https://iap-kpj.org

Karnataka Paediatric Journal

Original Article

To estimate the prevalence of thrombocytopaenia and its role as prognostic marker in patients of paediatric intensive care unit

Gurudutt Joshi[1], Hetal Budh[1]

[1]Department of Paediatrics, Surat Municipal Institute of Medical Education and Research, Surat, Gujarat, India.

***Corresponding author:**
Gurudutt Joshi,
Department of Paediatrics,
Surat Municipal Institute
of Medical Education and
Research, Surat, Gujarat, India.

joshigurudutt@yahoo.com

Received: 23 October 2021
Accepted: 14 December 2021
EPub Ahead of Print: 09 May 2022
Published: 22 June 2022

DOI
10.25259/KPJ_36_2021

Quick Response Code:

ABSTRACT

Objectives: Platelets play an important role in normal homeostasis and thrombus formation. They help in reducing vascular permeability, mediating inflammatory processes, promoting wound healing and host defence mechanisms. The aim of this was to estimate the prevalence of thrombocytopaenia, to categorise thrombocytopaenia according to the severity and to evaluate the role of thrombocytopaenia as a prognostic marker in patients admitted in PICU.

Materials and Methods: This was a prospective observational study over a period of 15 months. One hundred and eighty patients of age 1 month–17 years, critically ill, admitted in PICU or transferred from paediatric ward were enrolled. Those, who had thrombocytopaenia during admission or during PICU stay, were labelled as 'Thrombocytopaenia' group, while the remaining patients who did not have thrombocytopaenia were grouped as 'No thrombocytopaenia' group.

Results: The prevalence of thrombocytopaenia in PICU was 37.78% category wise, 35.29%, 33.82%, 19.12% and 11.76% of patients had mild, moderate, severe and very severe thrombocytopaenia, respectively. Mean duration of stay in PICU was more with severe and very severe thrombocytopaenia, followed by moderate and mild thrombocytopaenia, which was statistically significant (P = 0.00037). Mortality was higher in thrombocytopaenic group as compared to non-thrombocytopaenic patients expired, which was statistically significant (P = 0.001013).

Conclusion: The prevalence of thrombocytopaenia in this study was similar to other studies. Severity of thrombocytopaenia correlated well with the duration of PICU stay. Overall mortality was 22.22% in this study.

Keywords: Thrombocytopaenia, Prevalence, Paediatric intensive care unit

INTRODUCTION

The circulating life span of platelets is 10–14 days. Normal platelet count is 150–450 × 10^9/L. Decrease in platelet count below 150 × 10^9/L is labelled as thrombocytopaenia. Disseminated intravascular coagulation, increased destruction, reduced production, increased consumption and abnormal sequestration are mechanism of thrombocytopaenia. Thrombocytopaenia is a common complication in patients admitted to PICUs and may require transfusions.[1-5] The prevalence of thrombocytopenia varies in PICUs ranging from 13% to 60%.[6-9] Some of the drugs such as beta-lactams, linezolid, vancomycin and anticonvulsants such as phenytoin and valproic acid also cause decrease in platelet counts.[10-13] Implications of platelet count and its outcome have been studied in adult medical intensive care units but there are few studies and scarce

data available, as regards prevalence of thrombocytopaenia and its outcome in paediatric intensive care units (PICU), particularly in Indian setup; hence, this study was planned. Outcome of this study finding may add to the existing literature.

MATERIALS AND METHODS

This study was a prospective observational study conducted in PICU, over a period of 15 months (from 1 December 2018 to 29 February 2020). A study was approved by the 'Institutional Ethics Committee' and a written informed consent from the parent/guardian of enrolled patients was obtained. A total of 246 patients were enrolled, out of which 18 expired within 48 h of admission, 11 patients were discharged against medical advice (DAMA), 19 were transferred to paediatric ward after stabilisation of vitals within 48 h of PICU stay, 12 had deranged coagulation profile, five had received platelet transfusion in other setup before admission in PICU of our hospital and one patient had Glanzmann thrombasthenia, all these patients were excluded from this study. In addition, those patients, whose parents did not give consent, who had deranged coagulation profile, platelet function disorder and received platelet transfusion, were also excluded from the study. The remaining 180 patients were studied in detail and subjected to statistical analysis. Patients were studied for their entire duration of PICU stay (till discharge, transfer to paediatric wards, DAMA or death).

Sampling method

Platelet counts were performed as a part of routine investigations at the time of admission and as per treating physician but it was ensured that minimum of two investigations was done during the entire PICU stay. Any discrepancy in platelet count was counter confirmed by expert faculty. Patients with any of the platelet counts showing thrombocytopaenia during the duration of PICU stay were grouped into 'Thrombocytopaenic' group while the remaining patients who did not develop thrombocytopaenia during PICU stay duration were grouped into 'No thrombocytopaenic' group. Data were entered into predesigned pro forma. The lowest platelet count on admission or during PICU stay was used to grade the severity of thrombocytopaenia.

Statistical analysis

The sample size was calculated as per the average annual admissions in the PICU. The level of significance was 95%. The sample size calculated was 178 for the present study. Qualitative data were presented in the form of frequency (number) and percentage. Association between 'Thrombocytopaenia' and 'No thrombocytopaenia' with the qualitative variables was assessed by Chi-square test for 2×2 tables along with Yates correction and Fisher's exact test where Chi-square was not valid because of small counts. This analysis was done with the help of OpenEpi software. Quantitative data were represented by mean ± SD. For more than 2 rows and columns, R X C table for Chi-square testing was used for statistical analysis in OpenEpi software. Independent *t*-test and ANOVA test were applied for the evaluation of quantitative data wherever applicable. Odds ratio was applied for the evaluation of association between thrombocytopaenia and risk factors. Results were graphically represented where deemed necessary. Statistical analysis was done by MS Excel 2007, OpenEpi software (version 3.01) and SPSS 20 software. Graphical representation was done in MS Word 2007 and MS Excel 2007. $P < 0.05$ was considered statistically significant and confidence interval was at 95% confidence limit.

RESULTS

The classification of thrombocytopaenia[14] is as shown in [Table 1]. As shown in [Table 2], out of the 180 patients studied, 68 patients (37.78%) had thrombocytopaenia at least on a single occasion, while the duration of PICU stay, whereas 112 patients (62.22%) had platelet counts within the normal range. Fifty-nine patients from 68 patients had thrombocytopaenia on admission, whereas nine patients developed thrombocytopaenia during the PICU stay. The prevalence of thrombocytopaenia was observed to be 37.78% (i.e., 68 patients out of 180). Out of 180 patients, 92 patients (51.11%) are male and 88 patients are female (48.89%). Sex: Male predominance was observed with M: F ratio of 1.04:1. Age: The majority of the patients 64 (35.56%) were in the age group of 1–12 months, followed by 6–10 years and 11–15 years with 16 patients (16.11%) each. Mean age of the study population was 5.40 ± 5.94 years.

As shown in [Table 3], 68 patients had thrombocytopaenia, out of 180 patients enrolled, 24 patients (35.29%) had mild thrombocytopaenia, 23 patients (33.82%) had moderate thrombocytopaenia, 13 patients (19.12%) had severe thrombocytopaenia and 8 patients (11.76%) had very severe thrombocytopaenia.

Mean duration of PICU stay was 5.21 (~5) days and majority that is, 109 patients (60.59%) had <5 days of PICU stay. Ten patients (5.56%) had PICU stay of 5 days whereas 61 patients (33.89%) had PICU stay of more than 5 days, based on the mean duration of PICU stay, the study population was divided into three groups, with PICU stay lesser than, equal to and more than mean duration. As shown in [Table 4], the majority of thrombocytopaenic patients (51.47%) had PICU stay more than mean, while the majority of non-thrombocytopaenic patients (71.43%) had PICU stay of lesser than mean. Statistically significant difference ($P = 0.0003749$)

was observed with regard to the duration of PICU stay between the two groups. Hence, thrombocytopaenic patients required longer PICU stay duration as compared to non-thrombocytopaenic patients.

As shown in [Table 5], the mean duration of PICU stay for patients with thrombocytopaenia was 6.62 days, while it was 4.36 days in patients without thrombocytopaenia. Statistically significant difference was observed on comparison of mean PICU stay between the two groups (P = 0.00003585); hence, mean PICU stay was longer in thrombocytopaenic patients as compared to non-thrombocytopaenic patients.

As shown in [Table 6], mean PICU stay duration was more in severe thrombocytopaenia (10.15 days) followed by very severe thrombocytopaenia (8 days). There was statistically significant difference (P = 0.00037) observed on comparison of mean PICU stay with severity of thrombocytopaenia. Hence, the mean PICU duration is more for patients with severe and very severe thrombocytopaenia as compared to patients with mild and moderate thrombocytopaenia. No statistical test could be applied as it does not meet Cochrane criteria for Pearson Chi-square testing between severity of thrombocytopaenia and gender as well as age.

[Table 7] reflects that overall mortality observed in this study was 22.22% (40 patients out of total 180 patients studied). From the 140 patients (77.78%) that survived during the period of this study, 129 patients (71.67%) were given discharge after the completion of treatment whereas 11 patients (6.11%) had taken DAMA due to varied reasons such as personal, social or economical issues after being vitally stable and transferred to paediatric ward. Patients who had taken DAMA during the course of treatment and vitally unstable have been excluded from this study. Only those patients who had taken DAMA after being vitally stable and transferred to paediatric ward have been included in the study. Gender and age were not found to be statistically significant, as risk factors for thrombocytopaenia, as p value for both was 0.7019 and 0.6458, respectively.

[Table 8] depicts that 35.29% of thrombocytopaenic patients expired, while only 14.29% of non-thrombocytopaenic patients expired. Statistically significant difference was observed on comparison of mortality and thrombocytopaenia. Hence, mortality was more in patients with thrombocytopaenia as compared to patients without thrombocytopaenia. When gender was considered as risk factor for mortality in thrombocytopaenic patients, it was found to be statistically insignificant as P = 0.3858. No statistical test can be applied, to age, as a risk factor for mortality in thrombocytopaenic patients, as it did not meet Cochrane criteria for Pearson Chi-square testing.

Table 1: Grading of thrombocytopaenia.

Grade of thrombocytopaenia	Platelet counts (µL)
Mild	100,000–150,000
Moderate	50,000–100,000
Severe	20,000–50,000
Very severe	<20,000

Table 2: Prevalence of thrombocytopaenia.

Thrombocytopaenia	Number	Percentage
Present	68	37.78
Absent	112	62.22
Total	180	100

Table 3: Severity of thrombocytopaenia.

Severity of thrombocytopaenia	Number	Percentage
Mild	24	35.29
Moderate	23	33.82
Severe	13	19.12
Very severe	8	11.76

Table 4: Duration of PICU stay as a risk factor for thrombocytopaenia.

Duration of PICU stay	Number	Percentage	Thrombocytopaenia				Total
			Present		Present		
			Number	Percentage	Number	Percentage	
<5 days	109	60.56	29	42.65	80	71.43	109
5 days	10	5.55	4	5.88	6	5.36	10
More than 5 days	61	33.89	35	51.47	26	23.21	61
Total	180	100	68	100	112	100	180
Chi-square tests		**Value**		**df**		***P*-value**	**Association**
Pearson Chi-square		15.78		2		0.0003749	Significant

Mean duration of PICU stay of the study population was 5.21±3.63 days

Table 5: Comparison of mean duration of PICU stay between thrombocytopaenic and non-thrombocytopaenic group.

Thrombocytopaenia	Number of patients	Mean±SD	Minimum	Maximum
Present	68	6.62±4.04	2	16
Absent	112	4.36±3.07	2	22
Total	180	5.21±3.62	2	22

Independent *t*-test	Value	df	Lower limit	Upper limit	Mean difference	*P*-value	Association
Equal variance	4.24	178	1.208	3.311	2.26	0.00003585	Significant

Table 6: Association of mean duration of PICU stay and severity of thrombocytopaenia.

Severity of thrombocytopaenia	No. of patients	Mean PICU stay±SD	Min	Max
Mild	24	3.96±3.97	2	12
Moderate	23	6.91±4.07	2	13
Severe	13	10.15±4.26	3	16
Very severe	8	8.00±4.05	4	12

ANOVA test	Value	df	Mean square	*P*-value	Association
Equal variance	348.97	3	116.325	0.00037	Significant

Table 7: Outcome of patients.

Final outcome	Total no. of patients	Percentage
Survived	140	77.78
Expired	40	22.22
Total	180	100.00

As shown in [Table 9], the mean PICU stay duration is longer in expired thrombocytopaenic patients as compared to thrombocytopaenic patients who survived and these data were statistically significant ($P = 0.000029$). Maximum PICU stay was longer in expired thrombocytopaenic patients as compared to survived ones. Hence, longer PICU stay was associated with mortality in thrombocytopaenic patients and may be used as a mortality predictor in thrombocytopaenic patients.

DISCUSSION

Prevalence

The prevalence of thrombocytopaenia observed in various studies ranges from 25 to 60%. In this study, the prevalence was 37.78%. This is similar to the results shown in the studies conducted by Sah *et al.*[15] and Kaur *et al.*[1] where the prevalence of thrombocytopaenia was 34% and 32.36%, respectively. Relatively higher prevalence was observed in the studies conducted by Divecha *et al.*[8] (60.3%), Yilmaz *et al.*[6] (59.57%) and Mussa *et al.*[16] (44.61%), respectively, while relatively lower prevalence was observed in the studies conducted by Krishnan *et al.*[17] (25.3%) and Agrawal *et al.*[7] (25%). The difference in the prevalence of thrombocytopaenia may be attributed to the varying inclusion criteria of the different studies. Moreover, patients with burns have a separate ICU and hence not included in the present study. Almost all above studies had also male preponderance.

Age

Maximum age range was 1 month–18 years in the study of Mundkur *et al.*[18] The mean age of the patients in the present study was 5.4 years which is similar to the studies conducted by Mittal *et al.*[19] and Mussa *et al.*[16] The range of age groups of the study population in this study was 1 month–17 years, which is similar to that of the study by Mundkur *et al.*[18] who had included patients from 1 month to 18 years of age. The median age observed in our study was 36 months (3 years), which is similar to the study by Agrawal *et al.*[7] (2008), where a median age was 32 months. Yilmaz *et al.* (2013)[6] conducted a study which showed the median age of 24.

Severity of thrombocytopaenia

In this study, maximum patients 24 out of total 68 thrombocytopaenic patients that is, 35.29% had mild thrombocytopaenia followed in decreasing order by moderate thrombocytopaenia (33.82%), severe thrombocytopaenia (19.12%) and very severe thrombocytopaenia (11.76%). Similar results were observed in the study conducted by Sah *et al.*[15] where maximum (41.7%) patients had mild thrombocytopaenia (platelet count $<150 \times 10^9$/L) followed by 32.3% of patients with moderate thrombocytopaenia (platelet count $<100 \times 10^9$/L) and 26.4% of patients with severe thrombocytopaenia (platelet count $<50 \times 10^9$/L). Studies conducted by Mundkur *et al.*[18] and Kaur *et al.*[1] who showed higher prevalence of severe thrombocytopaenia 51% (platelet count $<50 \times 10^9$/L) whereas the study by Yilmaz *et al.*[6] showed lower prevalence (7.45%) of severe thrombocytopaenia as compared to our study. Thus, there is varying prevalence of severity of thrombocytopaenia.

Table 8: Association of thrombocytopaenia with mortality.

Outcome	Thrombocytopaenia		Total
	Yes (*n*=68)	No (*n*=112)	
Survived			
No.	44	96	140
%	64.71%	85.71%	77.78%
Expired			
No.	24	16	40
%	35.29%	14.29%	22.22%
Total			
No.	68	112	180
%	100.00%	100.00%	100.00%

Chi-square tests	Value	df	*P*-value	Association
Pearson Chi-square	10.8	1	0.001013	Significant

Table 9: Association of mean PICU stay duration with mortality in thrombocytopaenic patients.

Outcome	Number of patients	Mean PICU stay duration Mean±SD	Min.	Max.
Expired	24	9.58±4.04	2	16
Survived	44	5.00±4.01	2	12
Total	68	6.62±4.04	2	16

Statistical test	Value	df	Mean difference	*P*-value	Association
Independent t-test	4.48	66	0.1464	0.000029	Significant

Duration of PICU stay

In this study, the mean duration of PICU stay was found to be 5.21 (±3.63) days. The majority of patients (60.56%) had PICU stay duration of <5 days whereas 5.55% had PICU stay duration of 5 days and 33.89% had more than 5 days of PICU stay. The study conducted by Mundkur *et al.*[18] who showed that the median duration of PICU stay in mild and moderate thrombocytopaenia was 4 days and in severe thrombocytopaenia was 3 days. The median duration of PICU stay was 8 days (3–120 days) in the study by Yilmaz *et al.*[6] In the study by Mussa *et al.*,[16] PICU stay duration was divided into <7 days, 7–14 days and >14 days with 56.2%, 25.4% and 18.5% of study population, respectively. Agrawal *et al.*[7] found that 99 (71.1%) patients had PICU stay duration of <7 days while 20 (14.5%) had more than 14 days of PICU stay and 19 (13.8%) PICU stay of 7–14 days. The duration of PICU stay would depend on the type of diagnosis of the patients admitted in the PICU, treatment protocols and the outcome.

Duration of PICU stay and thrombocytopaenia

In this study as well as studies by Yilmaz *et al.*,[6] Mussa *et al.*,[16] Agrawal *et al.*[7] and Krishnan *et al.*,[17] longer duration of stay was observed in thrombocytopaenia group as compared to non-thrombocytopaenia group, which was statistically significant whereas in a study of Mittal *et al.*,[19] this difference was insignificant.

Outcome

Mortality was 22.22% in this study, which was comparable to Sah *et al.*[15] (26%), Mittal *et al.*[19] (20%) and Kaur *et al.*[1] (19.64%), whereas it was 37.2% and 53.07% in Yilmaz *et al.*[6] and Mussa *et al.*[16] study. The difference may be attributed to the different diagnosis of the patients and admission criteria in different studies.

Thrombocytopaenia and mortality

In this study, 35.29% of thrombocytopaenic patients expired while only 14.29% of non-thrombocytopaenic patients expired and this was statistically significant. Similarly, statistically significant association between mortality and thrombocytopaenia was observed in various studies as shown in table below. Kaur *et al.*[1] and Mittal *et al.*[19] observed that mortality among thrombocytopaenic and non-thrombocytopaenic patients was similar to this study. Higher mortality was observed among thrombocytopaenic patients in the studies by Sah *et al.*,[15] Yilmaz *et al.*,[6] Mussa *et al.*[16] and Agrawal *et al.*[7] while lower mortality was seen among thrombocytopaenic patients in studies by Mundkur *et al.*[18] and Krishnan *et al.*[17] Sah *et al.*[15] observed that there were 18 times more risk of mortality among thrombocytopaenic patient compared to non-thrombocytopaenic patients with odds ratio 18 at 95% CI. Mortality including this study was statistically significant in thrombocytopaenic group as compared to non-thrombocytopaenic group in all studies.

CONCLUSION

The prevalence of thrombocytopaenia in the PICU observed in this study was 37.78%, of which mild thrombocytopaenia was predominant (35.29%). Male preponderance was observed in this study. Duration of stay in PICU correlated well with a severity of thrombocytopaenia, also thrombocytopaenic patients had statistically higher risk of death; hence, thrombocytopaenia may be considered as an important risk factor for mortality.

Limitation of the study

Patients with burns could not be recruited in this study, as there was separate burns ward in the institute. Association of risk factors with a severity of thrombocytopaenia because could not be correlated as they were not meeting Cochrane criteria for statistical testing. The role of thrombocytopaenic drugs in causing thrombocytopaenia was not assessed.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Kaur A, Sethi GK, Goyal RK, Kaur A, Kaur R, Dhir SK, *et al*. Thrombocytopenia in paediatric ICU: Incidence, transfusion requirement and role as prognostic indicator. J Clin Diagn Res 2015;9:SC05-7.
2. Vasu BK, Sinha R, Verghese S. Thrombocytopenia and guideline-evaluated appropriateness of platelet transfusion in a tertiary care intensive care unit. ISBT Sci Series 2016;11:102-9.
3. Arnold DM, Crowther MA, Cook RJ, Sigouin C, Heddle NM, Molnar L, *et al*. Utilization of platelet transfusions in the intensive care unit: Indications, transfusion triggers, and platelet count responses. Transfusion 2006;46:1286-91.
4. British Committee for Standards in Haematology, Blood Transfusion Task Force. Guidelines for the use of platelet transfusions. Br J Haematol 2003;122:10-23.
5. Pont-Thibodeau GD, Tucci M, Robitaille N, Ducruet T, Lacroix J. Platelet transfusions in paediatric intensive care. Pediatr Crit Care Med 2016;17:e420-9.
6. Yilmaz S, Yildizdas D, Acipayam C, Bayram I, Ozcan N, Horoz OO, *et al*. The effect of thrombocytopaenia on outcome in critically ill children. Crit Care Shock 2013;16:48-57.
7. Agrawal S, Sachdev A, Gupta D, Chugh K. Platelet counts and outcome in the paediatric intensive care unit. Indian J Crit Care Med 2008;12:102-8.
8. Divecha C, Tullu M, Thombare T. An observational analytical study of causes, severity, risk factors and outcome of thrombocytopenia in a paediatric intensive care unit. J Pediatr Care 2020;6:73.
9. Patki V, Birru F, Patki VV. Decline in platelet count as a prognostic marker in critically ill children. J Pediatr Crit Care 2014;1:15-21.
10. Kleigman R. In: Scott J, Montogomery R, editors. Nelson Textbook of Paediatrics. 19th ed., Vol. 2. Amsterdam, Netherlands: Elsevier; 2014. p. 1714-22.
11. Gawaz M, Fateh-Moghadam S, Pilz G, Gurland HJ, Werdan K. Platelet activation and interaction with leucocytes in patients with sepsis or multiple organ failure. Eur J Clin Invest 1995;25:843-51.
12. Yeaman MR. The role of platelets in antimicrobial host defense. Clin Infect Dis 1997;25:951-68; quiz 969-70.
13. Priziola JL, Smythe MA, Dager WE. Drug-induced thrombocytopenia in critically ill patients. Crit Care Med 2010;38 Suppl 6:S145-54.
14. Schlappi C, Kulkarni V, Palabindela P, Bemrich-Stolz C, Howard T, Hilliard L, *et al*. Outcomes in mild to moderate isolated thrombocytopenia. Paediatrics 2018;142:e20173804.
15. Sah VK, Milan KC, Giri A, Niraula N. Association of thrombocytopenia and mortality in critically ill children admitted to PICU in tertiary hospital. Birat J Health Sci 2019;4:649-53.
16. Russul FM, Al Al-Alyasiri AA, Al-Marzoki JM. Prognostic value of platelet count in paediatric intensive care unit. Med J Babylon 2012;9:833-42.
17. Krishnan J, Morrison W, Simone S, Ackerman A. Implications of thrombocytopenia and platelet course on paediatric intensive care unit outcomes. Pediatr Crit Care Med 2008;9:502-5.
18. Mundkur SC, Upadhyay R, Hebbar SA, Kini P, Bhaskarananda N, Shashidhara S. A study to evaluate the prognostic significance of thrombocytopenia among critically ill children. Int J Contemp Pediatr 2019;6:540-4.
19. Mittal P, Barman ML, Ghanghoriya P, Ajmariya M, Khandare M. Platelet counts and outcome in paediatric intensive care unit. Eur J Pharm Med Res 2017;4:504-9.

How to cite this article: Joshi G, Budh H. To estimate the prevalence of thrombocytopaenia and its role as prognostic marker in patients of paediatric intensive care unit. Karnataka Paediatr J 2022;37:13-8.