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Leukocyte counts in falciparum malaria in African children from an endemic area

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Summary

Total leukocyte counts were done in 180 apparently healthy rural school children aged 6-12 years in a malaria endemic area in southwestern Nigeria. Total leukocyte counts and their distribution in aparasitaemic and asymptomatic parasitaemic children were similar. Total leukocyte counts, and the relationship between the density of parasitaemic and total leukocyte counts were studied in 55 consecutive children presenting with acute symptomatic falciparum malaria. Children without parasitaemia were older and had lower total leukocyte counts when compared with children with parasitaemia ($7.61 \pm 4.11 \times 10^9$/L Vs $9.04 \pm 5.0 \times 10^9$/L), but the difference was not statistically significant ($P > 0.05$). In non-hyperparasitaemic children and in hyperparasitaemic children with percentage infected red cells < 10%, there was poor correlation between density of parasitaemia and total leukocyte counts. However, at ≥10% parasitaemia, there was a positive correlation ($r = 0.55$; $P = 0.032$) between increasing parasitaemia and leukocytosis. Combination of hyperparasitaemia (> 5% parasitaemia) and leukocytosis ($> 12 \times 10^9$/L) occurred in 15% of the children and was not a poor prognostic index in the absence of other evidence of severe or complicated disease, as response to oral mefloquine was prompt. This would suggest that in African children from an endemic area, this combination is not a reliable indicator of severity or poor prognosis in falciparum malaria.

Résumé

Les comptes totaux des leucocytes sont faites chez 180 écoliers ruraux apparament en état de bonne santé et âgé de 6 à 12 ans dans une zone de malaria endémique au Sudouest du Nigéria. Les comptes totaux des leucocytes et leur distribution chez les enfants apparasitaemiques et ceux qui sont asymptomatiques parasitae miques sont similaires.

Les comptes totaux des leucocytes et le rapport entre la densité de parasitaemie et les comptes totaux des leucocytes ont été étudiés chez 55 enfants conséqutifs manifestant la malaria falciparum symptomatique aigue. Le enfants sans l'hyperparasitaemie étaient plus âgés et ils ont des comptes totaux de leucocytes plus basses par rapport aux enfants avec l'hyperparasitaemie (soit $7.61 \pm 4.11 \times 10^9$/L Vs $9.04 \pm 5.0 \times 10^9$/L), mais cette différence n'est pas statistiquement significative ($P > 0.05$).

Chez les enfants non-hyperparasitaemiques et les enfants hyperparasitaemiques dont le pourcentage de cellules rouges infectées est de < 10%, on note une pauvre correlation entre la densité de parasitaemie et les comptes totaux de leucocytes. Cependant, au niveau de ≥ 10% de parasitaemie, on note une correlation positive (soit $r = 0.55$; $P = 0.32$) entre la parasitaemie croissante et la leucocytose. La combinaison de l'hyperparasitaemie (> 5% de parasitaemie) et la leucocytose ($> 12 \times 10^9$/L) figure chez 15% des enfants et n'est pas un signe de pauvre pronostic en l'absence d'évidence supplémentaire de maladie sévère ou compliquée vu le fait que la réponse au méfloquine orale est prompte. Ceci suggère que pour les enfants Africains issus des zones endemiques, cette combinaison n'est pas un indicateur fiable de la sévérité ou du faux pronostic de malaria falciparum.

Introduction

In apparently healthy Africans as compared to Caucasians, leucopenia due to neutropenia is a well known phenomenon which has been attributed to genetic[1] or dietary factors[2,3,4,5]. Although the literature is replete with data on leucocyte counts in Africans there are few reports on leukocyte counts in African children suffering from *Plasmodium falciparum* malaria in endemic African countries. The present study was conducted primarily, (1) to

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establish the normal total leukocyte counts in rural school children from a malaria endemic area of southwestern Nigeria, (2) to determine the influence of parasite rate on total leukocyte counts, (3) to establish the range of leukocyte counts in children with acute symptomatic falciparum malaria and (4) to study the relationship if any, between the density of parasitaemia and leukocyte counts in children suffering from acute symptomatic falciparum malaria.

Methods and subjects

The study was in two parts; one was a study of total leucocyte counts in rural primary school children (both aparasitaemic and with asymptomatic falciparum parasitaemia), the other was a study of total leukocyte counts in urban children with acute symptomatic falciparum parasitaemia.

Study 1

One hundred and eighty apparently healthy rural school children aged 6 to 12 years, randomly selected from a total population of 403 children resident in 3 villages 15-20 kilometres north of Ibadan, southwestern Nigeria were studied between September 1990 and January 1991. At the beginning of the study (Week 0, rainy season) and eighteen weeks later (Week 18, dry season), all the children were screened for malaria parasitaemia by thick and thin blood films which were obtained from a finger prick and Giemsa-stained for parasite identification and quantification. Parasitaemia quantification was done as in a previous study[6]. Blood (2ml) was obtained from an antecubital vein by venepuncture and collected in dry sequestrene bottle at the same time of screening for parasitaemia. Total white blood cells count was done within 4 hours of collection. All samples were obtained between 8.00 a.m. and 10.00 a.m. An informed consent was obtained from the parents or guardians of all children before the commencement of the study.

Study 2

Fifty five consecutive children with acute symptomatic falciparum malaria reporting at the malaria clinic of the University College Hospital, Ibadan, Nigeria were studied between September, 1990 and January, 1991. The children were enrolled into the study if the following criteria were met: (a) pure *Plasmodium falciparum* parasitaemia, (b) no other complicating illness, (c) no history of antimalaria drug administration in the 2 weeks preceding presentation, (d) negative urine tests for 4-aminoquinolines (Dill-Glazko) and sulphonamides (lignin) and (e) consent of parents or guardians. Thin blood film was obtained from a finger prick and Giemsa-stained for parasite species identification and quantification. Parasitaemia quantification in thin blood films was done by counting 2,000 red blood cells in clear contiguous fields and finding the proportion parasitized. This was then expressed as percentage parasitaemia (percentage infected red cells). On the basis of percentage infected red cells, the children were divided into those without (≤ 5%) and those with (> 5%) hyperparasitaemia[7]. During the period of the study, all the children were treated with either 15mg or 25mg/kg body weight mefloquine orally and followed up daily for eight days (days 0-7), and weekly on days 14, 21 and 28 with clinical and parasitological examination in order to assess the therapeutic efficacy of mefloquine in acute falciparum malaria. The following parameters were determined; parasite and fever clearance time and the cure rate at day 28[8].

Values are given in text and tables as mean ± S.D. and differences between the groups where appropriate were compared using Student's t test. P values less than 0.05 were taken as significant.

Results

Of the 180 children, complete data were available in 127 children at 0 week and in 165 children at 18 weeks. The total leukocyte counts in apparently healthy aparasitaemic children and in apparently healthy children with asymptomatic falciparum parasitaemia are summarized in Table 1. The mean leukocyte counts in parasitaemic and aparasitaemic children at 0 week were similar with no statistical significant difference in the mean counts between the 2 groups. Similarly, at 18 weeks there was no significant difference in mean leukocyte counts between parasitaemic and aparasitaemic children and these were similar to the values at week 0. Although the sampling times correspond to mid-wet and mid-dry seasons respectively and showed a corresponding seasonal variation in parasite rate, there was no variation in the total leukocyte counts during this period. The distribution of leukocyte counts is shown in Figure 1. Peak leukocyte counts in the children were in the 4-5 x 10^9/L and 5-6 x 10^9/L range. Leukocyte counts greater than 8 x 10^9/L were encountered in less than 6% of the children.

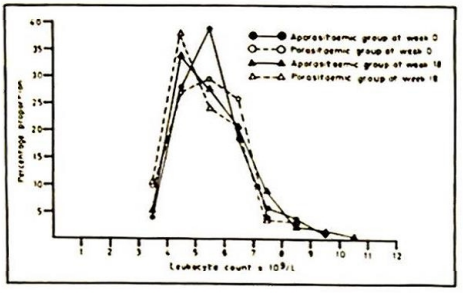

Fig. 1: Distribution of leukocyte counts in rural primary school children

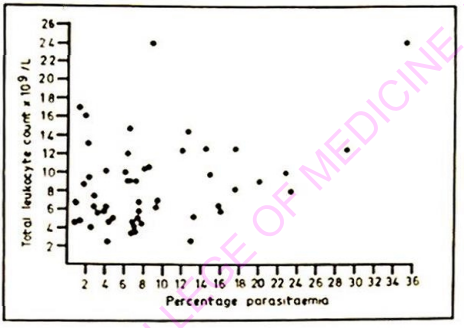

Fig. 2: Relationship between parasite density and leukocyte count in children with acute symptomatic falciparum malaria

Table 1: Total leukocyte counts in apparently healthy children without parasitaemia and in apparently healthy children with asymptomatic parasitaemia from a rural area of southwest Nigeria.

	Week 0		Week 18	
	Aparasitaemic	Parasitaemic	Aparasitaemic	Parasitaemic
No. of subjects	72	55	136	29
Parasite density/ul				
range	—	60-3,800	—	120-6,600
geometric mean	—	324	—	308
No. with parasite density 100/ul	—	18	—	4
Leukocyte count ($x10^9$/L)				
range	3.4-9.2	3.4-8.7	3.3-10.5	3.9-6.8
mean ± S.D.	5.54 ± 1.10	5.71 ± 1.22	5.62 ± 1.28	5.37 ± 1.19
95% confidence interval	5.28-5.79	5.39-6.04	5.40-5.83	4.83-5.91

Table 2: Clinical data and leucocyte count in African children with acute symptomatic falciparum malaria

	Non-hyperparasitaemic group	Hyperparasitaemic group*
Total No.	18	37
M:F	9:9	16:21
Age (year)		
range	1.7-11.0	0.75-12.0
mean ± S.D.	6.6 ± 2.9	4.3 ± 2.9
Percentage parasitaemia		
range	0.8-4.8	5.8-35.0
mean ± S.D.	2.57 ± 1.38	11.75 ± 6.97
Total leucocyte count $x10^9/L$		
range	2.5-16.0	3.5-26.0
mean ± S.D.	7.61 ± 4.11	9.04 ± 5.0
95% confidence interval	5.71-9.50	7.42-10.65
Parasite clearance time		
range	48-72	48-96
mean ± S.D.	50.2 ± 10.1	51.3 ± 12.1
Cure rate on day 28 (%)	100	100

*Defined as > 5% infected red blood cells in thin film

The clinical and parasitological data and leukocyte counts in children with acute symptomatic falciparum malaria are summarized in Table 2. Children with hyperparasitaemia were younger than those without hyperparasitaemia. In non-hyperparasitaemic children, mean leukocyte count was lower (7.61 ± 4.11 x 10^9/L) than in hyperparasitaemic children (9.04 ± 5.0 x 10^9/L), but the difference was not statistically significant (P > 0.05). Regression analysis of the relationship between parasite density and total leukocyte count showed that in non-hyperparasitaemic children, there was no correlation between the level of parasitaemia and leukocyte counts (Fig. 2). In fact, increasing parasitaemia from less than 1% to below 5% correlates negatively (r = -0.32; P = 0.19) with leucocyte counts. When hyperparasitaemic children were further subdivided into two groups, namely those with 5-9.9% and those with ≥ 10%, there was poor correlation between level of parasitaemia and leucocyte counts (r = 0.11; P = 0.60) in those with 5-9.9% parasitaemia. However, at ≥ 10%, increases in the level of parasitaemia correlates weakly positively (r = 0.55, P = 0.03) with increases in leucocyte counts (Fig. 2). Hyperparasitaemia and leucocytosis above 12 x 10^9/L was not associated with poor prognosis in the children studied since response to treatment was prompt in all patients and parasitaemia and fever cleared in all patients within 48-96 hrs of commencement of therapy. There was no significant difference in the parasite clearance times in patients with (51.3 ± 12.1 hrs) and without hyperparasitaemia (50.2 ± 10.1 hrs). Cure rate on day 28 was 100% in both groups.

Discussion

This study of leucocyte counts in African children from a rural area has shown that asymptomatic parasitaemia has little or no influence on leucocyte counts in children aged 6-12 years in an endemic area of malaria since similar values were found in all children irrespective of parasitaemia status. Also, despite a seasonal variation in parasite rate, there was no corresponding variation in leucocyte counts. The reported leucocyte counts in these rural children are in agreement with the range noted by several authors for similarly aged children and adults[2,3,4,9]. Leukocyte counts above 8 x 10^9/L were encountered in a small proportion of the children. It has been stated[3] that chronic low grade malaria is well known to cause neutropenia in humans, but this has not been possible to investigate in the present study.

In children from endemic areas, acute symptomatic malaria is a common occurrence as between 36-50% of patients presenting with fever may have parasitaemia[6-10]; of which about 16% may be hyperparasitaemic[6]. In the present study, children with hyperparasitaemia were younger than those without. The leukocytosis recorded in these patients was clearly attributed to *P. falciparum* parasitaemia because other causes of leukocytosis were ruled out by appropriate examination and tests and leukocytosis returned to normal by the end of 7 to 14 days of commencement of treatment with only antimalaria drugs. An interesting finding is that parasite density did not correlate with leucocyte counts if percentage parasitaemia was below 5% or 10%. However, at equal to or greater than 10% parasitaemia, parasitaemia correlates positively with leucocyte counts. It has been claimed that the combination of hyperparasitaemia (> 5% parasitaemia) and leucocytosis above 12,000/mm^3 constitute a poor prognostic index in severe or complicated malaria[7]. In the present study, approximately 15% of the children had a combination of hyperparasitaemia and leukocytosis above 12 x 10^9/L (Fig. 2) and yet had no other evidence of severe or complicated disease. These children responded promptly to oral antimalaria therapy. These findings support the assertation that greater than 5% parasitaemia may be well tolerated by semi-immune African children from an endemic area[11] and suggest that while hyperparasitaemia and leukocytosis above 12 x 10^9/L may indicate poor prognosis in the non-immune, this combination in the absence of other evidence of severe or complicated malaria is not a reliable indicator of severity or poor prognosis in semi-immune population of endemic areas.

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