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Vitamin A Supplementation of Malaria-infected Pregnant Women and Infant Birth Weight Outcomes A Case Study of Ebonyi State, Nigeria

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Abstract

A total of 152 malaria parasitaemic pregnant women of varying ages and gravidities, whose pregnancies had advanced up to the 6th months and above, were enrolled in the study. Seventy-six (76) each were randomised into supplemented and placebo groups. Venous blood was collected from each woman and examined for malaria parasitaemia, using standard parasitological techniques. Ten thousand international units of vitamin A was administered to the supplemented group once daily for three times per week. The placebo group also received vitamin A soft gels devoid of its active ingredients three times weekly. The regimen was continued as the women were followed up until delivery of their babies. Birth weights of the infants were determined with the use of weighing scales, within 72 hours post-delivery. Cross tabulations were used to calculate the percentages of low birth weights. The mean birth weights of the infants were analysed, using analysis of variance (ANOVA) and Fisher's least significance difference (FLSD), for mean separation. T-test was used to compare birth weight in supplemented group with those in the placebo group. Statistical significance was established at $p < 0.05$.

The multigravids dominated in the study. The primigravids had the least mean age while the multigravids had the highest. When the overall supplemented and placebo groups were compared the placebo groups had higher number of low birth weights that were statistically significant ($p < 0.05$) among the infants of the 8th month group women. The mean birth weights were generally statistically higher in the supplemented group than in the placebo group, except in a few cases with no significant differences. Vitamin A has proved to be efficacious in improving infant birth weights. Therefore, its supplementation to pregnant women at safe periods and dosages is advocated.

Keywords: Vitamin A, Supplementation, Malaria, Pregnancy, Birthweight

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Background

Vitamins are complex organic molecules which must be present in food in minute amount to enable growth, health and life to be maintained [1]. They are needed in small quantities and given to organisms that cannot synthesize them and most obtain them in their diet [2]. Vitamins are broadly divided into fat soluble and water soluble groups. Vitamin A is a fat soluble vitamin that comprises retinol, a preformed vitamin A originating from animal tissues, and beta-carotene, a provitamin originating from plant tissue. Vitamin A is an essential nutrient required for maintaining immune function, playing important role in the regulation of cell-mediated immunity and in humoral antibody response [3]. It is also essential for the growth and differentiation of epithelial cells as well as necessary in embryonic development [4]. It has been estimated that vitamin A deficiency affects 19.1 million pregnant women, the majority in Africa and South East Asia [5]. Vitamin A deficiency, defined as serum retinol < 0.70 mmol/L or the presence of abnormal impression cytology [6] is a serious public health problem in Nigeria, as it is in many Sub-Saharan Countries. Nigeria has been identified by the World Health Organisation as one of the categories of countries with the highest risk of vitamin A deficiency [7]. Vitamin A deficiency is more common among the rural poor and is always very much pronounced among pregnant women in such rural settings.

Inadequate intake of food, poor diet quality, or when micro nutrient are not readily release from foods, not absorbed efficiently or a combination of the factors may result in deficiency in one or more micro nutrients [8]. Supplementation of pregnant women with the recommended International Units (IU) of vitamin A could be a remedial measure to vitamin A deficiency. Vitamin A is transferred from the mother to the foetus across the placenta and vitamin A concentrations in the foetal blood are approximately half of those in the mother [9]. Retinol Binding Protein (RBP) is involved in the transfer of vitamin A from mother to embryo [10].

Malaria is endemic in 91 Countries with about 40% of the world population at risk [11,12]. World malaria report 2012 stated that Nigeria contributed 25% of all malaria cases in the 45 countries endemic for malaria in Africa [13]. In Nigeria, malaria is responsible for approximately 110 million clinically diagnosed cases annually and account for about 60% and 30% of outpatient visits and hospital admissions respectively [14].

Malaria in pregnancy is a common cause of severe maternal anaemia and low birth weight babies [15]. Infant birth weight is the weight of an infant taken within an hour after birth, to avoid possible post natal weight loss, and an infant is classified as either having Low Birth Weight (LBW), if the weight measured to the nearest 0.1 kg is less than 2.5 kg or is having Normal Birth Weight (NBW), if the weight is greater than or equal to 2.5kg. At least 17 million infants are born every year with low birth weights, representing about 16% of all newborns in the developing countries [16].

Maternal environment is an important determinant of birth weights and factors that can obstruct normal circulation across the placenta can also cause poor nutrition and oxygen supply to the foetus, thereby restricting growth. One of such factors is maternal undernutrition [17]. Evidence exists that suggest that infant outcome can be improved by improving the maternal nutritional status. Vitamin A has been reportedly stated to be effective in improving infant birth weight outcomes. Reports on the beneficial effects of vitamin A supplementation on birthweights have been published [18, 19].

Methods

The Study Area: The study was undertaken in some health centre, and rural villages within three rural communities in Ebonyi State. The communities are Ndubia, Agubia and Oshiri. Ebonyi state lies approximately within longitude 7 30’ and 8 30’ E and latitude 5´ 40’ and 6´ 45’ N and located in the South eastern region of Nigeria [20].

Study Populations: The study populations were pregnant women of varying age groups and gravidities, who were malaria parasitaemic and whose pregnancies had matured at least to the sixth month, and their infants when delivered. Women who had no malaria infection after diagnosis and whose pregnancies had not advanced to the sixth month were excluded.

Ethical Considerations: The study protocol was approved by the Primary Health Care Unit of Ebonyi State Ministry of Health. Informed consents were obtained from the participants.

Design of the Study: The study was a placebo-controlled randomized field trial that evaluated the effect of maternal vitamin A supplementation on infant birth weights.

Blood Collection and Determination of Malaria Parasitaemia: [The anatomical site for blood collection was cleaned with swab moistened with 70 % alcohol and was allowed to dry. (One) 1ml of venous blood collected from each woman was used to make thin and thick films that were examined for malaria parasitaemia according to standard parasitological techniques [21]

Supplement Administration and Monitoring: Ten thousand (10,000) International Units (IU) of vitamin A was administered to the pregnant women of the supplemented group three times per week [22]. Placebo (vitamin A soft gels devoid of their active ingredients) was also given to the placebo group three times weekly. The two groups were followed up and monitored to ensure high level of compliance to the intake of the regimen.

Determination of Compliance to Regimen: Compliance with the study regimen by each participant was determined by adding the number of the vitamin A soft gels taken by each participant from the time of enrolment into the study, and dividing them by the total number of soft gels the participant should have taken throughout the study.

Determination of Birth weights: Birth weights of the newborns were taken on weighing scales within a minimum of an hour after delivery and a maximum of 72 hours and were measured to the nearest 0.1kg.

Statistical Analysis

Cross tabulations were used to calculate the percentages of low birth weights. Differences in percentages were determined using Chi-square and Fisher's exact test. The mean birthweights of the infants were analyzed using Analysis of Variance (ANOVA) and Fisher's Least Significant Difference (FLSD) for mean Separation. Student's t –Test was used to compare birthweights in supplemented group with those in the placebo group. A p value less than 0.05 was considered statistically significant.

Results and Discussion

A total of 152 mother-infant pairs participated in the study, 76 in each of the supplemented and placebo groups. The mothers were all malaria parasitaemic at the beginning of the study and were at different gravidities (Table 1) and were also of varying age groups. Table 2 shows the mean age of the women. The multigravids dominated in number in both supplemented and placebo groups. Within the supplemented group, the mean age of the multigravids differed significantly from the rest of the gravidities. The primigravids had the least mean age while the multigravids had the highest mean age. In the placebo group, the mean age of the mothers differed across the gravidities, with the primigravids having the least mean age. When the supplemented group was compared with the placebo group, a statistically significant difference ($p < 0.05$) was obtained in the mean age of the primigravids, with women of the placebo group being younger.

Table 1: Population of follow-up mothers stratified by gravidity from vitamin A supplemented and placebo group mothers in Ebonyi state, Nigeria.

Gravidity	Supplemented Group(N= 76)	Placebo Group (N=76)
Primigravids	21(27.63%)	21(27.63%)
Secondgravids	24(31.58%)	21(27.63%)
Multigravids	31(40.79%)	34(44.74%)
Total	76(100%)	76(100%)

Table 2: Mean age of vitamin A supplemented and placebo group mothers in Ebonyi State, Nigeria

Gravidity	Supplemented Group(N= 76)	Placebo Group (N=76)
Primigravids	23.24 ± 4.43^{a}	$20.00 \pm 2.50^{a*}$
Secondgravids	25.63 ± 3.37^{a}	27.58 ± 4.20^{b}ns
Multigravids	30.20 ± 4.85^{b}	29.93 ± 3.83^{c}ns
Overall	26.93 ± 5.37	26.56 ± 5.50ns

Key: Values in a column with different alphabets as superscripts are significantly different (P< 0.05) NS=No significant difference (p> 0.05), determined by t – test; * significant difference (p< 0.05), determined by t-test.

Irrespective of the fact that the number of infants with low birth weights were more in the placebo group than in the supplemented group, there was no significant difference (p> 0.05) in prevalence of low birth across the months in both supplemented and placebo groups across all the gravidities. The overall prevalence of low birth weights among infants of vitamin A supplemented mothers was significantly higher (p< 0.05) among those whose mothers commenced taking the supplement at the 7th month of pregnancy when compared with others. When the supplemented and placebo groups were compared, the placebo group had higher low birth weights that were statistically significant (p< 0.05) at the 8th month.

Table 3: Prevalence of low birth weights (kg) among infants from vitamin A supplemented and placebo groups mothers in Ebonyi State Nigeria.

Month	**Supplemented**	**Placebo**
	Primigravids	
6th	$0(0.0)^{a1}$	$1(33.3)^{a1}$
7th	$0(0.0)^{a1}$	$0(0.0)^{a1}$
8th	$0(0.0)^{a1}$	$3(42.9)^{a1}$
9th	$0(0.0)^{a1}$	$1(25.0)^{a1}$
	Secondigravids	
6th	$0(0.0)^{a1}$	$1(33.3)^{a1}$
7th	$1(16.7)^{a1}$	$1(20.0)^{a1}$
8th	$0(0.0)^{a1}$	$1(16.7)^{a1}$
9th	$0(0.0)^{a1}$	$0(0.0)^{a1}$
	Multigravids	
6th	$0(0.0)^{a1}$	$1(50.0)^{a1}$
7th	$2(28.6)^{a1}$	$2(22.2)^{a1}$
8th	$0(0.0)^{a1}$	$1(12.5)^{a1}$
9th	$0(0.0)^{a1}$	$1(14.3)^{a1}$
	Overall	Overall
6th	$0(0.0)^{b1}$	$3(37.5)^{a1}$
7th	$3(21.4)^{a1}$	$3(15.8)^{a1}$
8th	$0(0.0)^{b2}$	$5(23.8)^{a1}$
9th	$0(0.0)^{b1}$	$2(12.5)^{a1}$

Key: Data were presented as frequency counts and compared using chi-square test and fisher exact test as approximate. Values in parenthesis indicate percentages. Percentage in a
Colum with different alphabets are significantly different percentages in a row with different figures are significantly different.

Table 4: Effect of maternal vitamin A supplementation on birth weights (kg) of infants from vitamin A supplemented and placebo group mothers in Ebonyi State, Nigeria.

Month	**Supplemented**	**Placebo**
	Primigravids	
6th	2.98 ± 0.46a	2.47 ± 0.06ans
7th	2.65 ± 0.21 a	2.62 ± 0.11ans
8th	2.82 ± 0.13 a	2.50 ± 0.12 a*
9th	2.95 ± 0.33 a	2.60 ± 0.18 a*
	Secondigravids	
6th	3.00 ± 0.00 b	2.70 ± 0.30ans
7th	2.63 ± 0.21 a	2.64 ± 0.13ans
8th	3.03 ± 0.27 b	2.73 ± 0.31ans
9th	2.80 ± 0.33 b	2.58 ± 0.08ans
	Multigravids	
6th	2.85 ± 0.50 a	2.95 ± 0.78ans
7th	2.79 ± 0.41 a	2.53 ± 0.12ans
8th	2.93 ± 0.37 a	2.61 ± 0.15 a*
9th	2.93 ± 0.38 a	2.69 ± 0.40ans
	Overall	
6th	2.94 ± 0.39 b	2.68 ± 0.39ans
7th	2.64 ± 0.19 a	2.58 ± 0.13ans
8th	2.93 ± 0.32 b	2.61 ± 0.21 a*
9th	2.87 ± 0.31b	2.64 ± 0.28a*

Key: Values in a column with different alphabets as superscripts are significantly different. ($p< 0.05$), NS= no significant difference ($p>0.05$), determined by t-test, *= significant difference ($p< 0.05$), determined by t-test.

Table 4 depicts effect of the vitamin A supplement on the mean birth weights of the infants. When the supplemented group was compared with the placebo group within the primigravids, significant difference ($p< 0.05$) were observed in the birth weights of the infants whose mothers were in the 8th and 9th month groups. Within the supplemented group of the secondigravids, a significant difference in mean birth weights was observed only among infants whose mothers started taking the vitamin A supplement at the 7th month of pregnancy. When the supplemented and placebo group birth weights were compared among the multigravids, significant difference was observed among infants of the mothers of the 8th month group.

In the supplemented group of the overall birth weight, weights of infants whose mothers started taking the supplement at the 7th month were significantly lower ($p< 0.05$) than those of other infants of mothers with different supplementation periods. Significant differences ($p< 0.05$) between supplemented and placebo groups was observed among infants of mothers at the 8th and 9th months.

Despite the fact that significant differences were not observed in some few cases, the birth weights were generally lower in the placebo group than in the supplemented group. The mean birth weights that were generally higher in the vitamin A supplemented group than in the placebo group is in consonance with the findings of Kumwenda and colleagues [19], who reported an increase in the birth weights of infants of human immunodeficiency virus- infected women who received vitamin A with iron and folate when compared with their counterpart placebo group that received daily doses of iron and folate alone.

The findings of this study also conforms with those of Jaya and Shatrugna [23] and Panth et al. [18], who found higher birth weights among the vitamin A supplemented group when compared with the placebo group. This study also agrees with the findings of Kaestal et al. [24]. However, this study disagrees with some reports of eelier studies. A trial from England conducted among South Asian immigrants with higher risks of lower birth weights than their British counter part reported no difference in birth weights [25]. In addition, a randomized blinded trial conducted among HIV positive women in Tanzania found no significant effect of the supplement in mean birth weights of their subjects [26].

The general higher birth weights observed in the supplemented group in comparison with the placebo group is an indication of vitamin A efficacy in the clearance of Malaria parasitaemia as have been reported by Davis et al. [27] and by Shankar et al. [28]. The parasite clearance potency of vitamin A might have mitigated in the prevention of infection of the placenta of the supplemented group by the malaria parasites, thereby preventing low birth weights and improving birth outcome.

Conclusion

Vitamin A has been reported to be generally beneficial to maternal and child health, including the function of improving birth weight outcome. Therefore, supplementing rural pregnant women with poor dietary habits and poor nutrition education, with the WHO recommended dose of vitamin A is advocated.

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