ISSN:0975-3583,0976-2833 VOL12,ISSUE05,2021

IS THROMBOCYTOPENIA A RISK FACTOR FOR SEPSIS IN NEONATES? : A PROSPECTIVE STUDY

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ABSTRACT

Background: Neonatal Sepsis is a systemic inflammatory response to infection and/or isolation of bacteria from the blood stream in the first 28 days of life.Thrombocytopenia, defined asplatelet count below 150×10^9/L, is a frequent problem in neonatal intensive care units, confounding the clinical course in 22–35% of intensive care admissions.Sepsis is the commonest cause of neonatal mortality; it is responsible for about 30-50% of the total neonatal deaths in developing countries.

Objectives: The aim of this study is to analyze the possible risk factors for neonatal thrombocytopenia, its association with neonatal sepsis and the outcome of neonatal sepsis.

Methods: This is a prospective study conducted on 68 babies in NICU of a tertiary care centre. The babies admitted in the NICU with platelet count below 150×10^9/L were taken into consideration. The study included consent by parents/guardian, data collection by meticulous history taking and clinical examination, appropriate laboratory investigations followed by statistical correlations.

Results: Study was conducted with 68 neonates having platelet countbelow 150×10^9/L. Risk factors of neonatal thrombocytopenia involved maternal factors like pre-eclampsia/ pregnancy induced hypertension, premature rupture of membranes, meconium stained liquor, multiparity as well as fetal factors like low birth weight, prematurity, birth asphyxia etc.There was male predominance (70%) amongst study population.Most of the study population had severe thrombocytopenia (47%) followed by moderate thrombocytopenia (42%) and mild thrombocytopenia (11%). 82.4% of study population survived while death occurred in 17.6%.

Conclusion: The present study concludes thatthere is an association of neonatal thrombocytopenia and sepsis. Thrombocytopenia is an earliest indicator as well as a prognostic marker of neonatal sepsis. Most common etiological factors include PROM, low

ISSN:0975-3583,0976-2833 VOL12,ISSUE05,2021

birth weight, prematurity, maternal GBS colonization, birth asphyxia, PIH, multiple gestation, chorioamnionitis and invasive procedures. Starting of empirical antibiotics becomes the mainstay of the treatment. If managed early and effectively, neonatal sepsis has promising outcomes.

Keywords: Early onset sepsis, Late onset sepsis, Neonatal Thrombocytopenia

INTRODUCTION

Thrombocytopenia, defined as a platelet count below 150×10^9/L, is a frequent problem in neonatal intensive care units, complicating the clinical sequence in 22–35% of intensive care admissions. One of the major causes of thrombocytopenia in neonates is sepsis and thrombocytopenia may rapidly become very severe with the lowest platelet count reached within 24–48 hours after onset of the infection. The importance of the relationship between thrombocytopenia and sepsis was emphasized by identifying thrombocytopenia as one of the most predictive, sovereign risk factors for sepsis-associated mortality in very low-birth weight neonates.[1] The classification of sepsis based on time of appearance as EOS (early onset sepsis) or LOS(late onset sepsis) is important as it aids in determining the most probable organism, mode of transmission and guide for empiric treatment. Thrombocytopenia is one of the earliest indicators of neonatal sepsis. Neonatal thrombocytopenia has been found to result in clinical bleeding.[2,3]

The important causes of thrombocytopenia in neonates are maternal infections, birth asphyxia, prematurity, intrauterine growth retardation, respiratory distress syndrome, and meconium aspiration syndrome and low birth weight.Severity of thrombocytopenia is correlated with mortality risk. Pre-clinical data suggest that thrombocytopenia contributes to mortality rather than simply being a proxy for disease severity.[4,5,6]The presence of a positive blood culture historically constituted the "gold standard" for the presence of neonatal sepsis. However, majority of the sepsis evaluations that are prompted by concerning clinical signs are associated with negative blood culture results. When blood and other sterile site cultures are negative, but the infant manifests signs consistent with infection they may be considered to have "clinical" sepsis. Importantly, a positive blood culture is not required to meet the consensus definition for sepsis.[7,8]

Thrombocytopenia is associated with a more disturbed host response in critically ill patients with sepsis independent of disease severity.[9]Though thrombocytopenia is so prevalent it is often ignored in the assumption that it will resolve spontaneously. However if it is not detected and managed properly can result in devastating complications.[10,11]The diagnostic approach should begin with clinical examination for bleeding signs. Initial laboratory tests should include a full blood cell count and coagulation studies.[12,13]In this study we therefore choose to present the characteristics of sepsis-related thrombocytopenia.

We have performed this study to evaluate the maternal and fetal risk factors related to neonatal thrombocytopenia. We have also studied the association of neonatal thrombocytopenia with sepsis in NICU admissions of a tertiary care hospital and to study the outcomes of neonates with thrombocytopenia.

MATERIALS AND METHODOLOGY

It is a prospective study of 68 newbornsadmitted with thrombocytopenia with platelet count $<150\times10^9$/L in a tertiary care hospital during a period August 2017 to December 2019 on 68 neonatal patients.All neonates admitted to NICU of a tertiary care hospital having thrombocytopenia with platelets counts $<150\times10^9$/L with consent were included in the study. All neonates admitted to NICU from August 2017 to December 2019 having thrombocytopenia with platelet counts $<150\times10^9$/L at a tertiary care hospital were considered.Approval from IEC (Institutional ethics committee) was taken.Consent was

ISSN:0975-3583,0976-2833 VOL12,ISSUE05,2021

obtained by parents or guardian.Detailed history was taken and certain maternal factors like pregnancy induced hypertension, premature rupture of membranes, meconium stained liquor, oligo/polyhydramnios and other maternal medical conditions were noted. Also fetal factors like low birth weight, prematurity, intra uterine growth retardation etc were observed.A brief clinical examination was performed. Signs of clinical sepsis like fever ,drowsiness, altered sensorium, decreased activity, respiratory distress, poor feeding, abdominal distension, bleeding tendencies, skin lesions were noted.Platelet counts were recorded since the day of thrombocytopenia and thereafter every 72 hours till the platelets counts became normal.Blood culture positivity, C- reactive protein and thrombocytopenia were correlated by appropriate test of significance.

Clinico- demographic distribution of the study population was accessed in table no. 1. As seen in the table 2, maternal factors were responsible for neonatal thrombocytopenia predominantly were parity- more prevalent in multigravida (68%), mode of delivery- more in normal vaginal delivery (74%), meconium stained amniotic fluid (21%), PIH/ Preeclampsia/ Eclampsia (8%) and Premature rupture of membranes (40%).

As seen in the table 3, fetal factors responsible for neonatal thrombocytopenia are gender- male predominance (70%), gestation- more in preterm babies (67%), age- more frequent in <5 days (61%), birth weight- more common in <2 kg (42%), birth asphyxia with APGAR score <7 at 1 min (15%). It was associated with clinical features like depressed activity (76%), tachypnea (62%), tachycardia (63%) and bleeding evidence (49%).

As seen in the table 4, most of the study population had severethrombocytopenia (47%) followed by moderate thrombocytopenia (42%) and mild thrombocytopenia (11%), CRP was raised in 78% of the study population and blood culture being positive in 53% of population.

As seen in the table 5, mean Hemoglobin, total leucocyte count, CRP was 16.5 ± 0.69, 20.1 ± 1.2, 26.9 ± 0.53 mg/L and 66918 ± 7619respectively. Amongst the neonates with mild thrombocytopenia, all 37 neonates survived; also in moderate thrombocytopenia all 17 neonates survived; whereas in severe thrombocytopenia, 2 neonates survived while death occured in 12 neonates [P value= 0.0001; Table 6]. Neonatal thrombocytopenia was associated with sepsis in 88% of study population while no signs of sepsis were seen in 12% of study population [Table 7]. As seen in the table 8,82.4% of the study population survived while death occurred in 17.6%.

Table no 1: Maternal factors of neonatal thrombocytopenia

Maternal factors	Variable	Frequency	Percentage
Parity	Primigravida	22	32
	Multigravida	46	68
Mode of delivery	NVD	50	74
	LSCS	18	26
Meconium stained amniotic fluid	Yes	14	21
	No	54	79
PIH/Preeclampsia/ Eclampsia	Yes	5	8
	No	63	92
PROM	Yes	27	40
	No	41	60

Table no 2: Fetal factors of neonatal thrombocytopenia

Fetal factors	Variable	Frequency	Percentage

ISSN:0975-3583,0976-2833 VOL12,ISSUE05,2021

Gender	Male	47	70
	Female	21	30
Gestation	Preterm	46	67
	Term	22	33
Age	< 5 days	42	61
	6- 10 days	23	34
	11-15 days	2	3
	>16 days	1	2
Birth Weight	<2 kg	29	42
	2-3 kg	25	37
	>3 kg	14	21
APGAR score at 1 min	<7	10	15
	>7	58	85
Clinical features	Depressed activity	52	76
	Tachypnea	42	62
	Tachycardia	43	63
	Bleeding evidence	33	49

Table no 3: Sepsis Screen

Investigations	Subgroup	Frequency	Percentage
Thrombocytopenia (platelets)	Mild	8	11
	Moderate	29	42
	Severe	31	47
C- reactive protein (CRP)	Raised	53	78
	Normal	15	22
Blood culture	Positive	36	53
	Negative	32	47

Table no 4: Investigations

Investigations	Mean	SD
Hemoglobin	16.5	0.69
TLC	20.1	1.2
CRP	26.9	0.55
Platelet count	66918	7619

Table no 5: Association of grades of thrombocytopenia with gestational age

Grades of thrombocytopenia	Preterm	Term	Total
Mild	2	35	37
Moderate	8	9	17
Severe	12	2	14

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Total	22	46	68

Chi square test, P value: 0.0001

Table no 6: Association of grades of thrombocytopenia with outcome

Grades of thrombocytopenia	Survived	Death	Total
Mild	8	0	8
Moderate	29	0	29
Severe	19	12	31
Total	59	9	68

Chi square test, P value: 0.0001

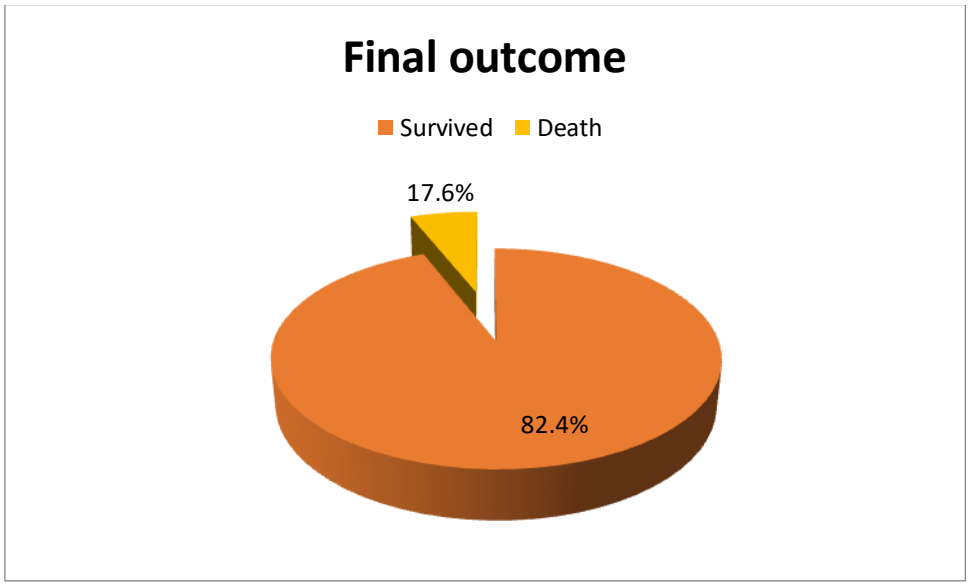
Table no 7: Association of neonatal thrombocytopenia and sepsis

Association of sepsis and thrombocytopenia	Frequency	Percentage
Neonates with thrombocytopenia and sepsis	60	88
Neonates with thrombocytopenia and no sepsis	8	12
Total	68	100

Table no 8: Final outcome amongst study population

Final outcome	Frequency	Percent
Survived	56	82.4
Death	12	17.6
Total	68	100.0

Graph 1: outcomes of survival and death



ISSN:0975-3583,0976-2833 VOL12,ISSUE05,2021

DISCUSSION

Neonatal sepsis is defined by systemic circulatory abnormalities (predominantly peripheral vasoconstriction, oliguria and ischemic damage to inner organs) and a variable spectrum of clinical signs, resulting from invasion of the bloodstream by bacteria and other pathogens, as well as from the ineffective host response, in infants up to their first month of life.[14,15] It results in one million deaths each year (42% in the first week of life). This amounts to 10% of all mortality under the age of five years. Neonatal sepsis is defined by: a) differential exposure to specific classes of infectious pathogens; b) the additional impacts of prematurity, low birth weight (LBW) and very low birth weight (VLBW); c) exposure to use of immunomodulatory drugs; and d) risks associated with therapeutic procedures in neonatal intensive care units.

In the present study, maternal factors like parity, mode of delivery, meconium stained liquor, PROM and PIH were associated with neonatal thrombocytopenia. multigravida mothers constituted 68% of the study population. Most of the study population had normal vaginal delivery (74 %)followed by LSCS (26%).PIH/PET/Eclampsia was present in 8 % of the study population, meconium stained amniotic fluid was present in 21 % of the population and PROM was present in 40 % of the study population.

Fetal factors associated with thrombocytopenia were gestation, birth weight, age, sex and birth asphyxia. In the present study, there was male predominance (70%) amongst the study population. These findings correlate well with the study conducted by EffatHisamuddin et al., in which male patients were 81(55.1%) while 66(44.9%) were female. Most of the study population had age of less than 5 days (61%) followed by 6 - 10 days (34%), 11 - 15 days (3%) and more than 16 days (2%).[16] In the study, 42(28.6%) patients were of age 6-10 days, 7(4.8%) were of age range 11-15 days and 7(4.8%) presented at age more than 15 days. There was higher number of preterm babies (67%) as compared to term babies (33%). Most of the study population had birth weight <2 kg (42%) followed by 2-3 kg (37%) and > 3 kg (21 %). APGAR score at 1 min< 7 was seen in 15 % of study population. Blood culture was positive in 53% of study population. In the present study, CRP level was raised in 78% of the study population. These findings correlate well with the study conducted by Sidra Younis et al., in which Blood cultures were positive in 64.4% and raised CRP was found in 64.5%.[17]

In the present study, most of the study population had severe thrombocytopenia (47%) followed by moderate thrombocytopenia (42%) and mild thrombocytopenia (11%). Similarly, in the study by Chate et al., reported that out of 54 neonates with sepsis, thrombocytopenia was present in 49/54 patients (90.74%); out of which severe thrombocytopenia was found in 21 (42.86%) neonates, moderate in 17 (34.69%), and mild in 11 (22.45%) neonates, respectively.[18]In the present study, out of 68 neonates with thrombocytopenia; 60 developed sepsis. Thus, platelet count may act as an early marker for the diagnosis of septicemia.

CONCLUSION

Thus, to conclude, maternal factors like parity, mode of delivery, meconium stained liquor, PROM, PIH and fetal factors like gestation, birth weight, age, sex, birth asphyxia are related to sepsis induced thrombocytopenia in neonates. Neonatal thrombocytopenia is not only associated with sepsis but is also a prognostic indicator which if managed timely gives promising outcomes.

ISSN:0975-3583,0976-2833 VOL12,ISSUE05,2021

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ISSN:0975-3583,0976-2833 VOL12,ISSUE05,2021