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A RETROSPECTIVE STUDY TO VALIDATE A CLINICAL SCORING SYSTEM FOR MANAGEMENT OF FEBRILE THROMBOCYTOPENIA

Medicine

Dr Asrar Ahmed Associate Professor and HOD, Dept of Medicine RUHSCMS. Jaipur

Dr Virendra Kr Goyal* Associate Professor, Dept of Medicine RUHSCMS Jaipur *Corresponding Author

ABSTRACT

Background: There are scoring system in place for many illnesses like stroke, malaria, and cardiac failure; however there is no system to evaluate patients presenting with febrile thrombocytopenia. Prasita shirsagar etal have tried to develop a scoring system for evaluating patients presenting with febrile thrombocytopenia for risk stratification, predicting patient outcome and optimization of care especially in resource poor countries.In present study we have tried to validate the scoring system developed by them.

Method: Objective: 1. To decide a protocol in the management of patiens with fever and thrombocytopenia based on risk score. 2. To develop screening or therapeutic guidelines (early warning score-EWS) in febrile thrombocytopenic patients and decide about therapeutic interventions Design: Retrospective study and development of a bedside scoring system based on Platelet Count, Temperature, Respiratory Rate, Blood Pressure. Pulse, CNS, Respiratory, Hematological, Hepatic and Renal complications in a hospital attached to a teaching institute in India Participants: All patients >18 years presenting with fever and thrombocytopenia with platelet count of <150 × 109/L.

Results: Number of patients requiring platelet transfusions decreases when total risk score is used for risk stratification and for transfusing platelets as against the platelet count at admission. Patients who died in our study had a platelet count at presentation between 20,000-1,00,000 though their total risk score was 17 and 18 respectively; hence platelet count alone should not be relied upon for platelet transfusion.Irrespective of the number of platelets transfused the prognosis is poor as the total risk score increases.

Conclusion: The platelet count is not the only indicator of transfusion.When we use total risk score instead of platelet count for classifying patients who need transfusions, number of patients who fall in severe risk category needing immediate transfusion reduces and haphazard use of platelets can be avoided. Patient outcome (death/survival), occurrence of complications and hematological manifestations (petechiae/purpura etc)are not dependent on platelet count at presentation. There is a significant association between risk category and patient outcome.

KEYWORDS

Introduction:

Thrombocytopenia is a haematological finding which is commonly seen in clinical settings. It may be the manifestation of common infectious diseases like dengue, malaria, leptospirosis or it may be due to life-threatening multisystem illnesses like DIC or thrombotic microangiopathies. Various viral infections (e.g., rubella, mumps, varicella parvovirus, hepatitis C, and Epstein-Barr virus), HIV may present with thrombocytopenia.

Other illnesses associated with febrile thrombocytopenia include meningococcemia, rat-bite fever, rickettsial infections, hantavirus, and other viral hemorrhagic fevers (e.g., Ebola, Lassa fever).

Historically thrombocytopenia is defined as a platelet count below the normal range for the population of - 2 standard deviations and the traditional value of 150 x 109 is supported by the National Health and Nutrition Examination Survey (NHANESIII) as the lower limit of normal.1About 0.9% of patients in the acute care setting and 25 to 41%of patients in the ICU setting account.

However an issue which has not been resolved is whether platelet count alone should be relied upon to initiate a platelet transfusion in acute medical settings and the number of platelets to be transfused.

Also definitions of mild, moderate and severe thrombocytopenia do not exist. As per Council of Europe Guide to the Preparation, Use and Quality Assurance of Blood Components the decision to transfuse platelets must not be based exclusively on the platelet count3 and must take patient's clinical condition into account.

However platelets are transfused based on platelet countsalone due to lack of guidelines Overzealous use of platelet transfusions overw helms blood banks jeopardising their supply in essential cases. As demonstrated by various studies thrombocytopenia is an early warning sign of sepsis and portends poor prognosis. Keeping these factors in mind we are validating a simple scoring system (total risk score) for management of thrombocytopenia in acute clinical conditions.

Aim

1. To decide a protocol in the management of patients with fever and thrombocytopenia
2. To develop therapeutic guidelines (early warning score-EWS) in febrile thrombocytopenic patients
3 To decide about therapeutic interventions in the form of platelet transfusions.

Material and Methods

A retrospective study spanning over a period of four months from June 2016-September 2016 was carried out in RDBP JAIPURIA HOSPITAL, Jaipur (attached to RUHSCMS,Jaipur).

A total of 93 subjects admitted to the medical ward or ICCU with fever and thrombocytopenia .

All the study subjects were identified to have thrombocytopenia defined as a platelet count of <150 × 109/L.Patient's younger than 18years, pregnant patients. patients on drugs causing thrombocytopenia (chemotherapy/immunosuppresant/antiplatelets.

previously diagnosed patients with chronic thrombocytopenia due to any cause were excluded.

Evaluation: Records of vital signs of the patients at time of admission were noted. Clinical examination findings of patients with respect to neurological status, respiratory,renal, haematological(petechiae, purpurae, ecchymosis or bleeding from any orifices) and other complications were noted. Routine investigations such as complete blood count, plasma glucose, urea,serum creatinine, bicarbonate, serum electrolytes, bilirubin,alanine aminotransferase were noted. In some of the patients cause of fever was found and tabulated accordingly. The study protocol was approved by the Institutional Human Ethical committee of RUHSCMS.

Statistical Analysis Statisticalanalysis was performed using the statistical software package SPSS (version 20).The non-parametric Chi-square test and t-test were also applied in comparative analysis results between different groups and to find significance (p) value. Mean values ,standarddeviation ,prevalence was assessed wherever relevant.

Results: The mean age of patients presenting with thrombocytopenia was 32.2 ± 13.2. 83.9% patients were male and 16.1 percent patients

were female.Mean number of platelets at admission was 46,225 and the mean number of bags of platelets transfused was two (Table 1).

Table 1: Platelet count and other parameters at admission and number of platelet packs given

	Platelet count	Platelets given	Pulse rate	Temp	RR	Systolic BP
Mean	46225.81 2	2.09	92.58	99.146	20.40	109.29
Median	39000.00	00	90.00	98.500	21.00	110
Std. Deviation	29108.167	2.058	13.167	1.4310	2.751	14.887

Early warning score was prepared as shown in the following table

Table 2:Clinical scoring system for thrombocypenia

	1	*2*	*3*
Platelet Count	*>1,00,000*	*20,000-1,00,000*	*<20,000*
Blood pressure	*>90*	*≤90*	
Pulse	*<100*	*≥100*	
Respiratory Rate	*<20*	*≥20*	
Temperature	*<100*	*≥100*	
*CNS complications**			*Present*
*Respiratory complications**			*Present*
*Haematological complications**			*Present*
*Hepatic complications**			*Present*
*Renal complications**			*Present*
**Zero if absent*			

There were two deaths in the cohort. Patients were assigned a score of1, 2 or 3 depending on parameters as mentioned in Table 1. Range of score as per scoring system is5 to 26 as per Table 1. As per our study minimum score was 6 and maximum score was 19.Best Cut-off was 16 with Sensitivity 100% and Specificity 98.9% for picking up adverse outcome of patients presenting with febrile thrombocytopenia. Hence 16 is taken as the cutoff for putting patients in the high risk category (Table 3).

For low risk category cut off is 7 as minimum score after considering parameters of temp, RR, BP, pulse and platelet count is 5. Presence of any complication pushes score to 8 and hence a score of more than 7 is placed in moderate risk category (Table 3).

Table 3: Test result variable(s): total risk score

Positive if ≥	Sensitivity	1-Specificity
5.00	1.000	1.000
6.50	1.000	.912
7.50	1.000	.703
8.50	1.000	.527
9.50	1.000	.418
10.50	1.000	.352
11.50	1.000	.264
12.50	1.000	.154
13.50	1.000	.098
14.50	1.000	.044
16.00	1.000	.011
17.50	.500	.011
18.50	.000	.011
20.00	.000	.000

4.3, 74.2 and 21.5% patients hada platelet count >1,00,000, 20,000-1,00,000 and <20,000 respectively (Table 4).

Table 4: Frequency and percentage of platelet count

Platelet count	Frequency (%)
>100,000	4 (4.3)
20,000-100,000	69 (74.2)
<20,000 20	20 (21.5)
total	93

29%, 67.7% and 3.2% ofpatients were in low, moderate and high risk category respectively (Table 5).

Table 5: Frequency and percentage oftotal risk score group

Total risk score	Frequency (%)
Low (6-7)	27 (29.0)
Moderate (8-15)	63 (67.7)
High (16-26)	3 (3.2)
total	93

As per the study done, in high risk group with score >16 (group 3) all the patients received platelets, in moderate risk group 33 out of 63 patients received transfusions while in low risk score category 2 patients out of 27 receivedtransfusions.1 patient with platelet count of more than 1,00,000, 16 patients in group 20,000-1,00,000 and all 20 patients with platelet count less than 20,000 were transfused platelets.

Patients who died in our study had a platelet count at presentation between 20,000 - 1,00,000 though their total risk score was 17 and 18 respectively. There is no significant difference across groups of platelet count in patient outcome (Table 6).

Table 6: Table comparing outcome (survival vs death) with platelet count categories

Platelet count	Outcome		
	survived	died	Total No.of patients (%)
>100,000	4 (100)	0 (0)	4 (100)
20,000-100,000	67 (97.1)	2 (2.9}	69 (100)
<20,000	20 (100)	0 (0)	20 (100)
Total	91 (97..1)	2 (2.9)	93 (100)

Since P<0.0001 there is a significant association between risk category and outcome. Patients
who fall in high risk category as per total risk score have a worse outcome (Table 7).

Table 7: Table comparing outcome with total risk score

Risk group	Outcome		
	survived	died	Total No.of patients (%)
Low (6-7)	27 (100)	0 (0)	27 (100)
Moderate (8-15)	63 (100)	0 (0)	63 (100)
High(16-26) 0 (0)	1 (33.3)	2 (66.7)	3 (100)
Total	91 (97..1)	2 (2.2)	93 (100)

Patients who survived had a mean total risk score of 9.51 and those who died had a score of 17.50

The outcome of the patients is dependent on the risk score and not only on the platelet count at admission. Irrespective of the number of platelets transfused the prognosis is poor as the risk score increases (Table 8).

Table 8: Comparison of platelet at admission,no of platelet received and total risk score with the outcome

	Mean	SD	SE	outcome		t-value	df	P
				Survived	Died			
Platelet at admission	46725.3	29227.5	3063.9	91		1.118	91	.267
	23500.0	3535.5	2500.0		2			
No. of platelets received	2.01	2.842	.298	91		5.994	91	.033
	5.50	.707	.500		2			
Total risk score	9.51	2.734	.287	91		4.112	91	.000
	17.50	.707	.500		2			

Discussion: Patients presenting with fever and thrombocytopenia may require emergent interventions and intensive care support. There is a need to develop a scoring system for thrombocytopenia which can predict case mortality, length of hospital stay and need of emergency interventions. There is a scoring system in place for many illnesses like stroke,6 malaria,7 and cardiac failure;8 however there is nosystem to evaluate patients presenting with febrile thrombocytopenia.

Adverse outcomes generally correlate with the severity of thrombocytopenia as demonstrated by PROTECT trial which included

a cohort of medical and surgical ICCU patients; however such a study has not been carried out in patients presenting with febrile thrombocytopenia.9

The only scoring system available for thrombocytopeniais for heparin-induced thrombocytopenia and there is a paucity of research in evaluating febrile thrombocytopenia.10 APACHE-II scoring system can be applied to these patients but it's too cumbersome and difficult to apply for bedside evaluation of the patient.11 We have tried to develop a scoring system which is free of interobserver variability, depends on few bedside variables and minimal lab parameters and is easy to remember. Patients presenting with febrile thrombocytopenia can be classified into low, intermediate and high risk depending on their score and accordingly decisions about their management, daily prognosis assessment and referral to higher centres can be made.

Platelet transfusion is indicated in all patients with platelet count less than 20,000 and otherwise stable, nonbleeding, and body temperature >100.4°F (38°C)or undergoing invasive procedure and platelet coun <10,000 who are otherwise stable and nonbleeding.12

Our study is done to find out the indication for platelet transfusions in patients with platelet count more than 20,000 who can have a poor prognosis and may require timely intervention. So we have graded the various clinical parameters to get a scoring system and rationalise the indications for platelet transfusion. The total risk score can be monitored frequently at bedside of patient to provide ongoing care. The scoring system will help in deciding about the urgency of transfusing platelets and number of platelets to be transfused.

If we depend on platelet count alone for transfusing patients as per standard recommendations, only four patients fell in low risk category who did not requireplatelet transfusions but were 27 patients in low risk category if we take a risk score under consideration for classifying patient risk. Hence the number of patients not requiring platelet transfusions is increased when total risk score is used for risk stratification and for transfusing platelets.If we depend on score group for classifying patients, only two patients fell in the severe category in whom transfusion is mandatory. If we depend on platelet count alone for transfusion, then 20 patients fell in this category for mandatory transfusion. There is a definite decrease in the number of patients who require transfusion if we rely on platelet count alone. Death occurred in patients irrespective of platelet count category which again proves the point that thrombocytopenia is not the only indication for poor prognosis of patient.

In our study platelet transfusion was given to patients in a haphazard manner irrespective of the degree of severity of thrombocytopenia. The platelet count and the total risk score comparison for transfusing platelets reveals that the platelet count is not the only indicator of transfusion. When we use total risk score instead of platelet count for classifying patients who need transfusions, number of patients who fall in severe risk category needing immediate transfusion reduces and haphazard use of platelets can be avoided.

In our study 0.09% of the study population had bleeding manifestations and these symptoms were not dependent on platelet count, hence all cases need not present with haematologica l manifestations. Since a patient presenting with a higher score had significantly worse outcome including death these patients should be adequately monitored and provided ICU care if necessary.

Platelet count at presentation was not related to poor prognosis. As per our study patients who died presented with a platelet count of more than >20,000 and one of the two patients who died didn't have any haematological manifestations. Hence platelet count or bleeding alone should not be relied on for gauging prognosis of patients with febrile thrombocytopenia. Similarly an otherwise stable patient with a low score in spite of presenting with severe thrombocytopenia can be closely monitored without platelet transfusion.

Conclusion: The dynamic and erratic course of thrombocytopenia requires close monitoring of the patient and careful decision making. The scoring system developed by Prasita shirsagar etal 13 may serve as reproducible,inexpensive bedside tools for evaluating throm bocytopenia and in guiding platelet transfusion therapy. It will help clinicians to be more judicious in transfusing platelets and it will guide early interventions in patients with a higher score so that these patients can make a complete recovery. Since this score has been developed on simple physiological parameters besides platelet count at presentation it will help in predicting case recovery and survival. This scoring system can fulfil the lacunae in evaluating febrile patients presenting with thrombocytopenia.The scores can be a guide to the management as below.

Low Risk Score (upto 7)
- No platelet transfusion required.
- No admission required.Monitor the platelet count.
- # Admission will depend uponfeasibility of monitoring plateletcount.

Moderate Risk Score (8-15)
- Admit the patient in ward.
- Consider transfusion of platelets after monitoring
- Revise the scoring system every 2-4 hours.

Severe Risk Score (16 and above)
- Admit in ICCU
- Transfuse platelets immediately

Limitation of Study
- Study was retrospective so no
- active intervention has been carried out.

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