ORIGINAL ARTICLES

Study to Document Pre Admission Risk Factors for Development of Severe Malaria and the Spectrum of It and Outcome in Different Categories of Hospitals in Malaria Endemic Zone of Bangladesh

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Summary :

As per inclusion and exclusion criteria based on World Health Organization formulated case definitions 1303 cases were screened. Out of these 909 severe malaria cases were selected at 3 different categories of hospitals of Chittagong zone. Hospitals were one Tertiary Health Care, 2 Secondary Health Care and 4 Primary Health Care providers which were, Chittagong Medical College Hospital, District General Hospitals and Thana Health Complex Hospitals respectively. The study area is the most malaria endemic zone of Bangladesh at the south-eastern part of the country. In this zone a National Malaria Control Program based on WHO sponsored country specific `Early Diagnosis Prompt Treatment' strategy has been in operation since 1994. In view of the high mortality and morbidity in presence of good care providing network and availability of effective drugs, this study envisaged documenting some preadmission factors in order to describe and if possible relate their influence on the outcome of SM cases. Moreover it tried to document the pattern and outcome of severe malaria cases at different tiers of hospitals. It was done over a period of 6 months in 1996 covering peak and off-peak seasons of malaria transmission. Data collector, who were designated Medical Officers of respective centers, were trained through workshop on the study, protocol, definitions, diagnosis, management and documentation. It was found that males in their 3rd decades were most frequent, significant numbers of pregnant cases, delays in initiating appropriate treatment, failure to recognize and prior use of first line antimalarials and significant mortality. The clinical patterns were different amongst different categories of hospitals, with severe ones were more at tertiary health care center with highest fatality, but as a whole all patterns are more frequent at secondary health care facility.

We conclude that more awareness and orientation training are needed both for the community and the professionals working in the endemic zone to ensure early diagnosis and prompt treatment. Secondary Health Care Hospitals should be more equipped for handling severe malaria cases and Chittagong Medical College Hospital should be made as a center of excellence for the same as it is the only tertiary health care provider at the perimeter of the malaria endemic zone of Bangladesh. Malaria issue should be incorporated in national MCH program. Further studies are needed including those directed to KAP.

Introduction

Mortality from malaria is often due to severe and complicated form. The World Health Organisation (WHO) had a target to reduce the malaria specific mortality by at least 25% by the year 2000 and 50% by 2010 by application of new strategy for control of malaria. Mortality due to malaria[1] remained high (around 25%) among severe malaria (SM) cases in Chittagong Medical College Hospital (CMCH), which is the only tertiary health care setup at the perimeter of most malarious zone of Bangladesh, Chittagong[2]. Till recently quinine resistance has not been documented in the malaria-affected areas of the country. Even then the mortality is found to be quite high in comparison to other malaria-affected countries. It is conceivable that there are some risk factors operating at the community and the sojourn till attendance at the appropriate facilities. SM is a medical emergency demanding immediate management and, appropriate care can only be provided at hospital setting, the lowest tier is the primary health care (PHC) one. Most of the patients of cerebral malaria admitted in CMCH have been found to have fever for about a week before hospitalisation and about 85% patients after a period of unconsciousness for more than 24 hours[3]. On the other hand there are some subtle SM criteria which can easily be overlooked like 'prostration' if one is not used to these. Obviously these factors influence the outcome even after appropriate treatment. Therefore it is imperative to describe the similar risk factors as far as possible to identify the modifiable aspects, which can be picked up by the national control program for prudent intervention.

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Aims of the study

This study has been done to describe various risk factors for the development of SM prior to admission in hospital and, to document the clinical patterns of SM at different categories of hospitals in Bangladesh.

Experimental Design and Methods :

All cases of SM admitted were documented in a Tertiary Referral Hospital, Chittagong Medical College Hospital (Tertiary Health Center - THC); two Secondary Health Care Facilities, Khagrachari and Bandarban District Hospitals (Secondary Health Center - SHC); and, 4 Primary Health Centers: Ramu, Teknaf, Matiranga and Fatikchari Thana Health Complex Hospitals (Primary Health Center - PHC); in high risk endemic area of Bangladesh, the southern and eastern part of the country. The period of study was six months from May to October 1998, which included pre-monsoon and post-monsoon. Diagnosis and management of SM were based on WHO guidelines customized in the 'National Guidelines for Clinical Management of Malaria[1]. An intensive care with minimum facilities required for nursing care, clinical monitoring, laboratory service and follow-up was established within the existing setups of CMCH and other study site hospitals. Ethical clearance was taken from the Ethical Review committee of CMC&H. Written informed consent was taken from the responsible person of each patient after elaborating the purpose of the study, the procedures and the implications. Attending doctors recorded base line data from tile patients on admission to hospital and ensured 12 hourly follow-up subsequently. For diagnosis of malaria thick and thin blood films were done for every patient. Depending on availability of blood glucose monitoring, renal and hepatic function assessment, chest x-ray, ECG and CSF study (in cerebral malaria cases only) were also done as indicated. The story preceding hospital admission was noted from tile accompanying person or patient (when able to communicate reliably) in a pre-designed proforma. A five day-long training course was arranged for twenty Medical Officers selected from all the participating hospitals to document the cases and manage them uniformly. All patients of SM were treated with parenteral quinine to be followed by oral formulation of the same as depicted by the national guidelines. Data were double entered and analysed utilizing EPINFO 6 software to determine the risk factors related to the development of SM. The different parameters of SM were compared in respect of different levels of care.

Results

Out of total screened 1308 cases, 909 fulfilled the selection criteria and enrolled for the study of which 58 patients died. Of these 339 (37.4%) cases admitted at PHCs, 382 (42.0%) at SHCs and 188 (20.6%) at THC. The male female ratio was 1.9 and mean age was 21.4 (± 14.4 SD, 95% CI 20.5 - 22.3) and maximum was 95, minimum 0.2 years with median value of 20 and mode 25. Of the female patients 39 (12.7.5.) cases were pregnant. 47.7% of cases had some form of antimalarials prior to admission within previous 2 weeks with a mean period of 2.4 (± 2.7) days. The case fatality rate was 6.4% and recovery without sequele 82.2%. But 1.4% cases recovered with some form of sequele. The outcomes of the other cases (N=91, 10%,) were not known because they left hospital before attaining the outcome.

Table – I

Description: Patient Profile of SM cases N=909	
Particulars	Total 909 (100%), PHCs 339 (37.4%), SHCs 382 (42.0%), THCs 188 (20.6%)
Sex: Male N (%)	601(66%)
Male female ratio	1.9
Pregnancy N.('%)	39(12.7%)
Mean Age (SD, 95% CI), Maximum, Minimum, Median and Mode	21.4 (14.4, 20.5-22.3) 95 0.2 20.0 25.0
Within 2wks AM usage N (%)	434(47.7%)
Period of prior AM usage Days (SD)	2.4 (2.7)
Case fatality	58(6.4%)
Recovery without sequele	747(82.2%)
Recovery with sequele	13(1.4%)

AM=Antimalarials, PHC=Primary Health Center, SHC=Secondary Health Center, THC=Tertiary Health Center

On admission-duration of illness, severe symptoms, inability to eat/drink (NPO: Non Per Os) and prostration were longest at the THC, and most of them were lowest at SHCs. The travel time was lowest at SHCs followed by THC and longest at the PHCs. The hospital stay was longest at THC followed by SHCs. These durations saving NPO were significantly different between different categories of hospitals.

All patterns of presentation of SM were found in cases at district hospitals (SHCs). Amongst the types as predominant presentation severe prostration ranked the top followed by hypoglycemia, unarousable coma. convulsion, severe anemia, impaired consciousness, hyperpyrexia and hyperparasitemia. Some cases of hemoglobinuria, jaundice, abnormal behavior, pulmonary edema, acute renal failure, shock, DIC/bleedings and acidosis were also encountered. Many of the cases had more than one type (7S.4%). Severe types of SM predomiently unarousable coma were more in tertiary care hospital (THC).

Table-II

Description: Different parameters with respect to different durations at different categories of hospitals

Particulars	Total N=909	PHC N=339	SHC N=382	THC N=188	P
Duration: Illness Days (SD)	6.2 (5.5)	5.7(3.4)	5.0 (3.9)	9.7 (8.9)	< 0.001
Duration: Severe symptoms Hours (SD)	41.3 (51.3)	37(48)	37(33)	59(78)	< 0.001
Duration: NPO Hours (SD) N	35(60) 293	26(21)49	31 (53) 102	41 (72) 142	> 0.1
Duration: Impaired Consciousness hours (SD) N	30.7 (54.8) 317	14 (14) 35	24(27) 142	42(78) 126	< 0.01
Duration: Prostration hours (SD) N	37(39) 448	34(39) 309	32(28) 58	70(57)81	< 0.001
Travel time: To reach hospital hours (SD) N	2(3.2)	3.2 (4.4)	1.0 (1.9)	1.9 (2.1)	< 0.00 l
Duration: Hospital stay Hours (SD)	107(76)	81 (43)	110(54)	147 (12G)	< 0.001

PHC=Primary Health Center, SHC=Secondary Health Center, THC=Tertiary Health Center

Table-III

Predominant Presentations of patients of SM by categories of hospitals

Presentations	Total = 909	PHC=339*	SHC=382*	THC=188*	P*
Severe prostration N(%)	379 (41.7)	248 (73.2)	101 (26.4)	30(16.0)	< 0.001
Hypoglycemia N(%)	135 (14.9)	9(2.7)	123 (32.2)	3 (1.6)	< 0.001
Unarousable coma N (%)	115 (12.7)	7 (2.1)	17(4.5)	91 (48.4)	< 0.001
Convulsion N(%)	99 (10.9)	23 (6.8)	54 (14.1)	22(11.7)	< 0.05
Severe anemia N(%)	53 (5.8)	10(2.9)	27(7.1)	16(8.5)	< 0.05
Impaired consciousness N(%)	44(4.8)	20(5.9)	16(4.2)	8(4.3)	NS
Hype pyrexia N(%)	39(4.3)	15 (4.4)	18(4.7)	6(3.2)	< 0.05
Hyperarasitemia N(%)	14(1.5)	4(1.2)	8(2.1)	2(1.1)	> 0.5
Hemoglobinuria N(%)	8(0.9)	0	6(1.6)	2(1.1)	NS
Jaundice N(%)	8 (0.9)	0	2(0.5)	6(3.2)	NS
Abnormal behavior N(%)	7(0.8)	I (0.3)	6(1.6)	0	NS
Pulmonaryedema N (%)	3 (0.3)	1 (0.3)	2(0.5)	0	NS
Acute renal failure N (%)	2(0.2)	0	2(0.5)	0	NS
Shock N(%)	2(0.2)	0	0	2(1.1)	NS
DIC/Bleedings N(%)	1 (0.1)	1 (0.3)	0	0	NS
More than one	678 (78.4%)	233 (8.7%)	353 (92.4%)	92(48.9%)	< 0.001

PHC=Primary Health Center, SHC=Secondary Health Center, THC=Tertiary Health Center

Table-IV

Outcome pattern of SM categories of hospitals N=909

Outcome	Total = 909 N (%)	PHC =339 N(%)	SHC=382 N(%)	THC N=188 N(%)	
Full Recovery	747 (82.2)	286 (84.4)	321 (84.0)	140 (74.5)	P > 0.05
Recovery with sequele	13(1.4)	9(2.7)	2(0.5)	2(1.1)	P < 0.05
Death	58(6.4)	5 (1.5)	19(5.0)	34 (18.1)	P < 0.01
Not known	91 (10.0)	39 (11.5)	40 (10.4)	12(6.4)	P < 0.05

PHC=Primary Health Center, SHC=Secondary Health Center, THC=Tertiary Health Center

747 (82.20%) cases recovered fully. But 13 cases (1.4%) had some sequele after recovery. The outcome of 91 (10%) cases was not known as they left the hospital without advice and or referred to other facilities. Case fatality was highest at THC followed by SHCs. But there was also differences of various outcome patterns among various categories of hospitals both significant and non significant as well.

Discussions

We have described the patient profile and time lines and presentations of patients admitted with SM in defferent categories of hospitals in high risk areas in Bangladesh for malaria. There is in operation the 'National Malaria Control Program' to control the malaria as per the WHO guidelines, which emphasizes on early diagnosis on clinical criteria and treatment with affordable and readily available 'chloroquine' as first line agent for uncomplicated malaria and parental quinine for severe category. For a successful campaign the need is to describe relevant influencing factors for appropriate addressing.

Patients were documented in three different categories of hospitals. Most cases were male of the age group of third decade. This signifies the sections of population who were economically active and are most exposed to the vector were affected. Therefore malaria is not only a health problem rather a developmental economic issue[4]. A significant number of patients were pregnant. Pregnancy is a susceptible state for SM, and carries more risk for case fatality. Studies in Thailand revealed that SM is 3 times more common amongst pregnant women[5]. The morbidity is also high in pregnant state as well. The 'National MCH Program' should develop guidelines for malaria with pregnancy and incorporate them in field operation.

The National Guidelines for Malaria emphasizes use of chloroquine as first line antimalarials (AMs) for all fever cases without focal signs for any other febrile illness in endemic zone. But it was found that more than half of the enrolled cases didn't get any AM prior to development of SM. This issue call for more awareness of the people and professional in this regard. The over all case fatality was 6.4%. In a hospital-based series in Papua-New-Guinea it was found that the mortality was 18%[6]. On the other hand the same was found in an ICU in Singapore to be 12.5%[7]. Compared to these, the mortality in our series is low. One of the reasons for this is the non homogeneity of study stations plus less severe patterns in most cases. About 1.4% of cases developed some form of sequele. Various neurological sequele, mostly psychiatric were described in cases of cerebral malaria but the association with malaria was doubtful[8]. So SM is not only regrettable for high mortality but also for lasting morbidity and or infirmity with related social and economic consequences. A study dedicated to describe the sequele is warranted in this behalf.

SM is a medical emergency, which needs immediate management in a hospital setup. The different durations, which were documented by this study from the onset to hospital admission, will provide some important insight. These durations: onset of illness, severe symptoms, impaired consciousness, prostration, travel time, and hospital stays are all found to be in appropriately prolonged leading to delay in starting specific management. The delay may be important contributing factor to influence the outcome. The travel time to hospital was found to be comparatively less if the commuter mechanism of the country is considered. Therefore the delays are possibly due to lack of awareness about the condition and consequences. Other authors in this region of Asia also observed this[9]. Even one can speculate this lack of awareness is also prevailing amongst the practicing and operational health care personnel. A KAP study is needed to describe the situation prevailing among people and professionals.

Detail examination of different durations by different categories of hospitals provided that these are more prolong in THC. This is possibly because of the fact that patients developing complications over time and more serious cases are used to seek admission at THC and or being referred from PHCs and SHCs. But surprisingly the travel time was lowest at the SHCs that should be supposed to be in between PHCs and THCs. This needs further study. But all the durations were found to be significantly different between different categories of hospitals saving duration of prostration.

Most of the patients had more than one types or presentation of SM, types as described by WHO. But out of these in descending order the most frequent types were: Severe prostration, Hypoglycemia, Unarousable coma, Convulsion, Severe anemia, Impaired consciousness, Hyperpyrexia and Hyperparasitemia. But in a small number of cases jaundice, abnormal behavior, pulmonary edema, shock and DIC/bleedings were also present. There was a striking difference between the THC and PHCs for different types with SHCs in between encountering most of the types that the other two

lacked in this series. But it was found that more severe types like unarousable coma and impaired consciousness were more frequent at THC. This feature emphasizes that the center of attention for SM management should be more focused to SHCs through making them more efficient in all respect.

The outcome data revealed that the case fatality was highest at THC followed by SHCs. This is lowest at the PHCs. As more severe cases with more serious types were conglomerated naturally and or by referral to THC and SHCs obviously the fatality rate was higher. So these centers should be upgraded and refurnished so that critical cases can be appropriately and comprehensively managed. A good number of cases, with insignificant difference between all categories of hospitals, left the hospital before the attainment of outcome. So outcome of these cases were unknown and therefore acting as an artefact for general implication of outcome data. The interpretation of those therefore needs some reservation for this reason.

Conclusion :
It can be concluded that more awareness and orientation training are needed both for the community and the professionals working in the endemic zone to ensure early diagnosis and prompt treatment. Secondary Health Care Hospitals should be more equipped for handling severe malaria cases and Chittagong Medical College Hospital should me made as a center of excellence for the same as it is the only Tertiary Health Care Provider at the perimeter of the malaria endemic zone of Bangladesh. Malaria issue should be incorporated in National MCH program. Further studies are needed to explore the situation critically.

Acknowledgement & Conflicts of Interest

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