

The Study of Platelet Indices in Acute Respiratory Tract Infections in Children Aged Between 2 Months -5 Years Visiting a Tertiary Care Hospital- A Cross-Sectional Study

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ABSTRACT

Background: Pneumonia is an inflammation of the lung tissue in the alveoli, caused by both infectious and non-infectious factors. Although platelets' primary function is haemostasis, recent studies have also explored their involvement in inflammation and immune response. **Objectives:** This study was conducted with the

objectives to determine the changes in platelet indices during an acute respiratory tract infection in children aged between 2 months to 5 years and to study the association of severity of acute respiratory tract infections with changes in platelet indices in children aged between 2 months to 5 years at the time of admission.

Methodology: This was a correctional study conducted among children with respiratory tract infections aged between 2 months to 5 years at a tertiary level hospital in South India. A total of 80 children were included in the study. A sample of 1 ml of venous blood was drawn from patients visiting the hospital and sent for Complete Blood Count analysis, from which platelet indices were obtained and recorded. **Results:** The median age of the study participants in this study was 12 months (inter quartile range 6 – 25 months). Majority of the subjects were males (60, 75.0%) in this study. Considering the association between various platelet indices and the severity of respiratory illnesses it was found that, the platelet count increased with increase in severity of illness ($p < 0.001$). Similarly, platelet distribution width ($p = 0.002$) and plateletcrit (< 0.001) increased with increased severity of the illness. Meanwhile mean platelet volume decreased with increased severity of the illness.

Conclusion: Platelet parameters show variation in the lower respiratory tract infections. As they can be determined as a part of routine complete blood picture analysis, they may be considered as markers of inflammation in the diagnosis of lower respiratory tract infections.

Keywords: Platelet indices, mean platelet volume, platelet distribution width, plateletcrit, acute respiratory infections, pediatric, inflammation, disease severity.

1. INTRODUCTION

Pneumonia is an inflammation of the lung tissue in the alveoli, caused by both infectious and non-infectious factors. It remains one of the leading causes of child mortality in developing countries, with an estimated 1.1 to 1.4 million children dying from it each year worldwide. The diagnosis of pneumonia is based on current clinical guidelines, which include

symptoms such as coughing, wheezing, fever, cyanosis, and difficulty breathing. Additionally, signs like tachypnoea, apnoea, cyanosis, sighing respiration, and rales and rhonchi during auscultation are key indicators. Chest X-rays (both anterior and posterior) and laboratory findings further aid in the diagnosis. Radiological imaging is used to differentiate between lobar pneumonia and bronchopneumonia.(1)

The WHO defines pneumonia as an acute episode characterized by cough or difficulty breathing, accompanied by tachypnoea (fast breathing). According to the protocol for children under 5 years old, simple (non-severe) pneumonia is indicated by a respiratory rate of ≥ 50 breaths per minute in infants under 12 months, and ≥ 40 breaths per minute in children aged 12-59 months. If pneumonia is accompanied by chest wall indrawing, it is classified as severe pneumonia. When pneumonia is accompanied by danger signs, such as inability to drink, excessive sleepiness, central cyanosis, convulsions, severe malnutrition, or persistent vomiting, it is considered very severe pneumonia. Due to the higher mortality risk in infants under 2 months, the diagnostic cutoff for pneumonia is ≥ 60 breaths per minute, and this is classified as severe pneumonia along with abnormal chest X-ray findings, such as consolidation or perihilar infiltration, with or without wheezing.(2) During an infection,

Although platelets' primary function is haemostasis, recent studies have also explored their involvement in inflammation and immune response. Platelets have the ability to attract leukocytes and release both pro-inflammatory and anti-inflammatory substances. Platelet activation has been associated with various diseases, including sepsis, inflammatory bowel disease (IBD), rheumatoid arthritis (RA), and acute lung injury. There is substantial evidence supporting the role of platelets in viral infections, with interactions reported between platelets and viruses such as adenovirus, dengue, hepatitis C, and Epstein-Barr virus (EBV). These interactions cause structural changes in platelets, which can alter platelet indices. Therefore, this study aims to examine changes in platelet indices during acute respiratory tract infections in children aged 2 months to 5 years. Although platelets have long been recognized as acute-phase reactants in inflammatory conditions, indicators of platelet activation and function, such as mean platelet volume (MPV) and platelet distribution width (PDW), are often overlooked. Recent research into infectious and systemic diseases has revealed significant findings related not only to platelet count but also to MPV and PDW.

This study was conducted with the objectives to determine the changes in platelet indices during an acute respiratory tract infection in children aged between 2 months to 5 years and to study the association of severity of acute respiratory tract infections with changes in platelet indices in children aged between 2 months to 5 years at the time of admission.⁵

2. METHODOLOGY

This was a cross-sectional study conducted among children with respiratory tract infections aged between 2 months to 5 years at a tertiary-level hospital in South India. The study was initiated following ethical approval from the institutional ethical committee and after obtaining informed written consent from the parents of the children. All children between 2 months to 5 years of age with respiratory tract infections during the study period, with ARI as defined by Integrated Management of Neonatal and Childhood Illness (IMNCI) guidelines, were included in the study. Children with diagnosed platelet disorders such as Bernard Soulier disease, Glanzmann's thrombasthenia, Hermansky Pudlak syndrome, Jacobsen syndrome and Lowe syndrome were excluded from the study. Patients with underlying chronic disease, a history of recent hospitalization within 2 weeks, and suspected hospital-acquired infection were not included in the study.

The sample size was estimated using the data from the study conducted by Sahin et al., with a confidence level of 95% with a margin of error of 0.2 in the mean. A total of 80 children were included in the study. A detailed history of the study subjects was recorded in a pre-tested proforma. All children with acute respiratory tract infections aged between 2 months to 5 years who visited RL Jalappa hospital during the study period were included in the study. A written informed consent for participation was obtained from parents or caregivers before enrolment. Detailed history, including the demographic characteristics of each child and duration of symptoms – fever, cough – was noted. Clinical examination findings of the respiratory system were recorded. A sample of 1 ml of venous blood was drawn from patients visiting the hospital and sent for Complete Blood Count analysis, from which platelet indices were obtained and recorded. A normal platelet count was accepted as 1,50,000–4,50,000/ μ L in children, and 6.5–12.0 fL for MPV, 0.10–0.28% for PCT, and

15.0–17.0 10 GSD for PDW were accepted as normal according to the hospital laboratory data.

The data was collected using Microsoft 365 Excel and analyzed using SPSS v27.0. The normality test (Shapiro-Wilk Test) was performed to analyze the data, and the results were expressed as frequency with percentage and mean with standard deviation or median with inter quartile range. Association between categorical variables was assessed using the Chi-square test or Fisher's exact test. Association between quantitative variables was assessed using an independent t-test. All the statistical analyses were carried out at a 5% level of significance, and results with a P value < 0.05 were considered statistically significant.

3. RESULTS

The median age of the study participants in this study was 12 months (inter quartile range 6 – 25 months). The majority of the subjects were males (60, 75.0%) in this study.

Table 1: Duration of symptoms

Duration of symptoms	Frequency	Percentage
Fever		
<7 days	53	66.3
>=7 days	27	33.7
Cough		
<7 days	51	63.7
>=7 days	29	36.3
Running nose		
<7 days	58	72.5
>=7 days	22	27.5
Noisy breathing		
<7 days	61	76.3
>=7 days	19	23.8
Hurried respiration		
1 day	6	7.5
3 days	3	3.8

In this study, 2 subjects had chest indrawing and one subject each had decreased activity (2.5%) as well as decreased feeding (1.3% each). The mean heart rate in this study was

117.76 ± 22.53 beats per minute. The mean respiratory rate was 38.73 ± 15.74 breaths per minute, and the mean temperature was 99.12 ± 1.62 degrees Fahrenheit.

Table 2: Distribution of other respiratory symptoms

Other respiratory symptoms	Frequency	Percentage
Nasal flaring	2	2.5

Suprasternal retractions	1	1.3
Subcostal retractions	1	1.3
Intercostal retractions	2	2.5
Wheeze	6	7.5
Stridor	2	2.5
Crepitations	66	82.5

Table 3: Association between platelet indices and respiratory disease severity

Platelet indices	Disease severity	N	Mean	Std. Deviation	95% Confidence Interval for Mean		P value
					Lower Bound	Upper Bound	
PLATELET COUNT	Mild	16	310.81	71.376	272.78	348.85	<0.001*
	Moderate	50	360.40	125.604	324.70	396.10	
	Severe	14	546.79	106.838	485.10	608.47	
	Total	80	383.10	136.980	352.62	413.58	
MEAN PLATELET VOLUME	Mild	16	9.319	.8758	8.852	9.785	0.005*
	Moderate	50	9.028	.8167	8.796	9.260	
	Severe	14	8.343	.7633	7.902	8.784	

	Total	80	8.966	.8670	8.773	9.159	
PLATELET DISTRIBUTION WIDTH	Mild	16	7.994	1.0535	7.432	8.555	0.002*
	Moderate	50	9.046	1.6453	8.578	9.514	
	Severe	14	10.093	1.6443	9.143	11.042	
	Total	80	9.019	1.6590	8.650	9.388	
PLATELETCRIT	Mild	16	.32250	.101357	.26849	.37651	<0.001*
	Moderate	50	.33820	.084339	.31423	.36217	
	Severe	14	.51643	.128159	.44243	.59043	
	Total	80	.36625	.118101	.33997	.39253	

*p value<0.05; Hence statistically significant

Considering the association between various platelet indices and the severity of respiratory illnesses, it was found that the platelet count increased with an increase in the severity of illness. Children with higher severity of illness had higher platelet count in this study, and this difference was statistically significant. Similarly, platelet distribution width and platelet crit increased with increased severity of the illness. Meanwhile, mean platelet volume decreased with increased severity of the illness.

Table 4: Association between CBC and respiratory disease severity

		N	Mean	Std. Deviation	95% Confidence Interval for Mean		P value
					Lower Bound	Upper Bound	
HAEMOGLOBIN	Mild	16	10.869	1.9345	9.838	11.900	0.305
	Moderate	50	10.212	1.8118	9.697	10.727	

	Severe	14	9.964	.9320	9.426	10.502	
	Total	80	10.300	1.7263	9.916	10.684	
TOTAL LEUCOCYTE COUNT	Mild	16	8.5306	2.71948	7.0815	9.9797	<0.001*
	Moderate	50	13.2162	5.53486	11.6432	14.7892	
	Severe	14	17.7336	2.64699	16.2052	19.2619	
	Total	80	13.0696	5.44055	11.8589	14.2804	
NEUTROPHILS	Mild	16	5.6956	4.11838	3.5011	7.8902	0.015*
	Moderate	50	23.9468	26.37775	16.4503	31.4433	
	Severe	14	28.4736	25.74742	13.6075	43.3397	
	Total	80	21.0887	24.63123	15.6073	26.5702	
LYMPHOCYTES	Mild	16	5.9169	3.07298	4.2794	7.5543	0.006*
	Moderate	50	15.8158	15.27653	11.4743	20.1573	
	Severe	14	23.0250	17.94805	12.6621	33.3879	
	Total	80	15.0976	15.10251	11.7367	18.4585	
MONOCYTES	Mild	16	2.8063	2.33874	1.5600	4.0525	0.277
	Moderate	49	3.6776	3.00694	2.8139	4.5412	
	Severe	13	4.5131	2.73886	2.8580	6.1682	
	Total	78	3.6381	2.85394	2.9946	4.2815	

BASOPHILS	Mild	16	.3094	.33147	.1327	.4860	0.412
	Moderate	50	.7528	1.36106	.3660	1.1396	
	Severe	14	.6057	.90068	.0857	1.1258	
	Total	80	.6384	1.15488	.3814	.8954	
EOSINOPHILS	Mild	16	1.6831	1.91306	.6637	2.7025	0.881
	Moderate	50	1.6958	1.72400	1.2058	2.1858	
	Severe	14	1.9471	1.46413	1.1018	2.7925	
	Total	80	1.7373	1.70313	1.3582	2.1163	

*p value<0.05; Hence statistically significant

In this study, TLC, neutrophils, and lymphocytes were found to be significantly associated with the severity of the respiratory illness, with each of these parameters increasing with an increase in severity of the illness. This difference was found to be statistically significant (p <0.05).

4. DISCUSSION

This was a cross-sectional study conducted among children with respiratory tract infections aged between 2 months to 5 years at a tertiary level hospital in South India with the objectives to determine the changes in platelet indices during an acute respiratory tract infection and to study the association of severity of acute respiratory tract infections with changes in platelet indices in these children.

Leukocyte count, ESR, CRP, and procalcitonin are the most often used acute-phase reactants in clinical practice; however, platelet parameters, such as platelet count, MPV, and PDW, may also function as acute-phase reactants in inflammatory disorders. (4) Secondary thrombocytosis often occurs in pediatric children with infections (5-7). Platelets and leukocytes are activated in reaction to microbial infections, and the platelet response has parallels to the leukocyte-mediated response. Leukocytes engulf bacteria, while platelets sequester germs in phagosome-like vacuoles, facilitating the rapid elimination of infections

(8). Thrombocytosis is prevalent in infections of the bone, joints, and pleural cavity. While it is mostly associated with bacterial infections exhibiting severe clinical development, high platelet counts are also seen in viral bronchiolitis and pneumonia. (9–11)

The mean age of the study participants in this study was 12 months, and a majority of the study participants were males in this study. The mean platelet count was higher in children with severe pneumonia in our study compared to mild and moderate pneumonia.

Prina et al. carried out a study of 2,423 patients with CAP, and reported that 2 percent had thrombocytopenia, 8 percent had thrombocytosis, and 90 percent had normal platelet counts.(12) The research also indicated that complex pleural effusion and empyema were more prevalent in individuals with thrombocytosis, but severe sepsis, septic shock, and hospitalization in critical care units were much more frequent in patients with thrombocytopenia. Patients with abnormal platelet counts had prolonged hospitalizations and elevated risks of death and re-hospitalization. The authors concluded that

thrombocytosis may serve as an indicator of disease severity. (12) In a separate study, Mirsaeidi et al. identified a substantial association between thrombocytopenia and thrombocytosis and death, and thrombocytosis was shown to be independently associated with the duration of hospital stay in patients with pneumonia.(8)

The authors proposed that abnormalities in platelet count were more indicative than abnormalities in leukocyte count for assessing the prognosis of pneumonia patients. Additional research, including pediatric patients, has shown analogous connections between thrombocytosis and worse clinical outcomes in pneumonia cases.

Both platelet count and size may fluctuate in proportion to their function. An elevation in MPV arises due to thrombopoietic stress, accompanied by enhanced megakaryocyte proliferation. An assessment of MPV and PDW together provides a more precise characterization of platelet volume distribution and quantifies variations in platelet volumes. PCT, conversely, denotes the proportion of platelets in a certain blood count.(13)

Platelet volume exhibits fluctuations in response to various clinical situations. Numerous studies have investigated the correlation between MPV and various inflammatory diseases, such as cystic fibrosis, ulcerative colitis, rheumatoid arthritis, FMF, neonatal RDS, upper urinary tract infections, and sepsis, whereas research on the clinical applicability of PDW and PCT is relatively scarce.(14–18)

In our study, platelet distribution width and platelet crit increased with increased severity of the illness. Meanwhile, mean platelet volume decreased with increased severity of the illness. Prior research has proposed two ways to elucidate the function of platelets in pneumonia. The first aspect pertains to the initiation of systemic inflammation. Platelets induce chemotaxis, leading to the release of several pro-inflammatory cytokines. Interleukin-6 (IL-6), a cytokine pivotal in the inflammatory response in community-acquired pneumonia (CAP), is thought to influence mean platelet volume (MPV). Additionally, cytokines like IL-3 and IL-6 stimulate megakaryocytes, leading to the generation of bigger and more reactive platelets. IL-6 levels are associated with illness severity in pediatric patients with CAP. (19,20) The second mechanism attributes thrombus formation to platelets, and the association between pneumonia and myocardial infarction in adults further substantiates this idea. (21)

5. CONCLUSION

Platelet parameters show variation in the lower respiratory tract infections. As they can be determined as a part of routine complete blood picture analysis, they may be considered as markers of inflammation in the diagnosis of lower respiratory tract infections. Taken together, platelet parameters have the power to indicate disease severity. We believe that their clinical use will increase as the relationship between platelets and infectious diseases is revealed through future studies

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