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Role Of Platelet Indices As Acute Phase Reactant In Acute Febrile Illness In Children.

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ABSTRACT

Acute febrile illness is illness with fever less than 2 weeks or shorter, with rapid onset, caused by diverse pathogens with no evidence of organ or system specific aetiology. Like C-reactive protein, platelets which are the part of natural immune system, can be during inflammatory reaction, so we studied 100 paediatrics patients over 8 months to evaluate the diagnostic value of platelet indices as an acute phase reactant. The mean Age of the patients was 5.77 years (SD=3.56) with range being 6 months to 14 years. Maximum children were presented and investigated between 24 to 48 hours of onset of fever. 67% children did not have any other sign at presentation except fever. CRP values correlated significantly with Platelet count and Mean Platelet Volume (MPV). There was negative correlation between CRP values and Mean Platelet Volume /Platelet Count (MPV/PT) ratio.

Keywords: Acute febrile illness, platelet count, platelet indices, C - reactive protein, acute phase reactant

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INTRODUCTION

Fever plays an important role in inflammation; in fact it is one of the four cardinal features of inflammation [1]. Fever can be classified based on duration as acute, subacute, and chronic [2]. Acute febrile illness is illness along with fever of 2 week or shorter in duration, with rapid onset, caused by diverse pathogens with no evidence of organ or system specific etiology. Comprehensive evaluation usually includes complete history and physical examination along with blood investigations like CBC, CRP (if available), blood culture and urine analysis, chest x ray, lumbar puncture [3]. CRP is one of the Acute Phase Reactant that influences multiple stages of inflammation and has both pro inflammatory and anti-inflammatory actions, although primary effect may be anti-inflammatory [4]. Like CRP, platelets which are the part of natural immune system, can be elevated in response as 'Acute phase reactant' during inflammatory reaction. Activated platelet with their micro particle can bind to leukocytes and stimulates mutual activation. Thereby platelets modulate leukocyte effector function and contribute to inflammatory and immune responses to injury or infection. Platelet enhance cytokine release and their interaction with neutrophils boost oxidative burst and phagocytosis. Depending on the underlying pathology platelet can enhance or diminish leukocyte cytokine production, indicating their interaction with leukocyte represent a fine balanced system to restrict excessive inflammation during infection [5]. Thrombocytosis or elevation in the peripheral blood platelet count is common in children who are further classified into primary or essential thrombocytosis and secondary thrombocytosis. Much rarer in children is primary thrombocytosis, which is divided into familial and essential. Secondary or reactive thrombocytosis in childhood results from increased thrombopoiesis, as a reactive process due to an underlying infection, chronic inflammation, injury, malignancy and surgical or functional splenectomy. Plateletocrit is the ratio of platelet volume to total blood volume; which is consistent with platelet volume in 100ml of blood. MPV is the ratio of plateletocrit to platelet count. Platelet indices are actual markers of platelet activation. They have been studied in metabolic diseases, vascular disorders, pregnancy, CKD, cirrhosis, malignancies, inflammatory and immune mediated disorders and infections. These indices have been studied in the diagnosis of individual infection. However, their role as acute phase reactant is not studied extensively in children with acute febrile illness so our study intended to do that.

MATERIALS AND METHODS

Study Design: Descriptive Cross-sectional study.

Study Duration: 1st September 2020 – 30th April 2021.

Study Setting: A tertiary pediatric care center in Western India.

Study Population: All children with acute febrile illness within age group 1 month to 16 years who were admitted in our institute within 48 hours of onset of fever.

Inclusion Criteria

- Children of both sexes aged 1 month to 16 years.
- Presentation within 48 hours of fever.
- Blood investigations taken simultaneously within 48 hours presentation.
- Fever more than 100 F.

Exclusion Criteria

- Children with hematological disorders affecting platelets.
- Children received antibiotic therapy or other medications affecting platelet count.
- Children who have received medications prior to presentation at our institute.
- Children whose parents refuse consent.

Data was collected using standard proforma meeting the objectives of the study. Case records of all the patients included in the study were obtained manually and data was analyzed. We obtained age, sex, presenting complaints, relevant past and personal history, vital signs, general and systemic examination, CBC and CRP along with it relevant investigations according to presenting complaints. Platelet indices

such as Platelet count, MPV, MPV/PT ratio were obtained. Each of the platelet indices was 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 are found out.

RESULTS

Table 1: Age wise Distribution

Age Group	Frequency	Percent
Upto 1 years	6	6.0
1 to 3 years	29	29.0
3 to 6 years	29	29.0
6 to 12 years	33	33.0
Above 12 years	3	3.0
Total	100	100.0

This study includes total 100 children with fever less than 48hrs of duration, out of them 6 children are between age 6 month to 1 year ,maximum children are between age1 year to 6 year that is 58 followed by 6 year to 12 year 33, there are 3 children who are beyond 12 years of age. The mean Age of the study sample was 5.77 years (SD=3.56) with range being 6 months to 14 years.

Out of 100 children who participated in the study 58(58%) were male and 42(42%) were female.

Table 2: Associated Symptoms Reported

Associated Symptoms	Frequency	Percent
Fever alone	55	55
Convulsion	18	18
Cough with fever	9	9
abdominal pain	4	4
fever with rash	3	3
fever with joint pain	3	3
fever with congestion of eyes	2	2
fever with burning micturition	2	2
swelling over body	1	1
fever with strawberry tongue	1	1
fever with anorexia	1	1
fever in k/c/o thalassemia	1	1
Total	100	100.0

Maximum children presented with fever as the only symptom (55%), followed by associated convulsions.

Table 3: Descriptive Statistics

	Mean	SD	Minimum	Maximum
Age	5.777	3.5644	0.6	14.0
Time since Onset	35.79	14.865	3	48
Temperature	101.39	1.034	100	104
Platelet count	335110.00	207418.228	10000	972000
MPV	8.150	1.9463	0.6	11.9
MPV/PT ratio	0.034696	0.0248253	0.0060	.1320
CRP	37.553	58.3920	0.0	343.0

The mean duration since symptom onset was 35.79 hours (SD=14.86) with minimum being 3 hours and maximum being 48 hours. Mean age of children was 6yrs with minimum age being 6months and maximum 14yrs. The mean recorded temperature was 101.39 OF with minimum recorded temperature was 100 OF and maximum being 104 OF. Mean platelet count was 3, 35,110 with minimum being 10,000 and maximum 9, 72,000. Mean MPV value is 8.150 with minimum being 0.6 to maximum 11.9. MPV/PT ratio mean was 0.034696 with minimum being 0.0060 to maximum 0.1320.

Table 4: Significant Correlations

Variables Compared		Co-efficient of Correlation (r)	P value	Interpretation
Age	Platelet Count	-0.203	0.04	Age had mild negative correlation with platelet values, whereas MPV/ PT ratio has mild positive correlation with age
	MPV/PT ratio	0.226	0.024	
MPV/PT ratio	Platelet Count	-0.714	<0.001	Platelet count had strong negative correlation with MPV/PT ratio and positive correlation with CRP values.
	CRP	0.174	0.004	
CRP	Platelet count	0.375	0.001	CRP values correlated significantly with Platelet count and MPV. There was negative correlation between CRP values and MPV/ PT ratio.
	MPV	0.369	0.006	
	MPV/PT ratio	-0.356	0.009	

Table 5: Correlations illustrated

	Age	Temperature	Platelet count	MPV	MPV/PT ratio
Platelet count	-0.203	-0.054			
	0.042	0.597			
MPV	0.082	-0.018	0.119		
	0.418	0.860	0.07		
MPV/PT ratio	0.226	-0.007	-0.714	0.369	
	0.024	0.948	0.000	0.004	
CRP	-0.003	0.171	0.375	0.369	-0.356
	0.979	0.090	0.001	0.006	0.009

Age had mild negative correlation with platelet values, whereas MPV/ PT ratio has mild positive correlation with age. Platelet count had strong negative correlation with MPV/ PT ratio and positive correlation with CRP values. CRP values correlated significantly with Platelet count and MPV. There was negative correlation between CRP values and MPV/ PT ratio.

DISCUSSION

Discussing about correlation of different platelet indices, age has mild negative correlation with platelet counts (P value 0.04) but MPV/PT ratio has mild positive correlation with age (P value 0.024). Whereas Vishwanathan et al [6] found that platelet count is lower in younger population as compared to older, but other indices showed no significant difference with respect to age.

It is known that IL-6 stimulates the synthesis of CRP and thrombocytosis. It is found that inflammatory disorders have high platelet count in almost all studies including K Pillai et al [7]. This study showed CRP value correlating significantly with platelet count. MPV is the most extensively studied marker of platelet activation as of now. MPV is indirect measurement of platelet function or activation. Reduced fragmentation of megakaryocytes in the bone marrow and splenic release of large platelets in sepsis i.e. increased demand of them may increase MPV and decrease in platelet release from marrow decreases MPV. As we have discussed discordance between concentrations of different

APR is common. Some may be elevated while others may not. Similarly, few reports which have evaluated relationship between infection and MPV. It has been studied in the diagnosis of infections like Hantavirus hemorrhagic fever, RSV, dengue, Pylori, UTI etc. Some studies found MPV values are higher in infection while others reported lower values. Zayeda et al [8] found MPV levels had a positive correlation with CRP. K Pillai et al found that MPV has significant negative correlation with CRP. In this study MPV has significant positive correlation with CRP. In a study by Gao et al [9], it was found that MPV was secondary to lactate in predicting mortality in patients with septic shock.

Some studies revealed that MPV/ PT ratio is associated with pathophysiological characteristic of many disorders can act as long term mortality predictor. K Pillai et al found MPV/PT ratio has significant negative correlation with CRP which is comparable to my study, where CRP is having negative correlation with MPV/PT ratio. But Lee et al [10] showed positive correlation between CRP with MPV/PT ratio in children with pneumonia. PDW and PCT as acute phase reactant haven't been studied in our study as values were not available with our analyzer.

Limitations

Though statistically significant, sample size studied was limited. Normal ranges for cell analyzer for platelet indices are not available, so that we could define lower and upper normal limits. Reference ranges may vary from machine to machine.

Analysis of platelet indices was performed using a single sample obtained at the time of admission only. This did not reflect how the values altered during the course of hospital stay, and how were the indices after improvement in patient's condition or on discharge.

Due to limited sample size, patients were not further categorized into specific subgroups depending on etiology. This would have given additional information.

We did not have an afebrile control group for platelet indices in normal children using same analyzer.

These results are from a single center study and may not be applicable in other areas or to a larger general population because of the variation in the local prevalence of acute febrile illnesses. So multi centric prospective study with specific age and diagnoses with follow up reports and comparisons with healthy controls would be required.

CONCLUSIONS

- Platelet indices have potential for clinical utility and which is supported by compelling evidences in certain clinical scenarios like acute febrile illnesses in children
- Age had mild negative correlation with platelet values, whereas MPV/PT ratio has mild positive correlation with age
- Platelet count had strong negative correlation with MPV/PT ratio and positive correlation with CRP values.
- CRP values correlated significantly with Platelet count and MPV. There was negative correlation between CRP values and MPV/PT ratio.
- Platelet indices can be useful as an acute phase reactant like CRP in acute febrile illness patient for evaluation of fever.
- As platelet indices are easy to perform, inexpensive and available with CBC report itself by using automatic haematology analyser, however they have limited clinical utility at present because they vary significantly and there is lack of definitive cut off values for specific analysers / and for specific diseases and age groups
- Therefore evaluation of retrospectively derived cut off values and standardization of platelet indices measurement should be emphasized in new prospective cohorts.
- There should be assessment of less researched platelet indices like PDW, plateletocrit in addition to MPV.
- Well designed and large scale prospective multicentric studies will help us further in establishing role of platelet indices.

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