Section: General Medicine

Original Research Article

UTILITY OF PLATELET INDICES IN PREDICTING MULTI-ORGAN DYSFUNCTION AMONG PATIENTS ADMITTED WITH TROPICAL FEVER

K. Thenmozhy[1], B. Umamaheswari[2], G. Vijayalakshmi[2], R. Sivaraman[2]

[1]Junior Resident, Department of General Medicine, Government Stanley Medical College, Tamilnadu, India
[2]Assistant Professor, Department of General Medicine, Government Stanley Medical College, Tamilnadu, India

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Corresponding Author:
Dr. R. Sivaraman,
Email: sivaraman63@gmail.com

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Abstract

Background: Platelet indices have been used to diagnose and predict tuberculosis, malaria, dengue, and septic shock infections. The present study was carried out to study the utility of platelet indices in predicting multi-organ dysfunction among patients admitted with tropical fever. **Materials and Methods:** This prospective cross-sectional study was conducted on 150 patients with fevers less than three weeks of duration and thrombocytopenia less than 1.5 lakhs. Patients with serologically proven Dengue, Scrub typhus, Leptospirosis and Microscopically confirmed malarial fever were admitted to a tertiary care centre in Chennai. IgM Dengue confirmed laboratory confirmation of Tropical fever, NS1Ag Dengue, IgM Leptospirosis, IgM Scrub typhus, microscopically confirmed and MP QBC positive malaria. **Result:** Male predominance was reported in the without MOD group, and females were higher in with MOD group. The mean age was 42.5±10.1 years in MOD patients and 34.3±9.9 years in those without MOD. Thrombocytopenia was reported to be significantly higher ($p<0.05$) in MOD group patients. Other haematological parameters like platelet crit, PDW (fL), MPV (fL), WBC, haemoglobin, and haematocrit were found significantly ($p<0.05$) abnormal in with MOD group. The renal parameters (urea, creatinine, ALT, AST), CNS, CVS sign, and abnormal chest and abdominal imaging were also significantly higher ($p<0.05$) in MOD patients. In a group with MODS, qSOFA scores were present in 74 subjects. **Conclusion:** Platelet indices are inexpensive and easily available. Only thrombocytopenia, creatinine, alanine transaminase, and abnormal chest radiograph could significantly predict MODS in patients with tropical fever.

INTRODUCTION

Megakaryocytes are the building blocks of platelets, which may produce 1500–2000 from a single megakaryocyte. Hemostasis, inflammation, wound healing, and angiogenesis are some of their physiological functions.[1] The three kinds of granules found in platelets produce hundreds of proteins and peptides. Mean platelet volume (MPV), platelet distribution width (PDW), platelet crit (PCT), mean platelet component, mean platelet mass, platelet component distribution width, platelet bigger cell ratio, and immature platelet fraction are platelet indices that are indicators of platelet activation. The MPV in femtolitres can be calculated from the ratio of the platelet crit to platelet count or from the geometric mean of the log transformation of the platelet volume distribution curve.[1] The PDW is calculated using a cutoff of 20% of the platelet size distribution width. The PCT is the proportion of the blood volume comprised of platelets.

In investigations, the prevalence of multi-organ dysfunction syndrome (MODS), defined as a malfunction in two or more organ systems, has ranged from 1/5th to 1/3 of patients with tropical fever.[2-4] One adult trial and one paediatric research compared MODS in tropical fever with non-MODS groups; platelet indices were not employed in either study. Platelet indices have been utilised to diagnose and predict various inflammatory, infectious, and malignant illnesses.[5-13] Septic shock, urinary tract infections, TB, H. pylori, spontaneous bacterial peritonitis, surgical site infections, hepatitis, pneumonia, malaria, and dengue are among the illnesses that have been researched.

Hence the present study was carried out to study the utility of platelet indices in predicting multi-organ dysfunction among patients admitted with tropical fever.

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MATERIALS AND METHODS

This prospective cross-sectional study was conducted on 150 patients with fevers less than three weeks of duration and thrombocytopenia less than 1.5 lakhs. Patients with serologically proven Dengue, Scrub typhus, Leptospirosis and Microscopically confirmed malarial fever were admitted to a tertiary care centre in Chennai. The study was carried out from October 2020 to October 2021. Institutional ethical committee approval and written consent were taken before the start of the study.

Inclusion Criteria

Patients of either sex aged more than 13 years. Patients with Acute Febrile illness of fewer than three weeks with IgM / NS1Ag / IgG positive Dengue, IgM positive Leptospirosis and Scrub typhus, microscopically confirmed malarial fever (Vivax / Falciparum) / MP-QBC positive patients.

Exclusion Criteria

Patients aged less than 13 years and serology negative. Patients with haematological malignancies, chronic liver disease, alcoholics, and autoimmune hepatitis. Patients on anti-platelets, heparin, chemotherapy and other drugs causing thrombocytopenia. Patients with platelet disorders, bleeding diathesis, HIV positive, sepsis and pregnancy were excluded.

Demographic, risk factors and clinical features, laboratory and radiological data, and mortality rates will be registered. IgM Dengue confirmed laboratory confirmation of Tropical fever, NS1Ag Dengue, IgM Leptospirosis, IgM Scrub typhus, microscopically confirmed and MP QBC positive malaria.

After collection, the Data will be compiled and entered into Microsoft Excel Sheet. The analysis will be done using the Statistical software SPSS version 16. All Continuous variables will be expressed as Mean and Standard Deviation, and all Categorical variables will be represented as percentages and proportions. The test will be considered Significant if P <0.05, at a 95% Confidence Interval.

RESULTS

There were 96 patients in the MOD group whereas 54 patients were without the MOD group. Male predominance was reported in the without MOD group, and females were higher in with MOD group. The mean age was 42.5±10.1 years in MOD patients and 34.3±9.9 years in those without MOD. In with MOD group, dengue was reported in the maximum patients 30 (31.25%), and in the without MOD group maximum patient found with malaria was 20 (37.03%). Vomiting/diarrhoea symptom was reported in a maximum of 80 patients for a group with MOD. A maximum of 47 patients were found with fever in a group without MOD. The duration of symptoms with more patients was more in the group with MOD (4 days) than without MOD group (2 days). In a group with MODS majority of them, 62 (64.58%), had hypotension. RR and PR were significantly higher ($p<0.05$) in MOD group patients, and low spO2 was reported in most MOD group patients. Thrombocytopenia was reported to be significantly higher ($p<0.05$) in MOD group patients. Other haematological parameters like platelet crit, PDW (fL), MPV (fL), WBC, haemoglobin, and haematocrit were found to be significantly ($p<0.05$) abnormal in with MOD group [Table 1].

Table 1: Demographic and other variables of patients in both groups

Parameters	Observation N		P-value
	With MOD (N=96)	Without MOD (N=54)	
Gender			
Male	41	32	
Female	55	22	
Age (mean± SD)	42.5±10.1 years	34.3 9±.9 years	P<0.05
Serology			
Dengue	30	11	
Scrub Typhus	28	18	
Malaria	23	20	
Leptospirosis	15	5	
Clinical Features			
Fever	59	47	<0.001
Headache	58	44	<0.05
Myalgia	49	26	>0.05
Abdomen Pain	76	21	<0.001
Arthralgia	22	9	>0.05
Rash	20	9	>0.05
Vomiting/Diarrhoea	80	19	<0.001
Duration of Symptoms (days)			
0	0	2	P<0.05
1	9	0	
2	25	15	
3	26	17	
4	28	10	

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5	7	9	
6	1	1	
SBP <90mm hg			
No	34	47	P<0.001
Yes	62	7	
RR (bpm) (mean± SD)	31.719±25.002	16.704±3.678	P<0.001
PR (bpm) (mean± SD)	122.2012± 15.391	93 ±10.374	P<0.001
SPo2 (% in room air)			
>93%	29	46	P<0.001
85-93%	45	7	
<85%	22	1	
Plateletcrit (%)			
Normal	13	48	P<0.001
<0.19	83	6	
Platelet <1,50,000			
>150000	0	3	P<0.001
50,000- 1,50,000	7	46	
20,000- 50,000	56	4	
<20,000	33	1	
PDW (fL)			
Normal	1	48	P<0.001
>16.3	95	6	
MPV (fL)			
Normal	18	48	P<0.001
<7.3	34	5	
>9.0	44	1	
WBC			
4,000- 11,000	26	26	P<0.05
<4,000	37	20	
>11000	33	8	
Haemoglobin			
10-16	38	50	P<0.001
<10	45	2	
>16	13	1	
Hematocrit			
36-56	54	36	P<0.05
<36	31	17	
>56	11	1	
Renal variables			
Urea	113	19	P<0.001
Creatinine	96	25	P<0.001
ALT	89	22	P<0.001
AST	95	20	P<0.001
CNS			
No	53	49	P<0.001
Yes	43	5	
CVS			
No	72	53	P<0.001
Yes	22	1	

The renal parameters (urea, creatinine, ALT, AST), CNS, CVS sign, and abnormal chest and abdominal imaging were also significantly higher ($p<0.05$) in MOD patients. In a group with MODS, qSOFA scores were present in 74 subjects, whereas, in a group without MODS, no patients had qSOFA scores [Figure 1]. The difference is statistically significant ($p<0.05$) [Table 2].

Table 2: Radiological parameters of Patients in both groups

Parameters	**Observation N (%)**		**P-value**
	With MOD (N=96)	**Without MOD (N=54)**	
Chest imaging			
Normal	14	46	P<0.001
Pleural effusion	49	7	
ARDS	23	0	
Alveolar haemorrhage	10	1	
Abdomen imaging			
Normal	19	47	P<0.001
Ascites/GB wall edema	39	7	
Organomegaly	38	0	
qSOFA scores			
No	22	54	P<0.001
Yes	74	0	
Oxygen support			

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No support required	10	48	P<0.001
Face mask/NRM	42	6	
NIV	25	0	
Endotracheal tube	19	0	
ICU stay			
No	41	54	P<0.001
Yes	55	0	
Duration of hospital stay (mean± SD)	7.2922±1.579	3.9259± 1.588	P<0.001

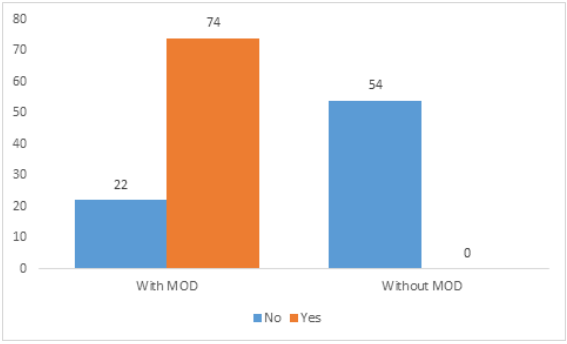

Figure 1: Observation of qSOFA score of patients in both group

DISCUSSION

Acute febrile illness is a fever lasting more than two days to 21 days. The most common features of many endemic diseases in India are fever, headache, chills, myalgia and fatigue. Common causes for AUFI are dengue and malaria, which are arthropod mediated, whereas leptospirosis and scrub typhus zoonotic diseases. Studies found thrombocytopenia, signs of a capillary leak and circulatory abnormalities.[14] Shahrabi et al. evaluated simple criteria to delineate these two and suggest that the presence of bleeding manifestation, thrombocytopenia (<1.4 lakhs) and leukopenia (WBC<5000/mm3) were associated with dengue.[15] Platelet indices have been investigated in various scenarios, including inflammatory disorders, infections, and malignancies. They are regularly assessed in automated haematology analysers at no additional expense.[16] MPV is the most often employed of these markers; bigger platelets have more granules and adhesion molecules and are linked to greater negative outcomes.[17] The role of MPV in diverse bacterial, mycobacterial, viral, and fungal infections has been investigated. Regression analysis revealed that our patient's MPV cutoff values of >7.3 fL and >9.0 were significant for MODS. This was a lower cutoff compared to that of other studies. In a study by Gao et al., an MPV >10.5 predicted mortality in septic shock.[5] MPV had high sensitivity and specificity for predicting spontaneous bacterial peritonitis with a cutoff of 8.7 at 95.9% and 91.7%, respectively, in cirrhotics.[9] In a study by Camara-Lemarroy et al., MPV had 82% sensitivity and 78% specificity to differentiate bacterial meningitis from tuberculous meningitis. MPV as a utility in dengue has varied with different studies. In Brazil, a higher MPV was found with the first vivax malaria infection and those with symptoms for >3 days.[18]

With tropical illnesses, including dengue, malaria, leptospirosis, and scrub typhus, thrombocytopenia is a typical symptom. Thrombocytopenia and rapidly declining platelet counts in dengue have been recognised as signs of severe illness.[19] In research on scrub typhus conducted in North India, thrombocytopenia was seen in most patients who met the criteria for severe sepsis.[20] The same study discovered that the only haematological markers effective at predicting organ failure were haemoglobin and total leukocyte counts. A similar observation was made in South Korea when leukocytosis and anaemia indicated severe scrub typhus.[21] In our study, MODS was substantially predicted by thrombocytopenia. According to Ritin et al., thrombocytopenia was the main factor contributing to MODS (defined as haematological dysfunction) in our research. In our investigation, thrombocytopenia was discovered in all individuals with MODS.[20]

Variability in platelet volume is shown by platelet distribution width. PDW rises with activated platelets that have pseudopodia. PDW has been employed in diagnosing acute pancreatitis, acute cholecystitis, and pulmonary TB, among other conditions. Elevated PDW was seen in vivax malaria, dengue, septic shock, and ascitic fluid infection. Orthopaedic patients and kids with a urinary tract infection caused by a gram-positive bacterium saw a decrease in PDW for deep surgical site infection. PDW among individuals with and without MODS differed significantly (p 0.05) in our research.[22]

Plateletcrit is the least studied among the four platelet parameters. They are decreased in dengue and septic shock. A platelet crit cutoff of ≤0.19 was significant (p<0.05) between patients with and without MODS.[5]

In a few studies, the determinants of the severity and mortality of severe scrub typhus have been examined.[21] Platelet indices have not been applied in the past to scrub typhus MODS prediction. While younger than Korean patients, our patients were of a similar age to those in the Chennai trial.[21-23] In our analysis, serum creatinine was a predictor, much like in Kim et al.[21] Studies by Premraj et al. and Kim et al. found that age and the lack of an eschar were risk factors for severe illness. Still, our investigation did not find these characteristics to be predictive.[21,23] In the Griffith et al. trial, which focused on patients needing critical care, respiratory problems were more prevalent.[24] We had 55 admissions into ICU in patients of MOD without the need for ventilation or renal replacement therapy,

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whereas Kim et al. reported 14 patients with ICU admission.[21]

The patients in our study had qSOFA scores of 0, 1, 2 and 3. The scores correlated well with systolic blood pressure, respiratory rate, leukocyte counts, and hepatic dysfunction achieving statistical significance ($p<0.05$), but not with ICU admission. However, there was no association of the qSOFA scores with any platelet indices. Patients with MOD showed higher qSOFA scores than those without MOD, reflecting its use in scrub typhus-related multi-organ failure.

CONCLUSION

A simple, non-invasive, inexpensive test is often required when prognostic common potentially fatal infections. This study thus explains a statistically significant correlation between altered platelet indices and the development of multi-organ dysfunction in acute febrile illness. Mean platelet volume and platelet crit positively correlate with low platelet count. Low MPV with low platelet count implies bone marrow suppression as a mechanism of thrombocytopenia in dengue infection. At the same time, platelet distribution width negatively correlates with low platelet count. A high value of platelet distribution width is seen in patients with low platelet count. Since platelet indices are easily available in most primary health centres in resource-limited settings, further studies are needed to validate the utility of platelet indices as a severity marker for better triaging in patients.

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