RESEARCH PAPER | Medical Science | Volume : 5 | Issue : 3 | March 2015 | ISSN - 2249-555X

A Study of Neurological Manifestations of Falciparum Malaria

KEYWORDS: Falciparum malaria, Neurological manifestations, Parasite Index.

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ABSTRACT *Objectives: To study relative frequency (prevalence) and profile of neurological manifestations of falciparum malaria and the outcome of falciparum malaria in general and of neurological involvement of falciparum malaria in particular.*

Methods: A hospital based prospective observational study of patients of acute febrile illness above 12 years of age. Diagnosis was based on clinical and serological data.

Results: A total of 70 patients were diagnosed with Falciparum malaria, with 67% males and 33% females, 26-40 year age group most affected. 48.6% presented with neurological manifestations. Altered sensorium was the most frequent neurological manifestation, followed by convulsions and hiccups. The mortality rate was 11.4%.

Conclusion: The study revealed that nearly half the number of patients with falciparum malaria have neurological manifestations. Mortality increases with age, decrease in hemoglobin levels and increase in parasitic index.

Introduction

Malaria is one of the most important parasitic disease of man caused by a protozoan from the genus 'Plasmodium' of which there are four human species: Plasmodium vivax, Plasmodium falciparum, Plasmodium ovale and Plasmodium malaria. Recently Plasmodium knowlesi[1] is also known to cause disease in humans. It is transmitted by female Anopheles mosquitoes. It is the leading cause of ill health in tropical and sub-tropical countries. In 2002, more than 2 billion individuals were exposed to malaria and an estimated 515 million clinical episodes of acute Plasmodium falciparum infection occurred[2]. More than 1 million people die from it every year[3].

Plasmodium falciparum is the most common cause of severe malaria. Incidence of malaria in India is about 2 million cases per year, which is about 40% of total number of cases outside Africa. Out of these, the proportion of falciparum malaria is between 35-43%, affecting both young and old persons, with children at particular risk[3]. Despite availability of several potent antimalarial drugs in the recent past, the mortality status has not changed.

The manifestations of severe malaria differ depending on the age of the patient and previous exposure[4]. In the first 2 years of life severe anaemia is a common presenting feature with seizures and cerebral malaria in older children; whereas in adults acute renal failure, acute pulmonary oedema, liver dysfunction, and cerebral malaria may all occur. Metabolic acidosis, mainly lactic acidosis, is common at all ages. Severe malaria is a multisystem disease, and the outcome often depends on the degree of vital organ dysfunction[5].

Severe neurological complications are associated with complicated and severe falciparum malaria. Cerebral malaria is one of the most dreaded complications. In falciparum malaria, 10% of all admissions and 80% of deaths are due to central nervous system involvement[6].

Cerebral malaria, multiple convulsions more than twice in 24 hours, impaired state of consciousness with behavioural change, confusion and stupor are the neurological manifestations of severe and complicated malaria[6-9]. Cerebral malaria is a rapidly evolving neurologic disease. It carries a fatality rate of more than 20% even in urban hospital settings where aggressive medical care is available[7, 10].

Hypoglycemia, convulsion, respiratory distress, circulatory collapse, metabolic acidosis and renal failure may aggravate or contribute to impaired consciousness in severe malaria[6-9, 11].

Falciparum malaria is also associated specifically with convulsions in uncomplicated patients of malaria. Several isolated case reports of various neurological syndromes like peripheral neuropathies, various movement disorders, myelopathies and stroke like syndrome have been described[9].

This study evaluated the relative frequency and the pattern of neurological manifestations of falciparum malaria in patients admitted to Sri Venkateswara Ramnarain Ruia Government General Hospital.

Objectives of the present study

1. To study relative frequency (prevalence) of neurological manifestations of falciparum malaria in patients admitted to Medical Department of S.V.R.R.G.G.Hospital.
2. To study the profile of neurological manifestations among patients with falciparum malaria.
3. To study the outcome of falciparum malaria in general and of neurological involvement of falciparum malaria in particular.

Materials and Methods

We did a hospital based prospective observational study in the department of general medicine, S.V.R.R.G.G.Hospital, Tirupathi, Andhra Pradesh.

Patients more than 12 years of age admitted with a provisional diagnosis of malaria were screened. Patients were recruited to study if they had had shown asexual forms of

Volume : 5 | Issue : 3 | March 2015 | ISSN - 2249-555X

Plasmodium falciparum in peripheral smear or quantitative buffy coat tested positive for Plasmodium falciparum.

Impaired consciousness was diagnosed if patients had inappropriate or incomprehensible verbal responses and did not respond to verbal commands. Assessment of the patient was delayed for 6 hr after a grand mal seizure to exclude postictal coma.

Severe anaemia was diagnosed in patients with hemoglobin level <5 g/dl. History and examination were recorded on standard forms on admission. Lumbar puncture was performed in those diagnosed as having cerebral malaria or with altered consciousness.

Patients were treated with a loading dose of 20mg/kg quinine dihydrochloride infused intravenously over a 4 hr period followed by 10mg/kg over 4hr every eight hrs until oral quinine could be tolerated. Quinine was continued for seven to ten days. Patients with anaemia were treated with blood transfusions as indicated clinically. Intravenous fluids were given as necessary. Episodes of hypoglycemia were treated with infusions of 25% intravenous glucose followed by 5% dextrose infusion. Convulsions were treated with diazepam intravenously. Patients in renal failure were treated conservatively. Patients were put on mechanical ventilation if clinically indicated.

Statistical Analysis: For continuous variables mean and range were calculated. Where appropriate, chisquare($\chi 2$) test is applied to test for significance. A 'p' value of < 0.05 is taken as a measure of significance.

Result and Observation

There were 11954 admissions in medical wards during the period February 2008 to july 2009. Of these 1972 patients were admitted with fever. 145 of these were diagnosed as having malaria, with 75 of them positive for plasmodium vivax and 70 positive for plasmodium falciparum. Three patients had both plasmodium vivax and falciparum. 248 of the smear negative fever patients responded to chloroquin.

Table.1: Age and sex distribution

Age group	Males	Females	Total
12-25	16	6	22
26-40	15	8	23
41-55	11	7	18
>55	5	2	7
Total	47(67%)	23(33%)	70(100%)

Overall, there were 67% males and 33% females of whom 2 were pregnant. 26-40 years age group constituted the majority among both males and females.

Table.2: Number of patients with neurological manifestations by age

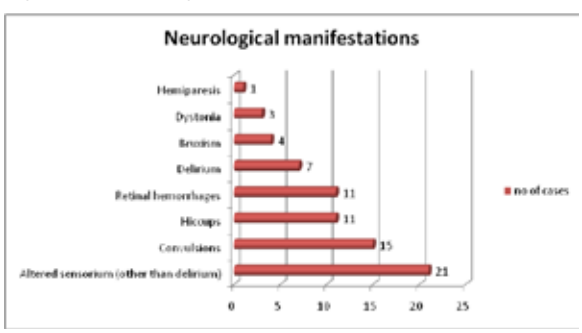
Age group	Total patients	Patients with neurological manifestations	Relative frequency(RF) of neurological manifestations
12-25	22	8	36.4
26-40	23	13	56.5
41-55	18	7	38.9
>55	7	6	85.7
Total	70	34	48.6

48.6% of the falciparum malaria patients had one or more neurological manifestations. Relative frequency of patients with neurological manifestations is higher in patients aged more than 55 followed by those in 26-40 years.

Majority of the patients were from Chittoor district(56%), followed by Kadapa district(31%) and Nellore district(7%). Even the neurological manifestations were maximum in patients from chittoor district(54%) followed by Kadapa district(41%).

Altered sensorium was the most frequent neurological manifestation, followed by convulsions and hiccups.In 7 of the 28 patients(25%) with impaired consciousness, this was the only indicator of severe malaria. By definition, none of the patients responded to commands or was making comprehensible sounds. 15 patients(21.4%) had seizures prior to admission. About 25% of patients had retinal hemorrhages. 10% of the patients were in delirium. 4 patients had tooth grinding as a symptom. 3 patients presented with abnormal involuntary movements and none of them were using any drugs prior to the presentation. One patient presented with hemiparesis.Positive Babinski sign was observed in 24 patients. Terminal neck stiffness was see in 15 patients. Lumbar puncture in 9 showed no abnormality. Seven of the patients with altered sensorium (25%) died. Patients responded to commands between one and three days after the treatment.

Figure 1: Neurological Manifestations.



As the parasite index increased, the percentage of cases with neurological manifestations increased and was 100% with parasite index of more than 20.

Eight patients (11.4%) died at a median time of 4 days after admission. The geometric mean peak parasite count was higher in fatal cases than in survivors.

Discussion

Neurological manifestations are commonly found among patients with falciparum malaria and the relative frequency of neurological manifestations in patients with falciparum malaria in this study is found to be 48.6%. This can be adopted as a measure of prevalence of neurological manifestations among patients with falciparum malaria in this geographic area.

Significant proportion of patients with falciparum malaria presented with one or more neurological manifestations.

Volume : 5 | Issue : 3 | March 2015 | ISSN - 2249-555X

Taking all the overlapping features together, neurological manifestations in decreasing order were altered sensorium other than delirium, convulsions, hiccups, retinal hemorrhages, delirium, bruxism, dystonia and hemiparesis. Similar manifestations were seen in other studies[13, 14].

According to WHO(1990), neck rigidity does not occur in patients of cerebral malaria, whereas it was observed in 15 patients at the time of admission. It was also observed in some patients in the Bikaner study conducted in 2002[14].

Seventeen percent of the patients had hiccups during the period of illness. This symptom appears to be important in predicting falciparum malaria. An earlier study also mentioned hiccups as a presenting symptom in 26.4% patients[12].

In this study, recurrent convulsions occurred in 21% of patients similar to the Bikaner study[14]. All the patients with parasitemia more than 20% had neurological manifestations.

There is a statistically significant difference in the mortality in the group of patients with neurological manifestations compared to those without neurological manifestations. This indicates that patients who have neurological manifestations have unfavorable prognosis compared to those without neurological manifestations. According to Dr.B.S.Kakkilaya, 10% of all admissions and 80% of deaths are due to central nervous system involvement in falciparum malaria[6]. In this study, 38.6% of all admissions and 87.5% of deaths were due to central nervous system involvement.

This study also included the outcome of falciparum malaria in general and of neurological manifestations in particular.

1. The relative frequency of falciparum malaria as a cause of fever in patients attending S.V.R.R.G.G.Hospital is 7.35%
2. Falciparum malaria was the cause of malaria in 48.27% of patients admitted with malaria.
3. Of the patients with falciparum malaria, 48.6% presented with neurological manifestations.
4. Altered sensorium, convulsions, retinal hemorrhages and involuntary movements were the commonest neurological manifestations.
5. Hyperparasitemia of more than 25% predicted neurological manifestations.
6. Neck rigidity was seen in 21.4% of patients.
7. Neurological complications, severe anaemia and hyperparasitemia were the major poor prognostic indicators.

Limitations

1. Only smear positive/QBC positive patients were included and repeat smear examination was not done in initial smear negative patients.
2. Glasgow coma scale was not included in the study
3. As S.V.R.R.G.G.Hospital is a tertiary care hospital and patients attending to the hospital are usually more seriously ill as compared to those attending primary health centers. Hence, these conclusions cannot be generalized to those patients.
4. Follow up was not possible in all patients as some were from faraway places and had visited the hospital in emergency.

Acknowledgements: I sincerely thank my Professor and guide Dr. M.S.Sridhar,Principal, SV Medical college, who guided me throughout and made this study possible.

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