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Research Article

SEVERITY ASSESSMENT WITH RISK PREDICTION USING MALARIA SEVERITY SCORE IN PATIENTS OF FALCIPARUM MALARIA

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ABSTRACT

According to the *World Malaria Report 2010*, there were 225 million cases of malaria and an estimated 781 000 deaths in 2009. Even if the diagnostic features of severe malaria have been set out by W.H.O, there are no objective criteria to quantify the severity of each complication. The aim of the study is to find out the usefulness of malaria severity score to predict to assess severity with risk prediction and design appropriate management measures. All adult patients (>18 years) of malaria presented to Department of Medicine of Sri R.L.JALAPPA Hospital and Research centre, for a period of one year. All Proven cases of P. *falciparum* malaria in adults. (Thin and Thick Smear study/ Rapid Card Test for malaria /QBC test) was included. Study was done in following steps

1. Enrolment of patients as per above criteria.
2. Defining Organ dysfunction as per Malaria severity score.
3. Defining 3 levels of severity of organ dysfunction as per Malaria Severity score.
4. Calculation of Severity score and statistical analysis.

GCS was impaired in 6.7%, 36.7 % had impaired serum creatinine and 50 % impaired blood urea. Total bilirubin was high in 27.7 %. Systolic blood pressure less than 90 mmHg was seen in 13.3 %, blood glucose was impaired in 3.3%. Haemoglobin was decreased in 46.7%, low platelets was seen in 36.7% and altered total counts in 26.6 %. In Total Organs involved, 6.66 % patient had five organ system involved that's highest in our study. Highest group was two organ involvements, i.e. 26.66 %. In the study it was observed that the majority 36.7% had a probability of death 3.1%. The maximum probability of death was 88.8% in 6.7% subjects. Though there were >40% probability of death among 10% of subjects all the patients survived by aggressive management in Medical Intensive Care unit with continuous monitoring, Artesunate based combination therapy and supportive care. Patient was observed and monitored 24 hours in Medical Intensive Unit and treated. Malaria severity score helps to assess severity and risk stratification and to allot better resources.

Malaria severity score can help physicians to assess severity and stratify the risk and allocated resources as per need in limited resource setting, a common scenario in our country. It`s helpful in predicting outcome as probability of death is given for each score and patient with high probability of mortality can identified , to provide more attention and quality care. Though further validation and trials , are needed with larger sample size.

Keywords: *Plasmodium Falciparum, Malaria Severity Score, Organ Dysfunction Score,*

INTRODUCTION

Just like the absence of sadness is not joy, the absence of disease is not health. The W.H.O States this, and all of us instinctively know it. Health is our greatest gift. It is GOD given, but the duty to nurture it is ours alone.

According to the World Malaria Report 2010, there were 225 million cases of malaria and an estimated 781 000 deaths in 2009. Malaria is one of the major public health problems in Karnataka and contributes about 7-10% of the total cases of malaria in the country (National Institute of Malaria research, 2011). In Kolar, Geographical reconnaissance ,revealed that irrigation tanks, wells and streams are the major breeding grounds for the mosquitoes *Anopheles culicifacies* and *An. Fluviatilis* , known vectors of malaria (National Institute of Malaria research, 2011). Kolar district has always been an endemic area for malaria (Muninarayana *et al.*, 2008). A study from Sri Devraj Urs Medical College showed that despite good

awareness about malaria, adoption of the mosquito control methods was poor in the area (Muninarayana *et al.*, 2008).

It has been observed that no two patients of falciparum malaria are same in severity (Mohapatra *et al., 2009*). Research on objective assessment of disease severity and prediction of mortality risk in malaria is lacking even if it frequently develops multiple organ dysfunction during the course of illness (Helbok *et al.*, 2005, Krishnan *et al.*, 2003). Objective risk assessment have been proved very useful for clinical decision making, in evaluating new therapies, in improving quality of treatment, and for proper utilization of resources in various critical conditions like sepsis, acute myocardial infarction etc (Mohapatra *et al.*, 2001).

Even if the diagnostic features of severe malaria have been set out by W.H.O, there are no objective criteria to quantify the severity of each complication. The aim of the study is to find out the usefulness of malaria severity score to predict to assess severity with risk prediction and design appropriate management measures.

MATERIALS AND METHODS

All adult patients (>18 years) of malaria presented to Department of Medicine of Sri R.L. Jalappa Hospital and Research centre, attached to Sri Devaraj URS Medical College, for a period of one year. All Proven cases of *P. falciparum* malaria in adults (Thin and Thick Smear study/ Rapid Card Test for malaria /QBC test) were included. Every patient will be evaluated by history, clinical examination and relevant investigations and stratified as per malaria severity score. Exclusion criteria are following: Diabetes mellitus, chronic renal failure, chronic liver disease, Coronary artery disease.

Sampling and Sample Size: All the confirmed cases of Plasmodium Falciparum reported to RLJH and SNR during the duration of one year was taken into study.

Method of Collection of Data: Data was collected by using pre-tested Proforma meeting the objectives of the study. The purpose of the study was carefully explained to the patients and informed consent was taken. Blood was drawn for Peripheral smear for malaria parasite and other investigations were sent for examination. Patients was examined and assessed on admission.

Study was done in following steps:

1. Enrolment of patients as per above criteria.
2. Defining Organ dysfunction as mentioned below.
3. Defining 3 levels of severity of organ dysfunction as mentioned below.
4. Severity score as mentioned below.

Criteria for diagnosis of organ dysfunction in malaria (Mohapatra *et al.*, 2009) modified with added component i.e blood arterial pH and HCO_3 (Longo *et al.*, 2012):

a) General :

1) Fever $\geq 101^0$F.

2) Presence of parasitic form of P. falciparum in peripheral smear or positive rapid card test.

b) Organ Specific Organ System Parameters for defining dysfunction

1. Neurologic	a) Glasgow Coma Scale $\leq$ 13
2. Renal (one or more)	a) S-creatinine $\geq$ 1.2 mg/dL
	b) B. Urea $\geq$ 36.0 mg/ dL
3. Hepatic	a) S. bilirubin $\geq$ 2.0 mg/dL
4. Respiratory	a) Respiratory rate $\geq$ 30/ minute
5. Cardiac (one or more)	a) Systolic blood pressure $\leq$ 90 mm Hg.
	b) Heart rate $\geq$ 120 beats / minute
	< 51 beats/min
6. Metabolic	a) Blood. Glucose $\leq$ 60 mg/dL
	b) arterial pH <7.3 [14]
	c) serum HCO_3 > 15 mmol/L [14]

7. Haematological (one or more)	a) Haemoglobin < 10.0 gm/dL
	b) Platelet count < 80,000/µL
	c) Total leukocyte count <4000/µL or > 12,000

Each parameter will be further sub divided and score will be allotted according the table below and analysed for severity assessment and outcome i.e full recovery or death will assed according to the severity.

Parameters of Range of variables for different Level of Severity Organ Dysfunction (Mohapatra *et al.*, 2009) modified with added component i.e blood arterial pH and HCO_3 (Longo *et al.*, 2012)

	Level-0	Level- I	Level-II	Level-III
1) *Neurologic:* GCS Score	14-15	10-13	7-9	0-6
2) *Renal:* B. Urea(mg/dl)	10.0-36.0	37.0-59.0	60.0-119.0	>120.0
S.Creatinine(mg/dl)	0.6-1.2	1.3-1.9	2.0-4.9	>5.0
3) *Cardiovascular*: Heart rate/min	51-119	120 -139	>140or<51	
Systolic Blood Pressure mmHg	90-160	70-89	41-69	
4) Respiratory: Respiration R/min	20-30	31-40	>41	
5) *Haematologic:* Hb. (gm/dl)	10.0-13.9	7.0-9.9	<7.0	
TLC (/cmm)	4001-16,000	2001-4000	<2000 or 10-20000	
Platelet (/cmm)	80,000-2,50,000	<80,000		
6) *Hepatic:* S. Bilirubin (mg/dl)	<2.0	≥ 2.0		
7) *Metabolic:* B. Glucose (mg/dl)	60.0-110.0	<60.0		
Blood [14]: arterial pH	>7.4	< 7.3		
serum HCO_3	> 15 mmol/L	<15 mmol/L		

Severity Score of each organ dysfunction with different level of severity (Mohapatra *et al.*, 2009)

Organ Dysfunction and Score	0	I	II	III
Neurologic	Score-0	Score-1	Score-3	Score-5
Renal	Score -0	Score -1	Score -3	Score -5
Cardiovascular	Score -0	Score -1	Score -3	
Respiratory	Score -0	Score -1	Score -3	
Hematologic	Score -0	Score -1	Score -3	
Hepatic	Score -0	Score -1		
Metabolic	Score -0	Score -1		

Statistical Analysis

Data was entered into Microsoft excel data sheet and analysis is done by using EPI INFO 7 Version. Descriptive statistics like frequencies and proportions are computed. 'P' Values and Pearson Correlation was computed for continuous variables. Total severity score and probability of death is calculated using the reference values.

RESULTS

In the study it was observed that majority of the patients were in the age group of 30 to 50 years i.e. (50%). It was observed that majority of the case were males i.e. 60% and 40% were Females.

In the study it was observed that majority of the patients had a GCS score of >13 i.e. 93.3%.

In the study it was observed that majority of the subjects had serum creatinine >1.2 mg/dl i.e. 63.3%. Serum Creatinine in majority 66.7% were at level – 0. 26.7% and 6.6% were at level I and level II respectively. There were no subjects at level III. It was also observed that 50% of the subjects had serum urea >36 mg/dl. Majority of subjects were in Level – 0 of severity with respect to Blood urea i.e. 56.7%. 26.7%, 13.3% and 3.3% were in Level I, Level II and Level III score.

In the study it was observed that majority of the subjects had serum bilirubin levels <2mg/dl i.e. 73.3%.

In the study it was observed that majority of the subjects had Heart rate <120 beats per minute i.e. in 96.7%. It was observed that majority of subjects were in Level – 0 of severity with respect to Heart Rate i.e. 93.3%. 3.3% and 3.3% in Level I and Level II Score. For Systolic Blood Pressure majority 93.3% were at level – 0 and 6.7% were at level I.

In our study it was observed that majority of the subjects had Serum Glucose Level >60 mg/dl i.e. in 96.7%. Majority of subjects were in Level – 0 of severity with respect to Blood Glucose i.e. 96.7% and 3.3% were in Level I Score.

In present study it was observed that majority of the subjects had pH Level >7.3 i.e. in 90%. Similarly for Arterial pH majority 90% were at level – 0 and 10% were at level I. Similarly for Serum HCO3 majority 96.7% were at level – 0 and 3.3% were at level I.

In the study it was observed that majority of the subjects had Hb% <10 i.e. in 46.7% , platelet count 80000 i.e. in63.3%.It was observed that majority of subjects were in Level – 0 of severity with respect to Hb% i.e. 56.6%. 26.8% and 16.6% were in Level I and Level II Score. Similarly for Total Leukocyte count majority 90% were at level – 0 and 6.7% were at level I and 3.3% at Level II. Similarly for Platelet count in majority 63.3% were at level – 0 and Low platelet was observed in 36.7% was at level I.

Criteria for Diagnosis of Organ Dysfunction in Malaria with Percentage of patients

	Criteria	n= 30
General	Fever ≥ 101^0F.	9 (30%)
	P. falciparum in peripheral smear or positive rapid card test	30 (100%)
Organ Specific		
Neurologic	Glasgow Coma Scale ≤ 13	2 (6.7%)
Renal (one or more)	a) S-creatinine ≥ 1.2 mg/dL	11 (36.7%)
	b) B. Urea ≥ 36.0 mg/ dL	15 (50%)
Hepatic	S. bilirubin ≥ 2.0 mg/dL	8 (26.7%)
Respiratory	Respiratory rate ≥ 30/ minute	0
Cardiac (one or more)	a) Systolic blood pressure ≤ 90 mm Hg	4 (13.3%)
	b) Heart rate ≥ 120 beats / minute or < 51 beats/min	1 (3.3%)
Metabolic	a) Blood. Glucose ≤ 60 mg/dL	1 (3.3%)
	b) arterial pH <7.3	3 (10%)
	c) serum HCO_3 > 15 mmol/L	29 (96.7)
Haematological (one or more)	a) Haemoglobin < 10.0 gm/dL	14 (46.7%)
	b) Platelet count < 80,000/µL	11 (36.7%)
	c) Total leucocyte count <4000/µL or > 12,000	8 (26.6%)

Table Showing Severity Score and Probability of death

Severity Score (Criteria B)	Probability of death (%)	Frequency	Percent
0	1.20	3	10
1	3.10	12	40
2	4.80	4	13.3
3	7.50	4	13.3
4	10.50	2	6.66
6	21.1	2	6.66
8	40.10	1	3.3
9	51.8	1	3.3
11	61.70	1	3.3
Total		30	100.0

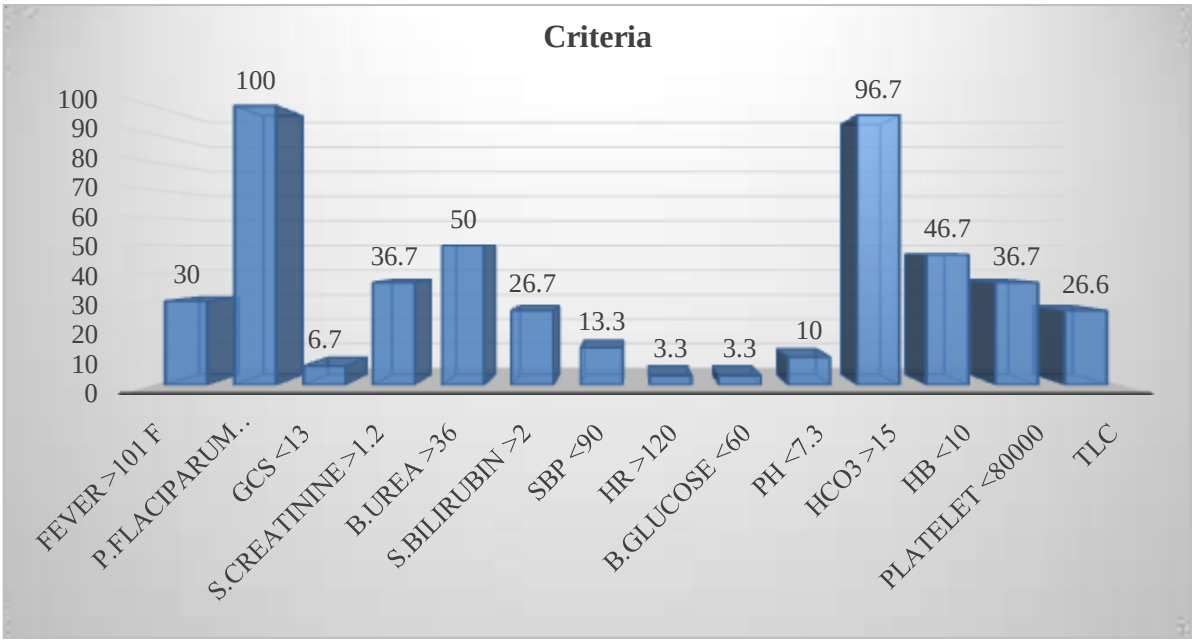

Figure 15: Bar Diagram showing Criteria for Diagnosis of Organ Dysfunction in Malaria

In the study it was observed that the majority 36.7% had a probability of death 3.1%. The maximum probability of death was 88.8% in 6.7% subjects. Though there were >40% probability of death among 10% of subjects all the patients survived by aggressive management in Medical Intensive Care unit with continuous monitoring, Artesunate based combination therapy and supportive care. Patient was observed and monitored 24 hours in Medical Intensive Unit and treated. Malaria severity score helps to assess severity and risk stratification and to allot better resources.

DISCUSSION

Malaria Severity Score for organ dysfunction used in our study is adapted from Malaria severity score by Mohapatra *et al.*, (2009). And this score is modified with extra component of pH and Bicarbonate from arterial blood gas analysis. In study by Mohapatra *et al.*, (2009) it was noted that severe malaria is a variable disease causing dysfunction of various organs in different combinations and with variable grades of severity, which was evident in our study too.

In our study GCS was impaired in 6.7%, 36.7 % had impaired serum creatinine and 50 % impaired blood urea. Total bilirubin was high in 27.7 %. Systolic blood pressure less than 90 mmHg was seen in 13.3 %, blood glucose was impaired in 3.3%. Haemoglobin was decreased in 46.7%, low platelets was seen in 36.7% and altered total counts in 26.6 %. In Total Organs involved, 6.66 % patient had five organ system involved that's highest in our study. Highest group was two organ involvements, i.e. 26.66 %.

In similar study by Mohapatra *et al.*, 2009, highest, 20.8 % patients had only organ dysfunction. In present study highest level of dysfunction is seen in the form of Renal and Haematological involvement, followed by Hepatic and cardiovascular involvement. A patient with highest number of organs involvement, does not necessary translates in high severity as level of severity can be low in each organ dysfunction. Similarly a patient with few organ system involvements can have high severity due highest levels of severity in each organ dysfunction level.

Uncomplicated Malaria accounts for 13.3% in our study whereas comparison 12.4% by Mohapatra *et al.*, 2009. In study by Mohapatra *et al.*, (2009) One organ dysfunction was 20.8 % were as 40% is noted in present study. Two organ dysfunction accounts for 17.1% in our study, in contrast with 26.66 %, by Mohapatra *et al.*, 2009. Similarly three organ dysfunction accounts for 10%, four organ dysfunction accounts for 3.33%, five organ dysfunction accounts for 6.66%, involvement of six organ dysfunction and

seven organ dysfunction was not noted in our study. In contrast in study by Mohapatra *et al.,* 2009 three organ dysfunction accounts for 18.2 %, four organ dysfunction accounts for 17.1%, five organ dysfunction accounts for 4.5%, involvement of six organ dysfunction and seven organ dysfunction was not noted. It can be due to the early treatment with chloroquine at primary health centre where patient presents first, hence prevented from reaching six or seven organ dysfunction.

Either a patient has involvement of several organs with low (level-I) to moderate (level-II) level of dysfunction or few organs with severe level (level-III) of dysfunction. In any such clinical situation the mortality risk is very high.

Each score has been further translated into probability of mortality (Mohapatra *et al.,* 2009). In this study it was observed that the majority 40 % had a probability of death 3.1 %. The maximum probability of death was 61.70 % in 3.3 % subjects. Though there were >40% probability of death among 10% of subjects all the patients survived by aggressive management in Medical Intensive Care unit with continuous monitoring, Artesunate based combination therapy and supportive care. Supportive measures like maintenance of hydration, antibiotics for any concurrent infections, blood transfusion, dialysis, ventilator support etc. were given according to individual needs. Patient with more than 40% probability of mortality was allocated resources aggressively with favourable outcome.

Teaño *et al.,* (2002) from Philippines proposed a clinical scoring index for predicting outcome in cerebral malaria. Scoring protocol was formulated and the 5 variables incorporated into the system, with a possible score of 0-14. Five factors were found to be significantly associated with an unfavourable outcome. Patients with impaired consciousness, multiple convulsions, laboured respiration, circulatory collapse and abnormal bleeding were all found to be highly associated with a poor prognosis.

Mishra *et al.,* (2007) from Ispat General Hospital, Rourkela, Orissa developed a scoring system (Malaria prognostic score) to predict outcome of adults suffering from severe P. falciparum malaria. The malaria score for adults was (MSA) = 1(severe anaemia) + 2 (acute renal failure) + 3(Respiratory distress) + 4 (cerebral malaria). The MSA ranges from 0 to 10. The mortality was 2% for MSA 0 - 2; 10% for MSA 3-4, 40% for MSA 5-6 and 90% for MSA 7 or more. The study results had shown that severe anaemia, acute renal failure, respiratory distress and cerebral malaria were the major factors influencing to the mortality rate of disease

Mohapatra and Das (2009) from Orissa have developed the Malaria Severity Score: a method for severity assessment and risk prediction of hospital mortality for falciparum malaria in adults. In a one more study by Mohapatra *et al.,* 2006 it was found that seven major organ dysfunction occurred commonly in malaria, basis for Malaria severity score based on organ dysfunction. For the assessment of the degree of severity, 12 different variables were extracted from the data base and grouped according to systems .Depending on the range of abnormal finding of the variables 3 levels of severity (I, II, and III) were determined . The level of severity was not equal for all types of Organ dysfunction (OD).

Neurologic and renal dysfunctions were with all the 3 levels of severity and received the maximum of 5 points for the most severe level of dysfunction, hence considered as most severe form of organ dysfunction.

Tangpukedee *et al.,* (2007) developed Malaria Severity Prognostic Score = 4.38 (schizontemia)+ 1.62 (gametocytemia) + 1.17 (dehydration) + 0.14 (overweight by body mass index; BMI) + 0.05 (initial pulse rate) +0.04 (duration of fever before admission) – 0.50 (past history of malaria in last 1 year) – 0.48 (initial serum albumin) –5.66. The results of the study had agreed with those studies that presence of schizontemia and gametocytemia in malaria patients affecting to the severity of disease.

In an earlier study, the APACHE II scoring for predictive outcome in cerebral malaria had been conducted by Wilairatana and Looareesuwan (1998). There were many variables used in the score system e.g., vital signs, serum electrolytes, serum creatinine, hematocrit, etc. However, the results of the study suggested that the APACHE II system was useful for stratifying the prognosis of group outcome in cerebral malaria patients with the accuracy of 95.8% (Wilairatana *et al.,* 1998).

The coma and malaria (CAM) score (Hanson *et al.*,2010), was developed using the multinational SEAQUAMAT trial conducted in Asia and was validated in 2 additional, large prospectively gathered

datasets from Vietnam and Bangladesh. The 5-point CAM score uses only a patient's GCS and the plasma base deficit and has strong predictive value for mortality. Results showed Acidosis (base deficit) and cerebral malaria (measured as Glasgow Coma Score) were the main independent predictors of outcome. The 5-point Coma Acidosis Malaria (CAM) score was simply derived from these 2 variables. Mortality increased steadily with increasing score. A CAM score <2 predicted survival with a positive predictive value and concluded that patients with a CAM score <2 at hospital admission may be safely treated in a general ward, provided that renal function can be monitored. The CAM score should not be used in isolation from clinical evaluation of the patient (Hanson *et al.,* 2010).

In another study by Lurdes *et al.,* (2012), severe cases of malaria in patients admitted to an ICU were reviewed retrospectively and identification of variables associated with in-ICU mortality performed. Malaria prediction score (MPS), malaria score for adults (MSA), simplified acute physiology score (SAPSII) and a score based on WHO's malaria severe criteria were applied.

Two prognostic scores of malaria were applied:

(1) Malaria Prediction Score (MPS) determined by: 2.13 + 0.02 × (age) + 0.25 × (creatinine) - 0.24 × (haemoglobin) + 3.05 (malaria cerebral criteria) + 0.8 (presence of pregnancy) + 0.8 (ventilated) (where age = age in years; creatinine is in mg/dl, haemoglobin in g/dl; presence of pregnancy, cerebral malaria or ventilatory support, when present = 1, when absent = 0);

(2) Malaria Score for Adults (MSA) was applied to all but three children and the score was determined by: 1 (severe anaemia) + 2 (acute renal failure) + 3 (respiratory distress) + 4 (cerebral malaria). The MSA ranges from 0 to 10

Fifty nine patients were included in the study, all but three were adults; 47 (79,6%) were male; parasitaemia on admission, quantified in 48/59 (81.3%) patients, was equal or greater than 2% in 47 of them (97.9%);the most common complications were thrombocytopenia in 54 (91.5%) patients, associated with disseminated intravascular coagulation (DIC) in seven (11.8%), renal failure in 31 (52.5%) patients, 18 of which (30.5%) oliguric, shock in 29 (49.1%) patients, liver dysfunction in 27 (45.7%) patients, academia in 23 (38.9%) patients, cerebral dysfunction in 22 (37.2%) patients, 11 of whom with Unrousable coma, pulmonary edema/ARDS in 22 (37.2%) patients, hypoglycaemia in 18 (30.5%) patients; 29 (49.1%) patients presented five or more dysfunctions. Comparing the four scores, the SAPS II and the WHO score were the most sensitive to death prediction. As per study severe malaria cases should be continued monitored in the ICUs. SAPS II and the WHO score are good predictors of mortality in malaria patients (Lurdes *et al.,* 2012).

In a study by Doherty *et al.,* 2013 retrospective study of patients with WHO severe falciparum malaria admitted to ICU at the Hospital for Tropical Diseases, London, UK. The relationship between clinical variables and risk of death or a prolonged ICU stay were examined with logistic regression. The predictive value of the MSA and CAM score were calculated. 124 patients were included. Cerebral malaria and acute kidney injury occurred earlier (median day 1) than acute respiratory distress syndrome (median day 3). Six patients had community acquired bacterial co-infection. Eight patients were co-infected with HIV, five of whom were newly diagnosed. The positive predictive value of a CAM score <2 or an MSA <5 for death were 12% and 22% respectively. The study showed that both a CAM score <2 and an MSA <5 identified patients who would survive. However, these scores had limited ability to predict mortality and it remains unclear what role, if any, they may play in clinical practice in areas of the world where malaria is not endemic. No clinical factor was associated with a poor outcome but given the low case fatality rate, as the study was under-powered to detect such a difference.

Some of the limitation in our study was that arterial blood gas analysis, may not readily available everywhere. And one of the major strength of study by Mohapatra at el was high number of patient and long duration of study, whereas in comparison our sample size may not be large enough. Being a tertiary care hospital many patient referred are already on treatment rendering them smear or rapid card test negative. Another factor responsible may be for changing prevalence of P.*Falciparum to* P.*Vivax.*

Conclusion

Malaria severity score can help physicians to assess severity and stratify the risk and allocated resources as per need in limited resource setting, a common scenario in our country. It`s helpful in predicting outcome as probability of death is given for each score and patient with high probability of mortality can identified , to provide more attention and quality care. Malaria severity score is good indicator of severity due its stratification of every organ dysfunction in different level of severity. Though further validation and trials, are needed with larger sample size.

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