

The incidence of clinical malaria detected by active case detection in children in Ifakara, southern Tanzania

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Abstract

Between July 2000 and June 2001, we used weekly active case detection (ACD) of clinical malaria episodes in 618 children aged <5 years to describe the epidemiology of malaria in Ifakara, southern Tanzania. *Plasmodium falciparum*-positive blood slides prepared from children with axillary temperature $\geq 37.5^{\circ}\text{C}$ were used to define clinical malaria and a rolling cross-sectional survey documented the prevalences of parasitaemia and anaemia. A random subsample of children was visited daily for 1 month at the end of the study to assess the effect of more frequent visits on estimated incidence rates. Only 50 (8%) children had 1 or more episodes of clinical malaria during the year, an overall incidence of 0.275 episodes/100 child-weeks-at-risk, with no age dependence. The maximum parasite prevalence of 25% was reached in children aged 4 years. The incidence of illness was significantly lower in children visited daily than in those visited weekly, suggesting a marked effect of frequent visits on estimated incidence rates. We conclude that the age pattern of malaria detected through ACD is a more robust epidemiological indicator than absolute incidence rate estimates and that, in contrast to the surrounding area, Ifakara town is subject to only moderate perennial malaria transmission.

Keywords: malaria, *Plasmodium falciparum*, epidemiology, active case detection, Tanzania

Introduction

A clear picture of the malaria epidemiology of a study site is required to assess the potential wider applicability of interventions assessed there. The entomological dimension is most frequently summarized as the number of infectious bites an individual receives per unit time, the entomological inoculation rate (EIR). Age-specific parasite, anaemia and spleen prevalences contribute to the epidemiological picture, as do hospital-based studies describing the clinical presentation of *Plasmodium falciparum* disease. The incidence of clinical disease may be documented by active or passive case detection. Active case detection (ACD), where people are visited regularly at home, describes the age pattern and temporal variations of disease without the influence of health-seeking behaviour. Passive case detection (PCD) depends on documenting episodes in children presenting to the health facility and may generate information of greater relevance from a health services perspective. In the assessment of a randomly assigned intervention either approach should generate useful efficacy estimates. However, as incidence rates generated by ACD are not comparable with those generated by PCD, the value of these measures in the description of the malaria epidemiology of different sites is limited. Possibly the most valuable information relates to the age pattern of clinical disease and death, as it not only reflects the intensity of transmission but also indicates the age group against which preventive interventions need to be targeted.

Ifakara town, situated in the Kilombero district of southern Tanzania, has been the site of a series of malaria and anaemia intervention trials. The EIR in several villages surrounding the town has been estimated at more than 200 infective bites per person per year (Tanner *et al.*, 1986; Lyimo, 1993; Smith *et al.*, 1993; Charlwood *et al.*, 1998) and an analysis of the age pattern of paediatric malaria admission and death in the district hospital showed a pattern typical of an area with intense malaria transmission (Schellenberg *et al.*, 1999). However, over recent years it has become

increasingly clear that the pattern of malaria in children from Ifakara town itself is different from that in the surrounding area. This paper uses a 1-year ACD study to describe the epidemiology of malaria in Ifakara town and discusses various methodological aspects of ACD.

Materials and Methods

Study area

The map (Fig. 1) includes the study area and indicates the homes of participating children. Ifakara is 1 of the 5 divisions of Kilombero district, in the Morogoro region of southern Tanzania. Ifakara division is split into 5 wards, 3 of which (Ifakara, Kibaoni and Lumemo) contribute to the study area described in this paper and have been used in previous studies (Menendez *et al.*, 1997; Hatz *et al.*, 1998; Acosta *et al.*, 1999; Schellenberg *et al.*, 2001, 2002). All villages in Ifakara ward (Ifakara Mjini, Lipangalala, Viwanja Sitini and Mlabani), Mbasa village from Kibaoni ward and Lumemo, Michenga, Mahutanga and Kiningina villages from Lumemo ward contribute to a total population of approximately 86 000 in the area. The 9 villages were selected as they are situated within ~6 km of the St Francis Designated District Hospital (SFDDH; $36^{\circ}40' \text{E}$, $8^{\circ}9' \text{S}$), ensuring good access to the PCD system based there. The area is subject to a long rainy season from March to June, followed by dry and dusty weather until November–December when light rains return.

Ifakara town is more heterogeneous than the surrounding villages but can be split into 2 main parts: a semi-urban centre with a population of ~50 000 (Ifakara Mjini, Viwanja Sitini and Mlabani) and the remaining, more rural, villages with a population of ~35 000. An unpaved road runs through the central area and is flanked by 2 smaller parallel streets, all lined with brick-built shops and bars. Some of these buildings have an electricity supply but few have piped water. Beyond these streets lie the densely populated residential areas which gradually merge with the more rural areas, similar to those involved in the Ifakara Health Research and Development Centre (IHRDC) Demographic Surveillance System (DSS), described in detail elsewhere (Armstrong Schellenberg *et al.*, 2001). Houses in this more rural area are typically made with mud or burnt brick walls and grass or corrugated iron roofs. Electricity is supplied to fewer houses and most people collect water from either the nearby Lumemo

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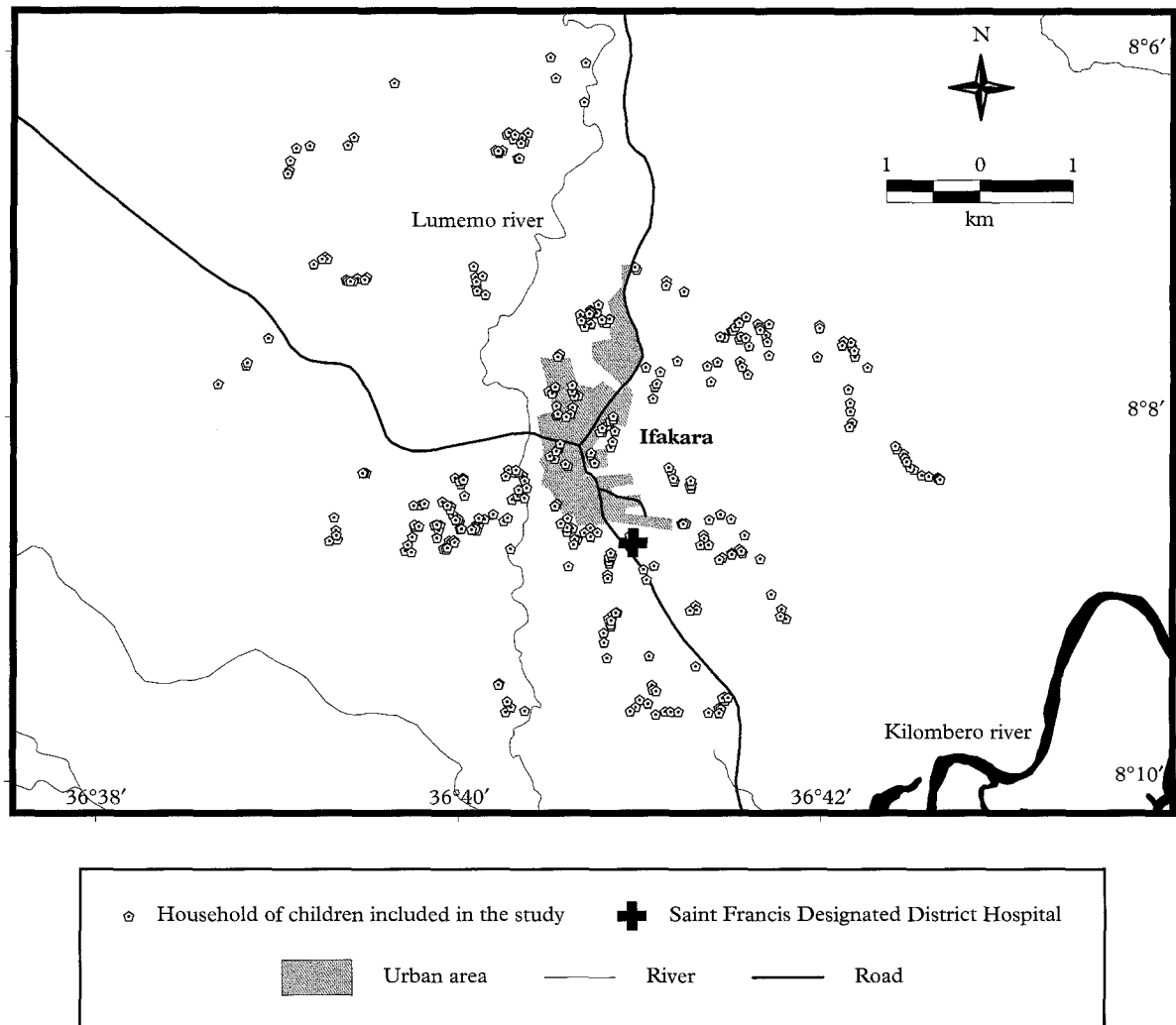


Fig. 1. Map of the Ifakara area, southern Tanzania, indicating the locations of study children's households.

river or shallow wells. Thick vegetation and abundant mosquito breeding sites are found between dwellings in these residential areas.

Selection and recruitment of study participants

Tanzanian households are arranged into 'cells' of about 10 (range 7–23), with one of the residents named as *balози*, or the 10-cell leader. An updated list of all *balозис* in the study area was obtained and 110 selected at random by a computer program. A random three-quarter sample of each selected *balози's* households was then generated by computer and written informed consent sought to enrol all children aged <5 years in each of these households. This approach was anticipated to provide approximately 100 children in each 1-year age group. Children who were not permanent residents of Ifakara or who were involved in other studies were not eligible to participate. To ensure that children in the youngest age groups were adequately represented during the whole of the study up to 8 children aged <1 month were recruited monthly from households in the original sampling scheme.

A recruitment form, completed at the child's home, documented demographic and socio-economic information. Data were also collected on factors which might be associated with the risk of malaria, such as use of a mosquito net, home ownership (whether owner-occupier or rented), type of roof, floor and walls, ownership of chickens, radio or bicycle, and the area of land

cultivated. Each house was geolocated using a Garmin GPS 12 (Garmin International, Olathe, KS, USA) which enabled calculation of the distance between the house and SFDDH using the Haversine formula (Sinnot, 1984). Each child was left with an identity card and the carer was given verbal and written instructions detailing how to access project clinical staff in the event of illness.

Follow-up

Between July 2000 and June 2001, home visits were repeated weekly, before 11:00, in order to minimize biases due to the diurnal variation in body temperature (Armstrong Schellenberg *et al.*, 1994). At each visit a prelabelled standard morbidity questionnaire was completed. Two blood slides were prepared from a finger-prick if the axillary temperature was $\geq 37.5^{\circ}\text{C}$ or there was a history of fever in the preceding 24 h. Carers were informed of blood slide results within 4 h and antimalarial treatment taken to them at home when necessary. A substudy investigated the effect on the detected incidence of fever of more frequent home visits. At the end of 1 year's complete follow-up, 1 in 7 children was randomly selected from the cohort and visited daily for 1 month, while the remainder of the cohort continued with weekly visits.

In the event of any illness, mothers were encouraged to take their child to the IHRDC-employed clinical officers operating the PCD system at SFDDH. De-

scribed in detail elsewhere (Schellenberg *et al.*, 1999), this system operates 24 h a day, every day of the year, to document illness episodes in study children. The same criteria for blood slide collection were used as at ACD visits. Free drug treatment was made available as required.

Each week, 10 children were randomly selected (2 from each 1-year age group) and a blood slide and packed cell volume (PCV) sample collected, regardless of fever. This rolling cross-sectional survey allowed assessment of temporal variations and the age dependence of asymptomatic parasitaemia and anaemia. Children with a PCV <25% were supplied with the standard anaemia treatment (14 d of ferrous sulphate and a treatment dose of sulphadoxine-pyrimethamine [SP]) and malaria episodes were treated with SP, which remains effective in the area (Schellenberg *et al.*, 2002). The study was approved by the IHRDC and national Medical Research Co-ordinating Committee ethical committees.

Quality control of field activities

Twenty randomly selected households were revisited by the field supervisor each week. He checked that fieldworkers had visited the household and whether children had reported a fever or had a blood sample collected. This information was checked against the original fieldworker's report. The field supervisor also accompanied fieldworkers on a small number of visits to ensure that all procedures were carried out correctly and sensitively.

Laboratory procedures

Laboratory tests were performed at IHRDC. Standard blood slide reading and storage procedures were followed, described in detail elsewhere (Alonso *et al.*, 1994). In brief, all slides were read twice and a computerized comparison routine used to identify slides with discrepant results which were then read a third time. The PCVs were measured in microcapillary tubes using a Hawkesley haematocrit reader after centrifugation. Red cell pellets remaining after PCV reading of samples collected at the rolling cross-sectional survey were stored at 4°C for up to 1 week before haemoglobin electrophoresis on cellulose acetate plates.

Data management and analysis

Data were double-entered into Microsoft FoxPro version 2.6 (Microsoft Corp., Seattle, WA, USA) databases and weekly completeness and internal integrity checks performed. Analysis was done using Stata version 7 (Stata Corp., College Station, TX, USA) according to a pre-agreed analytical plan. Clinical malaria was defined as a measured axillary temperature $\geq 37.5^\circ\text{C}$ in the presence of asexual *P. falciparum* parasitaemia. Episodes of clinical malaria detected at ACD visits, or at a PCD visit which occurred on the day of a scheduled ACD visit, were included in the analysis. A child did not contribute to the numerator or denominator for 28 d after a clinical malaria episode. Unless otherwise indicated, each weekly visit was considered as 7 d time at risk. The incidence of clinical malaria was compared between the different age groups using Poisson regression taking into account the 2-stage sampling procedure.

Results

A total of 649 children were invited to participate, of whom 618 (95%) gave informed consent. This included 550 children aged <5 years recruited in July 2000 and a further 68 children recruited shortly after birth during the course of the year. Fifteen children (2%) died (6 [40%] in infancy) and a further 15 (2%) withdrew. Basic descriptive features of the cohort are summarized in Table 1 and the age breakdown at recruitment is presented in Table 2. During the main

Table 1. Characteristics of 618 study children, Ifakara, Tanzania

	n (%)
Male gender	295 (47.7)
Owner-occupier of house	529 (85.6)
Roof type	
Grass	255 (41.3)
Corrugated iron	363 (58.7)
Floor type	
Earth	494 (79.9)
Cement	124 (20.1)
Wall type	
Mud	150 (24.3)
Mud bricks	29 (4.7)
Burnt mud bricks	439 (71.0)
Electricity supply to house	29 (4.7)
Assets ^a	
Bicycle	198 (32.0)
Radio	166 (26.9)
Chicken	223 (36.1)
Cow and/or pig	15 (2.4)
Television	6 (1.0)
Refrigerator	6 (1.0)
Mosquito net use	376 (60.8)
Last insecticide treatment (n = 376)	
<6 months ago	37 (9.8)
7–11 months ago	22 (5.8)
≥ 12 months ago	30 (8.0)
Never	287 (76.3)

^aOne or more of each.

study, 27 567 home visits were made and the child was present at 19 069 of these. Data were available from PCD at the time of a scheduled ACD visit for 192 additional contacts. Hence, data were available from 19 261 (70%) scheduled contacts and the following analyses are based on these data.

During the course of the year fever was reported on 302 (1.6%) occasions and a raised body temperature documented 171 (0.9%) times. Of these measured fevers, almost one-third (n = 53) were detected through PCD at the time of a scheduled ACD visit. The incidence of measured fever was strongly age-dependent (Fig. 2), being highest in infants (1.7 episodes/100 child-weeks-at-risk [CWAR], 95% CI 1.3–2.2), and falling during the second year of life before reaching a plateau in children aged 2 years (0.7 episodes/100 CWAR, 95% CI 0.48–0.93) ($P < 0.001$). There were also marked changes in the incidence of measured fever at different times of year (Fig. 3), with incidence rates of around 1.1 episodes/100 CWAR during July–December, and a peak of 1.8 episodes/100 CWAR in January falling gradually to a minimum of 0.1 episodes/100 CWAR in April (χ^2 test for heterogeneity = 43.9, $P < 0.001$). The incidence of measured fever was not associated with use of a mosquito net ($P = 0.9$) but increased significantly with increasing distance from SFDDH ($P = 0.001$) (data not shown).

Twenty-seven percent (87/328) of the blood samples collected from sick children during weekly visits were positive for asexual *P. falciparum*. Fifty (8%) children fulfilled the criteria for clinical malaria at least once, and 3 (0.5%) children had 2 episodes during the year. Sixteen of the 53 cases (30%) were detected by PCD. The geometric mean parasite densities of malaria episodes detected by PCD and ACD were 5513 (SD = 13 481) and 8406 (SD = 19 598), respectively ($P = 0.554$). The overall crude incidence rate of clinical malaria in children aged <5 years was 0.275 episodes/100 CWAR and did not vary significantly in the different 1-year age groups (Table 2). The inci-

Table 2. Age-specific incidence of clinical malaria in study children, Ifakara, Tanzania

Age (years)	n (%)	No. of cases	Child-weeks-at-risk	Incidence rate (95% CI) of clinical malaria ^a
0	191 (31)	9	3619	0.249 (0.129–0.478)
1	115 (19)	10	2981	0.335 (0.18–0.623)
2	158 (26)	10	5095	0.196 (0.106–0.365)
3	107 (17)	13	4875	0.267 (0.155–0.459)
4	47 (8)	11	2691	0.409 (0.226–0.738)
Total		53	19 261	0.275 (0.210–0.360)

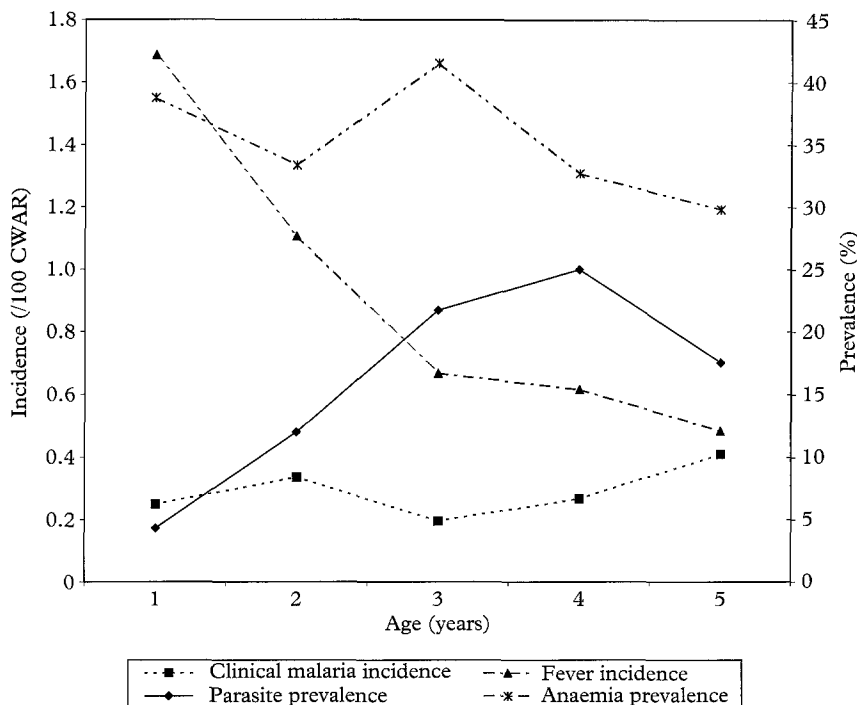
^aPer 100 child-weeks-at-risk. χ^2 test for heterogeneity (4 d.f.) = 3.40, $P = 0.494$.

Fig. 2. Relationship between age and incidences of clinical malaria and fever, and prevalences of parasitaemia and fever, in study children, Ifakara, Tanzania. Incidence was measured per 100 child-weeks-at-risk.

dence of clinical malaria was significantly associated with month of the year, reaching a maximum in January (Table 3), and was also significantly higher in children not sleeping under mosquito nets and in those living further away from the hospital. These temporal and geographical effects remained significant after Poisson multiple regression. Children sleeping in houses with iron roofs tended to have less malaria than those sleeping under grass roofs (Table 3).

A total of 435 visits were conducted as part of the rolling cross-sectional survey. A history of fever was reported in 4.1% ($n = 18$) of children and 1.1% ($n = 5$) had a measured pyrexia. Although 17% ($n = 72$) of samples were positive for *P. falciparum*, none of these was from a child with measured fever and hence no child fulfilled the case definition for clinical malaria on cross-sectional survey. There was marked age dependence of parasite prevalence (Fig. 2), with low levels in the first 2 years of life and a peak prevalence of 25% in 4-year-old children ($\chi^2 = 18.7$, $P = 0.001$). The variation with time in parasite prevalence did not reach statistical significance ($\chi^2 = 14.4$, $P = 0.21$). Over the course of the year, 35.9% (156/435) of children in the rolling cross-sectional survey were anaemic. Most of

the anaemia was mild, only 3% (12/435) having a PCV <25% and none having a PCV <15%.

Figure 2 shows that, as the incidence of fever decreases, the prevalence of asymptomatic parasitaemia increases. There was no clear variation with age of incidence of clinical malaria or the prevalence of anaemia. The marked temporal variation in the incidence of fever is shown in Fig. 3, and mirrors the changes in the incidence of clinical malaria. Both were maximal 1 month after the rainy season started. The highest parasite prevalence was observed 2 months after the peak in clinical malaria and fever. There was also marked temporal variation in the prevalence of anaemia ($\chi^2 = 31.2$, $P = 0.001$), the lowest prevalence occurring 1 month after the highest incidence of clinical malaria and one of the highest anaemia prevalences arising a month after the peak prevalence of asymptomatic parasitaemia.

The children selected for daily visits were similar to the remainder of the cohort in terms of age, distance between their homes and the hospital and reported use of a mosquito net (data not shown). During the 28-d period of daily follow-up the incidence rates of reported fever and measured pyrexia in children visited daily

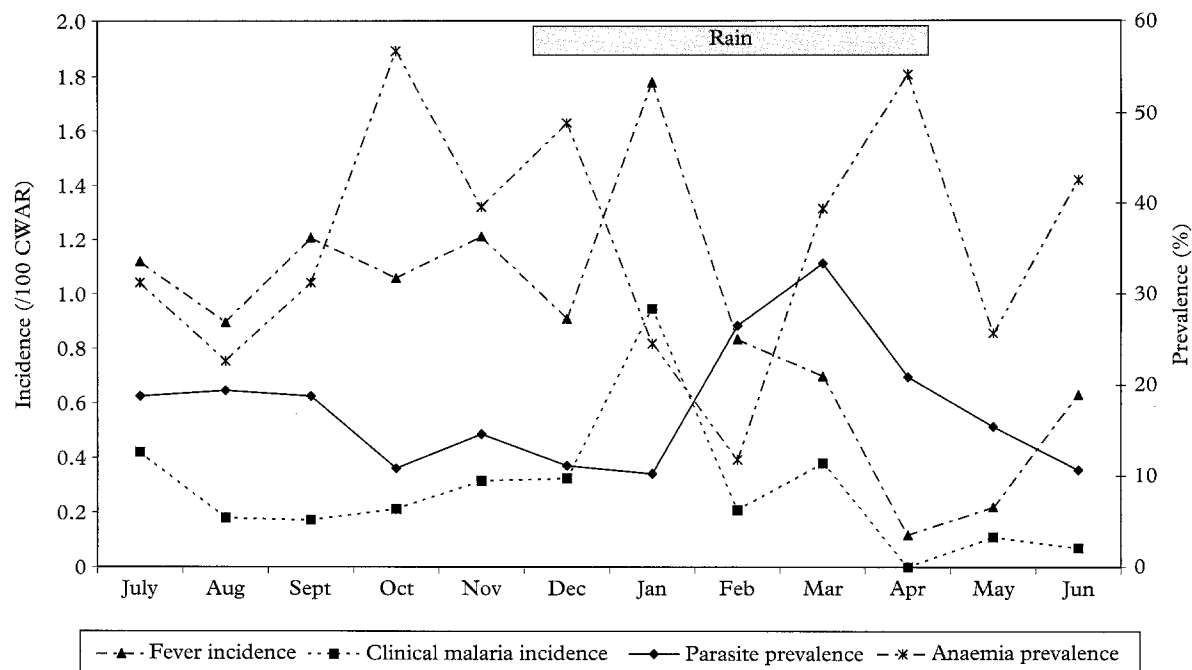


Fig. 3. Incidences of fever and clinical malaria, and prevalences of parasitaemia and anaemia, by month, in study children, Ifakara, southern Tanzania. Incidence was measured per 100 child-weeks-at-risk.

Table 3. Associations ($P < 0.1$) with incidence of clinical malaria in study children, Ifakara, Tanzania

Variable	No. of cases	Child-weeks-at-risk	Incidence rate (95% CI) of clinical malaria ^a
Month ($P < 0.01$)			
July	3	715	0.420 (0.135–1.301)
August	3	1678	0.179 (0.058–0.554)
September	3	1740	0.172 (0.056–0.535)
October	4	1891	0.212 (0.079–0.564)
November	6	1899	0.316 (0.142–0.703)
December	5	1542	0.324 (0.135–0.779)
January	17	1799	0.945 (0.587–1.52)
February	3	1442	0.208 (0.067–0.645)
March	6	1578	0.380 (0.171–0.846)
April	0	1722	0.000
May	2	1825	0.110 (0.027–0.438)
June	1	1430	0.070 (0.01–0.496)
Distance from hospital (km) ($P = 0.002$)			
0.3–1.39	10	6453	0.155 (0.083–0.288)
1.39–2.2	12	5908	0.203 (0.115–0.358)
2.2–5.2	31	6900	0.449 (0.316–0.639)
Mosquito net use ($P = 0.012$)			
Yes	23	11 595	0.198 (0.132–0.299)
No	30	7666	0.391 (0.274–0.56)
Roof type ($P = 0.077$)			
Corrugated iron	26	11 730	0.222 (0.151–0.326)
Grass	27	7531	0.359 (0.246–0.523)

^aPer 100 child-weeks-at-risk.

were significantly lower than those in children visited weekly, assuming each weekly visit represented 1 day's time at risk (Table 4). All children with a measured fever also gave a history of fever in the preceding 24 h. The incidence of attendance to PCD was slightly higher in children visited daily than in those visited weekly (Table 4).

Discussion

The Ifakara study area is a heterogeneous setting largely consisting of simple dwellings made of mud bricks with earth floors and grass roofs. Although the

study site is centred on Ifakara town the area can at best be described as semi-urban and there is little to distinguish the outskirts of the study area from the surrounding villages with high documented EIRs. However, the EIR of the Ifakara study area was recently estimated at 29 infective bites per person per year (Drakeley *et al.*, 2003) and, in the current study, only 8% of children had a malaria episode detected during the year of follow-up. There was no clear age pattern of clinical disease and the maximum parasite prevalence was only 25%, reached in children aged 4 years. Although there was significant month-to-month variation in the inci-

Table 4. Incidence of febrile illness and hospital attendance in study children visited daily or weekly at home, Ifakara, Tanzania

Endpoint	Daily visits (<i>n</i> = 84)						Weekly visits (<i>n</i> = 504)						
	Each visit = 1 d at risk			Each visit = 1 week at risk			Each visit = 1 d at risk			Each visit = 1 week at risk			
	No. of events	Days at risk	Incidence ^a	No. of events	Days at risk	Incidence ^a	No. of events	Days at risk	Incidence ^a	No. of events	Days at risk	Incidence ^a	<i>P</i> ^b
History of fever	4	1905	1.47	23	1644	9.79	23	11 508	1.40	23	11 508	1.40	0.883
Measured pyrexia	1	1975	0.35	8	1675	3.34	8	11 725	0.48	8	11 725	0.48	0.866
Presentation to PCD	36	2352	10.71	156	14 112	7.74	—	—	—	—	—	—	—

PCD, passive case detection.

^aPer 100 child-weeks-at-risk.^bCompared to estimates from daily visits.

dence of clinical malaria there were incident cases in all but 1 month. That the intensity of transmission was sufficient to induce some immunity is suggested by the observations that none of the parasitaemias documented through the cross-sectional survey were associated with fever and that the peak parasite prevalence occurred 2 months after the peak in incident malaria cases. However, the incidence of clinical malaria was similar in infants and older children, suggesting the rate at which immunity develops is slow, consistent with the low *P. falciparum* challenge. Taken together, these findings show that the Ifakara study area is one of low-to-moderate, perennial *P. falciparum* transmission.

Why was the intensity of malaria transmission so much lower in Ifakara than in the surrounding villages? No intervention was delivered through the project, although study children had good access to curative services and this may have influenced the incidence of clinical malaria detected. Our results suggest some other possible explanations. In addition to month of the year, the incidence of clinical malaria was significantly associated with reported use of mosquito nets and the distance between the child's home and the hospital. The protective antimalarial effect of mosquito nets has been well documented (Lengeler, 2003) and 61% of our study children slept under a mosquito net the night before recruitment to the study. The increasing risk of clinical malaria with increasing distance between the residence and SFDDH has been observed in studies detecting malaria episodes by PCD (Acosta *et al.*, 1999; Schellenberg *et al.*, 2001). It was not clear whether this association was due to differences in health-seeking behaviour, due to reduced availability of alternative malaria treatment outlets further from SFDDH, or whether exposure to *P. falciparum* increased with increasing distance from SFDDH. By using ACD the current study eliminated differences in health-seeking behaviour and this association is therefore most likely to be a function of increasing proximity of the households to mosquito breeding sites. The non-significant tendency for roof type to be associated with risk of malaria may reflect a predisposition of *Anopheles* mosquitoes for grass roofs over iron roofs as they are cooler, have more potential resting places and afford easier access through incompletely sealed eaves (Lindsay & Snow, 1988). However, this observation may also be explained by confounding associations between building materials and risk of malaria with socio-economic status or proximity to breeding sites.

Malaria is known to cause about 60% of the severe anaemia in infants in the study area (Menendez *et al.*, 1997) and the current study offers some insights into the mechanisms of malaria-related anaemia. There was markedly less severe anaemia than that seen in a large community-based cross-sectional survey in 4 districts in southern Tanzania (Schellenberg *et al.*, 2003), and only a non-significant decrease in the prevalence of anaemia with age. These 2 observations are consistent with the lower incidence of malaria in Ifakara than in the surrounding area, and may also reflect good access to curative services in the study area. The latter may also explain why the lowest prevalence of anaemia occurred a month after the peak incidence of symptomatic clinical malaria, when children would have had a haematological response to the treatment given. The importance of asymptomatic *P. falciparum* parasitaemia in the pathogenesis of anaemia is suggested by the maximal prevalence of asymptomatic parasitaemia being followed a month later by a peak in the prevalence of anaemia. However, these patterns should be interpreted with caution as several of the associations did not reach statistical significance.

Overall, only 26% of children with a history of fever or measured pyrexia were parasitaemic, underlining the poor specificity of fever as a marker for malaria. Furthermore, the marked age-dependence of fever, but

lack of age-dependence of clinical malaria, indicates a higher incidence of non-malaria febrile illnesses in infants than in older children. Co-morbidity may therefore be more likely in infants than in older children and may result in the age pattern of malaria morbidity being different from the age pattern of malaria-associated mortality. The change with age of the fraction of fevers attributable to malaria may justify the use of different malaria case definitions in different age groups.

It has been suggested that PCD may tend to detect more serious malaria episodes than ACD (Trape & Rogier, 1995). However the geometric mean parasite density in cases detected by PCD was similar to that in cases detected by ACD, although the relevance of parasitaemia as a marker of severity has been questioned in this setting (Schellenberg *et al.*, 1999). Nevertheless, the similarities in the patterns seen in ACD and PCD of parasite densities and the association between location of house and risk of malaria reassure that PCD in Ifakara is not biased by health seeking or geographical factors.

Classically, the time at risk within an ACD study starts at recruitment and ends when follow-up is complete, implying that weekly visits each contribute 7 d to the time at risk. However, it is inevitable that intermittent visits will miss a proportion of fever episodes and the incidence of disease will be underestimated. An alternative approach is to consider each visit as representing 1 day's time at risk, increasing the estimated incidence rates by a factor of 7. One would expect this to yield an incidence estimate similar to that obtained by visiting children on a daily basis. We were surprised, therefore, when daily visits to a random sample of the cohort generated incidence estimates substantially lower than those in which each weekly visit contributed one day to the time at risk. This may partly have resulted from individual febrile episodes each lasting several days, increasing the chance of their being detected by a weekly visit, and thus increasing the incidence of disease estimated by weekly visits. However, this would not explain the increased tendency of children visited daily to be brought to curative services at PCD. The children selected for daily visits were similar to the remainder of the cohort in those respects known to alter risk of illness, suggesting that the difference in incidence rates was largely due to the daily visits themselves, a so-called Hawthorne effect (Last, 1995). A possible explanation is that mothers of children visited more frequently developed a heightened awareness of their child's welfare and changed their caring patterns. This raises questions about the effect of weekly visits on estimated incidence rates, compared to no visits. An indication of this may be discerned from a comparison with infants from the same area involved in a contemporaneous intervention study (Schellenberg *et al.*, 2001). In that study, the incidence of clinical malaria episodes, detected by PCD only, was 0.42 episodes per infant per year, which compares with the 0.13 episodes per infant per year in the current study. This further supports the suggestion that visiting children at home by ACD greatly influences the estimate of incidence rates and reveals that ACD in Ifakara is less likely than PCD to give an accurate estimate of the true incidence of malaria. However, the size and direction of this Hawthorne effect may vary in different age groups and in different settings. A review of data from The Gambia suggests a significant increase in the incidence of malaria detected in children visited weekly compared to those visited monthly (Greenwood *et al.*, 1987) and a trend towards more episodes detected by daily compared to weekly visits (Snow *et al.*, 1989). For these reasons, and because of differences in study design and case definitions, more weight should be placed on the age pattern of disease than on the absolute incidence rates detected by ACD in different sites.

A final methodological consideration concerns the

malaria case definition. If it is accepted that each visit should represent 1 day's time at risk then it makes sense to include a history of fever in the preceding 24 h in the malaria case definition, and not just measured pyrexia. Although this will tend to reduce the specificity of the case definition it will increase its sensitivity and enhance the robustness of the rationale on which disease incidence rates are calculated.

In conclusion, the semi-urban Ifakara study area is subject to low-to-moderate perennial malaria transmission. The reduced intensity of transmission in comparison with the surrounding area is likely to be due to a combination of mosquito net use, reduced numbers of mosquito breeding sites in the centre of the study area and the better access to curative services. Including a history of fever in the malaria case definition may be rational when each ACD visit contributes 1 d to the time at risk. ACD visits appear to be associated with a marked Hawthorne effect, making the age-pattern of disease detected through ACD a more robust indicator of disease epidemiology than absolute disease incidence estimates.

Acknowledgements

This study would not have been possible without the goodwill and cooperation of the families of study children and their community leaders. We are also grateful to the Kilombero District Health Management Team, SFDDH and IHRDC staff for general support. This investigation received financial support from the Fondo de Investigaciones Sanitarias (FIS number 00/0803) and the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (TDR).

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Received 3 December 2002; revised 30 May 2003; accepted for publication 5 June 2003