Initial treatment of severe malaria in children is inadequate – a study from a referral hospital in Cameroon

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Background. Severe malaria, caused by *Plasmodium falciparum*, is potentially fatal, with a case mortality rate of 15 - 20%, despite treatment.

Aim. To document epidemiological and clinical features, including initial treatment, of severe malaria in children referred to a general paediatric unit in Cameroon.

Methods. A prospective cross-sectional study investigating characteristics of children admitted for severe malaria, confirmed with a positive thick blood smear.

Results. A total of 309 (29.2%) children were identified out of 1 060 admissions, of whom 52% were males and 48% females, and mean age 46.3 (1 - 180) months. Most children were aged <3 years; 43% were 1 - 3 years. The mean duration of symptoms before admission was 3.9 days (range: 1 - 30 days). Hyperpyrexia, severe anaemia and convulsions were the main clinical features in 37%, 32% and 25% cases respectively. In 60% of the subjects, some form of treatment had been administered at home, and 33% had consulted a primary health facility. In 85% of the malaria-infected children, quinine, artemisinin-based combination therapies (ACTs) and amodiaquine were respectively administered to 32%, 30% and 23% of the children. In ACTs-treated patients, 49% received inadequate doses; drugs used in their order of frequency were artemether + lumefantrine (76%), artesunate + amodiaquine (18%), and artesunate + mefloquine (6%). Only 16% of the mothers said they had used insecticide-treated bed nets (ITNs).

Conclusion. In most cases, there is a delay before consultation, with most children initially self-medicated at home. Initial consultations are at primary local health facilities where less effective drugs are prescribed at inadequate dosages. Recommended ACTs were also often prescribed at inadequate dosages. Education in the use of ITNs, home treatment of simple malaria, and appropriate use of ACTs should be promoted.

According to the World Health Organization (WHO), 40% of the world's population, in 100 countries, are exposed to varying degrees of malaria risk[1] – a significant cause of death and illness in children and adults in the tropics. Mortality (currently estimated at >1 million people per year) has risen in recent years, probably owing to increasing resistance to antimalarials.[2] The annual clinical case load may be well over 500 million, with between 1 and 3 million deaths, mainly among young children.[3]

The WHO states that malaria control requires an integrated approach comprising vector control and treatment with effective antimalarials.[2] In Cameroon, hospital statistics reveal that 35 - 45% of deaths are from the severe forms of malaria, with children <5 years and pregnant women carrying the greatest burden.[4] We aimed to document epidemiological and clinical features (including initial treatment) of malaria in patients presenting to our health care facility.

Patients and methods

Ours was a prospective cross-sectional study of all children admitted to the general paediatric unit of the Yaounde Gynaeco-Obstetric and Paediatric Hospital from 1 March to 30 September 2007. The patients included in the study were those in whom the diagnosis of severe malaria was confirmed after a complete physical examination, positive parasitaemia and other diagnoses excluded on admission and during the period of hospitalisation. The criteria of severity were those defined by the WHO.[5] A full blood count and a thick blood film were systematically done on admission. The thick blood smears were Giemsa-stained, and parasitaemia was expressed as number of parasites per microlitre (μl) of peripheral blood.

All patients with incomplete information and children <1 month old were excluded from the study. Data were analysed using Epi-info version 6 software.

Results

A total of 1 060 children were admitted to the unit, of whom 309 (29.2%) fulfilled the study inclusion criteria; 161 were boys and 148 girls. The mean age was 3.6 years (range 1 month - 15 years); 82% of affected children were <5 years old (range 1 - 60 months), of whom the largest number (72.8%) were <3 years (Figs 1 and 2). The three most frequent criteria of severity were hyperpyrexia, severe anaemia and convulsions (Fig. 3).

Home self-medication had been administered to 59.8%; about a third had received treatment from a primary health centre or another hospital; and only a minority (7%) had received no treatment (Fig. 4). Some form of malaria treatment had been taken by 51% of patients, and none by 45%. The three most consumed antimalarials were quinine (32%), artemisinin-based combination therapy (ACT) (29.6%) and amodiaquine (23%) (Fig. 5). In the majority (122, 72%) of the 170 patients who received antimalarial treatment, the doses were adequate. Among the 50 children who received ACTs, 38 (76%) had artemether + lumefantrine, 9 (18%) artesunate + amodiaquine, and 3 (6%) artesunate + mefloquine, with adequate doses in only 51% of the patients.
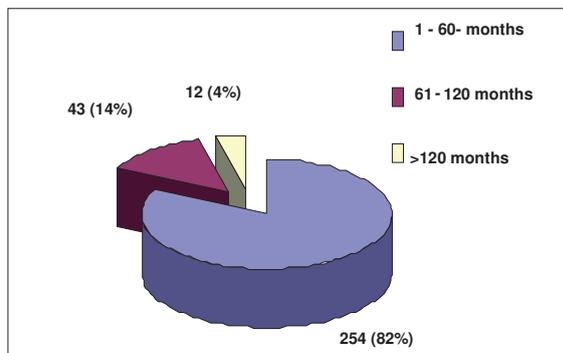

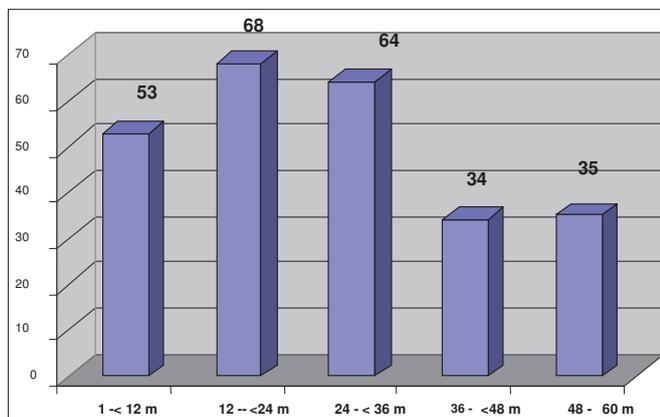*Fig. 1. Distribution according to age groups.*

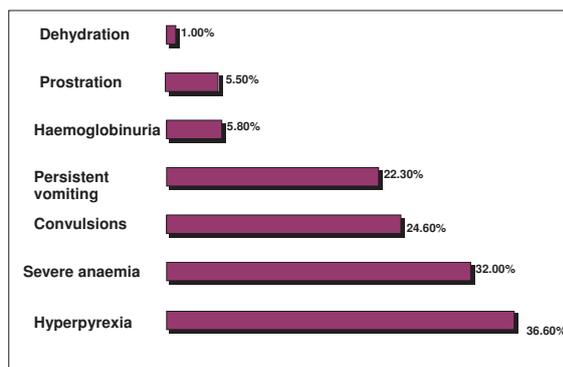*Fig. 2. Distribution of patients less than 5 years old.*

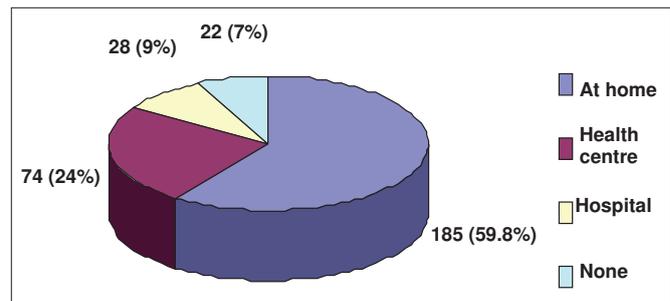*Fig. 3. Distribution of criteria of severity.*
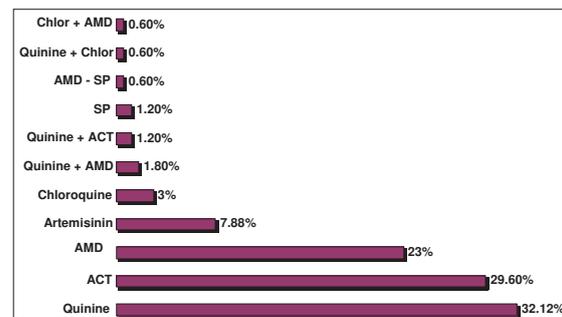

Fig. 4. Place of management before admission.

Fig. 5. Antimalarial drugs taken before admission (ACT = artemisinin-based combination therapy; AMD = amodiaquine; SP = sulfadoxine-pyrimethamine; Chlor = chloroquine).

Other drugs taken apart from antimalarials were antipyretics (84%), iron preparations (8.7%), antibiotics (6.5%), anticonvulsants (4.3%), de-worming compounds (4.3%), local concoctions (4.3%), anti-emetics (2.2%) and other mixtures (2.2%).

Only 49 (16%) of the mothers admitted had used and were using insecticide-treated bed nets (ITNs). Most patients (301, 97.4%) were completely cured and left the hospital well, 4 (1.3%) patients absconded, 2 (0.6%) died and 2 (0.6%) requested discharge because of financial constraints. Two patients died from severe anaemia despite repeated blood transfusions.

Discussion

The prevalence of severe malaria at 29.2% in our study is higher than frequencies reported by Tchokoteu *et al*.[6] (9.4% – Yaounde General Hospital), Chiabi *et al*.[7] (18.4% – Bertoua Provincial Hospital) and Zeidan *et al*.[8] (21% – Sudan). Our higher rate could be because of a higher index of suspicion of attending doctors, which is a direct result of the several training sessions on the appropriate use of the criteria of severity adopted by The Cameroon's Ministry of Public Health. It could also be that the study was carried out during a period of high transmission with heavy rains, as indicated by Chiabi *et al*.[7] Most patients were <5 years old, with a mean age of 3.6 years. This trend was also observed by other studies[6-11] and is consistent with the WHO's suggestion that, in parts of the world where endemicity of falciparum malaria is stable, severe malaria is mainly a disease of children from the first few months of life to the age of 5 years, because of acquisition of partial immunity.[5]

Hyperpyrexia, severe anaemia and convulsions were the three most frequent criteria of severity. Hyperpyrexia was also the most frequent symptom in other studies, e.g. at 36%[6] and 42.2%[10] in the Philippines. However, the most frequent symptoms differed in other studies.[12-14]

We used the WHO definition of hyperparasitaemia, which is defined as parasite density $\geq$200 000/μl.[15] We found a mean parasite density of 3 050/μl (range 50 - 39 500) of trophozoites of *Plasmodium falciparum*. The criteria of severity adopted by Cameroon[16] were modified from the previous[5] and most recent

WHO criteria of severity[2] and are designed for public health purposes. The appropriateness of any definition of severity varies with the use to which it is to be put, the facilities available and the clinical spectrum of disease in any given environment. Therefore, a definition that seeks to measure the clinical load on a health service needs to be broad and inclusive.[5]

In our study, the mean lapse between onset of symptoms and admission in our hospital was 3.9 days (range 1 - 30 days). This long duration in seeking appropriate treatment has also been observed in other studies.[8,17,18] Of our patients 59.8% had had some form of home treatment; this figure was similar to the 57.5% observed in one study[11] but high compared with those from other studies, of 9%[18] and 13.3%.[19] A possible explanation could be a high rate of self-medication with drugs from roadside vendors and over-the-counter sales from pharmacies.

Of the other drugs administered, antipyretics (especially paracetamol) were given to 84% of the children. These findings are consistent with observations from the last 2004 Demographic Health Survey in Cameroon.[4] Of the antimalarials taken before admission, quinine was the most frequently administered. However, adequate doses of all the antimalarials were administered in only 28% of the patients. ACTs comprising artesunate + amodiaquine and artemether + lumefantrine have been adopted in Cameroon to replace monotherapy since 2004 for the treatment of uncomplicated malaria. The fact that monotherapy was still most frequently prescribed suggests a need for public health education in our population. Among the 29.6% of children who received ACTs, the dose was adequate in only 51% of cases.

Other studies reported the most frequently used drug for the home treatment of malaria to be chloroquine (78.6% in Togo, with doses adequate in only 38.1% of cases),[20] chloroquine/quinine (41.8%, also in Togo),[21] sulfadoxine-pyrimethamine (13% in Tanzania),[22] chloroquine (37% in Uganda[23] and 85.6% in Sudan[19]) and chloroquine (17.5% in Ibadan).[17]

Only 16% of our patients' caregivers said they had mosquito nets. In the Cameroon's 2004 Demographic Health Survey,[4] 20.2% of the population had bed nets of which only 2% were insecticide-treated. Use of bed nets is low, according to many African studies, with a range of 5 - 61% of which less than 20% were insecticide-treated.[18,20-24] The high proportion of good outcomes in our patients, with only a few deaths, is similar to that reported in other hospital studies (no deaths in Yaounde;[6] 3.8% in Bertoua).[7] However, the overall outcome would probably have been different if the treatment started prior to admission had not been appropriately adjusted.

Conclusions

In our setting, severe malaria affects mostly children less than 5 years old, especially those of 1 - 3 years. Delays before consultation are the norm, with most children initially self-medicated at home. At primary health facilities, inappropriate drugs were prescribed at inadequate doses, and even the recommended ACTs, when used, were given at inadequate doses. In addition, ITNs were routinely not used.

We recommend improved education of public and primary care clinicians by the National Committee – Roll Back Malaria, particularly in the use of ITNs, home treatment of simple malaria and correct use of ACTs. Community-integrated management of childhood illness (C-IMCI) should be encouraged to reinforce home prevention and treatment and community involvement in the management of simple malaria.

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