Clinical Study of Complicated Malaria

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Abstract- Complicated malaria remains a major cause of morbidity and mortality worldwide this is a prospective study of clinical presentation, biochemical profile, prognosis and mortality of complicated malaria, in relation to severity of the disease, Age, Sex, and system involvement.

75 patients of complicated malaria diagnosed by peripheral smear examination admitted in Osmania General Hospital, were selected for the study. Detailed history, clinical examination, biochemical profile, blood tests and radiological studies were done to identify systemic involvement and severity of Malaria. In this study 66 patients (88%) of complicated malaria were due to plasmodium falciparum, 9 cases (12%) were due to mixed infections with plasmodium falciparum and plasmodium vivax. Among 75 patients 63(84%) were males and 12 females (16%) in the age group 12 to 66 years with mean age of 39 years.

Out of 75 patients 60% had jaundice, 60% had acute renal failure, 60% had anemia, 37% had cerebral malaria, and 37.33% had hypoglycemia.

Overall recovery rate was 82.6% while mortality was 17.35%. High case fatality was seen with acute respiratory distress syndrome (ARDS) (100%).

Index Terms- Complicated Malaria, Plasmodium Falciparum, Cerebral Malaria, Acute Respiratory Distress Syndrome.

I. INTRODUCTION

Malaria is the most important protozoan parasitic diseases of humans, transmitted by the bite of infected Anopheles mosquitoes. It is transmitted in 108 countries containing 3 billion people and causes nearly 1 million deaths each year.Five species of the genus Plasmodium cause nearly all malarial infections in humans. These are P. Falciparum , P. Vivax , P. Ovale, P. Malariae, and—in Southeast Asia—the monkey malaria parasite P. Knowlesi , Malaria occurs throughout most of the tropical regions of the world P. Falciparum predominates in Africa, New Guinea, and Hispaniola (i.e., the Dominican Republic and Haiti); P. Vivaxis more common in Central America. The prevalence of these two species is approximately equal in South America, the Indian subcontinent, eastern Asia, and Oceania. P. Malariae is found in most endemic areas, especially throughout sub-Saharan Africa, but is much less common. P. Ovale is relatively unusual outside of Africa and where it is found, comprises <1% of isolates[1]

According to Unicef, in India 80.5 per cent of people reside in malaria-prone areas 22 per cent population lives in areas with high transmission and approximately 30 per cent of disease burden is reported from children.[2]

According to National Vector Borne Disease Control Program, there were 10,67,824 malaria cases in 2012 and in 2013, the figure was 8,36,916. A Lancet report of 2010 said that malaria may be causing about 200,000 deaths a year in India among people below the age of 70 [2]. Most cases of complicated malaria are due to P. Falciparum. Almost all deaths are caused by falciparum malaria.[1]

W.H.O. GUIDELINES FOR CLINICAL DIAGNOSIS OF COMPLICATED MALARIA

Severe Falciparum malaria is defined as:
One or more of the defining criteria below

Defining Criteria	**Finding**
Cerebral malaria (unarousable coma)	Unarousable coma not attributable to any other cause in a patient with falciparum malaria. Coma should persist at least 30 minutes after a generalized convulsion to make the distinction transient post-ictal coma.
Severe normocytic anemia	Normocytic anaemia with hematocrit < 15% or haemoglobin 5 gm/ dl in the presence of parasitemia 10.000 parasites per ml.
Renal failure	Urine output < 400 ml in 24 hours in adults, or 12 ml per kg in24 hrs in children, failing to improve after rehydration, and with serum creatinine > 3 mg dl.

Pulmonary edema. ARDS	Radiological evidence of pulmonary oedema (Bilateral infiltrates in the lungs on chest film).
Hypoglycaemia	Whole blood glucose < 40 mg/dl
Circulatory collapse, shock	Hypotension (systolic blood pressure < 50 mm Hg in children -5 years old: < 70 mm Hg in adults) with cold, clammy skin
Spontaneous bleeding	Spontaneous bleeding from gums, nose, G1 tract or other sites, with laboratory evidence of Disseminated Intravascular Coagulation (DIC).
Repeated generalized Seizures	>3 observed seizures within 24 hours despite cooling
Acidemia or acidosis	Arterial ph < 7.25, plasma bicarbonate < 15 mmol/1lt
Hemoglobinuria	Dark red or black coloured urine with lab evidence of Hemoglobin in urine.

The 2000 WHO recommendations also include the following:	
Additional Criteria	**Finding**
Impaired consciousness	Impaired consciousness less marked than unrousable coma, can
but arousable	localize a painful stimulus
Prostration and extreme Weakness	Patient unable to sit or walk, with no other obvious explanation
Respiratory distress	Tachypnoea/deep breathing/nasal flaring /intercostal in drawing
Jaundice (Combined with evidence of other vital organ dysfunction)	Total bilirubin > 2.5 mg/dl
Hyperpyrexia	Rectal temperature > 40^0 C [3]

II. Material and Methods

75 cases of complicated malaria, diagnosed by peripheral smear examination, were studied in Department of Medicine at Osmania General Hospital.

Detailed history was recorded followed by thorough clinical examination to evaluate clinical status of the patient. Complete Blood Picture, Smear for MP, Liver Function Tests, Renal Function Tests, radiological studies were done. Both male and female above 12 years, Cerebral malaria / un arousable coma, Severe anemia, Renal failure, Pulmonary edema / ARDS,Hypoglycemia,Hypotension,shock,Bleeding,D1C,Acidosis,Macroscopic. haemoglobinuria ,severe Prostration or weakness, Jaundice ,Hyper pyrexia were included in the study. Known cases of chronic systemic illness involving Central Nervous System, renal, haematological, and respiratory and hepatobiliary systems were excluded. Patients with history of alcoholism and those taking hepatotoxic drugs were excluded.

III. RESULTS

Table: 1 Sample Composition

Total Number of Patients	75
Age Group	12 - 66
Male : Female	63 : 12
P. falciparum	66
Mixed Infections	9

Among the 75 cases of complicated malaria studied 63 were Males (84%) and 12 Females (16%) in the age group from 12 to 66 years with mean age of 39 years. 66 cases were due to P.falciparum, 9 cases (12%) were mixed infections with P.falciparum and P.vivax. Maximum number of cases (35) was falling in the age group of 31 to 40 years.

Table : 2 VARIOUS PRESENTATIONS IN COMPLICATED MALARIA

SI. No.	Presentation	No. of Cases	Percentage
1	Fever + Chills & Rigors	100	100
2	Jaundice	68	90.66
3	Oliguria	45	60
4	Altered Sensorium	34	45.33
5	Seizures	19	25.33
6	Abdominal Pain	11	14.66
7	Vomiting	18	24
8	Breathlessness	13	17.3
9	Myalgias	10	13.34
10	Loose Motions	3	4
11	Tremors	18	24
12	Bleeding gums	2	2.66
13	Unconsciousness	4	5.33
14	Epistaxis	1	1.33

All cases presented with moderate to high grade fever with chills and rigors. Jaundice was present in 68 patients (90.66%). Mean duration between fever and appearance of Jaundice was 5 days. Presentation with Oliguria was a frequent occurrence seen in 45 patients (60%). Neurological complaints like altered sensorium were seen in 34 patients (45.33%) and Seizures in 19 patients (25.33%). Tremors were seen in 18 patients (24%). Gastro intestinal symptoms like abdominal pain occurred in 11 cases (14.66%) and vomiting were seen in 18 patients (24%). Myalgias were seen in 10 patients (13.34%). Breathlessness was noticed in 13 cases (17.3%). 2 patients had bleeding gums and 1 patient had epistaxis.

Table : 3 Complications in Complicated Malaria

Sl.No	Complications	No. of cases	Percentage
1	Cerebral Malaria	28	37.33
2	Anemia	63	84
3	ARF	45	60
4	ARDS	4	5.33
5	Thrombocytopenia	45	60
6	Hypoglycaemia	28	37.33

Complications noticed in this study were, 63 (84%) had anaemia. 45 patients (60%) had oliguria with renal failure. Cerebral malaria and hypoglycaemia were noticed in 28 cases (37.33%). Thrombocytopenia was present in 45 patients (60%). ARDS was noticed in 4 cases (5.33%)

Table No. 4 Liver Function Tests

Sl.No	LFT (Unit)	Range	Mean
1	Sr. Bilirubin (mg%)	0.8 – 22	6.34
2	SGPT (Iu%)	60 – 227	130.81
3	Alkaline Phosphatase (KA)	6.22	12.41
4	SGOT (Iu%)	60 – 215	128.44

Sr. Bilirubin levels ranged from 0.8 to 22 mg.% with a mean of 6.34mg% . SGPT levels ranged from 60 - 227 u% with a mean of 130.81 u%. The mean SGPT for the expired patients was 131.46 u% and 127.12 u% in survivors. Mortality was low in patients with Sr. Bilirubin levels ranging from 2-10 mg% with a percentage of 5.66. Mortality with Sr.Bilirubin ranging from II - 20 mg% was 25% and from 21 - 30 mg% was 100%

Thrombocytopenia was detected in 45 patients (60%). Platelet count ranged from 0.6 3.1 lakhs in number, there was no mortality in these patients.

IV. DISCUSSION

Complicated malaria presents with protean manifestations and is associated with variety of complications. The processes of cytoadherence, rosetting, and agglutination are central to the pathogenesis of falciparum malaria. They result in the sequestration of RBCs containing mature forms of the parasite in vital organs (particularly the brain), where they interfere with microcirculatory flow and metabolism.[1]

In this study jaundice was noticed in 68 cases. Sr Bilirubin levels > 10 mg% were seen in 15 (22%) cases .7 patients with Sr bilrubin > 10 mg% expired and had associated multi organ involvement. 3 patients had associated cerebral involvement. 2 patients had ARDS with anemia and renal involvement was seen in 2 patients. SGOT elevation was seen but not more than 3 times of normal. In Mishra et al (1992) study 66% of patients had unconjugated hyperbilirubinemia with mild elevation of Sr. Transaminases. Similar observation was made by Wilairatana et al (1994) study.[12,14] Severe jaundice is associated with *P. falciparum* infections is more common among adults than among children and results from haemolysis, hepatocyte injury, and cholestasis. When accompanied by other vital-organ dysfunction (often renal impairment), liver dysfunction carries a poor prognosis. Hepatic dysfunction contributes to hypoglycaemia, lactic acidosis, and impaired drug metabolism [1] 45 patients in this study had oliguria and acute renal failure accounting to 60**%** of total cases. This is similar to the trends reported in Chawla et al (1989) study where 78% had oliguria with renal failure[6]. Similar observation was made in Dash et al (1991) study[7]. Out of 45 cases 8 patients expired (17.77%). All these patients had multi organ involvement like cerebral malaria**,** ARDS, anemia and high Sr. Bilirubin levels. 28 Patients had features of cerebral malaria accounting to 37.33**%.** 4 patients of cerebral malaria had neck stiffness and CSF was normal with clear fluid, normal proteins and WBC less than 10 / micro liter. Out of 28 patients 5 patients expired with a mortality rate of 17.85%. Multi organ involvement was observed with Cerebral Malaria**.** In Bags et al (1993) study the mortality rate due to Cerebral malaria was 22%.[5]

5.33% Patients in this study developed ARDS with associated complications like renal failure. Anemia and Jaundice. Mortality was 100%. Similar observations were made in Murthy et. al study (1989).[13]

Anemia was noticed in 63 cases (84%) with 12 deaths (19.04%) Mortality was more in association with cerebral involvement, renal failure, ARDS and markedly raised Sr. Bilirubin levels. Similar observations were made in 120 patients by Mathur et. al (1992) study.[10]

Thrombocytopenia was present in 45 cases. None of them had severe bleeding manifestations and none required transfusion, this study revealed that asymptomatic thrombocytopenia is a common manifestation of complicated malaria. Similar observations were made by Jadhav et al (2004) study were normal platelet count was present only in 21.6% cases.[8]

In this study 28 patients (37.33%) had hypoglycemia and Majority of patients had blood glucose levels of 40 to 50 mg% In this study out of 75 patients 62 recovered (82.6%) and 13 expired (17.35%). This mortality rate was comparable to the findings of Chawla et. al (1989) study, where it was 21% 7. In Anand et al (1992) study the mortality rate was 30%.5 all the expired patients had higher incidence of cerebral involvement, ARDS and renal failure. Many of them were having associated Jaundice and Anemia. Severe falciparum malaria constitutes a medical emergency requiring intensive nursing care and careful management In acute renal failure or severe metabolic acidosis, hemofiltration or haemodialysis should be started as early as possible. Parenteral antimalarial treatment should be started as soon as possible.[1]

V. CONCLUSION

Complicated malaria presents with Protean Manifestations. Jaundice**,** acute kidney in jury, cerebral malaria**,** Anemia when associated with multiple complications has high mortality. Retinal hemorrhages indicate poor prognosis**.** ARDS has bad prognosis and high mortality in association with other complications. Old age is found to be a poor prognostic factor. Delayed diagnosis and delayed treatment is another cause for poor prognosis.

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