European Journal of Molecular & Clinical Medicine

ISSN 2515-8260 Volume 9, Issue 7, Summer 2022

ORIGINAL RESEARCH

To assess the severity of plasmodium vivax malaria according to malaria severity score and its role in predicting mortality

[1]Dr Ravish Padda, [2]Dr Navjot Singh, [3]Dr Lydia Solomon

[1]Registrar, [2]Professor, [3]Associate Professor, Department of Internal Medicine, Christian Medical College, Ludhiana, Punjab, India

Correspondence:
Dr Lydia Solomon
Associate Professor, Department of Internal Medicine, Christian Medical College, Ludhiana, Punjab, India

Received: 07 September, 2022 Accepted: 11 October, 2022

ABSTRACT

Malaria is one of the most widespread infections in the tropics, and also one of the most dangerous. There are four types of Plasmodium causing malaria of which Plasmodium vivax and falciparum are common in India. There is a huge burden of disease and it is responsible for increased mortality and morbidity. Due to paucity of research to quantify the severity and to predict the mortality risk of vivax malaria even though it affects multiple organ system during the course of the disease, this study was undertaken, to assess the severity of P. vivax malaria according to malaria severity score (MSS). The Aim of this study was to analyze the role of Malaria Severity Score (MSS) in predicting morbidity and mortality in patients affected by Plasmodium vivax infection.

Methods: This was a prospective observational study conducted in department of medicine from 1st December 2019 to 30th September 2021, in a tertiary care hospital in North India. All adult patients with age more than 18 years, with plasmodium vivax infection were included in the study. The diagnosis of malaria was made on thick and thin smear with malarial parasite identification and/or RDT (Rapid diagnostic test) kits. Organ dysfunction (OD) of each patient was assessed based on clinical and laboratory parameters and categorized into various levels of severity. Each level was translated into a score and Malaria Severity Score was calculated.

Results: A total 55 P. vivax positive patients were included in the study. Mean age was 37.53 years. There were 35(63.64%) males and 20(36.36%) females. Most common symptom was fever (98.18%) followed by yellowish discoloration of eyes (30.91%), vomiting (16.36%), generalized weakness (9.09%), headache (5.45%), cough (3.64%), loose stools (3.64%), abdominal pain (3.64%) and hemoptysis (3.64%). Significant association was found between jaundice and renal failure and mortality (p-0.00163) and between platelet count less than 80000 and mortality (p- 0.018). Mean MSS was 4.45 ± 3.77. Mortality was seen in 4(7.27%) patients. Mean duration of hospital stay was 5.09 ± 2.22 days.

Conclusion: MSS >7 was a significant predictor of mortalityin P. vivax malaria patients (p <0.0001).

Keywords: Malaria Severity Score (MSS), Plasmodium vivax (P. vivax), Organ Dysfunction (OD)

INTRODUCTION

Malaria is caused due to five species of plasmodium, which infect the humans naturally. In majority of humans, the burden is because of the falciparum and vivax species of Plasmodium. The clinical course of malaria depends on numerous host and parasite related factors and is manifested by a multitude of signs and symptoms. The disease spectrum progresses from stage of asymptomatic parasitemia to uncomplicated malaria, to severe malaria, leading to death in some patients. The delay in the diagnosis can be one of the major factors linked to mortality in cases with severe malaria and thus we need to know the risk factors for severe malaria and its relation to morbidity and mortality. Due to paucity of research to assess the severity of P. vivax malaria according to MSS, this study was undertaken.

MATERIALS AND METHODS

This was a cohort study which was done in the Department of Medicine, in a tertiary hospital in North India, from 1st December 2019 to 30th September 2021, on 55 patients, whose age was more than 18 years, with P. vivax malaria infection, whose diagnosis was by staining the peripheral blood smear with Giemsa stain and detecting the asexual forms of P. vivax and/or rapid diagnostic test (RDT) kits, and by using the thick and thin blood smear of the patient under light microscope to assess the percentage of red blood cells that are infected (parasite density), during the time of admission. Assessment of OD was made based on clinical and laboratory parameters (Table 1).

Organ system involved	Criteria
Neurological	Glasgow Come Scale <13
Kidneys (one or more)	a. Urine output<750ml/24hours b. Serum creatinine>1.2mg/dl c. Blood urea>36mg/dl
Liver	Serum bilirubin>2mg/dl
Respiratory	Respiratory rate>30/minute
Heart (one or more)	Systolic Blood pressure<90mmHg Heart rate>120beats/min or<51
Metabolic	Blood glucose <60mg/dl
Hematological (one or more)	Hemoglobin <10gm/dl Platelet count <80,000/microlitre Total Leucocyte count<4000/microlitre or >12,000

Table 1: The Criteria used for diagnosis of organ dysfunction in malaria[1]

Organ dysfunction (OD) in malaria is noted by taking different criteria into consideration. Based on its severity of each organ involvement, a level was allotted (Table 2). Based on the variables of each organ involvement, the dysfunction in 7 organ systems were divided into 3 levels of severity (I to III), Central nervous system and Kidney dysfunctions, each had 3 levels of severity. Hematologic, cardiovascular, and respiratory dysfunctions had 2 levels of severity each whereas hepatic and metabolic dysfunctions had 1 level of severity. Level I, II and III severities of OD, were given 1,3, and 5 points respectively. A score of 0 was given if there was no organ failure.

Organ involved	Level 0	Level 1	Level 2	Level 3
Neurology Glasco Coma Scale	14-15	10-13	7-9	<7
Kidneys				
Blood Urea(mg/dl)	10-36	37-59	60-119	>120
Serum Creatinine(mg/dl)	0.6-1.2	1.3-1.9	2.0-4.9	>5.0
Urine Output (liters/day)	0.75-3.9	0.5-0.75	0.4-0.5	<0.4

Heart Heart rate(beats/min) Systolic Blood Pressure(mmHg)	51-119 90-160	120-139 70-89	>140 or< 51 41-69	
Respiratory Respiratory Rate (/min)	20-30	31-40	>41	
Hematological Hemoglobin (gm/dl) Total Leukocyte count(/cumm) Platelet count(/cumm)	10-13.9 4001-16000 80000-250000	7.0-9.9 2001-4000 <80000	<7.0 <2000	
Liver Serum Bilirubin(mg/dl)	<2.0	>2.0		
Metabolic Blood glucose (mg/dl)	60-110	<60		

Table 2: Organ specific parameters

Every level is translated into corresponding score to estimate the MSS (Table 3).

The Malaria Severity Score (MSS) is used to analyze the severity of disease among patients with malaria and to analyze the probability of risk of mortality [(1)]

The additive score in a patient is called the MSS which ranges from 0 to 21. Individually, each score was calculated for mortality risk. [(1)]

Organ Dysfunction and Score	**Severity Level**			
	I Score	**II Score**	**III Score**	**IV Score**
Neurological	0	1	3	5
Renal	0	1	3	5
Cardiovascular	0	1	3	
Respiratory	0	1	3	
Hematological	0	1	3	
Hepatic	0	1		
Metabolic	0	1		

Table 3: Different levels of severity and M.S.S. of each OD [(1)]

Total score was calculated and analyzed

STATISTICS

Microsoft excel sheet was used to enter the data, which was summarized using frequency distribution and descriptive analysis. Association of categorical variables was done by using Chi square test. To find the association of continuous variables between two groups, independent t-test or Mann-Whitney test were used. To compare the continuous variables between more than two groups, One Way ANOVA or Kruskal Wallis were used. P value <0.05 was considered significant. Using SPSS (Statistical Packages for Social Sciences, version 21.0. Armonk, NY: IBM corp.), all statistical analysis were performed.

RESULTS

This prospective study was conducted in the Department of Medicine, at a tertiary hospital in North India, which included 55 patients of age more than 18 years and confirmed diagnosis of Plasmodium vivax malaria on peripheral blood smear and/or RDT. Clinical and laboratory

parameters were noted and severity of malaria was assessed using Malaria Severity Score and results are as follows.

A total of 55 patients with P. vivax were included. The mean age was 37.53 years, with 35(63.64%) males and 20(36.36%) females. Most common symptom was fever (98.18%) followed by yellowish discoloration of eyes (30.91%), vomiting (16.36%), generalized weakness (9.09%), headache (5.45%), cough (3.64%), loose stools (3.64%), abdominal pain (3.64%) and hemoptysis (3.64%).

Significant association was found between jaundice, acute kidney injury and mortality (0.00163) and also between platelet count less than 80000 and mortality (p- 0.018).

The total Malaria Severity Score of the study subjects enrolled in study with maximum being 21 and minimum being 0, the mean malaria severity score was 4.45 ± 3.77.

Malaria Severity Score	Number of patients and their percentage	Total Mortality (percentage)
<5	35(63.64%)	0 (0.00%)
5 – 10	16 (29.09%)	1 (6.25%)
11 – 15	3 (5.45%)	2 (66.67%)
>15	1 (1.82%)	1 (100.00%)

Table 4 – Relationship of malaria severity score with mortality

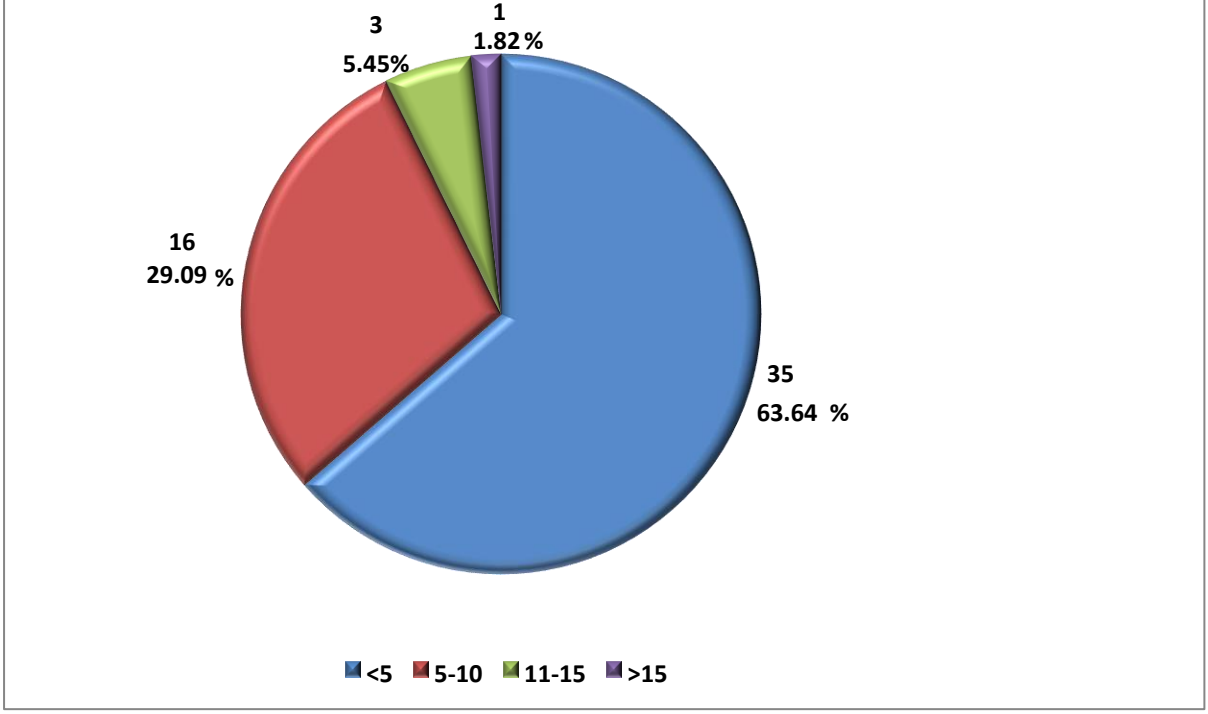

Figure 1: Distribution of risk of mortality and severity score of study subjects

Figure 1 and Table 4 shows that in majority of patients, 35(63.64%), the malaria severity score was less than 5, followed by 16(29.09%) having MSS between 5-10, 3(5.45%) having MSS between 11-15 and only one having MSS more than 15(1.82%).

The use of MSS has been seldom done in P. vivax which highlights the importance of the present study.

Variables	Total score
Area under the ROC curve (AUC)	0.978
Standard Error	0.0216
95% Confidence interval	0.897 to 0.999
P value	<0.0001
Cut off	>7
Sensitivity (95% CI)	100% (39.8 - 100.0%)
Specificity (95% CI)	90.2% (78.6 - 96.7%)
PPV (95% CI)	44.4% (13.7 - 78.8%)
NPV (95% CI)	100% (92.3 - 100.0%)
Diagnostic accuracy	90.91%

Table 5 -Receiver operating characteristic curve (ROC) of total malaria severity score for predicting mortality

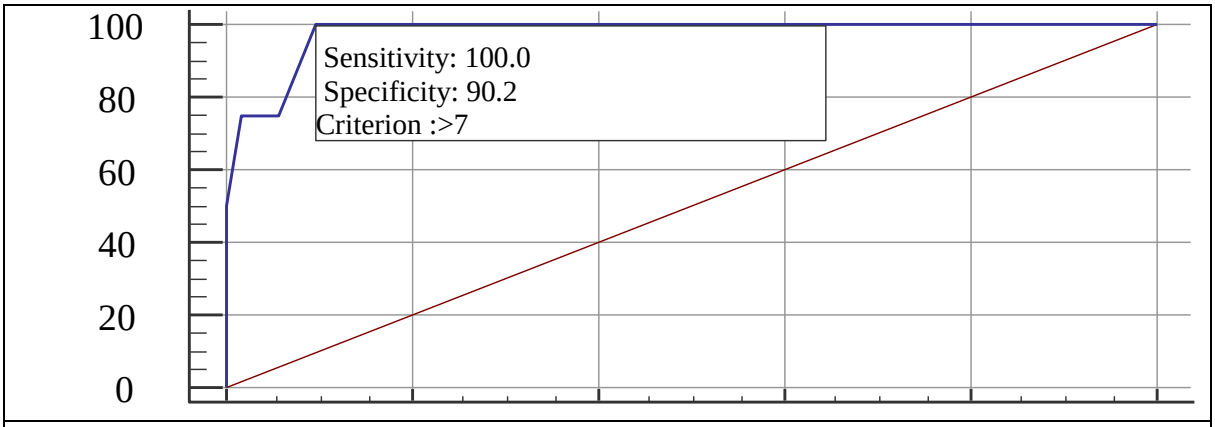

Figure 2 - Receiver operating characteristic curve of total score for predicting mortality

ROC curves above the diagonal line are considered to have reasonable discriminating ability to predict mortality. Interpretation of the AUC showed that the performance of total score (AUC 0.978; 95% CI: 0.897 to 0.999) was outstanding. A significant predictor of mortality of the total score at cut off point of >7 was made, with chances of correctly predicting mortality being 97.80%. Table 5 and Figure 2 show that among the patients who died, 100% of patients had total score >7. If total score >7, then there was 44.40% probability of mortality and if Total score ≤7, then 100% chances of no mortality. Among patients who were discharged, 90.20% of patients had Total score ≤7.

DISCUSSION

A number of factors, both of the host and the parasite, can vary the clinical course of the disease and is manifested by various signs and symptoms. The spectrum of disease varies from asymptomatic parasitemia to uncomplicated malaria, to severe malaria, even leading to mortality in few. One third of all malaria cases in India are due to P. vivax, with urban areas having a higher prevalence. [3]

It was observed that most common complication was jaundice (41.8%), followed by renal failure (40%) and pulmonary edema (1.82%). Convulsions and hypoglycemia were not seen

in any patients. There was a significant association between mortality and presence of Thrombocytopenia (p- 0.018), Jaundice (p-0.00163) and Renal failure (p-0.00163).

TOTAL MSS (MALARIA SEVERITY SCORE)

The Mean value of total score of study subjects was 4.45 ± 3.77 with median (25th-75th percentile) of 4(2-5). In majority 35(63.64%) of patients, MSS was less than 5, with no mortality seen in this group. Followed by MSS of 5-10 in 16(29.09%) patients, in whom 1 mortality was seen. MSS of 11-15 was seen in 3(5.45%) patients, and 2 moralities were seen in this group and MSS of >15 was seen in only 1(1.82%) patient.

In another study conducted in 2019, it was found that mean MSS in vivax positive patients was 2.98±1.8 (4 patients had MSS >6). [(4)]

In our study the final outcome of majority (92.73%) of patients was discharge while mortality was observed in (7.27%) of cases while study conducted by Saravu et al, reported mortality in 0.34% of cases, this is attributed to the large sample size of their study compared to our study. [(5)]

ROC curves above the diagonal line are considered to have reasonable discriminating ability to predict mortality. The performance of total score (AUC 0.978; 95% CI: 0.897 to 0.999) was outstanding, when interpretation of the area under the ROC curve was done. Total score of more than 7 was a significant predictor of mortality with 97.80% chances of predicting mortality correctly.

While in a similar study conducted by Lakhani et al observed that ROC curve of MSS showed that threshold on the curve corresponded to MSS of 9. Greater discriminant capacity was observed at MSS 9, in their study. Mean MSS to predict mortality was 7.37, 6.58 and 9.11 on days 0, 2 and 7 respectively. [(6)]

MSS score by day 7 gave prediction at a cut-off value of ≥9. With a 95% confidence interval (0.65-0.88), AUROC was 0.76.

CONCLUSION

Malaria is an important public health issue, even in the modern era, though there is a consistent decline in the incidence, with P. vivax being responsible for most of the cases of malaria nowadays. Its potential to cause life-threatening illness is a cause of concern, causing multi organ dysfunction and even death.

The delay in the diagnosis can be one of the important factors related to death in patients with severe malaria and thus there is a need to know the risk factors for severe malaria and its resulting morbidity and mortality. Every P. vivax malaria patient should be evaluated thoroughly for clinical or biochemical evidence for complications and Malaria severity score can guide the clinicians about the severity of the disease and predicting the mortality.

BIBLIOGRAPHY

1. 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.
2. Lacerda MV, Fragoso SC, Alecrim MG, Alexandre MA, Magalhães BM, Siqueira AM, et al. Postmortem characterization of patients with clinical diagnosis of Plasmodium vivax malaria: to what extent does this parasite kill? Clin Infect Dis. 2012;55: e67-74.
3. WHO. World malaria report: 2019; 2019. p. 1–282.
4. Kuncheria T, Chowta NK, Madi D, Chowta MN, Basavaprabhu A. Comparative assessment of clinic-laboratory profile of different species of severe malaria in a tertiary care institute in southern India. J Vector Borne Dis. 2019; 56:360-6
5. Saravu K, Kumar R, Ashok H, Kundapura P, Kamath V, Kamath A, et al. Therapeutic Assessment of Chloroquine-Primaquine Combined Regimen in Adult Cohort of

Plasmodium vivax Malaria from Primary Care Centers in Southwestern India. PLoS One. 2016;11: e0157666.

6. Lakhani JD, Chavda N, Shah C, Doshi M, Chordiya R, Panchasara S, et al. Malaria Severity Score in malaria section patients admitted in critical care wards. JCDR. 2021;15: OC30-3