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Malaria morbidity and mortality in children under three years of age on the coast of Benin, West Africa

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Abstract

Malaria morbidity and mortality were measured in a population of 1500 children under 3 years of age from April to December 1989. During monthly home visits, an average of 26 children in 1000 had fever, of whom 15 had parasitaemia. Children less than 6 months old had significantly fewer fever episodes, whether associated with parasitaemia or not. Overall, prevalence of fever with parasitaemia rose steadily from April to August, then decreased but reached a second peak in November. Peaks coincided with the 2 rainy seasons in April to June and September to October. Comparison with a control group demonstrated that children with parasitaemia exceeding 1000 infected red blood cells per microlitre of blood had fever significantly more often than children with lower levels of parasitaemia. The average number of fever episodes per child per year was 2·4, and 33% of these were estimated to be caused by malaria. All cause mortality was 26/1000/year and the malaria mortality rate was 8/1000/year. Malaria deaths were most frequent in the second year of life.

Introduction

Malaria is generally recognized as a major threat to health in Benin. Health staff are trained to give presumptive treatment for malaria whenever fever is detected. Paediatricians recommended chemoprophy-

data, the possibility could not be excluded that both interviewers and persons interviewed had been jumping to conclusions about the nature or cause of a disease, given the general awareness that malaria is the number one health problem in the country.

It thus seemed appropriate to document more objectively the magnitude of the malaria problem among young children in the project area. An extra component was therefore incorporated in a longitudinal study already in progress, to measure body temperature and to collect blood samples from selected children to verify the presence of malaria parasites.

Materials and Methods

Study area

The study area was situated on the Atlantic coast of south Benin in West Africa and covered 18 villages consisting of 138 hamlets. A village typically consisted of a nucleus or 'central hamlet' with a number of small hamlets spread around it. The median number of inhabitants per village was 550 (range 300–2000). The total population was 13 000. Compounds were numbered within villages. Each household in the area had a unique 4 digit number and each member a sequential number within the household. The dominating ethnic groups were Fon (55%) and Aizo (25%). Subsistence farming, horticulture for the nearby city,

Newborn children were enrolled on the first visit of the field-worker following birth. Children who reached the age of 36 months were no longer followed. Children who migrated in or out of the study area were similarly enrolled or considered lost to follow-up.

Morbidity

Rectal temperature was measured during each monthly visit by means of an ordinary mercury thermometer for at least one minute. At the beginning of the study it was verified that field-workers read the temperature correctly, and during the study this was regularly checked in the field. Whenever a child with fever (>37·9°C) was detected, a technician took a blood sample on the same day, prepared a thick and a thin blood film on the same slide, and filled a heparinated capillary tube with blood for determination of the packed cell volume (PCV).

For every child with fever a control from another household, who had been visited the same day, was selected without symptoms, with the same date of birth (±3 months), and living in the same ecological zone. The same procedures were followed for control children as for children with fever.

Duration of fever episodes

In a sub-sample of approximately 850 children comprising nearly equal numbers from the 3 ecological zones, the mother or guardian was asked if the child had been ill in the past 7 d. If such was the case, the interviewer asked how many days ago the illness had begun and for how many days it had lasted. The field-worker then ascertained the dates of onset and termination of the episode. If the child was ill on the day of the interview, a card was given to the mother on which squares indicated the days. The field-worker marked with a cross the days the child had been ill and the mother was asked to mark each following day with a cross if the child continued to be ill, or a circle if the child was better again. The field-worker retrieved the card towards the end of the month.

method and examined by one of 2 observers using a ×100 oil immersion objective and ×10 eyepieces.

The level of parasitaemia was determined from the thin blood film by dividing the number of infected red blood cells (IRBC) in 75 fields by the total number of red blood cells examined, which, from previous data, was estimated to be 280 per field (CHIPPAUX *et al.*, in press). Multiplication of the proportion of IRBC and the total number of red blood cells per µl yielded the estimated number of parasites per µl. The number of red blood cells per µl was estimated from the PCV by means of a linear regression equation based on data collected in 3 clinics in areas adjacent to the study area (CHIPPAUX *et al.*, in press). Detection of a single infected red blood cell in a thin film would result in an estimate exceeding 100 IRBC/µl. Thus a negative thin film indicated that fewer than 100 IRBC were present per µl of blood. Thick blood films were used to check for gametocytes in the blood and this information was dealt with separately. All parasites detected were *Plasmodium falciparum*, the dominant species in this area.

Statistical analysis

Odds ratios relating risk of fever to level of parasitaemia were estimated by maximum likelihood methods for matched case-control studies (BRESLOW & DAY, 1980) by means of the program MULTLR (CAMPOS-FILHO & FRANCO, 1989). The program automatically disregards cases for which the matched control is missing. Attributable risks were computed for each category of parasitaemia as $(r-1)/r$, where r is the odds ratio. The average of these category-specific estimates, weighted according to the proportion of cases in each category, is the population attributable risk (BRESLOW & DAY, 1980).

Likelihood ratio test statistics for heterogeneity or trend in the morbidity rates were derived from the comparison of hierarchic logistic models which described prevalence as a function of the independent categorical variables age, sex, ecological zone, or month of the year. The numbers of cases in different

Cumulative rainfall figures per month were provided by a meteorological station 5 km from the centre of the project area.

Results

Relationship of fever and parasitaemia

Children with fever (cases) were compared to asymptomatic controls. For 21 cases a matching control could not be found on the same day that the case had been detected. Thin blood films were positive for 58% of cases and 41% of controls. However, 92 cases (28%) had parasitaemia levels exceeding 1000 IRBC/µl of blood, compared with 16 controls (5%). Taking children with a negative thin blood film as reference, odds ratios increased as the level of parasitaemia increased (Table 1). The risk of having a fever for a child with more than 20 000 IRBC/µl was 43 times greater than for a child with a negative smear. The odds ratio was significantly elevated for levels exceeding 1000 IRBC/µl; below this level the excess risk was small and statistically insignificant. This was also true when finer subdivisions were used, in particular when parasitaemia levels were categorized as 100–500, 500–1000, 1000–1500, 1500–2000 etc. Only 24% of cases with parasitaemias of 100 to 1000 IRBC/µl could be considered to be caused by malaria, while this percentage was 84 or higher among cases with parasitaemia levels exceeding 1000 IRBC/µl. The level of 1000 IRBC/µl was considered a pathogenic threshold above which fever could be assumed to have been caused by malaria, while below it such a diagnosis would be less probable. Consequently, data have been presented for fever associated with any parasitaemia and separately for fever with severe parasitaemia (>1000 IRBC/µl).

Rainfall

The first rain fell in late March (Fig. 1) and rainfall increased steadily until June followed by a sharp drop in July and August, the short dry season. A second peak occurred in October, the short rainy season, and virtually no rain fell in November and December.

Malaria morbidity

Overall prevalence of fever varied between 20 and 38 per thousand per month (Fig. 2). The point prevalence of fever cases with parasitaemia increased steadily from 12 per thousand in April to 19 per thousand in August. This rise coincided with the increasing rainfall but continued for 2 months after the rains had practically stopped. Prevalence then decreased but rose to a second peak in November, 2 months after the beginning of the short rainy season. The prevalence of cases with parasitaemia levels >1000 IRBC/µl rarely exceeded 10 cases per thousand; it was highest in July and August. The proportion of infected cases who had parasitaemia >1000 IRBC/µl was 81% in August but only 25% in May and June. Statistical tests detected no significant difference between the monthly prevalence rates of fever (χ^2=14·4, 8 degrees of freedom [df]) or of fever and parasitaemia (χ^2=10·5, 8 df). Prevalence of fever with severe parasitaemia (i.e. >1000 IRBC/µl) showed significant month-to-month variation (χ^2=23·4, 8 df).

Children younger than 6 months had fever, whether or not associated with parasitaemia, significantly less often than children aged 7–35 months (Table 2). Prevalence of fever associated with severe parasitaemia increased with age from birth to the second year of life. There was no significant difference in prevalence of fever or fever associated with (severe) parasitaemia between boys and girls.

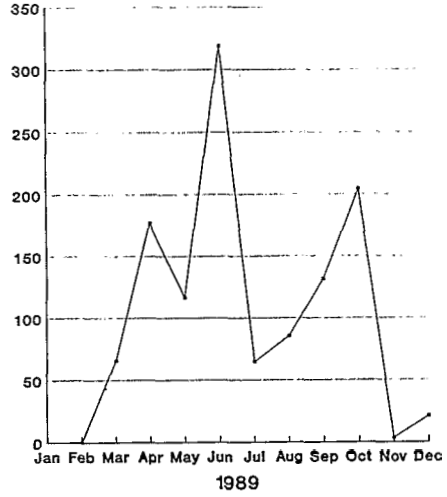

Fig. 1. Cumulative rainfall (mm) per month during one year on the coast of Benin, West Africa.

Table 1. Association of fever and malaria parasitaemia

Level of parasitaemia[a]	Cases of fever	Healthy controls[b]	Odds ratio[c]	95% confidence interval	AR[d]
≤100	136	177	1·00	–	
101–1000	97	108	1·32	0·89–1·95	24
1001–5000	41	12	6·30	2·25–15·03	84
5001–20000	21	3	12·06	2·93–49·69	92
>20000	30	1	43·27	5·42–345·25	98

[a]Information on parasitaemia was missing for 13 cases and 16 controls; expressed as number of infected red blood cells per µl of blood.
[b]Individually matched to cases for age, zone and day of visit.
[c]Computed by conditional logistic regression.
[d]Attributable risk (per cent) for each level of exposure.

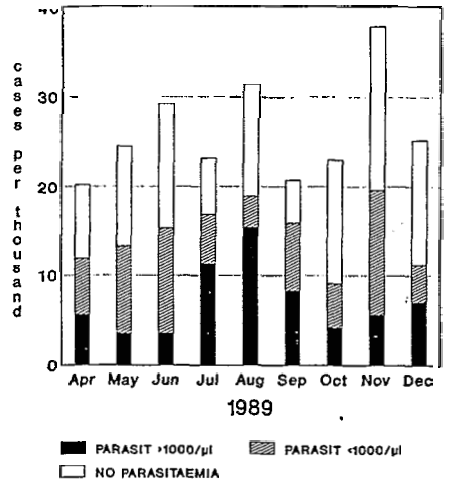

Fig. 2. Point prevalence of fever per month subdivided according to the associated parasitaemia level; Pahou, Benin, 1989.

Table 3. Packed cell volume (per cent) by level of parasitaemia for children with fever and individually matched controls[a]

Level of parasitaemia[b]	Cases of fever Mean	s.d.	Healthy controls[c] Mean	s.d.
≤100	36·6	4·5	36·5	4·2
101-1000	34·9	5·0	36·3	5·3
1001-5000	32·2	5·5	35·7	6·0
5001-20000	32·2	4·7	35·0	5·0
>20000	33·7	4·5	33·0	[d]
Total	34·9	5·0	36·4	4·7

[a]Numbers of observations in each category are given in Table 1; s.d.=standard deviation.
[b]Number of infected red blood cells per µl of blood.
[c]Matched for age, ecological zone and day of visit.
[d]Only one observation.

Fifteen thick blood films contained gametocytes; 4 of these films were from controls. Four of the 11 cases with gametocytes had negative thin films. Twenty-seven children had fever on 2 occasions, and 2 children had fever on 3 occasions.

Fever episodes had a median duration of 4 d. The average number of fever episodes per child per year was estimated as 2·4. Based on the distribution of parasitaemia levels among the controls, the population attributable risk, i.e. the proportion of all fever episodes caused by malaria, was estimated to be 33%.

Parasitaemia in afebrile children

The proportion of control children with a positive thin blood film varied from month to month between 32 and 53%. Thus seasonal variation was only slight and could not be distinguished from a purely random fluctuation. The proportion of infected controls was 29% among the 35 children below 6 months of age, compared to 43% among older children; it was 46% for boys and 36% for girls. These differences were not statistically significant. There was no difference between ecological zones.

Table 2. Malaria morbidity in a dynamic population of 1500 children visited monthly; Pahou, Benin, April to December 1989

	No. of visits	Fever[a] No.	Rate[e]	Fever[a] and parasitaemia[b] >100/µl No.	Rate[e]	>1000/µl No.	Rate[e]
Age (months)[d]							
0–5	2485	39	15·7[e]	24	9·7	7	2·8[f]
6–11	2381	72	30·2	36	15·1	14	5·9
12–23	3853	110	28·5	62	16·1	36	9·3
24–35	4191	114	27·2	66	15·7	35	8·4
Ecological zone							
Plateau	2325	65	28·0	35	15·1	23	9·9
Marshland	6055	146	24·1	86	14·2	38	6·3
Coastal strip	4530	126	27·8	68	15·0	31	6·8
Sex							
Male	6254	168	26·9	93	14·9	39	6·2
Female	6656	169	25·4	96	14·4	53	8·0
Total	12910	337	26·1	189	14·6	92	7·1

[a]Fever is defined as a rectal temperature>37·9°C.
[b]Information on parasitaemia was missing for 13 cases.
[c]Rate per thousand visits.
[d]Age could not be determined for two children.
[e]χ^2 for heterogeneity of rates: 14·9, 3 degrees of freedom, $P<0·005$.
[f]χ^2 for trend with age: 8·2, 1 degree of freedom, $P<0·01$.

Malaria and anaemia

Packed cell volume was lower in children with fever than in their matched controls. A break-down by level of parasitaemia (Table 3) revealed that cases and controls had similar PCVs in the absence of parasitaemia. When parasites were present, sick children had lower PCVs than healthy children for the same level of parasitaemia. A two-way analysis of variance controlling for level of parasitaemia showed that this effect was statistically significant (t=1·98, $P<0·05$).

Malaria mortality

There were 29 deaths during the study period among children less than 3 years of age, an annual

Table 4. Childhood mortality from all causes and from malaria in Pahou, Benin. Monthly follow-up April to December 1989

	Child-months	All causes		Malaria	
		Cases	Rate[a]	Cases	Rate[a]
Age (months)					
0–5	2539	11	52·0[b]	1	4·7
6–11	2491	4	19·3	2	9·6
12–23	4026	8	23·8	5	14·9
24–35	4355	6	16·5	1	2·8
Ecological zone					
Plateau	2424	8	39·6	4	19·8
Marshland	6335	15	28·4	3	5·7
Coastal strip	4652	6	15·5	2	5·2
Sex					
Male	6497	16	29·6	7	8·8
Female	6913	13	22·6	2	3·5
Total	13410	29	26·0	9	8·1

[a]Rate per thousand children per year.

study was higher in the second year or life.

A so-called pathogenic or pyrogenic threshold of 1000 IRBC/µl in the present data distinguished those for whom malaria was the most likely cause of their fever from those for whom the cause probably had another origin. This value seems very low in comparison with other reports. TRAPE *et al.* (1985) suggested 5000 IRBC/µl, BAUDON *et al.* (1986) 10 000 IRBC/µl, and BENASSENI *et al.* (1987) 15 000 IRBC/µl. CHIPPAUX *et al.* (in press) estimated in Benin a threshold of 6000 for children under 3 years of age. One factor which may have caused these differences is that both BENASSENI *et al.* (1987) and BAUDON *et al.* (1986) recruited their controls from among patients attending an outpatient clinic. Observations in Benin suggest that patients, although afebrile, have higher levels of parasitaemia than healthy subjects visited at home. Thus the recruitment of 'hospital controls' would result in an inflated estimation of the pyrogenic threshold. It has been suggested that this threshold will vary according to the degree of immunity of the population studied (CHIPPAUX *et al.*, in press), and

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