

Original article

Maternal and Neonatal Risk Factors for Thrombocytopenia in Preterm Infants

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ABSTRACT

BACKGROUND: Thrombocytopenia is a common problem in preterm neonates. Thrombocytopenic neonates are at an increased risk of life threatening complications. Hence this study was done with the objective to analyse maternal and neonatal risk factor associated with thrombocytopenia in preterm neonates.

METHODS: This prospective study was conducted in Department of Paediatrics, National Institute of Medical Sciences & Research, Jaipur. All intramural, singleton preterm neonates were included in the study. Maternal ANC history, clinical feature, perinatal events and neonatal features were recorded in a proforma. Enrolled neonates were screened for platelet count between 12-24 hour of life and later at 72 hour of life. Platelet count was repeated daily in thrombocytopenic infant. Statistical analysis was done using software SPSS version 23.

RESULTS: During the study period 5170 were born of which 183 were preterm babies. 168 preterm babies gave the consent for inclusion in the study. 56 (33.3%) neonates had thrombocytopenia. 35 (20.8%) neonates had early onset of thrombocytopenia and 21 (12.5%) had late onset. 24 (42.8%) had mild, 20 (35.7%) had moderate and 12 (21.4%) had severe thrombocytopenia. None of the maternal risk factors showed any statistically significant association with thrombocytopenia. Neonatal risk factors such Birth weight, Gestational Age, Intrauterine growth status, mode of deliver, requirement of resuscitation, Apgar Score (at 5 minutes), Delayed cry and presence of neonatal sepsis showed statistically significant association with thrombocytopenia.

CONCLUSION: Clinicians should lookout for thrombocytopenia in preterm neonates with these risk factors to avoid further complications which may arise due to thrombocytopenia.

Keywords: Preterm Neonate, Thrombocytopenia

Introduction

Thrombocytopenia is a common haematological problem in neonates, especially in preterm. It is defined as platelet count of less than $150 \times 10^9/L$ and is classified by severity as mild, moderate and severe and by age of onset as early and late.¹⁻⁴ 0.7-4% of all neonates have thrombocytopenia.^{2,5,6} Incidence of thrombocytopenia is higher in preterm babies

especially those who are sick, ranging widely from 20-40%.^{7,8} Thrombocytopenic preterm neonates are at an increased risk of intraventricular haemorrhage,^{3,9} necrotising enterocolitis,³ disseminated intravascular coagulation^{3,7,10} and mucocutaneous bleed.³ Even fatality is reported to be quite high in thrombocytopenic preterm neonates.^{3,7}

Because of severe morbidity associated with thrombocytopenia in a preterm, identification of risk factors are important for early diagnosis, identification of underlying cause and appropriate intervention in preventing the complication of thrombocytopenia.

Aims and Objectives

1. To analyse maternal risk factor associated with thrombocytopenia in preterm neonates.
2. To analyse neonatal risk factor associated with thrombocytopenia in preterm neonates.

Methodology

This Cross-Sectional Observational study was conducted in Neonatal Intensive Care Unit of National Institute of Medical Sciences and Research, Jaipur, India from 01/04/2015 to 31/3/2016.

All intramural, singleton preterm neonates of less than 37 weeks of Gestation were included in the study after taking a written, informed consent from one or both parents. Gestational age was calculated by estimating according to last menstrual period, combined with ultrasound and/or Ballard scoring if required. Details of demographic, clinical, laboratory data of mother and neonate recorded. All mothers were evaluated with respect to age, gravida, para, maternal medical illness, obstetrical illness, infections, medication during pregnancy and details of labour and mode of delivery. Family history of bleeding in parents and sibling was also recorded. Neonatal characteristics including resuscitation detail, Apgar score, birth weight and gestational age at birth were recorded.

Complete physical examination was done at enrolment and then once daily to identify the aetiology and risk factors for neonatal thrombocytopenia. All subjects were followed in hospital till recovery/death. Subjects enrolled in the study continued to receive routine management as per unit policy.

Enrolled neonates were screened for platelet count between 12-24 hour of life and later at 72 hour of life. Platelet count was measured by fully automated haematology analyser (KX-21, SYSMEX) along with Neubauer chamber and then confirmed by examination of slide after staining with Leishman's stain. Platelet Count of less than $150 \times 10^9/L$ was taken as cut off point for thrombocytopenia. Platelet count was repeated daily in thrombocytopenic infant.

Data obtained was entry and analysed in a Windows based statistical software IBM SPSS version 23.

Results

During the study period 5170 were born of which 183 were preterm babies. Amongst these preterm neonates parents of 168 preterm babies gave the consent for inclusion in the study. 56 (33.3%) neonates had thrombocytopenia. 35 (20.8%) neonates had early onset of thrombocytopenia (before 72 hours of birth) and 21 (12.5%) had late onset (after 72 hours of birth). 24 (42.8%) had mild thrombocytopenia (Platelet count $150 \times 10^9/L - 100 \times 10^9/L$), 20 (35.7%) had moderate thrombocytopenia (Platelet count $100 \times 10^9/L - 50 \times 10^9/L$) and 12 (21.4%) had severe thrombocytopenia (Platelet count $< 50 \times 10^9/L$).

Baseline demographic characteristics of the study preterm newborns are depicted in table 1.

Table 1: Description of baseline neonatal demographic characteristics

Characteristics	Mean ± SD
	Median (Range)
Gestational age(in weeks)	34.3 ± 1.54 34(28-36)
Birth weight in grams	1983 ± .419 1980 (900-2.640)
Sex; n (%)	
Male	100(59.5)
Female	68(40.5)
Growth status; n (%)	
AGA	163(97.02)
SGA	5 (2.9)

Baseline maternal demographic information is depicted in table 2.

Table 2: Description of baseline maternal demographic characteristics

Characteristics	Values
	N (%)
Maternal Age (In years)	
Mean ± SD	24.36±3.635
Median (Range)	24(18-34)
Gravida - Primi	89(52.9)
Maternal medical problems	23(13.6)
Hypertension	15(8.9)
Asthma	2(1.1)
Hypothyroidism	3(1.7)
AIDS	3(1.7)
Maternal obstetric problems	17(10.1)
Gestational hypertension	15(8.9)
Antepartum haemorrhage	2(1.1)
Maternal intake of drugs during antenatal period	18(10.7)
Evidence of maternal infection	33(19.6)
Maternal fever	10(5.9)
Foul smelling liquor	7(4.1)
Maternal leucocytosis	1(0.59)
PROM	15(8.9)

Various perinatal characteristics of the preterm infants are depicted in Table 3

Table 3: Description of baseline perinatal characteristics (n=168)

Characteristics	Values
	N (%)
Maternal medication	51(30.3%)
Antenatal steroid	21(12.5)
Antibiotic	10(5.9)
Pitocin	22(13.09)
Mode of delivery	
Spontaneous Vaginal	148(88.09)
Induced Vaginal	1(.59)
LSCS (Emergency)	15(8.9)
LSCS (Elective)	4(2.3)
Resuscitation level	
None	130(77.3)
Tactile Stimulation	13(7.7)
O ₂	3(1.7)
IPPV	16(9.5)
Chest compression	6(3.5)
Delayed cry	38(22.6)
Perinatal asphyxia	30(17.8)
Apgar Score at 1min.	
Mean ± SD	8.12±1.585
Median (Range)	9(3-9)
Apgar Score at 5 min.	
Mean ± SD	8.45±1.193
Median (Range)	9(4-9)

None of the maternal risk factors showed any statistically significant association with preterm neonates with thrombocytopenia. Analysis of various maternal risk factors between preterm neonates with and without thrombocytopenia shown in Table 4.

Table 4: Univariate analysis of various maternal risk factors between preterm neonates with and without thrombocytopenia

Putative risk factor		No. of patient with Thrombocytopenia (n=56)	No. of patient without thrombocytopenia (n=112)	P value
Maternal age (in years)		24.54 ± 4.173	24.28 ± 3.351	.665
Gravida	Primigravida	28(50%)	61(54.5%)	.585
	Multigravida	28(50%)	51(45.5%)	.585
Medical illness	Hypertension	7(12.5%)	8(7.2%)	.193
	AIDS	1(1.8%)	2(1.8%)	1
Obstetric Illness	P.I.H	7(12.5%)	8(7.2%)	.193
	A.P.H	0(0%)	2(1.8%)	.314
Medication during Pregnancy	Methyl Dopa	7(12.5%)	8(7.2%)	.193
	Thyroxin	0(0%)	3(2.7%)	.552
Evidence of Maternal infection	Maternal fever	5(8.9%)	5(4.4%)	.207
	Foul smelling liquor	4(7.1%)	3(2.7%)	.169
	Maternal leucocytosis	0(0%)	1(0.9%)	.478
	PROM > 24	8(14.3%)	7(6.2%)	.078
Medicine	Steroid	11(19.6%)	10(8.9%)	.08
	Antibiotic	5(8.9%)	5(4.4%)	.207
	Pitocin	6(10.7%)	16(14.3)	.518

Neonatal risk factors such Birth weight, Gestational Age, Intrauterine growth status, mode of deliver, requirement of resuscitation, Apgar Score (at 5 minutes), Delayed cry and presence of neonatal sepsis showed statistically significant association with preterm neonates with thrombocytopenia. Analysis of various neonatal risk factors between preterm neonates with and without thrombocytopenia shown in Table 5.

Table 5: Univariate analysis of various neonatal risk factors between preterm neonates with and without thrombocytopenia

Putative risk factor		No. of patient with thrombocytopenia(56)	No. of patient without thrombocytopenia (112)	P value
Birth weight (in grams)		1707.3 ± .445	2121 ± .330	<.001*
Gestational age (in weeks)		33.46 ± 1.81	34.72 ± 1.19	<.001*
Sex	Male	31(55.4%)	69(61.6%)	.270
Intrauterine growth status	SGA	4(7.1%)	1(0.9%)	0.043*
	AGA	52(92.9%)	111(99.1%)	0.043*
MOD	VD	45(80.3%)	104(92.8%)	.016*
	Emg. LSCS	9(16.1%)	6(5.4%)	.022*
	El. LSCS	2(3.6%)	2(1.8%)	.601
Resuscitation level	Required	14(25%)	8(7.2%)	.001*
	Not required	42(75%)	104(92.8%)	.001*
Apgar score at 5 min.	≤7	20(35.7%)	10(8.9%)	<.001*
Cry	Delayed	20(35.7%)	18(16.1%)	.004*
Congenital pneumonia		8(14.3%)	7(6.2%)	.078
Jaundice	Phototherapy	15(26.7%)	17(15.2%)	.071
	Exchange transfusion	1(1.7%)	1(0.89%)	.304
Sepsis		13(23.2%)	10(8.9%)	.012*

*Chi Square Test

SGA=Small for gestational age. AGA=Appropriate for gestational age. VD=Vaginal delivery. Emg=Emergency. El=Elective

Discussion

Neonatal thrombocytopenia frequently occurs in the sick neonates admitted to neonatal intensive care unit, and it can contribute to high mortality, and many of these infants are preterm. To prevent the preterm neonates from neonatal thrombocytopenia, or to evaluate a thrombocytopenic neonate, the mechanism and predisposing factors of thrombocytopenia must be investigated. Since aggressive therapy administered to thrombocytopenic infants also

increases the mortality, the determination of mechanism and risk factors are important in providing early diagnosis and intervention. Because otherwise healthy appearing neonates are not screened for thrombocytopenia, there is a need to identify high risk population. There are limited Indian studies till date conducted in a prospective fashion to identify risk factors associated with thrombocytopenia especially in preterm neonate.

In our study, out of 168 preterm babies 56 (33.3%) were found to be thrombocytopenic. Previous studies have revealed that incidence of thrombocytopenia in healthy preterm was found to be similar as compared to the incidence in healthy term neonate.¹⁰ Beiner ME et al⁹ found that 93 (31%) preterm neonates were thrombocytopenic out of 305 babies (gestational age between 27-35 weeks). Bonifacio L³ studied 1054 preterm neonates, out of which 94 (8.9%) had at least one episode of thrombocytopenia.

Studies have revealed that lesser is the birth weight more are the chances of thrombocytopenia. Present study also revealed that low birth weight was observed in infants with thrombocytopenia in comparison to those infants without thrombocytopenia and this difference was statistically significant. Bernis ME et al⁹ shown that thrombocytopenic preterms had a lower average birth weight than the non-thrombocytopenic preterm infants (1208 vs. 1597gram). Similar observation of lower the birth weight, greater the severity of thrombocytopenia was quoted by Bonifacio L.³

In our study, newborns with lower gestational age had a statistically highly significant association with thrombocytopenia as compared to newborns without thrombocytopenia. Beiner ME et al⁹ found that average gestational age was slightly lower though statistically significant in thrombocytopenic group (30.5 weeks) as compare to non-thrombocytopenic group (31.6 weeks). Bonifacio L et al³ revealed that mean gestational age of < 28 weeks or less had significant association with thrombocytopenia on preterms.

In our study, when comparing the neonatal characteristics of both groups we found that small for gestational age neonates had significant association with thrombocytopenia.

Newborns with appropriate gestational age were found to be a protective factor against thrombocytopenia in preterm newborns. Bonifacio L et al³ and Beiner ME et al⁹ reported similar results.

It was also revealed that newborns born by emergency LSCS had more association with thrombocytopenia as compare to preterms born by other methods and the difference was statistically significant.

Current study has statistically confirmed that preterm babies with delayed cry, those required Intermittent positive pressure ventilation or above and babies with perinatal asphyxia (≤ 7 Apgar score at 5 minute) had more chances of thrombocytopenia. Many studies have confirmed that hypoxia (Low 5 min Apgar score) induces neonatal thrombocytopenia. Incidences in thrombocytopenic term infant were found to be 18% by Mehta et al¹⁰ and 12.2% by Beina et al⁹. Our study did not associate any maternal risk factor with thrombocytopenia in preterm neonates. Early onset neonatal thrombocytopenia is most commonly observed secondary to placental insufficiency with maternal hypertension.¹¹ Thrombocytopenia was found in 5-36% of neonate of mothers which suffered from pregnancy induced hypertension.¹²⁻¹⁴ In contrast to other studies hypertension was not a risk factor for thrombocytopenia in study by Bonifacio L.³ PROM was found to be negatively associated with neonatal thrombocytopenia.^{3,9,10} It has been stated that prolonged PROM possibly serves as a protective factor against mild thrombocytopenia.⁹ Intrapartum steroid was found to be significant risk factor for neonatal thrombocytopenia in other studies.⁹

The current study had a few limitations that can be implied upon on future research. The study did not

include various immune causes of thrombocytopenia due to limitation of investigation available in the hospital. Study should be conducted on a large scale because some factors like sepsis should be evaluated in detail.

Conclusion

33.3% neonates of our study group had thrombocytopenia. There were no maternal risk factors associated with thrombocytopenia however

neonatal risk factors such as birth weight, mode of delivery (emergency LSCS), delayed cry, gestational age, small for gestational age and sepsis were associated with thrombocytopenia in the study group. Hence clinicians should lookout for thrombocytopenia in preterm neonates with these risk factors to avoid further complications which may arise due to thrombocytopenia.

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