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Original Research Article

Platelet indices as an acute phase reactant in infants admitted with acute febrile illness

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ABSTRACT

Background: The most common causes of thrombocytosis are infectious illnesses; platelet count is unaffected by fever duration. Infectious disorders such rotavirus gastroenteritis, respiratory syncytial virus infection, hepatitis B and C virus infection, brucellosis, and pulmonary tuberculosis, and also medical and non-medical situations, might impact mean platelet volume (MPV) readings. C-reactive protein (CRP) plasma concentration changes during infection or inflammation as part of the innate immune response. Aim was to investigate in children with febrile illness the correlation between platelet indices and CRP.
Methods: This hospital based descriptive study was conducted in post graduate Department of Paediatrics and Neonatology, an associated hospital of Government Medical College and Hospital, Srinagar, from December 2019 to November 2021. As per sample size calculation 3000 patients were included in the study. Patients of either sex, age from 1 month to 1 year of age with fever admitted in hospital were included in the study.
Results: There was a significantly positive correlation between platelet count and CRP. The sensitivity was highest for platelets at 96.67 and lowest for MPV 32.97 while as specificity was highest for white blood cells (WBC) at 94.4 for MPV was 92.22 and lowest for platelet (PLT) 30.77. Spearman rank correlation between platelet indices and CRP value children with fever with high CRP had a significantly high PT and it has significant positive correlation with CRP.
Conclusions: We found a strong link between CRP and platelet counts in patients. Platelet count, platelet distribution width (PDW), MPV, and plateletcrit (PCT) were all influenced.

Keywords: Platelet count, Mean platelet volume, Platelet distribution width, CRP

INTRODUCTION

Fever, often known as pyrexia, is a condition in which the normal body temperature is elevated above homeostasis.[1] Infectious, inflammatory, neoplastic, and other causes of fever can be categorized into four categories.

Fever in the paediatric population is usually grouped into 4 categories: fever in the neonate, fever with localizing signs, fever without source (FWS) and fever of unknown origin (FUO).

Fever is a condition in which the body temperature increases over normal levels, and according to Saladin's great scientific text, it is a good condition as long as it does not last or reach 44°C to 46°C, at which point it might be fatal or cause irreversible brain damage.[1,2]

The thermoregulatory centre, located in the preoptic portion of the anterior hypothalamus, regulates temperature. The hypothalamic set point keeps body temperature about 37°C in most people, but there can be significant fluctuation. Normal daytime temperatures

range from 36 to 37.8°C, with a high in the afternoon (5-7 p.m.) and a trough in the early morning (2-6 a.m.).

Fever is the most prevalent clinical complaint among paediatric patients, occurring in one-third of those admitted to the hospital.[1] Fever is a symptom of an underlying illness. In febrile individuals, tachycardia, irritability, chills, and cutis marmorata are common. Fever suppression boosts viral and bacterial agent reproduction and supports the body's acute phase reaction, according to several studies.[3] However, no previous research in the paediatric age range have looked at changes in platelet parameters in relation to the duration of fever (of infectious origin). One type of blood cell is platelets. However, because they lack a nucleus, some authors do not consider them to be cells. Platelets, however, behave similarly to cells in many respects. Platelets have an important role in haemostasis, according to researchers. Platelets also shield some tumour cells from the immune system. Platelets are also implicated in the immune system response to host defenses at the same time.[4] Atherothrombosis, inflammatory lung disease, inflammatory bowel illness, and inflammatory skin disease have all been linked to platelet-leukocyte interactions. Phospholipid vesicles are found in platelets and are released into the environment after viral or bacterial interaction. Infectious diseases can therefore impact platelet parameters. Platelet counts in the typical range are 150.000-450.000 per microliter.

The most common causes of thrombocytosis are infectious illnesses (viral and bacterial). Platelet count is unaffected by fever duration (based on the incidence of both thrombocytopenia and thrombocytosis). The average size and manufacturing rate of platelets are shown by the mean platelet volume (MPV). MPV levels are not affected by age or gender. Infectious disorders such rotavirus gastroenteritis, respiratory syncytial virus infection, hepatitis B and C virus infection, brucellosis, and pulmonary tuberculosis, and also medical and non-medical situations, might impact MPV readings.

Platelet distribution width (PDW) indicates active platelet release. Many studies have shown that PDW values differ in various diseases. Plateletcrit (PCT) describes circulating platelets in a unit volume of blood and is calculated using the formula given below.

$$PCT = Plt \times MPV$$

CRP belongs to the short pentraxin family of plasma proteins, which consists of five identical non-glycosylated peptide subunits that join to form a cyclic pentamer structure. CRP is created as a result of neutrophil and monocyte-mediated pro-inflammatory cytokine signaling. CRP plasma concentration changes depending on the pace of CRP production and the degree of infection. CRP plasma concentration changes during infection or inflammation as part of the innate immune response. CRP has a half-life of 19 hours in plasma and is excreted by the urinary system. CRP stimulates immune cells by attaching to Fc receptors (FcR) on leukocytes (monocytes, neutrophils, and myeloid lineage cells) and increasing IgG synthesis, thus linking the innate and adaptive immune systems. The anti-inflammatory actions are also aided by CRP FcR binding. CRP may be useful as a diagnostic marker for active inflammation and infection, according to some research. In response to active infection or inflammation, IL 6, IL 1, and TNF induce hepatocyte-mediated CRP production.

Our aim is to investigate in children with febrile illness the correlation between platelet indices and CRP.

METHODS

This hospital based descriptive study was conducted in post graduate Department of Paediatrics and Neonatology, an associated hospital of Government Medical College and Hospital, Srinagar, from December 2019 to November 2021. As per sample size calculation 3000 patients were included in the study.

Patients of either sex, age from 1 month to 1 year of age with fever admitted in hospital were included in the study. Age less than 1 month and more than 1 year, children with hematological diseases affecting platelets, not consenting, and children receiving iv antibiotics prior to admission in GB Pant Hospital were excluded in the study.

All children presenting to the hospital with fever, fulfilling the inclusion and exclusion criteria were enrolled in the study. An informed consent was taken from the parents or guardian of the patients.

Children admitted with fever between 1 month and 1 year of age, whose hemogram and CRP was done by the treating physician, were included in the study. Children with any hematological disorders affecting platelets, those who received antibiotic therapy or other medications affecting platelet count were excluded from the study. Data was collected from blood investigation reports of 3000 patients fitting inclusion criteria. Serial complete blood count (CBC) and CRP were done on days 1, 3 and 7 of admission. Each of the platelet indices were compared with CRP to find out the correlation between the two using Pearson correlation. By receiver operating characteristic (ROC) curve the cut off value for all platelet indices were found out.

Statistical analysis

The recorded data was compiled and entered in a spreadsheet (Microsoft excel) and then exported to data editor of statistical package for the social sciences (SPSS) version 23.0 (SPSS Inc., Chicago, Illinois, USA). Statistical software SPSS and Microsoft excel were used to carry out the statistical analysis of data. Descriptive statistics of data including percentages and means were reported. Categorical variables were presented in number and percentage (%) and continuous variables were

presented as mean±standard deviation (SD) and median. Graphically, the data was presented by bar and pie diagrams. A p value of less than 0.05 was considered statistically significant.

RESULTS

Of the 3000 patients included in our study, 1588 (52.9%) were males and 1412 (47.1%) were females. In our study mean platelet count was 312±180×109. The mean PDW was 9.81±1.49. The mean MPV was 8.31±0.93. The mean PCT was 0.22±0.07.

There was a significantly positive correlation between platelet count and CRP (p value <0.02) and r-correlation of 0.239, however all other platelet indices had a negative correlation with CRP.

Sex distribution i.e. 1588 male and 1412 female was not statistically significant (Table 1). Maximum and minimum age in months for male and female subjects, the maximum age was 12 months for both the groups the minimum age for males was 1.1 months and for females was 1.2 months. The mean±SD for males was 7.1±2.3 and for females was 6.7±2.3. The difference was not statistically significant (Table 2).

Table 1: The sex distribution of patients.

Gender	Number of patients
Male	1588
Female	1412
Total	3000

Table 2: Maximum and minimum age in months for male and female.

Age (in months)	Male	Female
Maximum	12	12
Minimum	1.1	1.2
Mean±SD	7.1±2.3	6.7±2.3

The mean height and weight of the males and females, the mean height was 54.6±13 and 53.6±13 for males and females respectively. There was no significant difference between the two (Figure 1).

Data concerning, white blood cell count (WBC), haemoglobin, MPV, PDW, PCT, platelet count, and CRP. The characteristics were not statistically significant between males and females (Table 3).

Table 4 depicts the correlation between platelet indices and CRP. There was a significantly positive correlation between PLT and CRP. However, all of the platelet indices had significantly negative correlation with CRP.

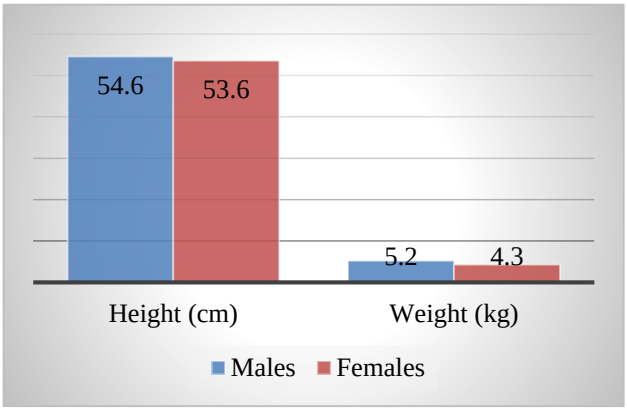

Figure 1: Mean height and weight of the males and females.

Table 5 depicts the best cut-off points, sensitivity and specificity of PLT and platelet indices. The sensitivity was highest for platelets at 96.67 and lowest for MPV 32.97 while as specificity was highest for WBC at 94.4 for MPV was 92.22 and lowest for PLT 30.77.

Table 6 presents data on the 1st, 3rd and 7th day after admission for males. The results are statistically significant for platelets and CRP (p value <0.001) and PCT and CRP (p value 0.116) while as they are not statistically significant for MPV, PDW and WBC.

Table 7 presents data on the 1st, 3rd and 7th day after admission for females. The results are statistically significant for platelets and CRP (p value <0.001) and PCT while as they are not statistically significant for MPV, PDW, PCT and WBC.

Table 8 depicts Spearman rank correlation between platelet indices and CRP value children with fever with high CRP had a significantly high PT and it has significant positive correlation with CRP (p value=0.003). MPV has negative correlation with CRP which is statistically significant (p value=0.0001). MPV/PT ratio has negative correlation with CRP which is statistically significant (p value=0.0001). PCT has positive correlation with CRP which is statistically significant (p value=0.022). PDW has a weakly positive correlation with CRP (not statistically significant).

Table 3: General characteristics of the study subjects.

Variable (mean±SD)	Males	Females	P value
WBC (mm^3)	7900.00±2113.89	7825.55±1925.38	0.722
Hemoglobin (g/dl)	12.12±1.35	11.89±1.50	0.632
PLT (140-440×109/l)	$382x10^9$±$153×10^9$	$3.12±1.80×10^9$	0.966
MPV (8.5-12.5 fl)	8.31±0.93	8.74±0.82	0.954

Continued.

Variable (mean±SD)	Males	Females	P value
PCT (0.21-0.23%)	0.23±0.13	0.22±0.13	0.239
PDW (10-17 fl)	9.81±1.49	10.32±1.37	0.543
CRP (mg/dl)	2.59±0.86	2.49±0.86	0.533

Table 4: Correlation of platelet indices with quantitative and qualitative variables.

Variables	P value	R correlation
PLT and CRP	0.02	0.239
MPV and CRP	0.02	-0.23
PDW and CRP	0.05	-0.193
PCT and CRP	0.04	-0.22

Table 5: Sensitivity, specificity and accuracy of PLT and platelet indices.

Variables	Cut-off point	Sensitivity	Specificity	AUC	95% CI	SE	P value
PLT	>252000	96.67	30.77	0.626	0.551-0.697	0.0419	<0.001
MPV	≤7.7	32.97	92.22	0.649	0.575-0.719	0.0409	0.972
PDW	≤8.9	37.36	83.33	0.622	0.547-0.693	0.0417	0.564
WBC	>10400	97.8	94.4	0.995	0.971-1.00	0.00251	<0.001
PCT	≤0.17	94.74	78.05	0.888	0.100-0.150	0.0101	0.944

Table 6: Data on the 1st, 3rd and 7th day after admission for males.

Variable (mean±SD)	Day 1	Day 2	Day 3	P value
WBC (mm^3)	7900.00±2113.89	7525.55±1925.38	7225.55±1925.38	0.772
Hemoglobin (mg/dl)	12.12±1.35	11.89±1.50	11.89±1.50	0.643
PLT (1.4-4.4×10^9/l)	382×10^9±153×10^9	312×10^9±1.80×10^9	302×10^9±1.80×10^9	<0.001
MPV (8.5-12.5 fl)	8.31±0.93	8.44±0.82	8.40±0.82	0.957
PDW (10-17 fl)	9.81±1.49	10.32±1.37	10.22±1.37	0.732
PCT (0.21-0.23%)	0.24±0.06	0.23±0.07	0.24±0.070	0.116
CRP (mg/dl)	22.59±3.86	12.49±1.96	2.49±0.86	<0.001

Table 7: Data on the 1st, 3rd and 7th day after admission for females.

Variable (mean±SD)	Day 1	Day 2	Day 3	P value
WBC (mm^3)	7500.00±2113.89	7525.55±1925.38	7225.55±1925.38	0.772
Hemoglobin (mg/dl)	11.42±1.35	11.29±1.50	11.49±1.50	0.643
PLT (1.4-4.4×10^9/l)	382x10^9±153×10^9	312x10^9±180×10^9	302x10^9±180×10^9	<0.001
MPV (8.5-12.5 fl)	8.31±0.93	8.44±0.82	8.40±0.82	0.957
PCT (0.21-0.21%)	0.21±0.18	0.23±0.22	0.25±0.17	0.116
PDW (10-17 fl)	9.81±1.49	10.32±1.37	10.22±1.37	0.732
CRP (mg/dl)	22.59±3.86	12.49±1.96	2.49±0.86	<0.001

Table 8: Spearman rank correlation between platelet indices and CRP value.

Variable	Correlation coefficient (Spearman rank correlation)	P value
PT (109/l)	0.148	0.003
PDW (fl)	0.054	0.277
MPV (fl)	-0.176	0.0001
PCT (%)	0.115	0.022
MPV/PT	-0.175	0.0001

Table 9 and Figures 2 and 3 correlated the studied markers with paediatric risk of mortality (PRISM) score, PRISM score had significant negative association with both platelet count (r=−0.420, p=0.001) and PCT (r=−0.442, p=0.001). And, it had a significant positive association with CRP level (r=0.497, p=0.001). ROC for PDW and MPV gives the area under the curve and sensitivity and specificity of these indices 0.622 and 0.649 respectively

for PDW and MPV. ROC for PLT and WBC gives the area under the curve and sensitivity and specificity of these indices.

Table 9: Correlations of PRISM score with CRP, platelet count and parameters.

Variable	PRISM	
	R	P
PLT	-0.420	<0.001
MPV	0.047	0.772
PDW	-0.040	0.776
PCT	-0.442	<0.001
CRP	0.479	<0.001

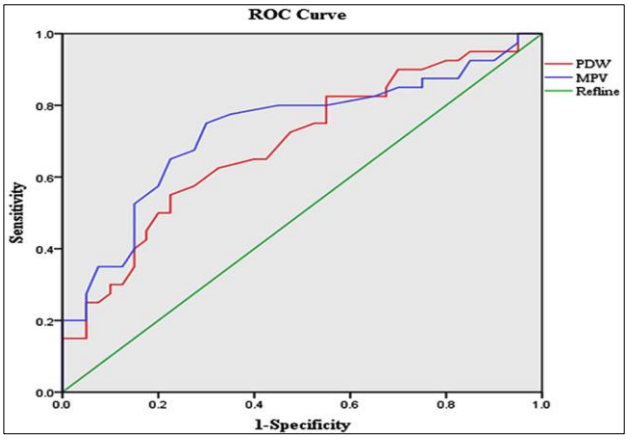

Figure 2: ROC for PDW.

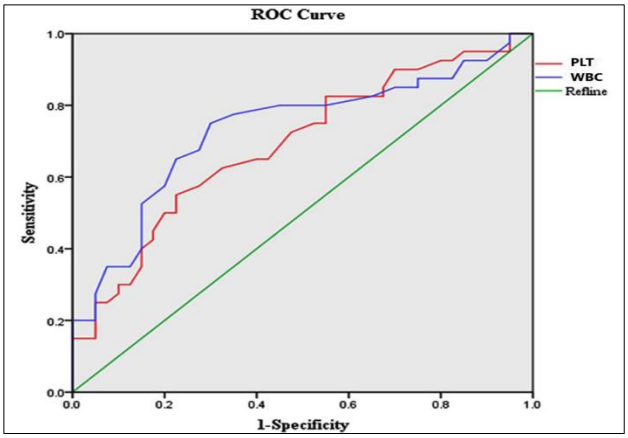

Figure 3: ROC for PLT.

DISCUSSION

Children with fever and high CRP had a significantly higher platelet count and a significant positive connection with CRP, according to our findings. The findings support those of Pillai et al who discovered that children with fever and high CRP had a considerably higher platelet count and a significant positive connection with CRP (p value=0.003).[5]

Zhang et al investigated the relationship between platelet indices and deep surgical site infection. PLT values were substantially higher in the case group than in the control group (303.00±139.27 versus 196.10±59.61 [109/µl], p=0.001).[6]

However, when it comes to MPV as an acute phase reactant, the same cannot be said. Some research found greater MPV values, while others found lower MPV values. Tekin et al found that the MPV's sensitivity and specificity were 81.4 percent and 86.3 percent, respectively, while utilising a cut-off value of 8.2 fl.[7] Various investigations on MPV in patients with infectious and inflammatory disorders produced inconsistent results. MPV had a substantial negative connection with CRP in our study, with a significant cut off value of MPV is ≤7.7 fl.

Patients with lower PLT count and PCT (p=0.001 and 0.001, respectively), increased MPV and PDW (p=0.014 and 0.004, respectively) had a significantly higher risk of mortality than those with normal platelet indices, according to Samuel et al.[8] According to Makwana et al, increased MPV, PDW, and PCT were related with a longer hospital stay and a longer fluid therapy requirement.[9] According to Srinivasa et al, MPV and PDW levels were greater in patients with culture-proven sepsis, particularly with gram-positive organisms. PDW had a negative connection with CRP in our study.[10]

PDW levels were considerably greater in difficult acute appendicitis compared to non-complicated acute appendicitis in research by Boshnak et al. In a case control study, Zainab et al discovered that the MPV/PCT, PDW/platelet count, and MPV/platelet count in the first sample after admission were accurate predictors of mortality, predicting 65 percent to 67 percent of fatalities.[11,12] Togan et al discovered that whereas the CRP level in patients with acute brucellosis was high, the MPV, PDW, and leukocyte counts in the study were all within normal limits.[13] In situations of acute brucellosis, CRP remains the most important inflammatory marker. In a study by Lee et al, the APN group had significantly greater WBC, ESR, CRP, and MPV levels than the lower UTI group. PDW, CRP, and platelet count were all positively linked with MPV.[14] CRP and MPV were found to be independent predictors of APN in multiple logistic regression studies. However, MPV had a lower area under the ROC curve than CRP. The results suggest that MPV can be an inflammatory marker in UTI, but the predictive value of MPV was not superior to CRP in the diagnosis of APN.

Kefeli et al discovered that MPV could be a helpful parameter to serve as an indicator for AP and a predictive factor for AP.[15] According to the findings of Icli et al, patients with infective endocarditis have enhanced platelet activation, and infective endocarditis therapy reduces platelet activation by lowering MPV.[16]

Limitations

Limitations of the study were non-categorization of fever into specific types and delay in the processing of samples affects various platelet parameters which many a times is the case in a resource limited setup as ours.

CONCLUSION

Patients' CRP and platelet counts were elevated at the time of admission. CRP and platelet levels decreased dramatically as the patient's health improved. Furthermore, our findings revealed a strong link between CRP and platelet counts in patients. Platelet count, PDW, MPV, and PCT were all influenced. Only MPV was replaced on the third day of the fever.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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