Hospital-based study of severe malaria and associated deaths in Myanmar

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The present study identifies factors that contribute to malaria deaths in township hospitals reporting large numbers of such deaths in Myanmar. Between July and December 1995, we identified a total of 101 patients with severe and complicated malaria by screening the cases admitted to hospital with a primary diagnosis of falciparum malaria. Unrousable coma and less marked impairment of consciousness with or without other severe malaria complications, in contrast to severe malaria anaemia, were associated with all malaria deaths. Adult patients with severe malaria were 2.8 times more likely to die than child patients, with the higher risk of death among adults probably being associated with previous exposure to malaria, delay in seeking treatment and severity of the illness before admission. In view of this, we consider that malaria mortality could be reduced by improving peripheral facilities for the management of severe malaria and providing appropriate education to communities, without stepping up vector control activities.

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Introduction

Malaria is a major public health problem in the WHO South-East Asia Region, where an estimated 23 million new cases occur annually. The disease is thought to cause 34 000 deaths each year in the region (*1*) and in Myanmar is a threat to about 60% of the population. In 1994 about 800 000 clinical cases of malaria and 4377 deaths from the disease were reported in Myanmar. However, estimates of the number of malaria cases and deaths in Myanmar were much higher and amounted to 3 475 085 and 6565, respectively, in 1994. At present, after several years of relative improvement, severity and mortality rates of malaria are increasing in the country.

Information on malaria as a clinicoepidemiological phenomenon is limited (*2, 3*). It raises a number of methodological issues such as definition, detection and monitoring of severe malaria, association of severity and deaths with risk factors and assessment of malaria mortality (*4*). Therefore, there is an urgent need for reliable clinicoepidemiological information on malaria as a life-threatening disease to understand better the underlying causes of its severity and related deaths, for policy-making, planning, monitoring and evaluation of disease-specific interventions.

The present study was carried out to identify factors that may contribute to malaria deaths so that guidelines can be set up to monitor and control the severe forms of the disease in Myanmar.

Materials and methods

Study area

The study was carried out in Myanmar in the following township hospitals, which reported large numbers of malaria deaths: Kalay, Tamu, Kawlin, Katha and Kalewa townships of Sagaing division; Yegyi township of Ayeyarwady division and Taunggyi, Yauksauk, Thibaw, Kyaukme, Lashio, Momeik townships of Shan state.

The study area is characterized by endemic and seasonal forest-related malaria, with *Anopheles minimus* and *A. dirus* being the principal vectors. The most prevalent parasite species, *Plasmodium falciparum*, which is resistant to chloroquine, sulfadoxine–pyrimethamine and mefloquine, also occurs in this area. The published malaria mortality and morbidity rates were in the range 19.03–45.84 per 100 000 population and 12.52–63.78 per 1000 population, respectively, in this area in 1994.

Hospital-based surveillance for severe and complicated malaria cases

Between July and December 1995, a total of 959 malaria cases (653 adults and 306 children) were admitted to the selected township hospitals in Sagaing, Ayeyarwady and Shan divisions/state. The majority of hospital malaria admissions were straightforward cases, admitted for social rather than medical reasons. Most of the severe and complicated malaria cases within the study area were admitted to township hospitals. A total of 101 severe malaria patients with impaired consciousness and severe

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anaemia were identified by screening the admissions to inpatient departments. The patient's name, date of admission, age, sex, address, occupation, history of illness before admission, antecedents regarding malaria exposure/protection, clinical features on first medical examination, initial laboratory findings, parasitological examination during hospitalization, provisional/final diagnosis and outcome were recorded on a standard form. Blood samples were taken for the detection of malaria parasites and determination of haemoglobin level. Thick blood smears were Giemsa-stained. The number of parasites per 200 leukocytes was multiplied by 40 to give a quantitative count per μl.

Local residents with a primary diagnosis of falciparum malaria were included in the study. All malaria cases with impaired consciousness and severe anaemia (*5*, *6*), as the subgroups of patients with severe and complicated malaria reported within the study area, were subdivided into two groups as follows:

- Group 1(a): Patients with impaired consciousness: Glasgow coma score >9/15), with or without other severe malaria complications such as circulatory collapse and shock, spontaneous bleeding, renal failure.
  Group 1(b): Patients with cerebral malaria, i.e. unrousable coma (Glasgow coma score <9/15), with or without other severe malaria complications such as pulmonary oedema, circulatory collapse and shock, and fluid, electrolyte and acid-base disturbances.
- Group 2. Patients with severe anaemia (normocytic anaemia with haemoglobin <5 g/dl) in the presence of parasitaemia >10 000 per μl, and no other severe manifestations and complications.

Statistical analysis

Data were analysed using the statistical software Epi Info 6. Proportions were compared using χ^2 tests. The rate ratios (*RR*), Taylor series 95% confidence limits for *RR* (RR_U and RR_L), and population attributable risk were also calculated (*7*).

Results

A total of 101 patients with severe falciparum malaria were included in the study (Table 1): 93 patients (92%) with impaired consciousness and other severe manifestations (Group 1) and 8 patients (8%) with severe anaemia (Group 2). The majority of patients in Group 1 were adults, while Group 2 consisted only of children (Fig. 1). There was a predominance of males among patients in Group 1 and females among patients in Group 2. All malaria deaths were reported among patients in Group 1. The proportion of deaths was higher among patients with cerebral malaria in Group 1(b) (26.0%) than among patients in Group 1(a) (18.6%). A total of 12 patients died (57% of all malaria deaths) within the first 24 hours of admission (Table 2).

Only children below 9 years of age developed severe malaria anaemia. Before and when they were admitted, cases with severe anaemia did not exhibit the typical manifestations of severe malaria such as impaired consciousness and convulsions. High fever with or without chills, rigors, profuse sweating and headache were the main symptoms of these patients. Most had palpable spleen on normal breathing.

The mean age of patients with severe malaria-related anaemia was 6.3 years, while the mean age of patients in Group 1 was 21.2 years. The mean haemoglobin level was 7.4 g/dl and 4.5 g/dl, respectively, among patients in Groups 1 and 2.

Risk groups

Rate ratios were used to compare malaria mortality among children and adults in Group 1. Comparison of numbers of severe cases and deaths indicates that adults were 2.8 times more likely to die from malaria than children, with the differences being statistically significant ($RR = 2.81$; $RR_L = 1.03$; $RR_U = 4.44$; $P<0.05$). It seems reasonable to assume that 52.1% of the malaria mortality involving the adult population was associated with factors that had no influence on the children (population attributable fraction = 52.1%).

Furthermore, among the adults, female patients were 1.14 times more likely to die from malaria than male patients, but the differences were not statistically significant ($RR = 1.14$; $RR_L = 0.90$; $RR_U = 1.44$; $P>0.10$).

Risk factors

Attempts to identify the risk factors leading to death among children and adults in Group 1 showed that there were no statistically significant differences

Table 1. **Characteristics of study patients with severe falciparum malaria**

	Patients with impaired consciousness (Group 1)		Patients with severe anaemia (Group 2)
	Rousable and other complications (Group 1(a))	Unrousable and other complications (Group 1(b))	
No. of severe cases	43	50	8
No. of deaths	8	13	0

Fig. 1. **Age distribution of severe falciparum malaria: patients with impaired consciousness and other severe complications (series 1) and severe anaemia (series 2)**

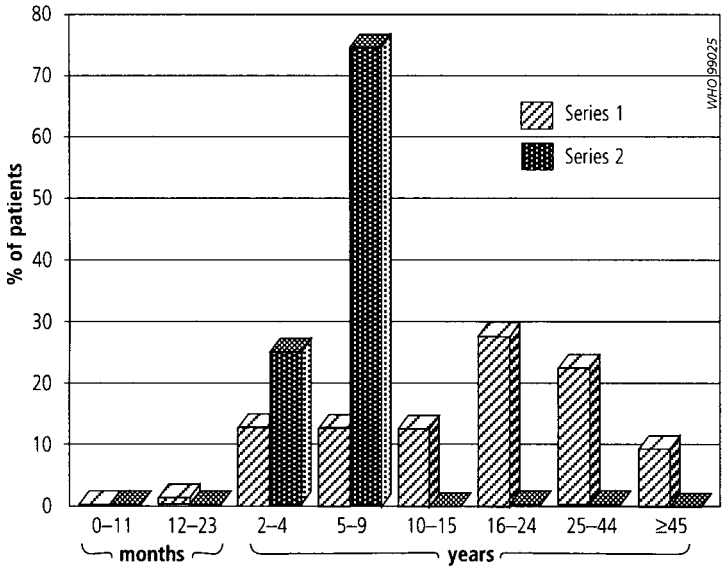
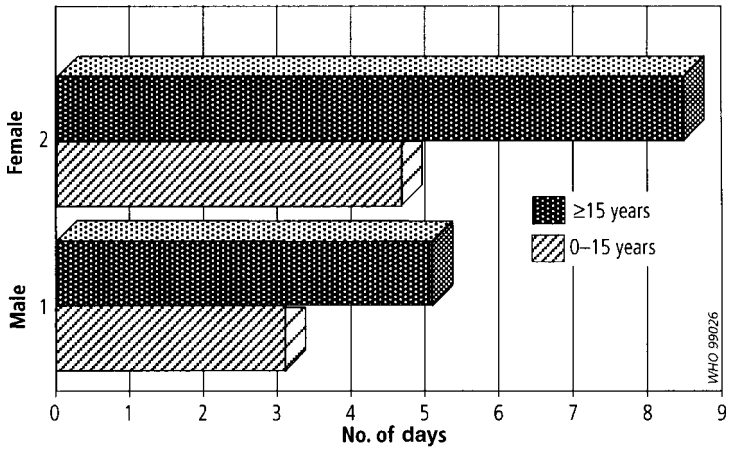


Table 2. **Occurrence of malaria deaths after admission among study patients**

	Time (hours)		
	<24	24–72	>72
No. of malaria deaths	12	5	4
% of total deaths	57	24	19

Fig. 2. **Mean duration of illness before admission among study patients with impaired consciousness and other severe malaria manifestations, by age and sex**



between them in terms of number of medical consultations, antimalaria treatment, number of malaria attacks before admission, previous hospitalization for malaria, use of bednets at and while away from home, as well as in manifestations of malaria on admission and antimalaria treatment during hospitalization (χ^2 test = 0.77-6.85; P>0.10).

In contrast, comparison of the mean duration of malaria before admission between males and females in different age groups indicates that the proportion of deaths increased with the duration of illness (χ^2 test =5.97;P<0.050). The highest proportion of deaths (38.9%) and the longest mean duration of illness (8.46 days) occurred among patients aged >15 years, while the lowest proportion of deaths (6.7%) and the shortest mean duration of illness (3.13 days) occurred in males aged <15 years (Fig. 2).

Significant differences also existed between children and adults in Group 1 in terms of the malaria manifestations exhibited before admission (χ^2 test = 17.86; P<0.05) and history of previous travel into malaria-risk areas (χ^2 test = 27.09; P<0.01).

Before admission, the typical manifestations of severe malaria, such as high fever, chills, rigors, profuse sweating, headache, drowsiness, impaired consciousness (semiconsciousness or/and unconsciousness) and convulsions were generally seen in adult patients, particularly females, while in children they were less common.

The proportion of patients who had previously travelled into malaria-risk areas was much higher in adult patients, particularly males. It was uncommon for children to travel from their place of residence (Fig. 3).

The mean duration of illness before admission among those who died from severe malaria was significantly longer than that among those who recovered, less than 1% level of significance (P = 0.0087). Differences in previous travel into malaria-risk areas between patients who died and recovered were also significant (χ^2 test = 4.53; P<0.05).

Discussion

The results of the study show that impaired consciousness (rousable or unrousable coma) with or without other severe malaria complications, in contrast to severe malaria anaemia, was associated with all deaths within the study area.

Cerebral malaria was one of the major causes of death (mortality rate = 26%) among patients with severe falciparum malaria. Most deaths occurred within the first 24 hours of admission. Similar findings have been presented by White & Krishna (*8*).

Significant differences were found in malaria mortality between adult and child patients with impaired consciousness and other severe malaria complications. It was estimated that adult patients were 2.8 times more likely to die from malaria than child patients and that 52.1% of malaria mortality among the adult population was probably associated with factors exerting no influence on the child population. These factors may be due to the differences in travel to malaria-risk areas (previous exposure) and in mean duration and manifestations of malaria illness before admission (delay in seeking treatment and severity of disease). Therefore, previous exposure to malaria, a long delay in seeking

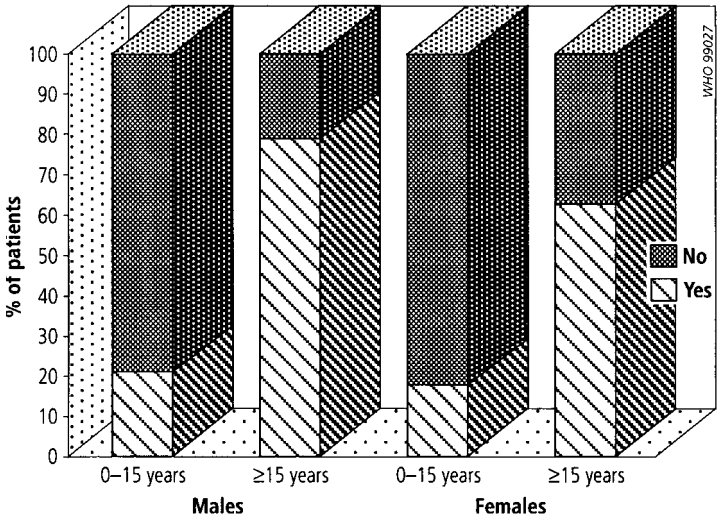
antimalaria treatment, and a high proportion of severe malaria manifestations among adult patients before admission can be considered as contributory factors to malaria deaths.

Adult females with severe malaria had a higher risk of dying than adult males, with delay in seeking treatment rather than previous exposure to malaria being a major contributory factor to the number of deaths among these women. Because of the relative rarity of deaths among severe cases of malaria, more data are needed to provide a better estimate of the role of suspected risk factors.

Determination of the reasons why adults died from malaria more frequently than children is of practical importance. If sociobehavioural factors are the most important determinant of such deaths, it may be possible to reduce malaria mortality significantly by improving peripheral diagnostic and treatment facilities for the management of the severe and complicated cases, and by providing appropriate health education, even before introduction of vector control methods to reduce malaria-related morbidity (*9*).

Considering the delay in seeking treatment and previous exposure to malaria as sociobehavioural factors leading to death from malaria, we expect malaria mortality in Myanmar can be reduced through increasing the awareness and participation of communities in malaria control. In addition, upgraded peripheral health facilities for early recognition and urgent treatment of severe malaria could play an important role in reducing such deaths. The need for urgent treatment is justified by the fact that some patients in our study died only 48 hours after the clinical features of severe malaria were first noted. ■

Fig 3. **History of travel into malaria-risk areas among study patients with impaired consciousness and other severe malaria manifestations before admission, by age and sex**



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Résumé

Etude hospitalière du paludisme grave et de la mortalité associée au Myanmar

Le paludisme demeure une cause majeure de décès et de morbidité grave au Myanmar. L'objet de la présente étude était de recenser les facteurs susceptibles de contribuer à ces décès dans les hôpitaux des petites localités signalant un nombre important de décès dus au paludisme au Myanmar.

Les résultats montrent que tous les décès relevés dans la zone étudiée étaient associés à une perte de conscience (coma plus ou moins profond) avec ou sans autres complications du paludisme grave. Le paludisme cérébral était l'une des principales causes de décès chez les malades atteints de paludisme grave à falciparum. La plupart des décès survenaient dans les 24 heures suivant l'admission à l'hôpital.

Les malades adultes étaient 2,8 fois plus susceptibles de mourir du paludisme que les enfants atteints de paludisme grave et, dans 52,1% des cas, la mortalité paludéenne dans la population adulte était probablement associée à des facteurs sans influence sur les enfants. Ces facteurs pouvaient inclure un voyage effectué dans une zone impaludée (exposition antérieure) ainsi que la durée moyenne (fait de tarder à solliciter des soins) et les manifestations du paludisme (gravité de la maladie) avant l'admission à l'hôpital. Les femmes adultes atteintes de paludisme grave risquaient plus d'en mourir que les hommes adultes. Le fait de tarder à solliciter des soins, plus qu'une exposition antérieure, était un important facteur de mortalité chez les femmes adultes. Etant donné la rareté relative des décès parmi les cas graves, des données plus nombreuses seront nécessaires pour mieux apprécier le rôle des facteurs de risque soupçonnés.

En considérant le fait de tarder à solliciter des soins et une exposition antérieure au paludisme comme des facteurs sociocomportementaux ayant contribué aux décès, nous pensons que la mortalité paludéenne au Myanmar pourrait être réduite grâce à une éducation sanitaire appropriée et l'amélioration des services diagnostiques et curatifs périphériques pour la prise en charge du paludisme grave et compliqué, même avant l'adoption de méthodes de lutte antivectorielle.

Resumen

Estudio hospitalario sobre el paludismo grave y la mortalidad asociada en Myanmar

El paludismo sigue siendo una importante causa de defunción y enfermedad grave en Myanmar. El objetivo del presente estudio consistió en identificar factores que pudieran contribuir a esas defunciones en los hospitales comarcales del país que notifican un elevado número de muertes por paludismo.

Los resultados muestran que la pérdida de conciencia (coma reversible o irreversible) con o sin complicaciones graves, a diferencia de lo que ocurre con la anemia palúdica grave, está presente en todas las defunciones registradas en la zona estudiada. El paludismo cerebral era una de las principales causas de muerte entre los pacientes aquejados de paludismo falciparum grave. La mayoría de las defunciones se produjeron durante las 24 horas siguientes al ingreso en el hospital.

Entre los pacientes con paludismo grave, el riesgo de defunción por esa causa era 2,8 veces mayor en los adultos que en los niños, y el 52,1% de la mortalidad por paludismo en la población adulta se asociaba probablemente a factores que no tenían ninguna influencia en los niños. Entre dichos factores cabe citar las diferencias relacionadas con los viajes a zonas con riesgo de paludismo (exposición previa) y la duración media (tardanza en buscar tratamiento) y las manifestaciones de la enfermedad (nivel de gravedad) antes del ingreso hospitalario. Las mujeres adultas con paludismo grave presentaban un mayor riesgo de defunción por esa causa que los varones adultos. Un factor contribuyente importante en las defunciones registradas entre las mujeres adultas fue la demora en la búsqueda de tratamiento, más que la exposición previa al paludismo. Dado que el número de defunciones registradas entre los casos graves es relativamente bajo, se necesitan nuevos datos para poder estimar con más precisión la influencia de presuntos factores de riesgo.

Considerando la demora en la búsqueda de tratamiento y la exposición previa al paludismo como factores sociocomportamentales que contribuyeron a las defunciones, esperamos conseguir una disminución de la mortalidad por paludismo en Myanmar mediante una educación sanitaria apropiada y mediante el mejoramiento de los servicios periféricos de diagnóstico y tratamiento que manejan casos de paludismo grave y complicado, antes incluso de aplicar métodos de lucha antivectorial.

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