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Original Article

Reactive Thrombocytosis in Febrile Infants and Children with Serious Bacterial Infection

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Abstract

Introduction: Serious bacterial infection (SBI) is common in infants and children. Many children with SBI at presentation have no identifiable cause other than fever. A simple, rapid, inexpensive diagnostic test that identifies SBI among febrile children is unattainable. Reactive thrombocytosis secondary to disease is a common finding in children. Platelet will behave as an acute phase reactant through the stimulation of platelet production by interleukin-6.

Aim: This study aims to estimate the incidence of reactive thrombocytosis among young infants and children with a SBI.

Methods: It was a prospective study conducted on infants and children aged between 2 months and 3 years admitted as inpatients in pediatric intensive care unit and intermediate care unit of the Pediatric Department in Tirunelveli Medical College and Hospital from May 1, 2018, and April 30, 2019.

Results: The general incidence of thrombocytosis was 42% in children with febrile illness. In children with thrombocytosis, 53.6% had SBI. Among children with SBI, 80% had thrombocytosis. In babies with non-SBI, only 27.1% had thrombocytosis. *P*-value was statistically significant when the platelet count was compared between SBI and non-SBI groups. The mean platelet count was higher in the SBI group. *P*-value showed statistical significance between mean platelet count in SBI and non-SBI group. The sensitivity and specificity of platelet in diagnosing SBI were 80.4% and 72%, respectively. Other parameters that help early recognition of febrile infants at risk of SBI are total white blood cell count, C-reactive protein, and pyuria.

Conclusion: The incidence of thrombocytosis was high in babies with SBI. Among babies with SBI, 80.3% had thrombocytosis. In babies with non-SBI, only 27.1% had thrombocytosis. Thus, thrombocytosis can be used as a predictor of SBI.

Key words: Febrile young infants, Serious bacterial infection, Thrombocytosis

INTRODUCTION

Thrombocytosis refers to a platelet count above the normal value. With the easy availability of platelet count as a part of routine cell count using an automated cell counter, thrombocytosis is more often observed in sick babies. Thus, an elevated platelet count has become an important clinical problem for differential diagnosis.[1,2] Serious bacterial infections (SBIs) such as urinary tract infection, bacteremia, bacterial meningitis, pneumonia, infection of soft tissue, and bones are common in the pediatric age group. These infants and children initially present only with fever with no other localizing signs. Fever is a very common cause of pediatric consultation. The physical examination cannot identify the focus of the infection in many patients, and this problem becomes more accentuated if the child is younger. Although most children have only minor infections, it is important to identify those children and infants with SBI to start antibiotic treatment early.[3] Simple, rapid, inexpensive diagnostic test that identifies SBI among febrile children is unattainable.

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Reactive thrombocytosis is a common finding in children secondary to infection. If these SBIs are not diagnosed or diagnosed late, it will delay the initiation of treatment, thereby increasing morbidity and mortality. The risk of SBI varies with age. The incidence is 8–14% of those under 1 month of age, 5–9% of those between 1 and 3 months of age, and in 3–15% of those between 3 and

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36 months of age.[4-6] Hence, it is essential to identify the SBI early to reduce mortality and morbidity. The diagnosis of SBI in febrile infants and children without apparent the focus of infection remains difficult. Blood culture is the gold standard investigation to detect occult bacterial infection. The disadvantage is the delay in the availability of culture results. The elevated total count with an increase in neutrophils suggests a bacterial infection. In infants and children having fever without focus, elevated C-reactive protein (CRP) may indicate bacterial infection but is not confirmative. Reactive thrombocytosis was a frequent finding in children with SBI. Thrombocytosis of more than 450,000 cells/mm^3 in combination with leukocytosis, elevated CRP, and pyuria may help in the early recognition of febrile young infants and children with SBI.[7]

Aim

This study aims to estimate the incidence of reactive thrombocytosis among young infants and children with SBI.

MATERIALS AND METHODS

This prospective study was conducted on infants and children aged between 2 months and 3 years admitted as inpatients in pediatric intensive care unit (PICU) and intermediate care unit (IMCU) of the Pediatric Department in Tirunelveli Medical College and Hospital. Inclusion criteria: All children aged between 2 months and 3 years admitted to our pediatric IMCU and PICU with fever <7 days (with axillary temperature >100), associated with or without chills and rigors, tachypnea/respiratory distress, meningeal signs/increased ICT, dysuria/pyuria, and GI manifestations. Exclusion criteria: Children who previously received antibiotics, either oral or parenteral, vaccination, children with anemia, myeloproliferative disorder, other inflammatory condition such as Kawasaki disease, acute, rheumatic fever, and fever with thrombocytopenia.

All patients admitted to the pediatric department who fulfill the inclusion criteria after getting consent from the parents were enrolled in the study. These babies were subjected to sepsis evaluation such as white blood cell (WBC) count, platelet count, CRP, and urine microscopy. In addition, other investigations such as urine culture, blood culture, CSF analysis, pus culture, stool culture, chest X-ray, and pleural fluid analysis were done depending on the clinical requirements. The WBC count and platelet count were analyzed using automated equipment by withdrawing 2 ml of blood in an EDTA tube during admission or during the hospital stay.

RESULTS

The total number study population was 164. The incidence of SBI in our study was 28% [Figure 1]. Among which, 11% of the population belonged to 2–3 months of age. The rest of the children belonged to 4–36 months of age [Table 1]. The incidence of SBI in infants <3 months was 58.3% compared to 36% in children aged between 4 and 36 months (P = 0.121). Out of 164 infants and children studied, 92 were male, and 72 were female in the study group. About 33% of males and 20.8% of females had SBI (P = 0.089). A total WBC count of more than 15,000/cu.mm was seen in 48% of the study population. Among the children with SBI, 44% have a total count of more than 15,000/cu mm (P = 0.001). The mean total count was high in the SBI group. The sensitivity and specificity of the total count in diagnosing SBI were

Table 1: Babies characteristics

Characteristics	No. of patients	Percentage
Age in years		
<3 months	19	11
4–36 months	145	89
Gender		
Male	92	56
Female	72	44
Total count		
>15,000	78	48
<15,000	86	52
CRP		
Positive	76	46
Negative	88	54
Urine microscopy		
PUS cells >5	34	21
PUS cells <5	130	79
Platelet count		
<4.5 lakh	95	58%
>4.5 lakh	69	42

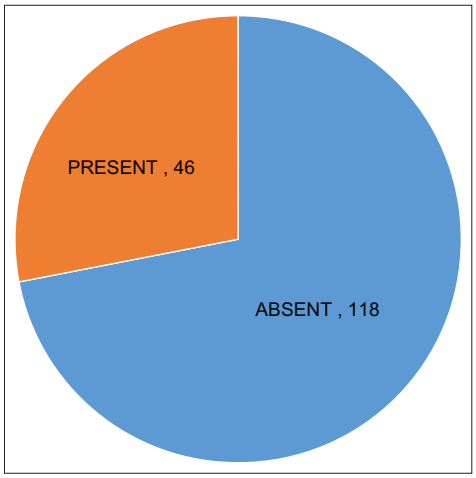

Figure 1: Serious bacterial infection

76.09 and 63.56, respectively. CRP >6 mg/dl was taken as positive. Among the study population, 46% of children have positive CRP. In the SBI group, 78% have positive CRP. Among the children with positive CRP, 50% had SBI. The sensitivity and specificity of CRP in diagnosing SBI were 82.67 and 67.8, respectively ($P = 0.001$). Among the study population, 42% have platelet count >4.5 lakh. In children with thrombocytosis, 53.6% had SBI. Among babies with SBI, 80% had thrombocytosis. Most of the babies with thrombocytosis had mild thrombocytosis ($P = 0.002$). The mean platelet count was higher in the SBI group. The sensitivity and specificity of platelet in diagnosing SBI were 80.4% and 72%, respectively. The mean platelet count was 5.97 lakh for UTI, 5.48 lakh for bacteremia, 5.8 lakh for osteomyelitis, 5.4 lakh for septic arthritis, 4.68 lakh for pneumonia, and 3.9 lakh for acute central nervous system infection, the mean platelet count in non-SBI was 3.88 lakh ($P = 0.007$) [Tables 2 and 3].

Among the study group, 21% had pus cells > 5/hpf. About 41.1% of children with >5 pus cells/hpf had SBI. Among the study parameters, CRP had high sensitivity and specificity followed by total count and platelet. When these parameters were combined, sensitivity and specificity increased.

Table 2: Distribution of serious bacterial infection according to babies characteristics

Characteristics	Serious bacterial infection	Percentage
Age in years		
<3 months	7	15.2
4–36 months	39	84.8
Gender		
Male	31	67.4
Female	15	32.6
Total count		
>15,000	35	76.1
<15,000	11	23.9
CRP		
Positive	38	82.6
Negative	8	17.4
Urine microscopy		
PUS cells >5	14	30.4
PUS cells <5	32	69.6
Platelet count		
<4.5 lakh	37	80.4
>4.5 lakh	9	19.6

Table 3: Distribution of diagnosis and platelet count

Diagnosis	No. of patients	Percentage	Platelet count	
			Mean	SD
UTI	20	43	5.97	0.86
Bacteremia	5	11	5.48	0.6
Osteomyelitis	2	4	5.8	0
Septic arthritis	1	2	5.4	0
Pneumonia	15	33	4.68	1.39
Acute CNS infection	3	7	3.9	1.21

CNS: Central nervous system

DISCUSSION

Olaciregui *et al.* found that 23.63% of the study group had SBI, while the incidence of SBI in our study was 28%.[8] The sensitivity and specificity of CRP in diagnosing SBI were 64 and 84% compared to 82.67 and 67.80 in our study. The higher sensitivity in our study was due to the lower cutoff of 6 as compared to 20 in the Olaciregui study. The sensitivity and specificity of leukocytosis >15,000/cu mm were 76.09% and 63.56%, which is not comparable with the Olaciregui study with sensitivity and specificity of 38% and 84%. Pulliam *et al.* studied children aged 1–36 months and found that 18% had SBI while the incidence in our study was 28%.[9] CRP with a cutoff of 7mg/dl had a sensitivity of 79.1% and specificity of 91%; the sensitivity was comparable to that of the sensitivity found in our study, that is, 82.67%. The lower specificity of CRP of 67.8% was due to the lower cutoff of CRP – 6 mg/dl. WBC count of ≥15,000/mm^3 had a sensitivity and specificity of 64% and 67%, respectively, comparable to sensitivity and specificity of 76.9 and 63.5 in our study. Heng and Tan found that 78% of cases of reactive thrombocytosis were due to infections.[10] A similar incidence was shown by Matsubara *et al.*, where 68% of thrombocytosis was due to SBI.[11] Fouzas *et al.* studied 408 infants and found that 25.2% had SBI.[12] Platelet count was significantly higher in infants with SBI compared to those without. In our study, the children with age group <3 years showed that the incidence of thrombocytosis was 42%. Out of that, 53.6% of thrombocytosis was due to SBI. Pratt *et al.* studied 128 children in the age group of 1–36 months. They found that 62% of the children had SBI.[13] The sensitivity of CRP at a cutoff of 7 mg/dl was 73% and specificity 81%. The sensitivity of WBC in predicting SBI was 82% and specificity was 69% with a cutoff of 15,000/mm^3. These values were comparable with those values in our study.

CONCLUSION

Among 164 children studied, the incidence of SBI was 28%. The age and sex of the child did not influence the incidence of SBI. Among the children with SBI, 44% had a total count of more than 15,000/cu mm. The mean total count was high in the SBI group. The sensitivity and specificity of the total count in diagnosing SBI were 76.09 and 63.56, respectively. In the SBI group, 78% had positive CRP. The sensitivity and specificity of CRP in diagnosing SBI were 82.67 and 67.8, respectively. The ability of CRP in diagnosing SBI was also fairly good. About 21% of the

study group had pus cells of >5/hpf in urine. About 41.1% of children with >5 pus cells had SBI.

Among the study population, 42% had a platelet count >4.5 lakh. In children with thrombocytosis, 53.6% had SBI. The incidence of thrombocytosis in SBI was 80%. The majority of cases with thrombocytosis had mild thrombocytosis. The mean platelet count was higher in the SBI group. The sensitivity and specificity of platelet in our study were 80.4%and 72%, respectively. Hence, platelet count can be used as a predictor of SBI. No single parameter had 100% accuracy in diagnosing SBI, but diagnostic accuracy can be increased when these parameters were combined.

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