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Original Research Article

Study on reactive thrombocytosis in febrile young infants with serious bacterial infection in a tertiary care hospital

Nasreen Chidhara*

Department of Pediatrics, Kanchi Kamakoti Child's Trust Hospital, Nungambakkam, Chennai, Tamil Nadu, India

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***Correspondence:**
Dr. Nasreen Chidhara
E-mail: nasreenchidhara29@gmail.com

ABSTRACT

Background: Thrombocytosis associated with multiple, simultaneous causative factors was also reported in many children. Among all patients with infections, osteomyelitis and septic arthritis were associated with higher platelet counts than other infections. This study was done to estimate the prevalence of reactive thrombocytosis among febrile young infants and to assess the utility of platelet count as a potential predictor of serious bacterial infection.
Methods: The study was a cross-sectional study conducted in the department of paediatrics, Kanchi Kamakoti child's trust hospital, Nungambakkam, Chennai. 140 children were included in the study. Venepuncture was done in all these children. Blood sample of 3 ml was collected in an EDTA tube for complete blood count and in another tube 2 ml of blood was collected for CRP.
Results: The prevalence of reactive thrombocytosis was 65.8% in the population with serious bacterial infection (SBI). The proportion of children having respiratory symptoms in the study population was 70%, which was the most common system affected. Gastrointestinal, CNS and genito-urinary symptoms were seen in 29.29%, 11.43% and 10.00% of subjects respectively. Other miscellaneous symptoms were reported in 4.29% of the patients.
Conclusions: The prevalence of SBI was highest (30.2%) in the 4 to 6 months age group. The prevalence of SBI in 1 to 3 months, 7 months and above age groups was 28.6% and 29% respectively.

Keywords: SBI, Platelets, Fever, Infant, Diagnosis

INTRODUCTION

Fever is the commonest chief complaint in infants aged less than three months attending either emergency departments or outpatient clinics. Numerous studies have reported that serious bacterial infections are common among such patients.[1] The overall prevalence of SBI seems to be 7-18% among such febrile infants. SBI has been a major cause of morbidity and mortality in children in the developing world, which accounts for about 60% of childhood mortality.[2] Early recognition and appropriate antibiotic treatment can significantly reduce morbidity and mortality.[3] Managing such patients is further challenged by the resultant complications and the sensitive nature of their health. Also, it is often hard to differentiate between infants with SBI and those with simple infections.[4] Definitive diagnosis of SBI necessitates a positive culture of the CSF, blood, urine or a physical examination to identify bacterial focus and radiography.[5] Owing to the generally unrevealing physical examination of the infants and the culture results are not readily available, it is challenging for the attending clinicians to decide the appropriate patient management based on history, physical examination and laboratory tests.[6] Considerable time has been spent to develop and implement screening tests to identify the biomarkers using which the physicians can reliably differentiate and diagnose febrile children having a

higher risk for SBI than those with low risk.[7] Many markers have been identified and seem to be closely associated with SBI. C-reactive protein (CRP), an acute-phase reactant that swiftly rises during infection, inflammation and trauma is one such marker. WBC count and differential count in the form of absolute neutrophil count (ANC) is another marker evaluated to be associated with most of the febrile infants.[8] The common causes of thrombocytosis reported by large-scale prospective studies among children are infection, hemolytic anemia, tissue damage, rebound thrombocytosis, chronic inflammation, renal disorders and malignancy.[9] Thrombocytosis associated with multiple, simultaneous causative factors was also reported in many children. Among all patients with infections, osteomyelitis and septic arthritis were associated with higher platelet counts than other infections Thrombocytosis secondary to infections was significantly more common in children under 5 years of age, whereas chronic inflammation, malignancy and renal disorders were more common causes of thrombocytosis in children over 5 years of age.[10]

METHODS

The study was a cross-sectional study conducted in the department of paediatrics, Kanchi Kamakoti child's trust hospital, Nungambakkam, Chennai after getting approval from institutional ethical committee. 140 children were included in the study from August 2019 to August 2020 (12 months). The study group involved young infants, presenting to the study setting with febrile illness and diagnosed with reactive thrombocytosis.

Inclusion criteria

The inclusion criteria was infants aged 29 to 365 days with temperature >38°C.

Exclusion criteria

The exclusion criteria was infants who had a fever for more than 72 hours and had received antibiotics or vaccination in the last 48 hours, age group <29 days and >365 days, infants with pre-existing hemato-oncological diseases and infants on chronic medication known to reduce platelet count. A thorough history was taken and a detailed physical examination was done. The findings were recorded in the proforma. Venepuncture was done in all these children, the blood sample of 3 ml was collected in an EDTA tube for complete blood count and in another tube 2 ml of blood was collected for CRP. Relevant necessary investigations such as urine routine examination, chest x-ray, urine culture, blood culture, CSF culture, or other X-rays were done for each subject based on the presenting complaints and thorough clinical examination. A platelet count of >4.5 lakhs/cu mm was taken as thrombocytosis. It was assessed in the lab using an automated blood analyzer.

Statistical analysis

The association between SBI, CRP positivity and thrombocytosis was assessed by calculating the odds ratio and its 95% CI. A chi-square test was used to assess the statistical significance of this association. The mean values of quantitative variables like TC and CRP were compared between people with and without thrombocytosis using an independent sample t-test. Mean differences and 95% CI were presented. A p value less than 0.05 was considered statistically significant. IBM SPSS version 21 was used for statistical analysis.

RESULTS

Table 1 shows a total of 140 participants were included in the analysis. There were 28 (20%) children between 1-3 months in the study population. The proportion of children between 4 to 6 months, >7 to 1 year were 43 (30.7%) and 69 (49.3%) respectively. The proportion of male children was 61.4% and female children were 38.6% in the study population.

Table 1: Descriptive analysis of age groups in study group (N=140).

Age groups	Frequency	Percent (%)
1-3 months	28	20
4-6 months	43	30.7
≥7 months-1 year	69	49.3

Table 2: Frequency distribution of respiratory symptoms in study group (N=140).

Respiratory symptoms	Frequency	Percent (%)
Cough	97	69.3
Fast breathing	65	46.4
Grunting	9	6.4

Table 3: Frequency distribution of gastrointestinal symptoms in study group (N=140).

Gastrointestinal symptoms	Frequency	Percent (%)
Loose stools	27	19.3
Vomiting	29	20.7
Blood in stools	0	0.0

Table 4: Frequency distribution of CNS symptoms in study group (N=140).

CNS symptoms	Frequency	Percent (%)
Seizures	13	9.3
Altered sensorium	5	3.6

Table 2 shows the number of participants with cough was 97 (69.3%) and fast breathing was 65 (46.45) in the study population. The proportion of subjects with grunting was 9 (6.4%).

Table 3 shows the number of participants with loose stools was 27 (19.3%) in the study population, while 29 (20.7%) of them had vomiting and none had blood in stools.

Table 4 shows the proportion of participants with seizures was 13 (9.3%) and altered sensorium was 5 (3.6%) in the study population.

Table 5: Frequency distribution of other symptoms in study group (N=140).

Other symptoms	Frequency	Percent (%)
Rashes	3	2.1
Soft tissue swelling	3	2.1
Tenderness of the swelling	3	2.1
Restriction of joint movements	0	0

Table 5 shows the number of participants with rashes was 3 (2.1%) and soft tissue swelling was 3 (2.1%) in the study group. The proportion of subjects with the tenderness of swelling and restriction of joint movements were 3 (2.1%) and 0 (0.0%) respectively.

Table 6 shows the mean HR was 128.0±22.85 in the study population. The mean RR was 45.67±13.14 and 14.82±0.453 was GCS in the study population.

Table 7 shows the number of participants with dehydration was 10 (7.1%) and anemia was 5 (3.6%) in the study population. The proportion of subjects with rashes was 2.1%. The proportion of subjects with skin or soft tissue swelling, warmth and tenderness were 2.1% each in the study population.

Table 8 shows the number of participants with thrombocytosis was 50 (35.7%) and 90 (64.3%) had no thrombocytosis in the study group. The number of participants with urine pus cells >5 was 14 (10.0%), 41 (29.3%) were observed to have urine pus cells 0 to 5. The proportion of subjects with positive CRP and blood c/s were 65 (46.4%) and 4 (2.9%) respectively. The number of participants with positive urine c/s was 7 (5.0%). The number of participants with positive CXR findings (suggestive of pneumonia) was 26 (18.6%). The number of participants who reported serious bacterial infection was 41 (29.3%). The odds of having thrombocytosis was 6.37 (95% CI 2.87-14.13, p<0.001) times higher in children with a serious bacterial infection when compared to non-SBI, which was statistically significant.

Table 9 shows the proportion of SBI was highest (30.2%) in the 4 to 6 months age group. The proportion of SBI in 1 to 3 months, 7 months and above age groups was 28.6% and 29%. The differences in the proportion of SBI across the age groups were statistically not significant. (p value 0.986).

Table 10 shows the proportion of thrombocytosis was highest (50%) in the 1 to 3 months age group. The proportion of SBI in 4 to 6 months, 7 months and above age groups was 37.2% and 29%. The differences in the proportion of SBI across the age groups were statistically not significant (p value 0.143).

Table 6: Descriptive analysis of vital signs in study group (N=140).

Vital signs	Mean±SD	Median	Max	Min	95% C.I. for EXP (B)	
					Lower	Upper
HR	128.0±22.85	120.00	204.00	98.00	124.24	131.88
RR	45.67±13.14	42.00	80.00	26.00	43.47	47.87
GCS	14.82±0.453	15.00	15.00	13.00	14.75	14.90

Table 7: Frequency distribution of general signs in study group (N=140).

General signs	Frequency	Percent (%)
Dehydration	10	7.1
Anemia	5	3.6
Rashes	3	2.1
Soft tissue swelling	3	2.1
The warmth of the swelling	3	2.1
Tenderness of the swelling	3	2.1

Table 8: Descriptive analysis of thrombocytosis in study group (N=140).

Thrombocytosis	Frequency	Percent (%)
Yes	50	35.7
No	90	64.3

Table 9: Proportion of children developing SBI in different age groups.

Parameters	SBI		Chi-square value	P value
	SBI	Non-SBI		
Age group				
1 to 3 months	8	20	0.029	0.986
	28.60%	71.40%		
4 to 6 months	13	30		
	30.20%	69.80%		
7 months or more	20	49		
	29.00%	71.00%		

Table 10: Proportion of children developing thrombocytosis in different age groups.

Parameters	Thrombocytosis		Chi-square value	P value
	Yes	No		
Age group				
1 to 3 months	14	14	3.89	0.143
	50.00%	50.00%		
4 to 6 months	16	27		
	37.20%	62.80%		
7 months or more	20	49		
	29.00%	71.00%		

DISCUSSION

SBI has been a major cause of morbidity and mortality in children in the developing world, which accounts for about 60% of childhood mortality.[11] Early recognition and appropriate antibiotic treatment can significantly reduce morbidity and mortality. In the process of proper diagnosis of SBI and for better prognosis in a variety of clinical settings in different patient groups, numerous diagnostic markers of sepsis have been suggested.[12] They include CRP, procalcitonin (PCT), soluble triggering receptor expressed on myeloid cells-1 (sTREM-1), hemoglobin scavenger receptor (CD163) and high mobility group box 1 (HMGB1), but results have been erratic and variable depending on the selection criteria of patients. Strategies to reduce the global burden of sepsis include prevention through immunization, early recognition, treatment, development of new diagnostics and therapeutics.[13] Of the total 140 participants, 28 (20%) children were between 1-3 months in the study population. The proportion of children between 3 to 6 months, ≥7 months to 1 year were 43 (30.7%) and 69 (49.3%) respectively. In one of their two studies, Mantadakis et al prospectively analyzed 892 infants of ≤3 months old, while in another the infants (469) were ≤4 months of age. The proportion of children with thrombocytosis was 35.7%.[14] In healthy pediatric subjects normal count platelet ranges between 250,000/muL and 450,000/muL. An elevated platelet count greater than 2 SD defines a condition of thrombocytosis. The prevalence of SBI in the study population was 29.3%.[15] In their study, Fouzas found a very large proportion of children (74%) having SBI. A considerable amount of evidence points to the finding that platelets can act like acute phase reactants and that their production is triggered by interleukin-6 by directly enhancing megakaryopoiesis or indirectly by stimulating hepatic thrombocytosis secondary to anemia. The odds of having thrombocytosis was 6.37 (95% CI 2.87-14.13, p<0.001) times higher in children with a serious bacterial infection, which was statistically significant.[16] In line with this finding Brown LST said that reactive thrombocytosis had the highest accuracy in differentiating infants with SBI with less false positive or false negative results and that it can be a useful tool that could help the clinician to look for further investigations in infants with SBI. On the contrary, several studies opined that clinical impression and routine laboratory tests were unable to accurately identify the presence of SBI. However, certain markers have been consistently identified with SBI like leucocytosis, elevated CRP, pyuria and thrombocytosis.[17] Olaciregui in their study on 377 children of whom 74% of them had SBI found that PCT and CRP as useful markers of SBI. Leucocytosis, specifically ANC a consequence of infections mainly of acute nature has also been observed to be associated with SBI.[18] A study by Bilavsky et al reported that apart from the common indicators of SBI like CRP and WBC even cytokines like interleukin-6 are also useful. Though among the various makers, raised serum CRP level is a better indicator of SBI, however, no marker, either alone or in combination, has demonstrated adequate sensitivity or specificity for the diagnosis of SBI in febrile infants.[19,20] In addition, thrombocytosis secondary to anemia is a matter of concern in this age group. Reactive thrombocytosis in combination with WBC, CRP and pyuria seems to be a useful tool that could help clinician to target further investigation and follow-up strategy.

CONCLUSION

Almost 30% of the study population had a serious bacterial infection. The prevalence of SBI was highest (30.2%) in the 4 to 6 months age group. The prevalence of SBI in 1 to 3 months, 7 months and above age groups was 28.6% and 29% respectively. There was a statistically significant association between thrombocytosis and serious bacterial infection in the study population.

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