A STUDY OF THE SPECTRUM OF PRESENTING SYMPTOMS, DIAGNOSTIC INVESTIGATIONS, TREATMENT AND OUTCOME OF SEVERE MALARIA IN THE ADMITTED CHILDREN OF KUWAIT TEACHING HOSPITAL, PESHAWAR, PAKISTAN

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Date Received:
August 09, 2015
Date Revised:
November 23, 2015
Date Accepted:
December 03, 2015

ABSTRACT

Objectives: To document the spectrum of presenting symptoms, diagnostic investigations, treatment and outcome of severe malaria in the hospitalized children of Kuwait teaching hospital.

Methodology: This was a descriptive study using patient case records of children admitted from 1st January till 31st December 2013. All children with malaria requiring admission and treatment with parenteral anti-malarial were categorized as severe malaria and included in the study. Data was analyzed using Microsoft office Excel 2007.

Results: 32 cases fulfilled the inclusion criteria. Fever was the commenest presenting symptoms present in 100% of cases (n=32). Fifty percent children (n=16) had pallor, 12.5 %(n= 4) cough, 9.3 %(n=3) had dysuria and 6.25 %(n=2) had fits recorded as additional presenting symptoms. 71.8% (n=23) had parasitological confirmation test before commencement of treatment .100% of this parasitological confirmation was done by peripheral blood smear/microscopy test. Out of the 23 who had microscopy done 60.86%(n=14) had negative result and 39.13%(n=9)were positive for plasmodium of which,88.88%(n=8)were vivax and 11.11%(n=1) was falciparum.93.75 %(n=30) of the parenteral anti-malarial used was intravenous quinine. All except one child 96.8 %(n=31) recovered with the anti-malarial treatment used.

Conclusions: Fever and pallor are the two most common presenting symptoms of hospitalized children with severe malaria. Microscopy remained the most common investigation for the diagnosis of malaria. Quinine is the most frequently used drug for severe malaria. The study highlighted the need to further improve the case management of severe malaria in children.

Key Words: Severe malaria, Children, WHO guidelines, Clinical manifestation, Management

This article may be cited as: **Saffiullah, Ali S, Salahuddin A, Salman M, Qureshi H. A study of the spectrum of presenting symptoms, diagnostic investigations, treatment and outcome of severe malaria in the admitted children of Kuwait Teaching Hospital, Peshawar, Pakistan. J Postgrad Med Inst 2015; 29(4): 288-93.**

INTRODUCTION

Malaria remained an important cause of mortality and morbidity in children. There are estimated 3.3 billion individuals worldwide who are at risk of malaria. Of these, 1.2 billion are categorized to be in the high risk category. In the areas with high risk of malaria more than one case is happening in every one thousand people living there According to World Health Organization (WHO) in the year 2013, the estimated mortality due to malaria was 584 000. Majority (90%) of these deaths were reported in Africa. More than four hundred and fifty thousand children under five years died worldwide due to malaria during this period. There are 97 countries which had continuing malaria transmission during the year 2014[1]. Pakistan is included in the Eastern Mediterranean Region. It is among the six countries with high malaria transmission in this region. 1 million confirmed malaria cases were reported in this region in 2013. 84% of these cases happened in two countries with Pakistan accounted for 27% and Sudan 57% of this burden of malaria. The mortality figures due to malaria in the region during 2013 were reported to be 1027. Pakistan was one of the two countries where more than 90% of

these deaths due to malaria happened, the other being Sudan. Pakistan accounted for (24%) and Sudan (67%) of these deaths due to malaria Plasmodium falciparum caused most cases of malaria in the region except in three countries, Pakistan, Iran and Afghanistan, where plasmodium vivax was responsible for the majority of cases[2].

Malaria spread by mosquito bite presents acutely with symptoms of fever, chills and sickness, usually a week to 10 days after the bite of infective mosquito. In paediatrics age group sever malaria often cause symptoms of pallor due to significant drop in haemoglobin, metabolic acidosis leading to respiratory distress and cerebral malaria[3].

WHO has published guidelines for the management of severe malaria in children. Plasmodium falciparum is more likely to cause severe malaria but plasmodium vivax can also manifest as severe malaria especially in children[4]. This study was conducted to document the spectrum of presenting symptoms, diagnostic investigations, treatment and outcome of severe malaria in the hospitalized children of a teaching hospital.

METHODOLOGY

This was a descriptive study conducted on the patient case records of children who were admitted with severe malaria in the paediatrics ward of Kuwait teaching hospital Peshawar. Kuwait teaching hospital, affiliated with Peshawar medical college, is a 250 bedded private teaching hospital in Peshawar, Khyber pakhtunkhwa, Pakistan. In the year 2013 the numbers of paediatrics admission were1174.Forty (3.4%) children were admitted with the diagnosis of Malaria.

Severe malaria is defined by clinical or laboratory evidence of vital organ dysfunction and though there are strict definition of severe malaria, WHO recommends a low threshold of starting parenteral anti-malarial in any child about whom a health care worker is concerned to have severe disease[4], and based on this for the purpose of our current study we classified a patient to had severe malaria who required admission and received parenteral anti-malarial. The study period was between January-December 2013. Information regarding demographics, symptoms at presentation, diagnostic investigation for malaria, treatment and outcome were recorded on a structured proforma.Data was then analyzed using Microsoft office Excel 2007. All the children with the diagnosis of severe malaria who were treated as in patient and had parenteral anti- malarial during the one year study period were included in the study. Children with malaria who were treated as outpatient and children who received oral anti -malarial were excluded from the study.

RESULTS

40 cases were identified who were treated as Malaria in the admitted patients during the study period. After applying our criteria 32 cases were selected for the study. 20(62.5%) were boys and 12(37.2%) were girls. Majority 21(65.6%) were > 5years of age and 11(34.3%) were <5 years of age. Mean age was 6.14 years (range 0.2 - 11 years). Fever was present as one of the presenting symptoms in all cases (100%, n=32).7 children (21.8%) had fever as the only presenting symptom.16 children (50%) had pallor recorded as additional symptom.5/16 of these children with pallor (31.25%) had documented moderate to severe anemia (Hb < 7%) and 3/16(18.75%) required blood transfusions. The distribution of spectrum of presenting symptoms is shown in the figure 1.Regarding the diagnostic investigations for malaria, 23/32(71.8%) had parasitological confirmation before commencement of treatment and 9/32(28.12%) had no parasitological confirmation and treated on clinical grounds only. All this parasitological confirmation was done by peripheral blood smear/microscopy and no rapid diagnostic tests (RDTs) were done. Out of the 23 who had microscopy done 14 (60.86%) had negative result and 9 (39.13%) were positive for plasmodium. Out of these 9 positive microscopy results, 8 (88.88%) were plasmodium vivax and 1 (11.11%) was plasmodium falciparum.

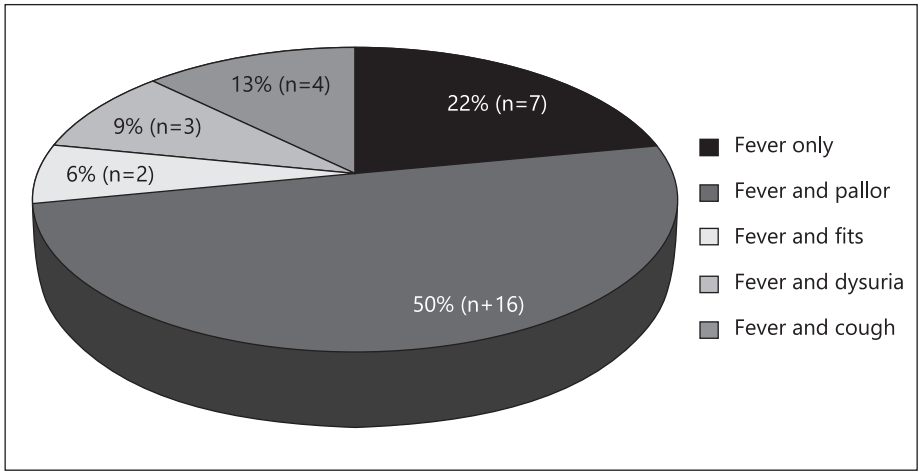
30/32 (93.75%) of the parenteral anti -malarial used was intravenous quinine.2 (6.25%) had intramuscular artemether and none had intravenous artesunate. The range of duration of stay in the ward was between 2 to 6 days with mean of 3.84 days .All except one child recovered with treatment. One patient died from disseminated intravascular coagulation (DIC).

DISCUSSION

The important fact about malaria remained that it can be prevented in the first place and even if acquired by an individual is totally treatable. The initial complaints of the patient may be confused with many other common illnesses and malaria may not be recognized. If not treated promptly, malaria caused by plasmodium falciparum and sometimes vivax lead to severe disease which can be fatal[3]. Therefore early and timely diagnosis and management with appropriate anti-malarial medications are important component to prevent death from malaria in susceptible individuals like small children and during pregnancy[4]. Many factors including age of the child, rate of malarial transmission and geographical territory determines the features of severe malaria in children[5,6].

In our study there were more boys than girls (62.5% vs. 32.7%). Previous study by Jalal-ud-din and colleagues on malaria in children in Mansehra region of

Figure 1: The distribution of spectrum of presenting symptoms in children with severe malaria.



Khyber Pakhtunkhwa Pakistan has shown even higher male to female ratio of 71.25 vs. 28.75 though that study was done in the outpatient cases of malaria[7]. This finding can be attributed to many reasons including the likelihood of boys spending more time outdoors making them susceptible to mosquito bites. This reason is even more likely to be the contributory factor in our study considering that most of the cases were more than 5 years of age who are likely to spend more time outside making them more likelihood to be exposed to mosquito bites.

Regarding symptoms on presentation fever was present in all 32 (100%) cases in our study. Data from a previous study from Federally Administrated Tribal Area (FATA), Khyber Agency, showed fever was the presenting symptoms in 98.5% of children with malaria. Additionally malaria caused by Plasmodium vivax was reported to be most commonly presented with high grade fever as compared to Plasmodium falciparum where chills and pallor were the common presenting symptoms[8]. Beg and colleague in a study from a tertiary hospital in Karachi also reported similar results. They reported fever to be one of the presenting features of malaria in 97% of their cases regardless of the species type[9]. Previous studies from abroad including studies from Latin America has shown fever to be present in more than 90% of inpatient cases of malaria though these studies subjects included both adults and children. In our study 7 (21.87%) children presented with the symptom of fever only as compared to these studies from Latin America where all the patients presented with more than one symptoms the other being headache, chills and sweating[10,11]. As fever could be the presenting symptoms of many other diseases in children, WHO recommended a high level of suspicion of malaria by a clinician to be the most vital component in clinical diagnosing it[4].

Pallor was the next most frequently reported symptoms in the cases of our study. 50 %(n=16) were reported to had pallor on presentation. Jan Mohammad and colleague in a previous study reported much higher percentage i.e. 96.6%, of their cases to had pallor[8]. The comparatively lower percentage of pallor in our study subjects could be due to the fact that we only looked pallor as symptom reported by parents and not the clinician examination finding as compared to the study by Jan Mohammad and colleagues who included pallor both as symptom and sign noticed by clinician during examination. Out of these 16 children with pallor, 31.25 %(n=5) had documented moderate to severe anemia (Hb <7gm/dl). Malaria is one of the known cause of anemia. Anemia in malaria is due to many factors including the breakdown of red blood cells and decrease production by suppression of bone marrow[12]. A previous study from Uganda showed the frequency of severe anemia to be 76.8% in hospitalized children with malaria though the study was done in children below 5 years of age and the cutoff of haemoglobin was <6gm/dl for severe anemia. Similar frequency of anemia(76.6%) were reported in a study from India in admitted children with malaria but the cut off used for severe malaria in this study was ,5gm/dl of haemoglobin[13,14]. Another study from Africa showed the frequency of anemia in children with malaria to be 54.4% though the children recruited in that study were treated on outpatient basis and did not required admission also plasmodium falciparum was the only specie of malarial parasite found in that study[15]. In our study 31.25% had documented anemia which is somewhat lower than these studies from Africa and India but this is likely to be an underestimation of the actual percentage because 50% of the children in our study had pallor as symptoms and majority were likely to had anemia so lack of laboratory test for checking and/or documentation of haemoglobin value in the

patient notes are likely to have contributed to this relatively low frequency of anemia. Severe anaemia is one of the main causes of mortality in paediatrics malaria cases[4]. We did not had any anemia related mortality in our patients with malaria. This could be due to the fact that all 3 children with severe anemia i.e. Hb ≤4 gm/dl in our study received blood transfusions.

Most of the cases in our study was caused by vivax and anemia in these cases might be the result of repeated infection and relapses. One of the other factors which has not been looked at in our study is the pre-existing iron deficiency and nutritional anemia in the studied children. The need for blood transfusion must be assessed with great care for each child. According to the WHO recommendation, in areas where malaria transmission is high, a blood transfusion is indicated with haemoglobin cut off of ≤ 4g/d irrespective of the clinical status of the patient. In children where haemoblobin is between 4-6gm/dl transfusion is indicated if the child has respiratory distress and acidosis, shock, cardiac decompensation, parasitemia >20% and clouding of consciousness[4]. In our study 3 out of 5 patients (60%) with documented moderate to severe anemia received blood transfusions. In all these patients hemoglobin level were less than 4gm/dl.

Two (6.2%) children had fits as presenting feature in addition to fever. A previous study from Thailand showed 7.7% children hospitalized with diagnosis of malaria had convulsions[16]. Febrile fits are common in children and its need to be differentiated from fits caused by malaria. In febrile fits post ictal phase is usually short and is less than 30 minutes. Other causes of fits with fever need to be considered when dealing with a child who have malaria and fits as the clinical manifestation of sepsis or invasive bacterial infection and sever malaria may mimic and some time most exist at the same time in a patient. According to WHO guidelines for treatment of severe malaria in children In children with suspected severe Maria and changes in the sensorium should be started on broad-spectrum antibiotic and course completed unless a bacterial infection can be ruled out. Ideally when possible Blood culture should be done on presentation in these children[4].

3(9.3%) children in our study had urinary symptoms in the form of dysuria .We assume that this could have resulted from concentrated urine in these children due to dehydration resulted from fever and reduce oral intake or could be due to coexisting urinary tract infection (UTI) though we neither looked at features of dehydration or urine examination including microscopy and culture for bacteria to rule out UTI in our study group. Okwara's et al, reported the prevalence of urinary tract infection of 13.3% in hospitalized children with malaria[17].

Four (12.5%) children had cough in addition to fever on presentation. A study by Gebre and Negash from Ethiopia reported cough to be one of the feature of severe malaria in 52% of children with severe malaria[18]. Symptoms of malaria may resembles pneumonia in children and can be difficult to differentiate between these two entities[19].

Most of the cases in our study where microscopy was positive showed plasmodium vivax. A previous study by Nicholas et al, reported cough to be more frequent manifestation of malaria caused by vivax or ovale (53%) as compared to falciparium (36%)[20].

Parasitological confirmation of suspected cases of malaria was done in 71.8% of cases and the rest were treated only on clinical grounds. The diagnosis of malaria on clinical grounds has a poor predictive value[21]. WHO recommends that all suspected cases need to be confirmed before commencement of treatment as it would help in diagnosis and also prevent unnecessary treatment. The only time its acceptable to treat only on clinical ground is that it facility for parasitological is not accessible or not readily feasible or the child is very unwell even then one should take a sample of blood and make a film which could be viewed later[4]. The possible reason for not confirming diagnosis in our patients could be the limited facility at night and out of hour, unwell child and lack of knowledge about the recommendations. In our study all the parasitological confirmation was done by microscopy. For routine clinical setting microscopy remained the gold standard for diagnosis detecting the type of species of malarial parasite

Rapid diagnostic tests (RDTs) can help to reach the diagnosis promptly in areas where accurate microscopy is not available or feasible[4]. In our study no RDT was done probably because of non availability of RDT kits, lack of awareness and cost of the service. The advantage of RDT especially out of hour is that it does not need personnel with experience in microscopy and also helpful if patient has been treated with anti-malarial recently .Though the RDTs presently available are somewhat less sensitive to find out P. vivax as compared to P. falciparum[4]. 60.8% of the microscopy was reported negative which could be due to many factors including the sampling, experience of personnel and prior use of anti malarial before the presentation in our hospital. Another factor associated with negative microscopy in severe falciparium malaria is the sequestration of malarial parasite to small blood vessels rather than circulating in blood stream. This factor could also have contributed to small extent in the negative microscopy results in our study[22].

Quinine was given in 93.7% as first line parenteral anti-malarial and only 6.2% received intramuscular artemether in our study. None of the children had intra-

venous artesunate.The use of quinine is likely to be because of its readily availability, people experience using it and lack of knowledge and advantages about artemether and artesunate. Though quinine is an acceptable alternative WHO recommends Artesunate as the first line parenteral anti-malarial for treatment of severe malaria[4]. It has many advantages and trial has shown its superiority over quinine. Artesunate clear the parasite much quicker than quinine and also eliminate the early ring stage of plasmodium from the circulation[23,24].

One child in our study group died. The mortality in our study was 3.12% (n=1). A study from Indonesia reported 2% mortality in hospitalized patients from malaria though the study included both children and adults[25]. whereas another study from India which included only hospitalized children showed a mortality of 3.3% in inpatient children with malaria which is comparable to our study results[14].

LIMITATIONS

There are few limitations of our study. We classify a child to have severe malaria who required hospital admission and received parenteral anti-malarial and the other clinical and laboratory investigations use to classify severe malaria were not included due to our resources constraint. Many other infections may have a bearing on the symptoms of the patients in our study. These could not be assessed systematically in the study due to our resource limited setting.

Preexisting other chronic medical problems, immune status, micronutrient deficiencies and malnutrition may have contributed to the severity of illness caused by malaria in our study group but again these were not looked into in the study.

But the fact that all most all children in our study were cured with parenteral anti-malarial (Few might have received other drugs like antibiotics as well) the link between the actual diagnosis and clinically treated diagnosis is at least probable.

Further larger prospective studies using the WHO criteria of clinical and laboratory components of classifying severe malaria and with the provision of more extensive tests to look into other associated diseases and conditions are needed.

CONCLUSION

Fever and pallor were the two most common presenting symptoms of hospitalized children with severe malaria. Microscopy remained the most common investigation for diagnosis of malaria in children .Quinine was the most frequently used anti-malarial drug for severe malaria in our study. There is a need to further improve the case management of severe malaria including using rapid diagnostic tests (RDTs), where appropriate, and intravenous artesunate. This can be done by introducing management protocol for severe malaria and regularly updating doctors on the malaria treatment incorporating the current WHO guidelines.

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CONTRIBUTORS

SU conceived the idea, planned the study, and drafted the manuscript. AS helped acquisition of data and did statistical analysis. MSHQ helped acquisition of data and manuscript writing. SA supervised the study, data analysis, manuscript writing and critical revision. All authors contributed significantly to the submitted manuscript.