A STUDY OF MANIFESTATIONS OF SEVERE FALCIPARUM MALARIA IN BIDAR DISTRICT

Vijay Kumar B. A¹, Sandeep Patil², Sajjal Balte³, Shivraj B. Patil⁴

HOW TO CITE THIS ARTICLE:

Vijay Kumar B. A, Sandeep Patil, Sajjal Balte, Shivraj B. Patil. "A Study of Manifestations of Severe Falciparum Malaria in Bidar District". Journal of Evolution of Medical and Dental Sciences 2014; Vol. 3, Issue 28, July14; Page: 7811-7817, DOI: 10.14260/jemds/2014/2977

ABSTRACT: OBJECTIVES: Severe falciparum malaria is a critical illness resulting in multi-organ dysfunctions and death severe malaria is defined by the World Health Organization as qualitative variable. The purpose of this study is to devise a scoring system for predicting outcome in severe falciparum malaria. **METHODS:** 100 cases of severe falciparum malaria diagnosed as per the WHO criteria, were evaluated to determine the parameters which were significantly associated with mortality. Of all the parameters studied, five variables namely cerebral malaria (GCS<11), Renal failure (Creatinine >3mg/dl), respiratory distress (Respiratory rate>24/min), jaundice (bilirubin >10mg/dl) and Shock (Systolic BP<90mm of Hg.) were all found to be associated with a poor prognosis. **RESULTS:** The five selected parameters were analyzed using the odds ratio and new scoring system named as GCRBS score was designed with a possible score from 0-10. With a cut-off score of 5, the GCRBS score predicted mortality with a sensitivity of 85.3% and a specificity of 95.6%. **CONCLUSION:** The GCRBS score is an easy to calculate and apply. Of the 5 parameters, 3 are clinical which can be determined at bedside and only 2 are biochemical which can be done in any laboratory. The most important advantage of this scoring system is that all the 5 parameters are to be assessed quantitatively for allotting a score, which would eliminate the possibility of observer bias.

KEYWORDS: Falciparum malaria, scoring system.

INTRODUCTION: Malaria is an important cause of death and illness in children and adults, especially in tropical countries. As per World malaria report 2010 malaria accounted for a total of 220 million cases globally causing 7 lakhs deaths in 2009. Of these 32 million cases were in South East Asian Region causing 40000 deaths. ¹India reports approximately two-thirds of all confirmed malaria cases in the South East Asia Region, with five states accounting for 60% of these cases: Orissa, Chhattisgarh, Madhya Pradesh, Jharkhand and West Bengal.¹ However in a recently published article the malaria deaths per year in India to be around 2 lakhs with only Orissa accounting for more than 60 thousand deaths.²

WHO enumerates a list of complications for severe falciparum malaria but the importance of each complication has not been assigned. ^{3, 4}For the patients with critical illness various scoring systems have been devised to determine the prognosis. Since severe falciparum malaria is associated with high mortality, a SCORING system for predicting the outcome will be of great help for the treating clinician in identifying patient needing more intensive medical care and to prognosticate the chances of survival.

Mishra et al devised a Malaria Score for Adults⁵ (MSA) prognosticate the outcome in severe falciparum malaria. This score is based on four parameters namely severe anemia, acute renal failure, respiratory distress and cerebral malaria. With a cut-off score of 5, the sensitivity and positive predictive value for mortality was 88.5% and 92.8% respectively.

ORIGINAL ARTICLE

Parameter	Value	Death	Survival	ODDS ratio	P value	Score allotted
	<x	A	b	a x d		
	x	C	d	b x c		
GCS	<7	11	8	9.281	<0.0001	3
	≥7	12	81			
	<11	19	50	3.705	0.0291	1
	≥11	4	39			
Creatinine (in mg/dl)	≥3	20	40	5.778	0.0003	2
	<3	3	49			
Respiratory Rate (per min)	>24	12	13	6.378	0.004	2
	≤24	11	76			
Bilirubin (in mg/dl)	≥10	16	23	6.559	0.002	2
	<10	7	66			
Systolic BP (in MM of Hg)	<90	7	10	3.456	0.0443	1
	≥90	16	79			

Table1: Calculation of ODDS RATIO and allotment of score to each parameter per sensitivity

Parameter		Score
GCS	3-6	3
	7-10	1
	11-15	0
Creatinine (in mg/dl)	>3	2
	≥3	0
Respiratory Rate (per min)	>24	2
	≤24	0
Bilirubin (in mg/dl)	≥10	2
	<10	0
Systolic BP (in MM of Hg)	<90	1
	≥90	0

Table 2: The GCRBS Score

Wilairatana et al in a Bangkok, Thailand applied the APACHE II⁶ scoring to stratify the prognosis in patient of cerebral malaria. With the cutoff point at a score of 24, the APACHE II score stratified the patient's mortality outcome with 94.8% accuracy.

Teana R et al. proposed a Clinical Scoring Index⁸ for predicting outcome in cerebral malaria with a possible score of 0-14. Level of consciousness, multiple convulsions, labored respiration, circulatory collapse and abnormal bleeding were the parameters taken for calculating the score. With an optimum score of 7, it could predict mortality with a sensitivity of 91% and specificity of 95.6%.

MK Mohanpatra, SP Das devised a Malaria Severity Score⁸ for Severity Assessment and Risk Prediction of Hospital Morality for falciparum Malaria in adults. There is a score for each organ dysfunction according to its severity level and for each score there is also a probability of mortality.

MATERIAL AND METHODS: This study was conducted in the department of Medicine, Bidar Institute of Medical Sciences, Bidar, Karnataka.

ORIGINAL ARTICLE

A total number of 60 patients diagnosed to be severe falciparum malaria as per WHO criteria 2006⁴ admitted to medicine ward were taken into the study. Malaria diagnosis was confirmed by Thick or thin smear/ optimal test/ Immunochromatographic test positive for falciparum malaria.

A detailed clinical evaluation of each patient including history and physical emanation was done. Investigations including hemoglobin, DC, TLC, Serum Urea, Serum Creatinine, Liver function test and Arterial blood gas analysis was done for all patients.

All the cases were treated with Artesunate (2.mg/kg stat IV followed by 2.4mg/kg at 12 and 24 h and then daily followed by a full course of an effective ACT (Artemisinin-based combinations therapy). Supportive therapy was give as per standard recommendations on packed cell/ fresh blood) was given in patients with Hematocrit<20% or with bleeding manifestation/ DIC.

Mechanical ventilation was provided to patients with pulmonary edema/ARDS. Inotrope support (Dopamine/ Nor-adrenaline) was given in patients with shock not improving with IV fluids. Patients with renal failure requiring dialysis were given Hemodialysis sessions as per need.

Score	Survival	Death	Sensitivity	Specificity
<x	a	b	$(a/a+c) \times 100$	$(d/b+d) \times 100$
$\geq X$	c	d		
<3	41	0	46.1%	100%
≥ 3	48	23		
<4	67	0	75.2%	100%
≥ 4	22	23		
>5	76	1	85.3%	95.6%
≥ 5	13	22		
<6	85	7	95.5%	69.6%
≥ 6	4	16		
<7	85	13	95.5%	43.5%
≥ 7	4	10		
<8	88	19	98.8%	43.5%
≥ 8	1	4		

Table 3: Computation of sensitivity and specificity for GCRBS score

ORIGINAL ARTICLE

Clinical finding, hematological and biochemical investigations were analyzed using SPSS v16 and Instat 3 software. Variable which had significant correlation to clinical outcome were subject to chi-square analysis (or Fischer exact probability test where applicable) with a variable considered significant if $p \leq 0.05$. The clinical parameters associated with an unfavorable outcome were analysed using the Odds ratio. In this study, the Odds ratios express how many times a clinical parameter is likely to be found in the death group as compared to the survival group.

The computed odds ratios were divided by three to avoid a wide range of score. This is possible because there was no computed odds ratio equivalent to zero. The highest possible score is 10, while the lowest is 0. The higher the score, the poorer the prognosis.

The proposed scoring index was tested on the original 60 patients diagnosed with severe falciparum malaria. The score for each patient was obtained by adding the specific values designated from the presence of the clinical parameters. Sensitivity and specificity for each clinical score were computed and the values obtained were plotted on an ROC¹⁰ (Receiver Operating Characteristic) curve to determine the best cut-off point. Malaria Score for Adults,⁵ APACHE II Score⁷ and Clinical Scoring Index⁸ was also calculated for all cases and compared using standard statistical methods.

RESULTS: The study to develop the score included 60 severe malaria patients with 9 deaths. The cases had a mean age of 35.8 ± 15.1 years. Only 8 cases were female of which 2 died. There was no significant difference in the age and sex of the survival and death group.

ORIGINAL ARTICLE

Scoring system	Cut-off score	Sensitivity (%)	Specificity (%)
Apache II	24	98.8	17.4
MSA	5	63	95.6
CSI	7	91	7
GCRBS	5	85.3	95.6

Table 4: Comparison other scoring systems

All the variable were analysed (viz., age, gender, Glasgow Come Score (GCS) hyperpyrexia, hypotension, severe anemia, acute renal failure, jaundice, hypoglycemia, respiratory rate). Of these cerebral malaria (GCS<11), Renal failure (Creatinine>3gm/ dl), Respiratory distress (Respiratory rate>24/min), Jaundice (Bilirubin>10mg/dl) and Shock (Systolic BP<90 mm of Hg) were significantly associated with death ($p<0.05$) (Table 1).

The computed odds ratios for the 5 clinical parameters that were shown to be significantly associated with poor outcome are shown in table associated with poor outcome are shown in Table 1. Table 2 shows the proposed GCRBS score for predicting outcome in severe falciparum malaria. A score of 5 was selected as the best cut-off point with sensitivity of 84.8%, specificity of 94.9% (Table 3).

As seen in the ROC curve (figure 1), this cut-off point is the best compromise between maximum sensitivity and maximum specificity and therefore the best cut-off in terms of predicting unfavorable outcome in sever falciparum malaria. Table 4 shows the comparison between sensitivity and specificity of GCRBS score with other score at their respective cut-off scores.

DISCUSSION: The critical course of severe malaria is variable depending on the presence of one or several complications. There are numerous severity-of-illness scoring systems that have been developed and validated as tools to accurately assess populations of critically ill patients. Currently, the most commonly utilized scoring, system are the PACHE (Acute Physiological and Chronic health Evaluation), system, the MPM (Mortality probability model), and the SAPS (simplified acute physiology score) system, all designed to predict outcomes in critical illness.

In this study APACHE II⁶, Clinical Scoring Index (CSI)⁸ and malaria Score for Adults⁵ (MSA) and specificity were calculated for each and sensitivity and specificity were calculated at the cut-off scores determined in the original studies. In contrast to the study by Wilairatana et al in our study only 4 patients in the death group has a APACHE II score of 24 or more resulting in a very lower specificity of 16.4%. Similarly at a CSI score of 7 the sensitivity and specificity was 90.8% and 69.5% respectively in our study as compared to a sensitivity of 91.8% and specificity of 94.9% in the study by Teana R et al.

The results for MSA score were also quite different. Compared to a sensitivity of 88.9% in the study by Mishra et al at a cut off score of 5, the sensitivity turned out to be just 62.9% in the current study.

The APACHE II score is difficult to remember cumbersome to calculate and needs sophisticated laboratory. The MSA and CSI score although simple and easy to calculate have subjective variables which would increase the observer bias. Hence, there has always been a need of a

ORIGINAL ARTICLE

simple, easy to apply score with quantitative variables so that observer bias can be minimized. The present GCRBS score is an attempt in that direction.

As seen in the previous studies cerebral malaria and acute renal failure are the major contributors to death. Since the neurological status of cerebral malaria patient can vary from disoriented to stupor to coma, GCS being an easy to calculate quantitative variable. Similarly a respiratory rate of more than 24 has been ARDS which has a high case fatality rate. But contrary to the previous studies jaundice has been found to be an important predictor of mortality in this study. We observed that with increase in bilirubin level the death rate also rises, more steeply with bilirubin levels >10 mg/dl.

The GCRBS score has a possible score of 0 to 10 higher the score poorer the outcome. 5 parameters are required for its calculation namely GCS, Creatinine, Respiratory rate, Bilirubin and Systolic BP (mnemonic GCRBS). Out of these only two (Creatinine and bilirubin) are laboratory parameters and the rest there are clinical parameters which can be easily determined at the bedside. Then a score is allotted to each parameter as shown in Table 2 and their sum gives the GCRBS score. The most important advantage of this scoring system is that all the 5 parameters are to be assessed quantitatively for allotting a score.

REFERENCES:

1. World malaria Report 2010;
www.who.int/malaria/world_malaria_report_2010/en/index.html.
2. Dhingra N, Jha P, Sharma VP, Cohen AA, Jotkar RM, Rodriguez PS, Bassani DG, Suraweera W, Laxminarayan R, Peto R, for the Million Death Study Collaborators. Adult and child malaria mortality in India a nationality representative mortality survey. *Lancet* 2010; 376:1768-74.
3. WHO: Severe Falciparum Malaria. *Trans R Soc. Tropical Med Hyg* 2000; 94:S1-S90.
4. WHO 2006: Guidelines for the treatment of malaria; 2nd edition
5. Saroj K Mishra, Pinaki Panigrahi, Rajalaxmi Mishra, Sanjib Mohanty. Prediction of outcome in adults with severe falciparum malaria: a new scoring system. *Malaria Journal* 2007, 6:24 doi:10.1186/1475-2875-6-24
6. Knauss WA, Drepper EA, Wagner Dp, Zimmermann JE. APACHE II- a severity of diseased classification system. *Critical Care Medicine* 1985; 13:818-829.
7. Wilairatana P, Looareesuwan S. APACHE II scoring for predicting outcome in cerebral malaria. *Journal of Tropical Medicine and Hygiene* 1995; 98: 256-260.
8. Taeno R, Robles AM, Dimaano E. A Clinical Scoring Index for Predicting Outcome in Cerebral Malaria. *Phill Journal Microbiolinfet Dis* 2003;32:43-4.
9. Mohapatra MK, Das SP. The Malaria Severity Score: a Method for Severity Assessment and Risk Prediction of Hospital Mortality for Falciparum Malaria in Adults. *JAPI* 2009;57:119-26.
10. Zweigh MH, Campbell G. Receiver-operating characteristic (ROC) plots: a fundamental evaluation tool in clinical medicine. *Clinical Chemistry* 1993;39:561-577.
11. DS Walsh. *The Journal of Infectious disease*; 1999, Oxford Journal; P. vivax infections, primaquine resistance; [www.oxfordjournal:Medicine:Vol180\(4\)\(issue4\):1282-87](http://www.oxfordjournal:Medicine:Vol180(4)(issue4):1282-87).
12. B.Saha. Severe Falciparum Malaria-predicting The Outcome;[www. apiindia.org:2011:469-74](http://www.apiindia.org:2011:469-74).
13. HD Mazigo. Co-infection with P. falciparum malaria: *Parasites & vectors*: 2010;
www.parasitesandvectors.com/content/3/1/44

ORIGINAL ARTICLE

14. Mishra. A Rare case report of fatal fulminate hepatic failure in a child due to mixed vivax and falciparum malaria: hindwai publishing corporation; 2011; [www.hindwi.com/ journals/crpe/2011/614054](http://www.hindwi.com/journals/crpe/2011/614054).

AUTHORS:

1. Vijay Kumar B. A.
2. SandeepPatil
3. SajjalBalte
4. Shivraj B. Patil

PARTICULARS OF CONTRIBUTORS:

1. Associate Professor, Department of General Medicine, BRIMS, Bidar.
2. Senior Resident, Department of General Medicine, BRIMS, Bidar.
3. Junior Resident, Department of General Medicine, BRIMS, Bidar.
4. Junior Resident, Department of General Medicine, BRIMS, Bidar.

NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Vijay Kumar B. A,
Associate Professor,
Department of Medicine,
Bidar Institute of Medical Sciences,
Bidar.
Email: vijayvb8@gmail.com

Date of Submission: 26/06/2014.

Date of Peer Review: 27/06/2014.

Date of Acceptance: 02/07/2014.

Date of Publishing: 11/07/2014.