The impact of a national impregnated bed net programme on the outcome of pregnancy in primigravidae in The Gambia

U. D'Alessandro[1,2], P. Langerock[1], S. Bennett[3], N. Francis[4], Kabir Cham[5] and B. M. Greenwood[1,3] *[1]Medical Research Council Laboratories, P. O. Box 273, Banjul, The Gambia; [2]Department of Parasitology, Institut de Médecine Tropicale Prince Léopold, B-2000 Antwerpen, Belgium; [3]London School of Hygiene and Tropical Medicine, Keppel Street, London, WC1E 7HT, UK; [4]Department of Histopathology, Charing Cross and Westminster Hospitals Medical School, London, W6 8RF, UK; [5] Ministry of Health and Social Welfare, Banjul, The Gambia*

Abstract

In 1992, the Gambian national impregnated bed net programme (NIBP) introduced insecticide treatment of bed nets into half of the primary health care villages in The Gambia. One component of the evaluation of this programme was the determination of whether it had any impact on the outcome of pregnancy in primigravidae. From February 1992, 651 primigravidae were recruited into the study. Less than 50% of them used an insecticide-treated bednet. During the rainy season the prevalence of *Plasmodium falciparum* among primigravidae was lower, fewer babies were classified as premature, and the mean birth weight was higher in villages where treated bed nets were used than in control villages. Therefore, during the rainy season, despite the low use of insecticide-treated bed nets by Gambian primigravidae, the NIBP had some impact on the outcome of pregnancy, particularly on the percentage of premature babies, and this was probably due to the decreased risk of malaria infection achieved during this period.

Keywords: malaria, *Plasmodium falciparum*, insecticide-treated bed nets, pregnancy, The Gambia

Introduction

Several studies have established that pregnancy increases the risk of malaria infection (BRABIN, 1991). Susceptibility to infection and the severity of the clinical manifestations of malaria are determined by the level of pre-pregnancy immunity, which, in turn, depends largely on the intensity and stability of malaria transmission (MITABINGWA, 1994). In highly endemic areas, such as most of sub-Saharan Africa, the effects of malaria on mother and fetus are less severe than in places with low or unstable transmission but malaria still has important consequences for pregnancy, especially in primigravidae (TAUFA, 1978; BRABIN, 1983, 1991; MCGREGOR, 1985, 1987). Maternal malaria causes anaemia which contributes significantly to maternal morbidity (MENENDEZ, 1995) and mortality (FULLERTON & TURNER, 1962). Maternal malaria is also associated with reduced birth weight, especially in first-born children; this has been attributed to impaired intra-uterine growth, premature delivery, or both (KORTMAN, 1972; MCGREGOR, 1984).

For many years the main malaria control strategy during pregnancy has been chemoprophylaxis, recommended for all pregnant women living in malaria endemic areas (WHO, 1984), but no final consensus has been reached on the efficacy of this intervention (GARNER & BRABIN, 1994). Some studies have shown that chemoprophylaxis reduces maternal anaemia and increases birth weight (MORLEY *et al.*, 1964; HAMILTON *et al.*, 1972; GREENWOOD *et al.*, 1989), while others have failed to confirm these findings (COT *et al.*, 1992; NOSTEN *et al.*, 1994). Insecticide-treated bed nets, which are effective at reducing malaria in children and in adults (COI *et al.*, 1995), offer a possible alternative approach to the control of malaria in pregnancy. However, only one trial on the effect of insecticide-treated bed nets on malaria in pregnancy has been reported so far (DOLAN *et al.*, 1993); this showed a decrease in the incidence of maternal anaemia but no beneficial effect on birth weight.

On the basis of the results of several preliminary trials (SNOW *et al.*, 1987; ALONSO *et al.*, 1991), the government of The Gambia initiated, in 1992, a national impregnated bed net programme (NIBP) which had the initial objective of introducing insecticide-treated bed nets into all large villages over a period of 2–3 years using the established primary health care (PHC) system. The UK Medical Research Council laboratories were asked to evaluate the impact of this programme on childhood mortality and morbidity in order to determine whether the results achieved in controlled trials could be reproduced in a nation-wide programme (D'ALESSANDRO *et al.*, 1995a). Another component of the evaluation was to find out whether the programme had any impact on the outcome of pregnancy in primigravidae, the group of pregnant women most vulnerable to malaria. The results of this component of the evaluation are reported here.

Address for correspondence: Dr Umberto D'Alessandro, Department of Parasitology, Institut de Médecine Tropicale Prince Léopold, Nationalestraat 155, B-2000 Antwerpen, Belgium.

Subjects and methods

Study area and implementation

Details of the implementation of the programme and of its impact on mortality and malaria morbidity in children under the age of 10 years have been described elsewhere (THOMSON *et al.*, 1994; D'ALESSANDRO *et al.*, 1995a, 1995b). In brief, 5 sentinel sites were selected for the epidemiological evaluation to reflect the varied cultural and ecological differences found within The Gambia. Within these areas, 104 PHC villages were identified and allocated at random to 2 groups. The programme, which involved the treatment of existing bed nets with 20% permethrin, was implemented in one group of villages in June–July 1992 and in the other group in June–July 1993. Eighty-one of the 104 villages were chosen to evaluate the impact of this intervention on the outcome of pregnancy in primigravidae between 1 August 1992 and 31 July 1993.

Evaluation

Primigravidae were identified throughout the study period and their gestational age assessed by history and palpation as early as possible during pregnancy. A blood sample for determination of parasitaemia and haemoglobin level was collected by finger-prick around 32 weeks of gestation and after delivery. On the same occasion, body temperature was determined using a digital thermometer and questions were asked on the usage of bed nets and their treatment with insecticide. New-born infants were weighed with a digital scale as soon as possible after birth and every second day for 2 weeks after birth. This series of weights was used to adjust the birth-weight for those babies who were not weighed immediately after delivery. New-born infants not weighed within 2 weeks after birth were excluded from the analysis. Every month the digital scales were checked with standard weights.

Maturity of the new-born child was assessed using the simplified method developed by PRIMHAK & MACGREGOR (1989), which is based on the presence or absence of plantar creases and on the diameter of mammary tissue. Babies without plantar creases and or with mammary tissue less than 0·5 cm in diameter were classified as premature. The assessment was done by a trained field assistant within 48 h after delivery. Information on the survival of new-born infants was collected until the end of July 1994.

Haemoglobin was determined immediately after blood collection using a portable β-haemoglobin photometer (Hemocue®). Thick blood films were prepared, stained and examined as previously described (GREENWOOD & ARMSTRONG, 1991).

At the time of delivery, trained traditional birth attendants (TBAs) collected a placenta biopsy, one thick blood smear from the maternal side of the placenta, and one from the cord. Placental and cord blood films were stained with Giemsa's stain and examined for malaria parasites. A placental biopsy, fixed in buffered formol saline, was embedded in wax by standard methods, sectioned and stained with haematoxylin and eosin and by the periodic acid–Schiff technique. Sections were examined by light microscopy and under polarized light for the presence of malaria parasites and malaria pigment. Placentas were classified as showing features of active infection (parasites), chronic infection (pigment), or both as described previously (BULMER *et al.*, 1993).

All primigravidae who were infected with malaria parasites and/or who were severely anaemic (haemoglobin ≤8 g/dL) were treated with a course of chloroquine and supplied with iron and folic acid until delivery.

Statistical methods

Two statistical analyses were carried out: (i) primigravidae from villages with insecticide-treated bed nets were compared with those from control villages (intention-to-treat analysis); (ii) primigravidae who slept under an insecticide-treated bed net were compared with those having an untreated bed net or no net at all, regardless of their village of residence (individual protection analysis).

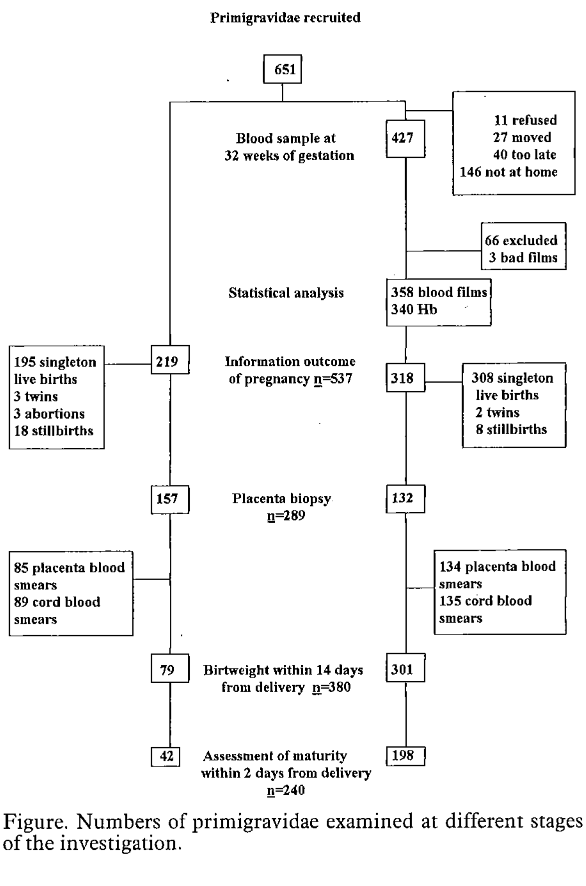

Figure. Numbers of primigravidae examined at different stages of the investigation.

Table 1. Bed net usage by primigravidae in villages where insecticide was available for the treatment of bed nets and in control villages

Area[a]	Availability of insecticide	No. of subjects	No net	Untreated nets	Treated nets
18	Yes	46	20 (43·5%)	4 (8·7%)	22 (47·8%)
	No	48	13 (27·1%)	35 (72·9%)	0
2	Yes	53	23 (43·4%)	10 (18·9%)	20 (37·7%)
	No	59	32 (54·2%)	27 (45·8%)	0
3	Yes	72	10 (13·9%)	12 (16·7%)	50 (69·4%)
	No	93	22 (23·6%)	70 (75·3%)	1 (1·1%)
4	Yes	64	30 (46·9%)	9 (14·1%)	25 (39·1%)
	No	56	21 (37·5%)	35 (62·5%)	0
5	Yes	70	22 (31·4%)	23 (32·9%)	25 (35·7%)
	No	85	25 (29·4%)	60 (70·6%)	0
Total	Yes	305	105 (34·4%)	58 (19·0%)	142 (46·5%)
	No	341	113 (33·1%)	227 (66·5%)	1 (0·3%)

[a]See D'ALESSANDRO *et al.* (1995a).

Data were analysed using SPSS for Windows® (version 6.1). The χ^2 test, analysis of variance, and multiple logistic regression were used as appropriate.

Results

Study cohort

From February 1992 onwards, 651 primigravidae, who delivered after 31 July 1992, were recruited into the study (Figure); 308 (47·3%) lived in villages with treated bed nets. The study cohort consisted of young, uneducated women (mean age 17 years; range 13–28 years) whose main occupation was farming. Although 55% of them had received some education (primary, secondary or Koranic school), 79·3% were unable to read and 90·2% were unable to write. The ethnic groups represented most frequently were Mandinka, Sarahuli, Fula and Wollof.

Less than 70% of primigravidae used a bed net and, in villages where insecticide was available, only 46·5% of the primigravidae slept under a treated bed net (Table 1).

A blood sample was collected at about 32 weeks of gestation from 427 of the study primigravidae (65·6%). Eleven refused and 27 had moved away. Forty (6·1%) were recruited too late in their pregnancy and 146 (22·4%) were not at home at the time of follow-up. In 66 cases, the 32 weeks' gestation blood sample was collected before the evaluation of the first intervention year started (1 August 1992) and these samples were excluded from the analysis; 3 samples were unusable (Figure). Eighty-eight (24·6%) of the remaining 358 primigravidae were parasitaemic; most of them (98%) had *Plasmodium falciparum*. Only *P. falciparum* infections were considered in the following analysis. Primigravidae with *P. falciparum* peripheral parasitaemia had a significantly lower haemoglobin level than those who were not parasitaemic (9·2 g/dL vs. 9·9 g/dL; P=0·002).

Information on the outcome of pregnancy was collected for 537 primigravidae (82·4%), although for some the birth weight of the new-born child was not available. The majority of women delivered at home (57·4%) and most of them were assisted by a TBA or by a friend or relative. There were 503 singleton (93·7%) and 5 twin (0·9%) live births, 26 still births (4·8%) and 3 abortions (0·6%). A blood sample was collected after delivery from 387 (59·4%) of the 651 primigravidae. The mean interval between collection of first and second blood samples was 5·7 weeks.

Three hundred and eighty babies were weighed within 14 d after delivery, 79·5% within 3 d and 95% within 7 d. An estimated birth weight was calculated, taking into account the number of days between delivery and weighing. Women who had not been resident in their village for the past 2 months and those who delivered twins were excluded from this analysis. Severely anaemic women (at 32 weeks of gestation) gave birth to significantly smaller children (2549 g vs. 2754 g; $P=0{\cdot}003$).

Placental biopsies were collected from 289 women, placental blood smears from 219, and cord blood smears from 224. The mean birth weight was significantly lower for mothers with a placental blood smear containing malaria parasites (2549 g) than for those without (2738 g; $P=0{\cdot}04$). There were more prenatal deaths (still births and neonatal deaths) among mothers with a positive placental slide (7/42, 16·7%) than among those with a negative one (4/176, 2·3%; $P<0{\cdot}001$).

Signs of maturity were assessed within 48 h in 48% (240/503) of live-born children. Severely anaemic women (at 32 weeks of gestation) were more likely to deliver preterm babies (11·8% vs. 5·0%), although the difference was not statistically significant ($P=0{\cdot}23$). Placental malaria was not associated with the delivery of premature children ($P=0{\cdot}68$), suggesting that the more likely outcome of placental infection was the delivery of small-for-term rather than premature babies. Seventeen children (7·6%) had malaria parasites in their cord blood.

Information on the survival of children 2 years after birth could be collected for 319 of those whose birth weight was known. Low birth weight babies (<2500 g) or more (12/213, 5·6%; $P=0{\cdot}007$ by survival analysis). However, this difference disappeared after controlling for prematurity ($P<0{\cdot}76$). Premature babies had a significantly higher risk of dying in the first 2 years of life (5/22, 22·7%) than the other children (19/279, 6·8%; $P=0{\cdot}001$ by survival analysis). There were 5 deaths among premature children; these happened during their first 2–3 months of life.

Intention-to-treat analysis

During the rainy season (August–December) the parasite rate was significantly lower in primigravidae living in villages where treated bed nets were used than in control villages (Table 2). No difference between treated and untreated villages was found during the dry season (January–July). No significant difference in parasite density was found between villages with treated bed nets (geometric mean 218·7 parasites/μL) and control villages (geometric mean 128·8 parasites/μL; $P=0{\cdot}21$).

Haemoglobin levels were measured at 32 weeks of gestation in 340 primigravidae. During the dry season, the mean haemoglobin level was higher among primigravidae in villages with treated bed nets than in control villages (10·0 g/dL vs. 9·6 g/dL), although the difference between groups was not statistically significant ($P=0{\cdot}11$). However, the prevalence of severe anaemia (haemoglobin ≤8 g/dL) was significantly lower in villages with treated bed nets (6·3%) than in control villages (20·0%) (odds ratio [OR] 0·27, 95% confidence interval [CI] 0·07–0·93; $P=0{\cdot}03$). During the rainy season no difference between the 2 groups of villages was found in either the mean haemoglobin level (9·6 g/dL vs. 9·7 g/dL; $P=0{\cdot}75$) or the prevalence of severe anaemia (20/101, 19·8% vs. 16/95, 16·8%; $P=0{\cdot}72$).

After delivery, no difference in parasite prevalence or mean haemoglobin level was found between women living in villages with treated bed nets or in control villages (data not shown). However, all primigravidae who were parasitaemic and/or severely anaemic around 32 weeks of gestation were treated, and this may have influenced the haematological data after delivery.

The prevalence of still births and abortions did not vary with season, nor between villages with treated bed nets and control villages. However, perinatal mortality (still births and neonatal deaths) was higher in control villages (27/277, 9·7%) than in villages with treated bed nets (14/252, 5·6%), particularly during the rainy season, but the difference between groups was not statistically significant ($P=0{\cdot}1$).

During the rainy season, the percentage of premature children was lower in villages with treated bed nets than in control villages (Table 2) The summary OR, after stratifying by season of delivery, was 0·44 (95% CI 0·12–0·92; $P=0{\cdot}04$). This did not change after controlling for chloroquine use during pregnancy, age, or marital status.

Overall, there was no difference in mean birth weight between villages with treated bed nets and control villages. however, babies born during the rainy season in villages with treated bed nets were, on average, 130 g heavier than those born in control villages (Table 2). The difference in birth weight found in the rainy season between the 2 groups of villages disappeared when the babies classified as premature were excluded from the analysis. During the dry season the mean birth weight of babies born in control villages was 135 g higher than that of those born in villages with treated bed nets.

The prevalence of positive placental blood slides was similar between the 2 groups of villages (20·6% in villages with treated bed nets vs 17·9% in control villages; $P=0-73$), as was the prevalence of positive cord blood films (6·5% vs. 8·6%; $P=0{\cdot}72$). One hundred and one placenta biopsies (52 from villages with insecticide-treated bed nets and 49 from control villages) were chosen for histological examination. The prevalence of pla-

Table 2. Prevalence of malarial parasitaemia at 32 weeks of gestation and of premature births and the mean birth weight of infants among primigravidae according to village group

	Villages			
Season	Treated nets[a]	Control	Odds ratio[b]	*P*
Parasitaemia				
Rainy	24/107 (22·4%)	35/96 (36·5%)	0·50 (0·26, 0·98)	0·04
Dry	12/66 (18·2%)	15/89 (16·9%)	1·09 (0·42, 2·70)	0·99
Total	36/173 (20·8%)	50/185 (27·0%)	0·70 (0·42, 1·19)	0·21
Prematurity				
Rainy	5/82 (6·1%)	11/59 (18·6%)	0·28 (0·08, 0·97)	0·02
Dry	1/40 (2·5%)	2/59 (3·4%)	0·73 (0·02, 11·1)	1·00
Total	6/122 (4·9%)	13/118 (11·0%)	0·42 (0·13, 1·25)	0·08
Mean birth weight[c] (g)			Difference	
Rainy	2699 (457)	2569 (500)	+130	0·04
Dry	2658 (227)	2793 (208)	−135	0·05
Both	2682 (464)	2679 (491)	+3	0·93

[a]Bed nets were treated with insecticide only once, at the beginning of the rainy season.
[b]95% confidence limits in parentheses.
[c]Standard deviation in parentheses.

Table 3. Prevalence of prematurity and mean birth weight of infants among primigravidae according to use of bed nets

Season	Bed nets Treated[a]	Untreated or none	Odds ratio[b]	P
Prematurity				
Rainy	1/35 (2·9%)	14/105 (13·3%)	0·19 (0·01, 1·51)	0·11
Dry	0/16	3/81 (3·7%)	0	1·00
Total	1/51 (2·0%)	17/186 (9·1%)	0·2 (09·02, 1·34)	0·13
Mean birth weight[c] (g)			Difference	
Rainy	2739 (398)	2610 (501)	+129	0·09
Dry	2759 (538)	2726 (453)	+33	0·70
Both	2748 (460)	2662 (483)	+85	0·14

[a]Bed nets were treated with insecticide only once, at the beginning of the rainy season.
[b]95% confidence limits in parentheses.
[c]Standard deviation in parentheses.

Table 4. Summary of the main findings[a]

	Intention-to-treat analysis[b]		Individual protection analysis[c]	
	Rainy season	Dry season	Rainy season	Dry season
Parasitaemia (32 weeks)	↓*	–	–	–
Severe anaemia (32 weeks)	–	↓*	–	↓*
Perinatal mortality	↓	–	–	–
Premature new-borns	↓*	–	↓	–
Birth weight	↑*	↓	↑	–

[a]↑=Increase, ↓=decrease, –=no difference. Statistically significant changes ($P<0·05$) are indicated by an asterisk (*).
[b]Primigravidae living in treated villages vs. those in control villages.
[c]Primigravidae using insecticide-treated bed nets vs. those with untreated nets or no net.

centas showing signs of chronic or active infection was similar between the 2 groups of villages (75% in villages with treated bed nets vs. 73·5% in control villages; $P=1·00$).

Individual protection analysis

During the dry season women who used treated bed nets were less likely to be anaemic (3·1%) than those who used an untreated bed net or no net (17·0%; $P=0·04$). No difference was found during the rainy season.

The risk of delivering a premature child was lower in women who slept under insecticide-treated bed nets than in those without a net or with an untreated bed net (Table 3). After controlling for chloroquine use, season of delivery, age, and marital status the OR was 0·17 (95% CI 0·02–1·37; $P=0·09$).

Primigravidae who used insecticide-treated bed nets delivered heavier babies than those who used an untreated net or no net at all, particularly during the rainy season (Table 3).

The main findings of the study are summarized in Table 4.

Discussion

This study was carried out on the assumption that, if the NIBP was to have any effect on the outcome of pregnancy, it would be most evident in primigravidae who are more susceptible to malaria than pregnant women of higher parity, at least in areas of high malaria endemicity like The Gambia (McGregor *et al.*, 1983). As the NIBP is a national public health measure, the primary analyses undertaken were on the effectiveness of the overall programme—i.e., an intention-to-treat analysis rather than a study of the efficacy of insecticide-treated bed nets in pregnancy, although this was investigated also. The level of bed net usage among the primigravidae in the study cohort was unexpectedly low and the percentage of those who used an insecticide-treated bed net was even lower. Thus, although 80% of bed nets in villages where insecticide was available were treated (D'Alessandro *et al.*, 1995a), the percentage of primigravidae who used an insecticide-treated bed net was less than 50%. One possible reason for this finding was that the great majority of primigravidae were young teenagers, probably of low social status and therefore less aware of village health activities. In Nigeria, Okonofua *et al.* (1992) showed that pregnant adolescent girls were less likely to receive antenatal care and to adopt appropriate measures for the prevention of malaria. Despite these problems, the intervention had some impact on the outcome of pregnancy. A subsidiary analysis of data for women who used an insecticide-treated bed net during pregnancy and those who did not was also undertaken, and its results generally supported those of the analysis of effectiveness. However, women who did not use an insecticide-treated bed net may have been disadvantages compared with those who did, introducing potential confounding for this comparison. These data must, therefore, be treated with caution.

During the rainy season there were significantly fewer primigravidae with parasitaemia in villages with treated bed nets than in control villages, although there was no difference in the prevalence of severe anaemia or in the mean haemoglobin level. In pregnancy, the peak prevalence of *P. falciparum* parasitaemia occurs at 9–16 weeks of gestation (Brabin, 1983; Brabin *et al.*, 1988, 1990). This can lead to anaemia (Kortman, 1972; Fleming *et al.*, 1984; McGregor, 1984) and there is no correlation in individuals between haemoglobin level and parasite density (Brabin, 1991). In this study, a first blood sample was obtained around 32 weeks of gestation fro women in their third trimester of pregnancy who had probably been exposed to malaria during the previous rainy season. Therefore, insecticide-treated bed nets had an effect on malaria prevalence but not on severe anaemia, which may have been a reflection of an infection acquired during the preceding rainy season. This is supported by the lower prevalence of severe anaemia in villages with treated bed nets during the dry season and in women using insecticide-treated bed nets. These women were in their first or second trimester of pregnancy during the preceding rainy season, when the NIBP may have protected then from malaria infection.

During the rainy season there were fewer preterm babies in villages with treated bed nets than in control villages, and women who used insecticide-treated bed nets were less likely to deliver a preterm baby than women who used untreated nets or no nets at all. Premature labour can occur in malarious women (BRABIN, 1991), but it has been described mainly in non-immune mothers or those with a low level of acquired immunity and is more likely when malaria occurs in the third, rather than in the second, trimester of pregnancy (HERD & JORDAN, 1981). Because of the difficulties of defining prematurity, it has not been used as an end point in previous community-based studies of the outcome of pregnancy in The Gambia (GREENWOOD *et al.*, 1989). The simplified method of PRINHAK & MCGREGOR (1989), which has been shown to have good sensitivity (78%) and specificity (91%), has provided an opportunity of investigating the effect of insecticide-treated bed nets on prematurity. This method has never been validated in Africa, so some misclassification may have occurred. However, most of the premature children had a birth weight lower than 2500 g and their mean birth weight (1921 g) was significantly lower than that of mature babies (2579 g). Premature babies also had a lower mean survival time than children classified as mature. The consistency of these findings suggests that, although not perfect, this method may be reliable and that the decrease in prematurity rates observed where treated bed nets were used and among individuals who used treated bed nets was real.

During the rainy season the mean birth weight of children born in villages with treated bed nets was 130 g higher than that of those born in control villages and, at the individual level, a similar difference was found between insecticide-treated bed net users and other women. This difference was based mainly on babies classified as premature and it disappeared when they were excluded from the analysis. Therefore, it is possible that the intervention, in reducing parasite prevalence during the rainy season, reduced the delivery of preterm babies and thus brought about an increase in the mean birth weight. The reduction of parasite rate in the rainy season. However, the increase in mean haemoglobin level in villages with treated bed nets was probably not large enough to being about an increase in mean birth weight.

It is recognized that the cause of low birth weight in malarious mothers is multifactorial (MENENDEZ, 1995). The results of this study suggest that malaria can cause delivery of low birth weight children in at least 2 ways. One is the delivery of small-for-term babies as a result of a malarial infection which occurred early in pregnancy, producing maternal anaemia and placental parasitization. The other is the delivery of preterm babies, due to an acute infection of the mother during the third trimester or pregnancy. It is on this last mechanism that the NIBP seems to have had its major impact.

Acknowledgements

We thank the MRC field staff at MRC Farafenni and Basse, especially Samba Cham and Kebba Keita, and Ms Linda Williams and Mr Shabbar Jaffar for statistical advice and Dr Christian Lengeler for his helpful comments. This study received financial support from the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (TDR).

References

Alonso, P. L., Lindaay, S. W., Armstrong, J. R. M., Conteh, M., Hill, A. G., David, P. H., Fegan, G., de Francisco, A., Hall, A. J., Shenton, F. C., Cham, K. & Greenwood, B. M. (1991). The effect of insecticide-treated bed nets on mortality of Gambian children. *Lancet*, **337**, 1499–1502.

Brabin, B. J. (1983). An analysis of malaria in pregnancy in Africa. *Bulletin of the World Health Organization*, **61**, 1005–1016.

Brabin, B. J. (1991). *The risk and severity of malaria in pregnant women. Applied filed research in malaria reports*, no. 1. Geneva: UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (TDR).

Brabin, B. J., Brabin, L. R., Sapau, J. & Alpers, M. P. (1988). A longitudinal study of splenomegaly in pregnancy in a malaria endemic area in Papua New Guinea,. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, **82**, 677–681.

Brabin, B. J., Ginny, M., Alpers, M., Brabin, L., Eggelte, T. & Van Der Kaay, H. J. (1990). failure of chloroquine prophylaxis for falciparum malaria in pregnant women in Madang, Papua New Guinea. *Annals of Tropical Medicine and Parasitology*, **84**, 1–9.

Bulmer, J. N., Rashee, F. N., Francis, N., Morrison, L. & Greenwood, B. M. (1993). Placental malaria. I. Pathological classification. *Histopathology*, **22**, 211–218.

Choi, H. W., Breman, J. G., Teutsch, S. M., Liu, S., Hightower, A. W. & Sexton, J. D. (1995). The effectiveness of insecticide-impregnated bed nets in reducing clinical malaria: a meta-analysis of published results. *Americn Journal of Tropical Medicine and Hygiene*, **52**, 377–382.

Cot, M., Roisin, A., Barro, D., Yada, A., Verhave, J. P., Carnevale, P. & Breart, G. (1992). Effect of chloroquine chemoprophylaxis during pregnancy on birth weight: results of a randomized trial. *American Journal of Tropical Medicine and Hygiene*, **46**, 21–27.

D'Alessandro, U., Olaleye, B. O., McGuire, W., Langerock, P., Aikins, M. K., Thomson, M., Bennett, S., Cham, M. K., Cham, B. A. & Greenwood, B. M. (1995a). Reduction in mortality and in morbidity from malaria in Gambian children following the introduction of a National Insecticide Impregnated Bednet Programme. *Lancet*, **345**, 479–483.

D'Alessandro, U., Olaleye, B. O., McGuire, W., Thomson, M. C., Langerock, P., Bennett, S. & Greenwood, B. M. (1995b). A comparison of the efficacy of insecticide-treated and untreated bed nets in preventing malaria in Gambian children. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, **89**, 596–598.

Dolan, G., ter Kuile, F. O., Jacoutot, V., White, N. J., Luxemburger, C., Malankirii, L., Chongsuphajaisiddhi, T. & Nosten, F. (1993). Bed nets for the prevention of malaria and anaemia in pregnancy. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, **87**, 620–626.

Fleming, A. F., Harrison, K. A., Briggs, N. D., Attai, E. D. E., Ghatoura, G. B. S., Akintunde, E. A. & Shah, N. (1984). Anaemia in young primigravidae in the guinea savanna of Nigeria: sickle-cell trait gives partial protection against malaria. *Annals of Tropical Medicien and Parasitology*, **78**, 395–404.

Fullerton, W. T. & Turner, A. G. (1962). Exchange transfusion in treatment of severe anaemia in pregnancy. *Lancet*, **i**, 75–78.

Garner, P. & Brabin, B. (1994). A review of randomized controlled trials of routine antimalarial drug prophylaxis during pregnancy in endemic malarious areas. *Bulletin of the World Health Organization*, **72**, 89–99.

Greenwood, B. M. & Armstrong, J. R. M. (1991). Comparison of two simple methods for determining malaria parasite density. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, **85**, 186–188.

Greenwood, B. M., Greenwood, A. M., Snow, R. W., Byass, P., Bennett, S. & Hatib-N'jie, A. B. (1989) The effects of malaria chemoprophylaxias given by the traditional birth attendants on the course and outcome of pregnancy. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, **83**, 589–594.

Hamilton, P. J. S., Gebbie, D. A. M., Wilks, N. E. & Lothe, F. (1972). The role of malaria, folic acid deficiency and haemoglobin AS in pregnancy at Mulago Hospital. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, **66**, 594–602.

Herd, N. & Jordan, T. (1981). An investigation of malaria during pregnancy in Zimbabwe. *Central African Journal of Medicine*, **27**, 62–68.

Kortman, H. F. C. M. (1972). *Malaria and pregnancy*. MD thesis, Universiteit van Amsterdam, Utrecht, Drukkerij Elinkwijk.

MacGregor, I. A. (1984). Epidemiology, malaria and pregnancy. *American Journal of Tropical Medicine and Hygiene*, **33**, 517–525.

MacGregor, I. A. (1987). Thoughts on malaria in pregnancy with consideration of some factors which influence remedial strategies. *Parasitologia*, **29**, 153–163.

MacGregor, I. A., Wilson, M. E. & Billewicz, W. Z. (1983). Malaria infection of the placenta in The Gambia, West Africal its incidence and relationship to stillbirth, birthweight and placental weight. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, **77**, 232–244.

Menendez, C. (1995). Malaria during pregnancy: a priority area of malaria research and control. *Parasitology Today*, **11**, 178–183.

Morley, D., Woodland, M. & Cuthbertson, W. F. J. (1964). Controlled trial of pyrimethamine in pregnant women in an Afri-

can village. *British Medical Journal*, **i**, 667–688.
Mutabingwa, T. K. (1994). Malaria in pregnancy: epidemiology, pathophysiology and control options. *Acta Tropica*, **57**, 239–254.
Nosten, F., ter Kuile, F., Maelankiri, L., Chongsuphajaisiddhi, T., Nopdonrattakoon, L., Tangkitchot, S., Boudreau, E., Bunnag, D. & White, N. J. (1994). Mefloquine prophylaxis prevents malaria during pregnancy: a double-blind placebo-controlled study. *Journal of Infectious Diseases*, **169**, 595–603.
Okonofua, F. E., Feyisetan, B. J., Davies-Adetugbo, A. & Sanusi, Y. O. (1992). Influence of socioeconomic factors on the treatment and prevention of malaria in pregnant and non-pregnant adolescent girls in Nigeria. *Journal of Tropical Medicine and Hygiene*, **95**, 309–315.
Primhak, R. A. & MacGregor, D. F. (1989). Simple maturity classification of the newborn infant. *Annals of Tropical Pediatrics*, **9**, 65–69.
Snow, R. W., Rowan, K. M. & Greenwood, B. M. (1987). A trial of permethrin-treated bed nets in the prevention of malaria in Gambian children. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, **81**, 563–567.
Taufa, T. (1978) Malaria and pregnancy. *Papua New Guinea Medical Journal*, **21**, 197–206.
Thomson, M. C., D'Allessandro, U., Bennett, S., Connor, S. J., Langerock, P., Jawara, M., Todd, J. & Greenwood, B. M. (1994). Malaria prevalence is inversely related to vector density in The Gambia, West Africa. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, **88**, 638–643.
WHO (1984). *Advances in Malaria Chemotherapy*. Geneva: World Health Organization, technical Report Series, no. 711.

Received 12 January 1996; revised 15 May 1996; accepted for publication 15 May 1996

Announcements

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE

The *Transactions of the Royal Society of Tropical Medicine and Hygiene* is issued bi-monthly (six parts per year) and publishes not only papers presented at Society meetings and symposia but also papers and correspondence submitted from all over the world on every aspect of tropical medicine and international health. Supplements on specialist topics are published from time to time.

The *Transactions* is available to Libraries and non-Fellows at an annual subscription of £120.00. It is dispatched by accelerated surface post at no extra charge.

The annual subscription for Fellows is £50.00. Applications for Fellowship must be made on the correct form, obtainable from the address below. The rate for *bona fide* students is £25.00.

Further information and application forms for Fellowship can be obtained from:

The Honorary Secretaries
Royal Society of Tropical Medicine and Hygiene
Manson House
26 Portland Place
London, W1N 4EY, UK
Telephone: +44 (0) 171 580 2127
Fax: +44 (0) 171 436 1389

Subscription orders from libraries and non-Fellows should be sent to:

Royal Society of Tropical Medicine and Hygiene
Subscription Department
Unit 67, Raglan House
St. Peter Street
Maidstone, ME16 0SN, UK
Telephone: +44 (0) 1622 756668
Fax: +44 (0) 1622 679774

President's Fund

The aim of the fund is to sponsor prospective Fellows from developing countries, who are at present unable to join because their country's fiscal rules prevent them from paying the subscription.

The fund known as *The President's Fund for Overseas Fellows in Developing Countries*, is used to sponsor deserving candidates for full Fellowship of the Society for a period of three years.

The Society relies on donations from Fellows (including Honorary and Life Fellows).

Any Fellow willing to donate to the President's Fund in order to help sponsor a Fellow from a developing country, is asked to write to Manson House.