Morbidity from falciparum malaria in Natal/KwaZulu

P. N. SONI, B. L. SHARP, S. NGXONGO, V. GATHIRAM

Abstract **Plasmodium falciparum malaria is endemic in the northern KwaZulu areas of South Africa. The clinical morbidity produced by this parasite has not been studied since the institution of the present malaria control programme. Fifty-nine patients were prospectively studied at a peripheral clinic during the peak malaria season; symptoms and signs of the infection, parasite loads, haemoglobin values and leucocyte counts were recorded in all patients. Haemoglobin and leucocyte counts were also measured in 37 control subjects without malaria. The commonest symptoms were persistent headache (100%), rigors (98%) and myalgia (93%). None of the patients presented with coma, pulmonary oedema, hypoglycaemia or algid malaria. Splenomegaly was found in 49%, hepatomegaly in 20% and mental confusion in 5% of patients. Mean parasite load was 1,71% and 57% of patients had parasite loads of <1%. Anaemia of <10 g/dl was significantly more frequent ($P <$ 0,0001) in the patient group than in the control group. Leucopenia (white cell count < 4,0 x 10^9/l) was present in 12 of 50 patients in whom it was measured compared with 2 controls (P = 0,0175). The results show a wide range of morbidity, without severe complications as presenting manifestations. Symptomatic infection in the presence of low parasite loads suggests that there may be little or no immunity in this population.**

S Afr Med J 1993; **83:** 110-112.

Department of Medicine, University of Natal, Durban
P. N. SONI, F.C.P. (S.A.)
V. GATHIRAM, M.D., F.C.P. (S.A.)
Research Institute for Diseases in a Tropical Environment of the South African Medical Research Council, Durban
B. L. SHARP, PH.D.
KwaZulu Department of Health, Jozini, KwaZulu
S. NGXONGO, M.SC.

Accepted 30 Jan 1992.

The impact of malaria is felt most in Africa. Here the climate, poverty, poor sanitation, and ignorance provide ideal conditions for the parasite to breed.[1] Malaria is endemic in all countries of tropical Africa, where the prevalance rate in children exceeds 50% in most areas, with *Plasmodium falciparum* malaria accounting for between 80% and 99% of cases.[1] More than 1 million children die each year from *P. falciparum* malaria in Africa alone,[1] where the problem has been aggravated by mosquito resistance to a wide range of insecticides and the parasite's resistance to chemotherapeutic agents.[2]

Falciparum malaria is endemic in the northern KwaZulu areas of South Africa.[3] The morbidity produced has not been studied in this region since 1931 when Swellengrebel *et al.*[4] found a high prevalence as well as a high parasite load in residents of this region before the institution of the present malaria control programme. Malaria has been a notifiable disease in the RSA since 1958 and all dwellings in the endemic malaria area have been subject to the annual intra-domiciliary application of DDT. The malaria control programme in Natal/KwaZulu as a whole is considered to be highly effective.[3] This is illustrated by the low malaria case fatality rate and low incidence between 1976 and 1985. The agricultural and industrial development of large

parts of the province since the late 1920s and early 1930s is a further indication of this.[3] The control programme includes mass blood examinations and routine active surveillance in areas of high endemicity, resulting in earlier diagnosis and treatment. Chloroquine resistance was first noted in the study area in 1985.[5]

Since 1984 malaria notifications have increased substantially.[6] An outbreak in 1987 produced 4 830 recorded cases of clinical malaria in this region, far in excess of the number of cases reported annually over the 11-year period, 1976 - 1986 (mean 648; range 75 - 1199).[7] The morbidity and clinical profile of the disease have not been studied in this region since the institution of the present control programmes. A cross-sectional study was designed to describe the clinical manifestations and determine the severity of *P. falciparum* infection in this area.

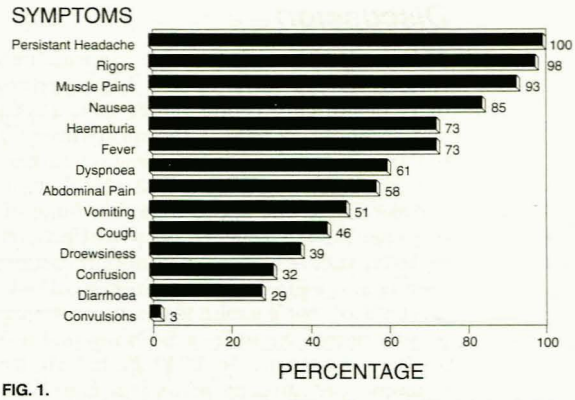

FIG. 1.
Bar diagram of symptoms in 59 patients with acute falciparum malaria.

Patients and methods

The study was conducted in 1989 during the months of March and April, the peak season for the disease in this region.[3] Patients were studied at the Ndumu clinic in the rural Ingwavuma district. This is a primary health care centre and a point of first contact for the population in this district. A total of 59 patients, 5 years of age and over, infected with *P. falciparum* were obtained by sequential sampling and included in this study.

Informed consent was obtained for the patients, and from the guardians in the case of minors. Patients were subjected to a systemic enquiry as to their symptomatology and examined clinically for signs of malaria. The clinical assessment closely followed the guidelines of the WHO Malaria Action Programme.[8] In the majority of patients, the duration of the illness was not recorded; in those in whom it was available, this was thought to be unreliable.

Urine samples from the patients were tested for the presence of blood and protein using dipsticks (Ames). Blood samples were drawn for later haematological analysis and blood smears were quantitatively examined for an estimation of parasite load. All patients were treated by the KwaZulu health authorities with sulphadoxine-pyrimethamine (Fansidar; Roche).

Blood samples for haematological comparison were drawn from a control group of 37 volunteers aged 5 years and over. This group consisted of healthy subjects living in the same endemic area and studied during the same malaria season. They had not suffered from malaria during this season, and their blood smears were negative for *Plasmodium* spp. Haemoglobin estimation and white cell counts (WCCs) were performed using a Cell-Dyne analyser. Student's *t*-test was used for comparison of means and the χ^2-test for comparison of categoric data. Where the expected cell sizes were less than 5 in the 2×2 case, Fisher's exact test was used.

Results

Of the 59 patients studied, 33 were female and 26 male. Their mean age was 22 years (range 5 - 60 years). The control population consisted of 27 females and 10 males, with a mean age of 26 years (range 5 - 60 years).

Fig. 1 shows the frequency of occurrence of symptoms. Persistent headache, rigors and myalgia were the most common; these were present in 100%, 98% and 93% of patients respectively.

The mean temperature was 38,5°C (range 36,8 - 40,5°C). Mild jaundice was detected in 2 patients. The mean pulse rate was 102/min and no patients presented with algid malaria, although systolic blood pressure was less than 100 mmHg in 21 patients (35,6%).

Splenomegaly (mean 2,4 cm; range 1 - 8 cm) was found in 29 patients (49%). Hepatomegaly was detectable in 12 patients (20,3%). The mean increase in liver size was 2 cm (range 1 - 4 cm). Thirty-two patients (54%) felt dull or drowsy and 3 (5%) were confused. None of the patients presented with hypoglycaemia and the mean blood sugar level was 6,4 mmol/l (range 3,6 - 11,4 mmol/l). No patients presented to the clinic in coma or with pulmonary oedema.

Proteinuria was detected in 95% of patients, although in the majority (81,3%) this was mild (trace to +). Haematuria was detected in 59%, including 14 patients with severe (++++) haematuria on dipstick testing. The majority of patients (57%) had parasite counts of < 1%. Five patients (8,5%) had hyperparasitaemia, i.e. > 5%. Mean parasitaemia was 1,71% (range 0,01 - 10,74%).

Haemoglobin levels were measured in 50 patients and the mean was 10,8 g/dl (range 6,9 - 16,9 g/dl). The mean for the control group was 12,1 g/dl (range 8 - 14,6 g/dl). This difference was statistically significant (P = 0,0019). Thirty-five of 50 patients compared with 16 of 37 controls had a haemoglobin level of < 12 g/dl (P = 0,12). From Fig. 2 it is apparent that a severe anaemia (under 10 g/dl) occurred significantly more often in patients (40%) than in controls (5%) ($P < 0,0001$).

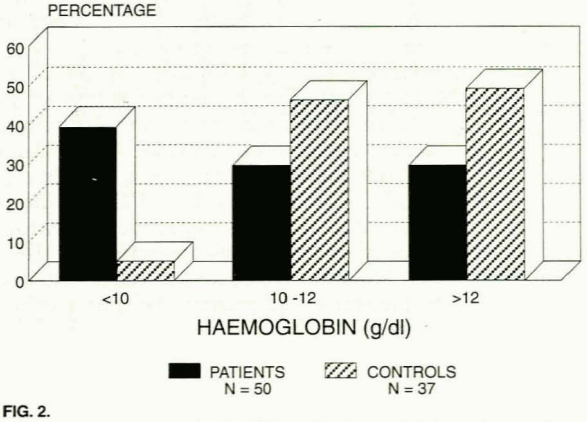

FIG. 2.
Haemoglobin analysis in 50 patients and 37 control subjects.

There was no statistical difference (P = 0,2669) between the mean leucocyte counts in the patient group ($6,1 \times 10^9$/l, range 2,3 - 20 $\times 10^9$/l) and the control group ($6,7 \times 10^9$/l). Leucopenia (< $4,0 \times 10^9$/l) occurred significantly more frequently in patients (12) than controls (2) (P = 0,0175). Leucocytosis (> $11,0 \times 10^9$/l) was found in 4 patients and none of the control population.

Discussion

This study differs from other clinical studies in South Africa[9,10] in two ways. Firstly, it was performed at a primary health care centre rather than a referral hospital, and secondly, it reflects the morbidity of *P. falciparum* malaria in residents of the region rather than South Africans returning from travels elsewhere in Africa. It is apparent from the above data that none of the patients presented with severe complications of falciparum malaria, such as coma, pulmonary oedema, hypoglycaemia and algid malaria. Symptomatic infection in the presence of low parasite loads in most patients suggests that there may be little or no immunity to *P. falciparum* in this population. In 1949 Field[11] showed that poor outcome was directly related to high parasite density, although the reverse was not true. This implies that the level of parasitaemia is not the only factor determining malaria mortality.

The common symptoms were all nonspecific and many also occur in other infections, such as typhoid fever; however, the presence of these symptoms may be a useful marker of malarial infection in mass screening programmes. Similar results have been reported from other southern African countries, like Zimbabwe[12-14] and Tanzania.[15] These data also concur with those of Goldstein[16] in his study of non-immune American soldiers in Vietnam. Respiratory and gastro-intestinal symptoms were commonly found (Fig. 1). The presence of a soft splenomegaly in almost half the patients is a useful clue to diagnosis.

Proteinuria and haematuria were also common. Mild proteinuria may occur with any febrile illness. In malaria the deposition of malaria immune complexes on the glomerular basement membrane may result in an acute nephritis with resultant haematuria and proteinuria. Haematuria may also be a result of *Schistosoma haematobium* infection of the bladder. This possibility was not investigated in our patients, although it is well documented that adjacent districts in northern KwaZulu have a high prevalence of *S. haematobium* infection.[17]

Anaemia is a prominent feature of the infection. The combination of haematuria and anaemia suggests red cell destruction as the primary cause of the anaemia. However, no correlation was observed between malaria parasite density and haemoglobin level. This observation concurs with the results of Olweny *et al.*[18] Haemoglobinopathies are rare in South Africa and therefore unlikely to play a role in anaemia.

Leucopenia was reported in 30%[16] and 33%[19] of American soldiers in Vietnam suffering from acute *P. falciparum* infections and occurred with a similar frequency (24%) in our patients. Typhoid fever, which is also endemic to this study area, can also produce a leucopenia. This makes a low WCC in the presence of a febrile illness a less sensitive indicator of malaria. Leucocytosis was also uncommon in the above studies[16,19] of uncomplicated malaria and its occurrence should raise the possibility that another disease is involved.

In conclusion, the clinical manifestations of falciparum malaria in the Natal/KwaZulu area of South Africa are similar to those in other malarious areas. The severity of infection ranged from an influenza-like illness to high fever with convulsions. However, severe complications were not observed. The clinical manifestations produced by low parasite loads suggest a much lower level of acquired immunity than that suggested by Swellengrebel *et al.* in the same area in 1931. This needs to be verified by further studies.

We wish to thank the nursing staff of Ndumu Clinic, David Mthembu and Sandy Fay, for their invaluable assistance in the data collection. We are also grateful to Dr Murray Short from the KwaZulu Department of Health for permission to perform this study and Ms Eleanor Gouws from the South African Medical Research Council for statistical assistance. This work was supported by a grant from the South African Medical Research Council.

REFERENCES

1. Wernsdorfer WH. The importance of malaria in the world. In: Kreier JP, ed. *Malaria*. New York: Academic Press, 1980.
2. Bruce-Chwatt LS. *Essential Malariology*. London: Heinemann Medical Books, 1980.
3. Sharp BL, Ngxongo S, Botha MJ, Ridl F, Le Sueur D. An analysis of 10 years of retrospective malaria data from the KwaZulu areas of Natal. *S Afr J Sci* 1988; **84:** 102-106.
4. Swellengrebel NH, Annecke S, De Meillon B. Malaria investigations in some parts of the Transvaal and Zululand. *Publications of the South African Institute for Medical Research* 1931; **4:** 245-274.
5. Herbst JM. Taylor LA, Joubert SM. *In vitro* chloroquine-resistant *Plasmodium falciparum* malaria in the Natal/KwaZulu area. *S Afr Med J* 1985; **69:** 749-750.
6. Sharp BL. Aspects of the epidemiology of malaria in Natal Province. Ph.D. thesis, University of Natal Medical School, 1991.
7. Freese JA, Sharp BL, Ngxongo SM, Markus MB. *In vitro* confirmation of chloroquine-resistant *Plasmodium falciparum* malaria in KwaZulu. *S Afr Med J* 1988; **74:** 576-578.
8. Warrell DA, Molyneux ME, Beales PF, eds. WHO Division of Control of Tropical Diseases: severe and complicated malaria. *Trans R Soc Trop Med Hyg* 1990; **84:** suppl 2, 1-65.
9. Jairam KT, Monteagudo FSE, Moch SL, Havlik I. Malaria at Johannesburg Hospital. *S Afr Med J* 1990; **78:** 467-469.
10. Eales L. Imported malaria in Cape Town: a life-threatening hazard. *S Afr Med J* 1972; **46:** 2053-2061.
11. Field JW. Blood examination and prognosis in acute falciparum malaria. *Trans R Soc Trop Med Hyg* 1949; **43:** 33-48.
12. Basset MT, Taylor P, Bvirakare J, Chiteka F, Govere E. Clinical diagnosis of malaria: can we improve? *J Trop Med Hyg* 1991; **94:** 65-69.
13. Stein CM, Gelfand M. The clinical features and laboratory findings in acute *Plasmodium falciparum* malaria in Harare, Zimbabwe. *Cent Afr J Med* 1985; **31:** 166-170.
14. Schmitz B, Gelfand M. A study of the clinical features of malaria in Rhodesia. *Cent Afr J Med* 1976; **22:** 83-88.
15. Mkawagile DSM, Kihamia CM. Relationship between clinical diagnosis of malaria and parasitaemia in adult patients attending Mwananyamala Dispensary, Dar-es-Salaam. *Cent Afr J Med* 1986; **32:** 2-5.
16. Goldstein E. A clinical study of falciparum and vivax malaria in Vietnam servicemen. *Milit Med* 1968; **133:** 991-996.
17. Schutte CHJ, Van Deventer JMG, Lamprecht T. A cross-sectional study on the prevalence and intensity of infection with *Schistosoma haematobium* in students of northern KwaZulu. *Am J Trop Med Hyg* 1981; **30:** 364-372.
18. Olweny CLM, Simooya OO, Boatin B, Syabula CS, Ngoma N, Njelesani EK. Preliminary investigation of the relationship between malaria, anaemia, parasite density, malaria specific antibody and syphilis reactivity in Ndola Central Hospital, Zambia. *Cent Afr J Med* 1985; **31:** 197-203.
19. Reiley CG, Barrett O'Neill. Leucocyte response in acute malaria. *Am J Med Sci* 1971; **262:** 153-158.