ORIGINAL ARTICLE

Hematological indices in febrile neonates with malaria parasitaemia in Calabar

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ABSTRACT

Background: Normal hematological indices has been determined in Nigerian newborns and found to be lower compared to their Caucasian counterparts. This was attributed to genetic factors. Malaria is endemic in Nigeria and is one of the major causes of ill health and death. Anemia is an important manifestation of malaria. Resistance by malaria parasites to antimalarial drug exacerbates the situation by continuous hemolysis. **Aim:** To determine the hematological indices in febrile newborn with malaria parasitemia. **Materials and Methods:** One-hundred fifty neonates (0-28 days) with fever admitted into the Newborn Unit of University of Calabar Teaching Hospital, over a 6 months period, were recruited consecutively. Blood film for malaria parasites and samples for full blood count were obtained and sent to the laboratory before commencement of the treatment. Data analysis was with SPSS version 14. **Results:** One-hundred fifty babies were recruited into the study. Most (85.3%) of the babies were aged ≤7 days. Six babies (4%) had malaria parasitemia. *Plasmodium falciparum* was the only species identified. All the babies that had parasitemia were anemic (mean hemoglobin [Hb] concentration of 12.6 g/dl) even when parasite count was low (average of 30.6/µl) though this could not be attributed solely to malaria. None of these neonates was transfused. All the other hematological indices were within the normal range of healthy newborn population irrespective of parasitization. **Conclusion:** Neonatal malaria does occur in our environment. While it does not affect the white blood indices, it lowers neonatal Hb. It is recommended that Hb concentration be estimated in newborns with malaria to reduce infant morbidity and mortality in our environment.

Key words: Hematological indices, malaria parasitemia, newborn

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INTRODUCTION

Malaria is endemic in Nigeria and is one of the major causes of ill health and death.[1] Anemia is an important manifestation of malaria. Anemia in malaria is caused by hemolysis of the infected red blood cells (RBC's), sequestration of the erythrocytes in the spleen and other deep organs, and suppression of erythrocytes production in the bone marrow by the malarial pyrogen-induced cytokines.[1,2]

It has been estimated that severe malarial anemia causes between 190,000 and 974,000 deaths each year among children below 5 years of age. Although blood transfusion may be life-saving in this situation, it also exposes children to the risk of HIV and other blood-borne diseases.[3]

Normal hematological indices in the newborn have been established in the Caucasians and have been found not to be the same for African neonates.[4-6] Studies done by Onwukeme *et al*. in Jos,[4] Scot-Emuakpor *et al*.[5] in Benin, and Effiong *et al*. in Ibadan[6] documented values for Nigerian neonates and showed variations in hematocrit values in full term newborns within same country which was thought to

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be due to several factors such as site and time of sampling, vessel used, fetal-maternal, or maternal-fetal transfusion. The lower values in African newborns compared to the Caucasian values was attributed to genetic (intrinsic) factors. Also noted is the definite pattern of progressive drop which is obtainable in the Caucasians.

There is need to evaluate the hemoglobin concentration (Hb Conc.) and other hematological indices of febrile newborn with emphasis on those with malaria parasitemia and to correlate it with the malaria parasite density. This is to determine if there is a relationship between malaria parasite density and Hb Conc. in newborns with fever to avert delays in early laboratory diagnosis of anemia and treatment.

MATERIALS AND METHODS

This prospective, cross-sectional, and analytical hospital-based study was conducted among neonates admitted in into the Newborn Unit of the University of Calabar Teaching Hospital (UCTH) from the November 3, 2010 to the May 8, 2011. The unit had earlier been described by Udo *et al*.[7] Sample size was calculated using the formula $n = Z^2 pq/d^2$.[8]

Inclusion criteria were neonates with temperature ≥37.5°C or recent history of fever, who had not received antimalarials or antibiotics at least 2 weeks prior to the enrolment into the study and whose parent(s) or guardians had given consent.

Ethical clearance was obtained from the Ethical Review Committee of the UCTH before commencement of the study.

A statement of the study was made available to the parents so that they could understand what the study entailed and a signed informed consent was obtained from the parents or guardians who gave consent.

All consecutive babies (0-28 days) who met the inclusion criteria were recruited until the desired sample size was obtained. Detailed clinical history, covering both the antenatal and perinatal periods, was obtained for every baby enrolled. Also, physical examination including anthropometry was performed on the babies.

Two blood films (thick and thin film) for malaria parasite and samples for full blood count were taken before commencement of treatment and 4 weeks after treatment at follow-up. Both thick and thin blood films were prepared and stained with 2% freshly prepared Giemsa stain. Thereafter, it was read using ×100 objective lens with oil immersion[9] within 24 hrs of collection of blood by the first investigator, assisted by the laboratory scientist. These slides were validated independently by the microscopist with Institute for Tropical Disease Research and Prevention and a World Health Organization certified laboratory scientist attached to the Department of Pediatrics Research Laboratory.[9]

The parasite density was derived by the formula: Parasite per microliter = Number of parasites/Number of leucocytes × 8000, where 8000 represents the mean leucocyte count of children, which when multiplied with the ratio of parasites to leucocytes in a given field equals the parasite density.[9] Parasite density was classified for the purpose of categorization of the babies into; + (1 parasite/ field), ++ (2-19 parasites/field) and +++ (>20 parasites/field). The thin films were used for speciation of *Plasmodium*.[9]

Two milliliters of blood was collected in a labeled EDTA bottle by the investigator and sent to the hematology laboratory within 30 min of collection. Where this was not possible, the samples were refrigerated at 4-8°C for a period not >12 hrs. This was used to determine the total white blood cell count and differentials, Hb level, packed cell volume, and platelets, using an automated machine: Particle counter, model PCE - -210, Erma Inc., Tokyo, Japan.

An experienced clinical hematologist, stained, viewed, and reported the blood film picture following standard procedure,[10] with the active participation of the first investigator. Correction for total white cell count, when numerous nucleated erythrocytes are counted, was calculated as follows:

Total differential white blood cells counted × total white blood cell divided by total differential white cell counted × total nucleated RBC

Nucleated RBCs were reported as count per 100 white blood cells.

A working diagnosis of neonatal sepsis and neonatal malaria was considered in every febrile neonate. All the babies were commenced on first-line antibiotics therapy for neonatal sepsis in the unit and antimalarial drug in line with the National Malaria Treatment Policy for newborns.[11]

Results were collected with the aid of the case record form designed for the study. Data were analyzed using SPSS version 14 statistical software (SPSS Inc. Released 2006. SPSS Statistics for Windows version 14.0. Chicago: SPSS Inc). The results were presented in tables, charts, and graphs. Frequency, sample means, and percentages were calculated for the necessary variables.

Pearson's correlation was used to determine the relationship between malaria parasite density and the values of the Hb Conc. of the babies. Statistical significance of difference was determined using Chi-square (χ^2) for dichotomous variables and *t*-test for continuous variables. The level of significance was set at $P < 0.05$.

RESULTS

A total of 150 subjects aged 0-28 days were consecutively recruited. The study population was made of 87 (58.0%) males and 63 (42.0%) females with a male:female ratio of 1.4:1. Age category 0-7 days represented 128 (85.3%) of the subjects. The mean age of the study population was 4.2 ± 5.9 days and was not normally distributed, with the median of 2.0 days. The difference in ages was not statistically significant (P = 0.71).

The average age of the mothers was 28.1 ± 4.9 years.

One hundred thirty- six (90.7%) mothers booked for the antenatal care either in UCTH or at other health facilities.

Six (4.0%) of the newborn population had malaria parasitemia. *Plasmodium falciparum* was the only species identified. Four (66.6%) of the six babies with malaria parasitemia were aged under 7 days, indicating that they were congenital infections. The other two babies were aged 14 and 23 days, respectively. The age-related differences in malaria parasitemia were not statistically significant (Fisher's exact = 0.15)

Table 1 shows the hematological indices in the febrile neonates. The mean Hb Conc. of the study population was 14.6 ± 10.9 g/dl. The mean Hb Conc. for those with malaria only was 12.3 ± 1.0 g/dl while it was 12.8 ± 3.2 g/dl for those with septicemia in addition. The Hb Conc. were lower than that of other categories of newborns, but the differences were not statistically significant (P = 0.91). None of these neonates required a blood transfusion.

The total white cell count was the highest (19.15 ± 8.13) in newborns with malaria alone compared to that for newborns with malaria/septicemia co-infection then followed by those with septicemia only. Neutrophils values were higher in the newborn with co-infection while lower than the mean in those with malaria alone, while the lymphocytes were highest in newborns with malaria alone. Platelets count was relatively the same for all the newborns. These differences did not reach statistical significance level.

Table 1: Comparison of the mean hematological indices in the neonate with malaria parasitemia and those without

	ANOVA				
Laboratory indices (mean ± SD)	Malaria only	Malaria + septicemia	Septicemia only	Nil malaria/ septicemia	*P*
WBC (×10⁹)	19.15±8.13	17.3±10.3	13.2±7.5	12.3±5.82	0.31
NEUTR (%)	48±5.66	53.8±7.13	53.17±21.05	50.4±16.4	0.85
LYMPHO (%)	50.5±3.54	44.25±8.02	44.3±20.2	47.3±16.0	0.79
HB Conc. (g/dl)	12.25±0.95	12.83±3.21	15.13±14.03	14.1±2.64	0.91
PCV (%)	36.25±0.64	38.1±9.1	41.9±8.24	42.81±7.76	0.47
PLT	230±66.47	202±34.52	209.9±92.7	222.7±94.1	0.85

WBC – White blood cell; NEUTR – Neutrophils; LYMPHO – Lymphocytes; HB Conc. – Hemoglobin concentration; PCV – Packed cell volume; PLT – Platelets; SD – Standard deviation

All the 150 newborns recruited in the study were seen at follow-up at the Newborn Outpatient Clinic as scheduled. None of the babies had symptoms, and all suckled actively at the breast. Repeat Hb Conc. was all within the normal range for age and blood film for malaria parasite was negative. They were consequently discharged from follow-up.

DISCUSSION

The mean Hb Conc. for the parasitized babies was lower than those of nonparasitized babies although the differences did not reach statistical significance. Other hematological indices remained same as in nonparasitized neonates. These observations are, however, inconclusive since the number of those with parasitemia was quite small. The malaria parasite density in this study was low and is similar to that obtained by other authors.[12-14] This could be explained by the high maternal immunity from prior malaria infection in endemic areas, high rate of antimalarial prophylaxis used by the mothers of the study population, maternal use of artemisinin-based combination therapy to treat malaria in pregnancy, the fetal Hb that does not support malaria parasite growth, and low transmission rate in dry season as the climatic conditions and period of the year, influence intensity of malaria transmission in a given locality.[15,16]

Good proportion of the subjects in this study was assessed long after delivery and it was therefore not feasible to include the cord parasitemia as a variable in the study, to ascertain if it was associated with the drop in Hb Conc.

CONCLUSION

Neonatal malaria does occur in our environment. While it does not affect the white cells indices, it lowers the neonatal hemoglobin. It is recommended that hemoglobin concentration be estimated in newborns with malaria to reduce infant morbidity and mortality in our environment. In addition blood film for malaria parasite microscopy should be done for neonates with fever in our environment.

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Conflicts of interest

There are no conflicts of interest.

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