Improved infant hemoglobin (Hb) and blood glucose concentrations: The beneficial effect of maternal vitamin A supplementation of malaria-infected mothers in Ebonyi State, Nigeria

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ABSTRACT

One hundred and fifty-two malaria-infected pregnant women whose pregnancies had advanced to the 6th month were randomised into two study groups – supplemented and placebo groups, after obtaining their approved consents. Ten thousand international units of vitamin A soft gels were administered to the supplemented group three times per week. Vitamin A soft gels devoid of their active ingredients were administered thrice weekly to the placebo group. Two hundred thousand international units of vitamin A was administered to the supplemented groups within 8 weeks postpartum. Placebo was given to the control group at same time after delivery. The regimen was continued in the two groups at three-month intervals until 12 months. Quarterly, 3 ml of venous blood was collected from each infant in the two groups and was used for the estimation of hemoglobin concentrations and determination of blood glucose levels. Hemoglobin concentrations were estimated using hemiglobincyanide method while the blood glucose levels were determined with a glucometer. Analysis of variance, Fisher's least significant difference and *t*-test were used for data analysis. Statistical significance was established at $p < 0.05$. Both hemoglobin concentrations and blood glucose levels were significantly ($p < 0.05$) higher in the supplemented group than in the placebo group. The malaria infection mitigating effects of maternal vitamin A supplementation have been established in the present study and supported by previous studies. Vitamin A supplementation, fortification of foods with vitamin A and diversification of diets, are advocated for maintenance of good health and protection against some infectious diseases.

KEYWORDS

hemoglobin; blood glucose; maternal; vitamin A; malaria

Introduction

Vitamin A is a fat-soluble micronutrient of great importance in the maintenance of good health and growth. Many clinical trials in infants and children have reported the potency of vitamin A supplements in protecting against illnesses [1]. The health maintenance and protective roles of vitamin A are centered mainly on its ability in modulating immunity. Reports of *in vivo* and *in vitro* studies carried out on both humans and animals indicated that vitamin A and its metabolites play vital roles in the regulation of both innate and acquired immunity [2,3]. In spite of the positive roles of vitamin A in public health, its deficiencies are prevalent in resource-constrained parts of the world, where it contributes to maternal and child morbidities and mortalities. It has been reported that approximately 7.8% of pregnant women in Africa had night blindness and 15.3% had low serum retinol which are indicators of vitamin A deficiency [4]. Food diversification, food fortification and supplementation with vitamins among other measures are approaches to tackling the problems of micronutrient malnutrition.

Malaria is a public health problem that is seriously ravaging both maternal and child health in many parts of the world especially in Africa. It has been reported that approximately 50 million women become pregnant annually and more than 50% of them reside in Africa [5]. Malaria in pregnancy has devastating effects on both maternal and infant health. It can result in maternal anemia, intrauterine growth restriction, still birth, pre-term birth, low birth weight, among other morbidities, and in severe forms, can lead to maternal mortalities and other sequelae in the health of any surviving infant. This study reports improved infant hemoglobin and blood glucose concentrations resulting from vitamin A supplementation of malaria-infected pregnant women in Ebonyi State, Nigeria.

Materials and methods

The study area

The study was carried out in Ebonyi State, a state that is part of the tropics and lies in longitude 7°30' and 8°30' and latitude 5°40' and 6°45' [6]. Ebonyi State has two

distinct seasons (the rainy and dry) in a year. The former starts from April and ends in October while the latter commences from November and stops in April.

The study population

The study population was 152 malaria-infected pregnant women of varying age groups, at second trimesters of pregnancy, and their infants when born. Since the study involved both the pregnant women and their infants when delivered, the women in addition to their own agreement consented for their newborns who were minors, before the study commenced on them (the infants).

Design of the study

The study was a placebo-controlled randomised field trial that evaluated the effect of maternal vitamin A supplementation on infant hemoglobin and blood glucose levels. Seventy six pregnant women were randomised to each of the supplemented and placebo groups.

Ethical considerations

Postpartum and infant vitamin A supplementation was not a routine supplementation program in Nigeria during the time of the study. The study protocol was approved by the Primary Health Care Unit of Ebonyi State Ministry of Health. Informed consents were obtained from the participants (pregnant women), who also gave approval for the enrollment of their infants when delivered. Comprehensive ethical precepts with respect to carrying out research on humans were duly observed in the study.

Supplement administration and monitoring

Ten thousand international units of vitamin A soft gels were administered to the supplemented group three times weekly starting from their 6th month in pregnancy. The placebo arm received the vitamin A soft gels devoid of their active ingredients also three times per week. The regimen was continued until the women delivered. On delivery of their babies, the supplemented group mothers received 200,000 IU of vitamin A within 8th week postpartum. The supplementation was continued every 3 months until the study was over after the 12th month. Placebo was also given at same frequencies to the non-supplemented group mothers until the study was over. Village-based health workers (VBHW_s) assisted in the administration of the supplement and monitoring of compliance to the in-take of the supplement.

Blood collection

Four milliliters (4 ml) of venous blood was collected quarterly from each infant. A drop ($\approx 25 \mu\text{l}$) of the blood was

used in the determination of blood glucose concentrations in situ while 3 ml of the blood was collected into an EDTA container and transported to the laboratory. In the laboratory, 20 μl (0.02 ml) of the blood in the EDTA container was used for the determination of the hemoglobin levels.

Estimation of hemoglobin concentrations

The hemoglobin–cyanide (cyanmethemoglobin) method as outlined by Lewis et al. [7] was used to estimate the hemoglobin concentrations of the infants.

Determination of blood glucose concentrations

The blood glucose levels of the infants were determined in situ with the use of a glucometer (ACCU-CHEK (R) Advantage).

Statistical analysis

Data collected were analyzed using analysis of variance, Fisher's least significant difference, and *t*-test. Statistical significance was established at $p < 0.05$.

Results

In the placebo group of the primigravids, significant difference ($p < 0.05$) in the hemoglobin concentrations was observed among infants of mothers that commenced taking the supplement at the 7th and 9th months of pregnancy. When the supplemented group was compared with the placebo group, significant differences ($p < 0.05$) were observed in all the months except at the 7th month. When the supplemented group was compared with the placebo group among the secundigravidae, significant differences ($p < 0.05$) were observed in the hemoglobin concentrations of infants of mothers in all the months except in those of the 6th month. Within the placebo group of the multigravids, the mean hemoglobin levels of infants whose mothers started taking the placebo at the 7th month differed only from those at the 8th month. When the mean hemoglobin concentrations were compared between the supplemented and placebo groups at the overall levels, significant differences ($p < 0.05$) were observed across the months, with hemoglobin levels of infants of placebo groups being smaller than those of the supplemented group (Table 1).

Table 2 depicts the effect of maternal vitamin A supplementation on blood glucose concentrations of the infants. Among the supplemented group, there was no significant difference ($p > 0.05$) in the mean blood glucose concentrations across board from the primigravids through multigravids down to the overall. Within the placebo group, significant differences ($p < 0.05$) in the mean blood glucose concentrations were observed

Table 1. Effect of maternal vitamin A supplementation on hemoglobin concentrations (g/dl) of infants from supplemented and placebo group mothers in Ebonyi state, Nigeria.

Month	Supplemented (N = 76)	Placebo (N = 76)
Primigravids (N = 21) Primigravids (N = 21)		
6th	11.06 ± 1.16 ^a	9.93 ± 0.49 ^{ab*}
7th	11.03 ± 0.97 ^a	10.35 ± 0.90 ^{b ns}
8th	11.01 ± 0.88 ^a	10.09 ± 0.92 ^{ab*}
9th	10.63 ± 1.16 ^a	9.85 ± 0.75 ^{a*}
Secundigravids (N = 24) Secundigravids (N = 21)		
6th	11.08 ± 0.73 ^a	10.16 ± 1.31 ^{a ns}
7th	10.99 ± 0.88 ^a	10.46 ± 0.97 ^a
8th	11.19 ± 0.90 ^a	10.75 ± 0.74 ^{a*}
9th	11.05 ± 0.87 ^a	10.30 ± 0.96 ^{a*}
Multigravids (N = 31) Multigravids (N = 34)		
6th	11.01 ± 1.00 ^a	10.59 ± 0.98 ^{ab ns}
7th	11.22 ± 0.93 ^a	10.33 ± 1.10 ^{a*}
8th	11.04 ± 0.95 ^a	10.81 ± 0.78 ^{b ns}
9th	11.07 ± 0.81 ^a	10.54 ± 1.03 ^{ab*}
Overall (N = 76) Overall (N = 76)		
6th	11.04 ± 1.02 ^a	10.23 ± 0.97 ^{a*}
7th	11.11 ± 0.90 ^a	10.38 ± 1.02 ^{a*}
8th	11.07 ± 0.91 ^a	10.49 ± 0.88 ^{a*}
9th	10.95 ± 0.96 ^a	10.31 ± 0.99 ^{a*}

Notes: 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. Months from 6th to 9th stand for gestation age of pregnant women on commencement of the vitamin A regimen.

Table 2. Effect of maternal vitamin A supplementation on blood glucose concentrations (mg /dl) of infants from supplemented and placebo group mothers in Ebonyi State, Nigeria.

Month	Supplemented (N = 76)	Placebo (N = 76)
Primigravids (N = 21) Primigravids (N = 21)		
6th	59.12 ± 4.39 ^a	53.00 ± 5.34 ^{a*}
7th	60.00 ± 4.67 ^a	52.09 ± 3.74 ^{a*}
8th	60.05 ± 5.43 ^a	50.77 ± 5.58 ^{a*}
9th	58.71 ± 3.60 ^a	51.15 ± 4.66 ^{a*}
Secundigravids (N = 24) Secundigravids (N = 21)		
6th	0.00 ± 0.00	52.21 ± 8.63 ^a
7th	59.75 ± 4.50 ^a	55.31 ± 4.79 ^{a*}
8th	60.97 ± 5.40 ^a	53.21 ± 5.79 ^{a*}
9th	60.15 ± 4.03 ^a	53.71 ± 4.72 ^{a*}
Multigravids (N = 31) Multigravids (N = 34)		
6th	58.44 ± 3.90 ^a	50.26 ± 5.40 ^{a*}
7th	59.29 ± 6.48 ^a	51.14 ± 5.22 ^{ab*}
8th	58.66 ± 4.27 ^a	53.22 ± 5.28 ^{bc*}
9th	58.61 ± 3.84 ^a	54.80 ± 5.24 ^{c*}
Overall (N = 76) Overall (N = 76)		
6th	58.72 ± 4.80 ^a	51.81 ± 6.37 ^{a*}
7th	59.54 ± 5.53 ^a	52.40 ± 5.10 ^{a*}
8th	59.79 ± 5.02 ^a	52.64 ± 5.70 ^{a*}
9th	59.28 ± 3.97 ^a	53.51 ± 5.19 ^{a*}

Notes: 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. Months from 6th to 9th stand for gestation age of pregnant women on commencement of the vitamin A regimen.

among the multigravids in some months. However, when the supplemented groups were compared with the placebo groups, statistical significant differences ($p < 0.05$) were observed in all cases and in all cases, the mean blood glucose levels of the infants were higher among the supplemented groups than in the placebo groups.

Discussion

Vitamin A supplementation has been reported to boost levels of hemoglobin and reduce anemia. Zimmermann et al. [8], reported a significant increase in hemoglobin concentrations after administering 200,000 IU of vitamin A to children in Morocco. Jimenez et al. [9], also reported a favorable effect of vitamin A supplementation on hemoglobin concentrations in Venezuela. The greater hemoglobin levels observed in this study in infants born by the vitamin A supplemented group in comparison to those born by the women in the placebo group is in line with the findings of Kumwenda et al. [10], who reported a decrease in anemia in vitamin A supplemented women in Malawi. However, the findings of the present study disagree with those of Miller et al. [11], who reported that vitamin A supplementation had no effect on hemoglobin or anemia on infants.

Overall, the mean blood glucose levels of the infants were significantly higher ($p < 0.05$) among the supplemented group than in the placebo group. The lower blood glucose concentrations in the placebo group could be as a result of metabolic effects of the malaria parasites and their disruptive activities on the blood glucose concentrations and homeostasis of the host.

Plasmodium parasites have been reported to increase glucose concentrations in the infected red blood cells by 50–100 folds and that most of the glucose is metabolised to lactic acid [12]. The parasites have been described as being highly dependent on glucose and very sensitive to oxidative stress [13]. The mechanisms and rates of glucose metabolism by *Plasmodium falciparum* in the more infected red blood cells (placebo group) may have been reduced, reversed or blocked in the erythrocytes of the less infected (vitamin A supplemented group) by the vitamin A supplement.

The primigravids have been widely reported to be more susceptible to malaria than the other gravidities. In this study, the authors examined the effects of vitamin A supplementation of malaria-infected pregnant women on hemoglobin and blood glucose concentrations of the infants and analysed the outcomes according to gravidities, to find out if the results of such a study could be similar to what is obtainable in malaria with respect to gravidity-based susceptibility.

Conclusion

The levels of concentrations of blood glucose in malaria-infected hosts have been reported by previous studies. Kayode et al. [14] reported hypoglycemia in their study on malaria and typhoid co-infection. In the present study, it is interesting to note that even though the mean blood glucose levels observed among the placebo group did not reach hypoglycemic levels (<40 mg/dl), some reduced concentrations on individual basis close to

hypoglycemic levels were observed. The findings of the present study are in conformity with those of Onyesom and Agho [15] in Edo State, Nigeria. The findings also agree with Mizushima et al. [16] and with Binh et al. [17]

Micronutrients play significant roles that cannot be neglected in public health and wellness. Their beneficial roles have been reported by previous studies. They are recognised to boost both cell-mediated and humoral immune response of the body [18]. Vitamin A is essential for vision, bone growth, reproduction and cell differentiation [19].

Vitamin A supplementation of malaria-infected pregnant women, in this study, significantly ($p < 0.05$) improved the mean hemoglobin and blood glucose concentrations of the infants. In addition, this study indicated that the trends of susceptibility to malaria by gravidity were not strictly observed in the case of mean hemoglobin and blood glucose concentrations as these two parameters were not strictly affected according to gravidity. Vitamin A supplementation, fortification of foods with vitamin A and diet diversification are advocated for maintenance of good health and protection against some infectious diseases.

Conflict of interest

No potential conflict of interest was reported by the authors.

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