Original article:

Clinical Profile and Outline of Complex Plasmodium Falciparum Malaria: a Retrospective Observational Study in Kerala

Ajit Kovil[1*], Baby Paul[2], Lipin Prasad[3]

[1*]Assistant Professor, [2]Professor, [3]Senior Resident, Department of General Medicine, Travancore Medical College, Umayanalloor, Kollam, Kerala, India.

Corresponding Author: Dr Ajit Kovil, Assistant Professor, Department of General Medicine, Travancore Medical College, Umayanalloor, Kollam, Kerala

Abstract:

Introduction: Malaria remains a major socioeconomic burden on community and accounts for 85% of global infectious disease burden. Our aim is to study clinical features, complications and factors affecting outcome of patients with complicated *P. falciparum* Malaria.

Materials and Methods: Present study was conducted at Travancore medical college umayanallor Kollam, Kerala India. This study is approved by ethical committee Travancore medical college. Consecutive adult patients with age > 18 years with smear positive *P. falciparum malaria* with various complications admitted to medical wards and intensive care unit were included in this retrospective study.

Result: During the retrospective study period, 80 patients who proved parasitiologically positive for *P. Falciparum* were studied and following observation were made. Total 62 (77.5 %) were males and 18 (22.5 %) were female patients with mean age of 32±18 years and 29±12 years for females. Age, gender, parasitic index and total serum bilirubin were not statistically significantly associated outcome of complicated *P. falciparum* malaria.

Conclusion: Early diagnosis and prompt treatment will reduce the mortality due to malaria. Early recognition of pulmonary involvement and timely intubation and artificial ventilation is vital to improve outcome of complicated *P.falciparum* malaria.

Keywords: Plasmodium Falciparum,Malaria, Infectious Disease

Introduction

Complicated *Plasmodium falciparum* Malaria is a syndrome and a disease of protean, clinical manifestations including jaundice, ARF, ARDS and multi-organ failure. Malaria remains a major socioeconomic burden on community and accounts for 85% of global infectious disease burden.[1]It is an important cause of morbidity and mortality irrespective of age group in subtropics and tropics. In the Southeastern Asian Region of World Health Organization (WHO) of 1.4 billion people living in 11 countries (land area; 8,466,600 km^2; i.e., 6% of global area), 1.2 billion are exposed to the risk of malaria, most of whom live in India.[2]

P. falciparum cases fluctuate between 1 to 1.2 million; thus *falciparum* malaria accounts for 50 % malaria in the country. India contributes about 70 % of malaria in the South East Asian Region of WHO. Although annually India reports about two million cases and 1000 deaths attributable to malaria, there is an increasing trend in the proportion of *Plasmodium falciparum* as the agent. The mortality in Malaria is due to *Plasmodiumfalciparum*. The considerable mortality and morbidity in *falciparum* malaria is due

to its protean manifestation, multi-organ involvement and delay in diagnosis and failure of administration of treatment promptly.Recently there is a changing trend not only in the clinical manifestations but also the complications, and more and more patients are presenting with ominous systemic manifestations.[3,4] All cases of *falciparum* malaria are potentially severe and life threatening medical emergency. A major reason for progression from mild through complicated to severe disease is missed or delayed diagnosis. Severe disease is treated with parenteral administration of adequate, safe doses of appropriate anti-malarial drugs. Supportive management of complications such as coma, convulsions, metabolic acidosis, hypoglycemia, electrolyte disturbances, renal failure, secondary infections, bleeding disorders and anemia are also important. Severe and complicatedmalaria is characterised by multi-organ involvement including acute lung injury (ALI), acute respiratorydistress syndrome (ARDS) and ARF. Recent years have witnessed a multi-organ failure, ALI and ARDS are being increasingly reported in *falciparum* malaria.[5]There is scanty literature and published studies on complicated *P. falciparum* malaria in Kerala.

Materials and methods

This study was a single centre retrospective observational study on complicated *P. falciparum* malaria conducted at Travancore medical college umayanallor Kollam, Kerala India. This study is approved by ethical committee Travancore medical college. Consecutive adult patients with age > 18 years with smear positive *P. falciparum malaria* with various complications admitted to medical wards and intensive care unit, from May 2012 to February 2013 were included in this retrospective study. Total 1500 patients were admitted with history of fever due to various etiologies. Total 250 patients were admitted with *P. vivax*malaria and mixed infections. Total 80 patients were included in present study with complicated *P. falciparum* malaria. As the coexistence of other diseases may influence the outcome of complicated malaria, patients with diseases like diabetes mellitus, chronic renal failure, chronic liver disease, rheumatic heart disease, coronary artery disease, and associated infections like pneumonia, urinary tract infection, leptospirosis, H1N1 and viral hepatitis were excluded. Cerebrospinal fluid analysis, abdominal ultrasound, chest radiograph, and serological markers for viral hepatitis were done to exclude these diseases. All patients who had a positive blood smear for *P. Falciparum* Malaria were included in this study. Patients who are peripheral smear negative but treated with anti malarial drugs (so called clinical Malaria) and other malarias (*Plasmodium vivax, Plasmodium ovale, Plasmodiummalariae*) were excluded.

On admission, peripheral blood smears were collected for Giemsa staining and subsequently every 12 hours to assess parasitemia. Parasite count with stage identification and index was determined. Blood was collected for estimation of glucose, urea, creatinine, sodium, albumin, bilirubin, aspartate amino transferase (SGPT), alanine amino transferase (SGOT), and for haematological investigations such as haemoglobin, platelet count, total leukocyte count, and prothrombin time (PT). Arterial blood gas analysis in patients with respiratory distress was done in 14 patients. The pH, PCo2, and PO2 were gauged and chest radiograph was done in 5 cases for diagnosis of respiratory distress and pulmonary edema. The diagnosis of malaria was made with

detection of asexual form of *P. falciparum* from Giemsa stained peripheral blood smear.

Results

Total 80 patients were included in present study with complicated *P. falciparum* malaria. Data is collected from Medical record sections of Travancore medical college. During the retrospective study period, 80 patients who proved parasitiologically positive for *P. Falciparum* were studied and following observation were made. Total 62 (77.5 %) were males and 18 (22.5 %) were female patients with mean age of 32±18 years and 29±12 years for females.Clinical profile of P. falciparum complicated malaria was shown in table 1. Mean and standard deviation of laboratory parameters of complicated P. falciparum malaria were shown in table 2 and Clinical presentation and complications of complicated malaria patients listed in table 3.

In multivariate analysis(MANCOVA) late presentation, ARF, hypotension, ARDS, thrombocytopenia, absences of splenomegaly, convulsions and hypoglycemia were associated with prolonged hospital stay, high mortality and poor outcome ('p' = 0.001). Age, gender, parasitic index and total serum bilirubin were not statistically significantly associated outcome of complicated *P. falciparum* malaria.

Table 1: Clinical profile of P. falciparum complicated malaria

Symptom	Number of patients	Percent
Fever		
1. Intermittent	**57**	**(71.25%)**
2. Remittent	**14**	**(17.5%)**
3. Continuous	**9**	**(11.25%)**
Generalized weakness nausea/anorexia	**65**	**(81.25%)**
Vomiting	**36**	**(45%)**
Altered sensorium	**11**	**(13.75%)**
Unconscious	**23**	**(28.75%)**
Convulsion	**4**	**(5%)**
Meningeal signs	**3**	**(3.75%)**
Papilloedema	**2**	**(2.5%)**
Hypoglycemia	**1**	**(1.25%)**
Jaundice	**47**	**(58.75%)**
Pallor	**39**	**(48.75%)**
Headache	**34**	**(42.5%)**
Hypotension	**12**	**(15%)**
Oligurea	**4**	**(5%)**
Breathlessness	**7**	**(8.75)**
Bleeding tendency	**2**	**(2.5%)**
Hepatomegaly	**26**	**(32.5%)**
Spleenomegaly	**28**	**(35%)**

Table 2: Mean and standard deviation of laboratory parameters of complicated P. falciparum malaria

Laboratory parameter	Mean± Standard deviation
Hb (gm%)	6.3 ±1.5
TC (cmm)	9840±2400
Platelet count (cmm)	76,000±27,000
BUL (mg%)	87±46
Sr. Creatinine (mg%)	5.9 ±3.6
Total bilirubin (mg/dL.)	11.9 ±2.3
SGOT (U/L)	196 ±29
SGPT (U/L)	174 ±32
Alpo4	200 ±27
Prothrombin time	1.6 ±0.3
pH	6.6 ±0.45

Table 3: Clinical presentation and complications of complicated malaria

Number ofcomplicationsTotal	Duration of hospital stay (days)	Patients (n= 73)	Death (n= 8)
Single complication			
Cerebral malaria	**8**	**16**	**0**
Jaundice	**9**	**17**	**0**
Anemia	**7**	**16**	**0**
Two complications:			
Jaundice with ARF	**6**	**4**	**0**
Jaundice with anemia	**13**	**14**	
Three complications:			
Cerebral malaria withjaundice with anemia	**15**	**7**	**4**
Multiple complications			
Cerebral malaria withARF with ARDS withthrombocytopenia	**5**	**6**	**5**

Discussion

We compared our results with various studies withdifferent geographic area. *Kochar et al*. in their study of532 patients with *P. falciparum* malaria observed that,cerebral malaria (25.75 %), hepatic involvement (11.47 %),spontaneous bleeding (9.58 %), severe anemia (5.83 %),ARDS (3 %) and renal failure (2.07 %) were the importantmanifestations.[6] Overall mortality was 11.09 %. Moralitywas highest in ARDS (81.25 %) followed by severe anemia(70.97 %), renal failure (45.45 %), jaundice (36.06 %)and cerebral malaria (33.57 %). Mortality was very high(82.35 %) in those persons who presented with more than 3 syndromes together. These findings are comparablewith our study were case fatality rate with multi-organdysfunction was 80 % with ARDS and ARF. Mishra SKet al.in their study stated that the severe malaria is invariablycaused by *Plasmodium falciparum* and acute renal failure andjaundice are more common among adults.[7]It wasobserved that 72 of 440 patients with microscopicallyand polymerase chain reaction (PCR) confirmedmonoinfection of *P. vivax*had severe manifestationsand these were jaundice 33 (45.8%) severe anemia, 11(15.3%), respiratory distress with acidosis, eight (11.1%),acute renal failure, seven (9.7%), cerebral dysfunctionwith convulsions, six (8.6%) and abnormal bleeding,six (8.6%). Our observations showed 32 of 201 patientsinfected with *P. vivax*had renal failure 21 (10.4%) hadjaundice, 19 (9.5%) had cerebral dysfunction withconvulsions, 15 (7.46%) had severe anemia, seven (3.5%)had abnormal bleeding and anemia (.5%).[6]Few reportswere observed from elsewhere in recent years.8-10 *P. falciparum* was responsible for 80.9% cases of renal failurein malaria; whereas, *P. vivax*was responsible for 11.7%.[11] Severe manifestations with *P. vivax*monoinfection are similar to those of severe *P. falciparum* infection and include cerebral malaria with generalized convulsions and status epilepticus,[12] severe anemia,5 hepatic dysfunction and jaundice,[13] acute lung injury, ARDS and pulmonary edema, shock, splenic rupture,14 acute renal failure,[15,16] and severe thrombocytopenia with or without bleeding from different parts of the body. Considering increasing trend of multiorgan dysfunction in complicated malaria and various other diseases, there is pressing need of development of emergency medicine faculty in urban as well as rural India to reduce morbidity and mortality.

Conclusion

Early diagnosis and prompt treatment will reduce the mortality due to malaria. Early recognition of pulmonary involvement and timely intubation and artificial ventilation is vital to improve outcome of complicated *P.falciparum* malaria. Multi-organ failure was the commonest cause of death. Currently, high quality intensive care, early institution of artificial ventilation and daily intensive renal replacement therapy and avoidance of nephrotoxic drugs are standard practice of the prevention and management of ARDS with ARF.

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