44)	t-value	p-value
Vit. C (mg/dl)	3.5±0.5	2.5±0.4	5.8424	0.001 (S)
Vit. E (mg/dl)	0.92±0.15	0.66±0.09	8.3045	0.001 (S)
Age (yrs)	27.0±3.6	26.6±3.2	0.4164	>0.05 (NS)
Vaginal delivery n (%)	161 (97.6)	18 (40.9)	-	-
Caesarean section n (%)	4 (2.4)	26 (59.1)	-	-
Variables (mean±SD)	**Newborn ≥2.5kg (n=164)**	**Newborn <2.5kg (n=45)**	**t- value**	**P-value**
Vit. C (mg/dl)	4.5±0.6	3.3±0.4	1.0703	>0.05 (NS)
Vit. E (mg/L)	7.7±1.2	5.3±0.9	4.5155	0.001 (S)

n=Number of subjects, P=Significant level (2-tailed), S='t' -test significant, NS=T- test non-significant birth weight, birth length, head circumference and Apgar score. This is consistent with some previous reports,[32,33] that serum vitamin C level during the second trimester had positive correlation with birth weight and birth length. Also, Scholl et al.,[34] reported that higher serum vitamin E of mothers at week 28 were positively associated with several indicators of fetal growth. Master et al.,[35] reported that mothers with lower vitamin E level had newborns with lower birth weight compared to newborns from mothers with higher serum vitamin E level. However, Wang et al.,[14] found no significant relationship between maternal serum vitamin E or vitamin C at delivery and newborns birth weight, birth length or head circumference. Tamura et al.,[13] reported that maternal vitamin E levels at 18 and 30 weeks of gestation were not related to birth outcomes.

Also significantly lower level of serum vitamin C in the mother has been associated with increased early neonatal morbidity and mortality, still birth, premature delivery and low birth weight.[36,20] Vitamin E deficiency during pregnancy may cause miscarriage, preterm birth, and intrauterine growth restriction.[37] Supplementation of vitamin C could help to prevent the development of such complications of pregnancy like gestational hypertension, intrauterine growth retardation.[38] Vitamin C supplementation is particularly important in pregnant women as its deficiency has been shown to affect placental structure and facilitates placental infection both of which results in increased risk of premature rupture of placental membranes and premature births.[39] It is observed in this study that mothers that delivered low birth weight newborns (<2500 gm) had significantly lower levels of serum vitamin C and vitamin E than mothers that delivered normal birth weight newborns (≥ 2500 gm). This is consistent with a previous report[27] that low birth weight child (<2500 gm) suffers with greater oxidative stress as compared with normal birth weight newborn (>2500 gm) and they were found to be relatively deficient in their antioxidant status. This present study is also consistent with another report[40] that preterm babies have fewer lipid-soluble antioxidant vitamins in their serum compared to term infants, and that preterm infants are more susceptible to oxidative stress. Besides, it had been previously reported that dietary intake was positively correlated with maternal plasma levels of vitamin C and E.[28]

Antioxidants are very vital in protecting cells and tissues from deleterious effects of oxidative stress,[41] thus decreased antioxidant defense in the presence of increased oxidative stress as in pregnancy can impair fetal growth. Even though few literatures on the effect of antioxidant vitamins on birth outcome exist, our present study suggests that maternal serum concentrations of vitamin C and E were associated with birth outcome. It should be noted that in relatively well nourished pregnant women there is tendency to have improved fetal growth. Limitation of this study was that although vitamin intake during pregnancy was determined, the study did not measure 24 hours recall of dietary intake. The present study does not suggest that only adequate vitamin C and E status may single handedly improve birth outcome, so caution should be taken while using supplements containing antioxidant vitamin C and E during pregnancy.

CONCLUSION

This study observed a significantly higher cord serum vitamin C and non significant lower vitamin E in newborns compared to their mothers. It is elucidated from this study that antioxidant vitamins C and vitamin E status has effect on birth outcome of the newborn, as poor antioxidant vitamins status is reflected in low birth weight, small head circumference and small birth length. Therefore vitamin C and E supplementation may be beneficial to the mother and fetus.

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Authors Contribution:
CII - Concept and design of the study, reviewed the literature, laboratory analysis, data collection, statistically analyzed and interpreted the data, manuscript preparation and critical revision of the manuscript; **NCM -** Concept, collected data and review of literature and manuscript preparation and helped in correction of manuscript; **JIA -** Conceptualized study, designed the study, collected data, and prepared first draft of manuscript and critical revision of the manuscript, co-supervised the study; **CNN** - concept of study, data collection, manuscript preparation and review of study; **IOO-** Concept and design of study, collected data, manuscript preparation, review of study and Supervision of the study.

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