International Journal of Contemporary Pediatrics
Chib R et al. Int J Contemp Pediatr. 2016 May;3(2):616-620
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: http://dx.doi.org/10.18203/2349-3291.ijcp20161050

Research Article

Estimate the incidence and pattern of reactive thrombocytosis among febrile young infants with serious bacterial infection

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Received: 26 February 2016
Accepted: 31 March 2016

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ABSTRACT

Background: Thrombocytosis or elevation in the peripheral blood platelet count to values >400,000/µL is common in infancy and childhood, occurring in 3 to 13% of children. The objective of study was to estimate the incidence and pattern of reactive thrombocytosis among febrile young infants with serious bacterial infections (SBIs).
Methods: The study was conducted in the Postgraduate Department of Pediatrics, G.B. Pant hospital, an associated hospital of Govt. Medical College Srinagar, which is a referral tertiary care hospital for the children of Kashmir valley. The study was a prospective non-randomized study conducted from April 2011 to March 2012. All infants of age 30-89 days admitted in hospital with rectal temperature >38°C/100.4°F without an apparent focus of infection on history and clinical examination were included in the study.
Results: The incidence of reactive thrombocytosis >4 lakh/mm3 in our study was 33 out of 39 (84.6%) in SBI versus 60 out of 110 (54.5%) in Non-SBI, which was statistically significant in SBI, p value < 0.05. Mean platelet count in urinary tract infections was 5.3 lakh/mm3, bacterial meningitis 5.2 lakh/mm3, occult bacteremia 4.9 lakh/mm3, pneumonia 4.7 lakh/mm3 and 3.9 lakh/mm3 across Non-SBI.
Conclusions: The incidence of reactive thrombocytosis >4 lakh/mm3 in our study was significantly higher in SBI (84.6%) than in Non-SBI (54.5%), p value < 0.05. Mean platelet count was highest in urinary tract infections followed by bacterial meningitis, occult bacteremia and pneumonia. So platelet count >4 lakh/mm3, reactive thrombocytosis, being simple and easy test to perform can be used for early prediction of SBI.

Keywords: SBI, Platelets, Fever, Infant, Diagnosis

INTRODUCTION

Thrombocytosis or elevation in the peripheral blood platelet count to values >400,000/µL is common in infancy and childhood, occurring in 3 to 13% of children.[1] Thrombopoietin (Tpo) is the key regulator of platelet production in humans, and is primarily expressed in the liver, and to a lesser extent the kidney, bone marrow and other organs.[2] Thrombocytosis is of two types, primary thrombocytosis which is divided into familial and essential and secondary thrombocytosis also known as reactive thrombocytosis in childhood results from increased thrombopoiesis, as a reactive process due to causes like, Infections (e.g., of the respiratory tract, gastrointestinal tract, central nervous system, skeleton and others), Iron deficiency anemia, hemolytic anemia, bleeding, Connective tissue diseases, malignancies, drugs, trauma, burns, and intense exercise.[3-8]

Reactive thrombocytosis seems to affect up to 15% of hospitalized children.[1,9,10] It is more common in neonates, particularly premature ones and up to 2 years of age and less common in older children. In most children with reactive thrombocytosis, platelet counts are modestly elevated up to 700,000/µL. Moderate thrombocytosis (platelets between 700,000 and 1,000,000/µL) occur in 6–8% of children with reactive thrombocytosis, while platelets >1,000,000/µL occur in less than 2% of Children with reactive Thrombocytosis, but may be more common in critically ill children.[5,10] Infections, both viral and

bacterial, are by far the most common cause of secondary thrombocytosis in childhood. Presently, infections of the respiratory tract account for 60-80% of cases of secondary thrombocytosis in children, followed by infections of the urinary and gastrointestinal tracts, and of the bones.[5,6,9,11-13]

Sick infants less than 3 months of age present a management challenge, as many of these have no identifiable source of fever, and the prevalence of serious bacterial infection (SBI) in this age group is high.[14-17] The most commonly suggested strategy for the febrile neonates admitted to a hospital is to undergo full sepsis work up.[16-17] The objective of our study was to estimate the the incidence and pattern of reactive thrombocytosis among febrile young infants with serious bacterial infections (SBIs).

METHODS

The study was conducted in the postgraduate Department of Pediatrics G.B. Pant hospital, an associated hospital of Govt. Medical College Srinagar, which is a referral tertiary care hospital for the children of Kashmir valley. The study was a prospective non-randomized study conducted from April 2011 to March 2012.

Inclusion criteria

All infants of age 30-89 days admitted in hospital with rectal temperature >38°C/100.4°F without an apparent focus of infection on history and clinical examination.

Exclusion criteria

Infants having fever more than 72 hours, and who had received antibiotics or vaccination within 48 hours of presentation.

Approach

All patients who had fulfilled, the inclusion criteria, underwent sepsis screening including WBC count, platelet count, blood culture, urine microscopy and culture and CRP. Lumbar puncture for cerebrospinal fluid (CSF) analysis and culture, pleural tap for pleural fluid analysis and culture as well as stool culture and chest radiographs, were obtained at the discretion of the attending pediatrician.

The WBC count with differential and the platelet count were quantified using automated laboratory equipment (Sysmex KX-21). Blood cultures were monitored by an automated system (Bac T/ALERT 3D). Urine was obtained by urethral catheterization using a sterile technique. A careful urinalysis, on a fresh urine sample, can identify children with a high likelihood of UTI to enable presumptive treatment while awaiting results of urine culture, the WBC in the urine were quantified by standard microscopic examination and expressed as WBC >5 leukocytes/high power field in a centrifuged sample or >10 leukocytes/mm^3 in an uncentrifuged sample.[19] The urine, CSF, pleural fluid and stool cultures were monitored using standard laboratory techniques. Normal CSF was defined as, clear in colour, WBCs up to 5/mm^3, proteins 10 to 40mg/dl, glucose content about 60% of the blood glucose level in a healthy child and polymorphonuclear cells were always taken abnormal in all patients.[20]

Serious bacterial infection

Was defined as occult bacteremia, urinary tract infection (UTI), bacterial meningitis, pneumonia. Isolates such as Staphylococcus epidermidis in the blood culture were considered contaminants unless they were isolated from more than two consecutive cultures. Urinary tract infection was defined as growth of single known pathogen on urine culture with ≥100,000 cfu/mL of urine obtained by urethral catheterization. Confirmation of the diagnosis on urine culture is necessary [(19)]. Definite pneumonia was defined as consolidation on chest radiograph plus any of the following signs, a positive blood culture for a pathogenic organism or culture of a pathogenic organism from pleural fluid sample. Probable pneumonia was defined as consolidation alone.[21]

Occult bacteremia was defined as a pure growth of a single pathogenic micro-organism on blood culture of a febrile young infant without any apparent focus of infection on history and clinical examination. Probable bacteremia was defined as the growth of two or more types of bacteria.[21] Definite bacterial meningitis was defined as isolation of organism on CSF culture. Probable bacterial meningitis was defined as abnormal CSF on analysis with sterile CSF culture.[20] Only patient with definite bacterial infection, was taken as serious bacterial infection.

RESULTS

Total number of admissions to hospital during the period was 25640. Total number of patients with fever without an apparent focus of infection on history and clinical examination, admitted to hospital was 180. Total number of patients fulfilling the inclusion criteria was 149. 31 patients out of 180 were excluded out of the study, as among these, 12 had fever for more than 72 hours, 3 had received vaccination, 16 were treated with antibiotics within 48 hours of presentation.

Thrombocytosis >4lakh/mm3 was positive in 93 (62.4%), TLC ≥15000/mm^3 in 44 (29.5%), C-Reactive Protein ≥2mg /dl was in 35 (23.5%), Blood Culture in 9(6%), Urine Examination for Pus Cells > 5/mm^3 in 31 (20.8%), Urine Culture 16 (10.7%), CXR for Bacterial Pneumonia and Pleural Fluid Analysis/culture for separation of pathogen responsible for bacterial pneumonia was in 9 (6%), CSF Culture was positive in 6 (4%) and Stool culture was positive in nil, in one patient *Escherichia*

Coli was isolated in both urine culture and blood culture, three contaminated blood cultures of Staphylococcus epidermidis were also noted. There was no case of bacterial pneumonia positive for blood culture.

Table 1: Depicting investigations across febrile young infants.

Investigation		N	%
Thrombocytosis>4lakh/mm^3		93	62.4
TLC ≥15000/mm^3		44	29.5
C-Reactive Protein ≥2mg/dl		35	23.5
Blood Culture	Sterile	140	94.0
	Escherichia Coli	1	0.7
	Klebsiella	2	1.3
	Methicillin Resistant Staphaureus	3	2.0
	Staphylococcus aureus	3	2.0
Urine Examination for Pus Cells/mm^3	>5	31	20.8
	≤5	118	79.2
Urine Culture	Sterile	133	89.3
	Escherichia coli	11	7.4
	Klebsiella	5	3.4
CXR for Pneumonia	+Ve	9	6.0
Pleural Fluid culture	+Ve	9	6.0
CSF Analysis	Abnormal	6	4.0
	Normal	99	66.4
	Not done	44	29.5
CSF Culture (n=105)	Sterile	99	94.3
	Group B Streptococcus	2	1.9
	Escherichia coli	2	1.9
	Methicilline Resistant *Staphylococcus aureus*	2	1.9
Stool culture	+Ve	0	0.0

Table 2: Depicting infectious causes of illness in febrile young infants.

Final diagnosis	%
Bronchiolitis	30.9
Acute viral exanthem	26.8
Non bacterial enteritis	14.1
Urinary tract infection	10.7
Pneumonia	6.0
Occult bacteremia	5.5
Bacterial meningitis	4.0
Environmental hyperthermia	2.0

Table 3: Total SBI and non-SBI across study.

SBI	N	%
Present	39	26.2
Absent	110	73.8

Total number of patients with SBI and Non-SBI were 39 and 110 respectively out of 149 patients included in the study.

Table 4: Depicting serious bacterial infection in febrile young infants.

Final diagnosis	%
Urinary tract infection	10.7
Pneumonia	6.0
Occult bacteraemia	5.5
Bacterial meningitis	4.0
Non-SBI	73.8

Above table depicts the percentage of SBIs across the total 149 febrile young included in the study. So, the prevalence of SBI in our study was 26.2% (39 out of 149 patients were positive for serious bacterial infection). Urinary tract infection in 16 which was 41.0% of the SBIs (i.e. out of 39 SBIs), pneumonia 9 (23.1%), Occult bacteremia 8 (20.5%) and bacterial meningitis 6 (15.4%).

Age, gender and residence were non-significant across SBI and Non-SBI groups, P value non-significant (>0.05). Thrombocytosis >4lakh/mm^3 was significantly higher in SBI, 33 out of 39 (84.6%) versus Non-SBI 60 out 110 (54.5%), P value < 0.05, also C - reactive protein and Total leucocyte count was significantly high in SBI than Non-SBI, p value <0.05.

Table 5: Comparing investigations across SBI and Non-SBI.

		Serious bacterial infection				p value
		+Ve		-Ve		
		N	%	n	%	
Age (day)	30 to 59	23	32.9	47	67.1	0.082 (NS)
	60 to 89	16	20.3	63	79.7	
Gender	Male	20	26.7	55	73.3	0.891 (NS)
	Female	19	25.7	55	74.3	
Reidence	Rural	30	25.6	87	74.4	0.778 (NS)
	Urban	9	28.1	23	71.9	
Thrombocytosis >4lakh/mm^3	Yes	33	35.5	60	64.5	0.001 (Sig)
	No	6	10.7	50	89.3	
C-Reactive Protein	+Ve	20	57.1	15	42.9	0.000 (Sig)
	-Ve	19	16.7	95	83.3	
Total Leucocyte Count	≥ 15000/mm3	20	45.5	24	54.5	0.001 (Sig)
	< 15000/mm^3	19	18.1	86	81.9	

Mean platelet count in urinary tract infections was 5.3 lakh/mm^3, bacterial meningitis 5.2 lakh/mm^3,occult bacteremia 4.9 lakh/mm^3, pneumonia 4.7 lakh/mm^3 and 3.9 lakh/mm^3 across Non-SBI. Mean platelet count was highest in urinary tract infections followed by bacterial meningitis, occult bacteremia and pneumonia.

Table 6: Means platelet across each SBI and non-SBI.

Serious bacterial infection	N	Platelet Count (lakh)/mm^3 in SBI	
		Mean	SD
Pneumonia	9	4.7	1.1
Bacterial meningitis	6	5.2	0.6
Occult bacteremia	8	4.9	1.6
Urinary tract infection	16	5.3	1.0
Total	39	5.1	1.1
Non-SBI	110	3.9	1.6

Table 7: Minimum, maximum and median of platelets across SBI and Non-SBI.

	Platelet count (lakh)/mm^3				
	Pneumonia	Menin-gitis	Occult Ba-cteremia	UTI	Non SBI
Median	4.9	5.0	4.7	5.2	4.1
Minimum	2.9	4.6	2.4	3.4	0.4
Maximum	6.0	6.1	7.2	7.5	7.4

DISCUSSION

Finally total number of patients fulfilling the inclusion criteria was 149. The purpose of this study was, to estimate the incidence and pattern of reactive thrombocytosis among febrile young infants with serious bacterial infection (SBI).

The prevalence of SBI in our study was 26.2% (39 out of 149 patients were positive for serious bacterial infection), Hsiao AL et al studied 429 infants out of which 44 (10.3%) patients were diagnosed with serious bacterial infection, in another study Pulliam PN, et al studied seventy-seven patients and they enrolled SBI in 18% of the patients and Annick Galetto-Lacour et al studied 99 patients and noticed serious bacterial infection in 29%.[15,22,23] Prevalence of SBI was quite high in our study which was conducted at a tertiary care, referral centre, to which more sick patients are referred, so this can be the reason for high prevalence of SBI in our study.

The total number of males in this study was 75 (50.3%) and females 74 (49.7%),SBI was reported in 20 (26.7%) males and 19 (25.7%) females, P value >0.05, so gender by itself was not a risk factor for SBI, another study by Hsiao AL et al. studied that gender distribution among SBI, of 218 male infants, 23 (10.6%) had SBI compared with 21 (10.0%) of 211 female infants, this study also showed no gender bias.[15]

C-Reactive Protein (CRP) in the study was statistically significant in SBI patients vs Non-SBI patients, P value <0.05, similar results were shown by Allen L. Hsiao, et al in which mean CRP value was significantly higher in subjects with SBI compared to those without (2.7±3.7 vs 0.9±1.4 mg/dL, respectively; p value <0.05).[15]

All 149 patients 30–89 days old were divided into two age groups 30-59 days old and 60 -89 days old, there were 23 patients in SBI and 47 in Non-SBI of 30 -59 days age, and 16 in SBI and 63 of Non-SBI of 60–89 days age. There was almost equal distribution of the patients, of 30-59 and 60-89 days of age across SBI, so SBI was independent of age groups across study, P value >0.05, another study conducted by Hsiao AL et al showed that the youngest infants in the study, 57-89 days of age, were not statistically significant more likely to have SBI compared with the oldest infants, who were 150–179 days of age (8.8% vs 12.9%), and were no more likely than those aged 120–149 days.[15]

Total no. of SBI in our study was 39 (26.2%) out of 149 studied patients. Urinary tract infection in 16 which was, 41.0% (out of 39 SBI's), pneumonia 9(23.1%), Occult bacteremia 8(20.5%) and bacterial meningitis 6 (15.4 %). Urinary tract infection was most common followed by pneumonia, then occult bacteraemia and finally bacterial meningitis ,another study conducted by Fouozas S et al. had also shown urinary tract infection as the most common SBI with 88 (85.4%) out of 103 followed by occult bacteraemia 9 (8.7%) then pneumonia 6 (5.8%) and bacterial meningitis 2 (1.9%).[18]

The incidence of thrombocytosis >4 lakh/mm^3 in our study was significantly higher in SBI than Non-SBI, 33 patients out of 39 (84.6%) in SBI versus 60 out of 110 (54.5%) in non-SBI and all over incidence of thrombocytosis in febrile young infants was 93 out of 149 (62.4%). A similar study conducted by Fouozas S et al had shown similar results, that thrombocytosis was significantly higher in SBI than Non-SBI, 88 out of 103 (85.6 %) in SBI versus 165 out of 305 (53.5%) in Non-SBI and all over incidence of thrombocytosis in febrile young infants was 253 out of 408 (62.4%).[18]

The mean platelet count (lakh/mm3 ± 1SD) in our study was 5.1±1.1 in SBI versus 3.9±1.6 in Non-SBI which was statistically significant in SBI, p-value <0.05, another study by Fouozas S et al had shown similar results, platelet count with median of 513000 /mm3 in SBI versus 398000/mm^3 in Non-SBI, statistically significant in SBI than Non-SBI, p value <0.05.[18]

Mean platelet count in urinary tract infections was 5.3 lakh/mm^3, bacterial meningitis 5.2 lakh/mm^3, occult bacteremia 4.9 lakh/mm^3, pneumonia 4.7 lakh/mm^3 and 3.9 lakh/mm^3 across Non-SBI. So reactive thrombocytosis was highest in urinary tract infections followed by bacterial meningitis, occult bacteraemia and pneumonia and least in Non-SBI.

CONCLUSION

To conclude, incidence of reactive thrombocytosis >4 lakh/mm^3 in our study was significantly higher in SBI (84.6%) than in Non-SBI (54.5%), p value <0.05. Mean platelet count was highest in urinary tract infections followed by bacterial meningitis, occult bacteraemia and pneumonia. So platelet count >4 lakh/mm^3 i.e. reactive thrombocytosis, being simple and easy test to perfom can be used for early prediction of SBI.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Chib R, Rashid M, Kumar S. Estimate the incidence and pattern of reactive thrombocytosis among febrile young infants with serious bacterial infection (SBI). Int J Contemp Pediatr 2016;3:616-20.