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Evaluation of gestational age as a risk factor for thrombocytopenia in preterm neonates

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Abstract

Background: Thrombocytopenia is a common problem in preterm neonates. Thrombocytopenic neonates are at an increased risk of life threating complications. Hence this study was done with the objective to analyse gestational age as a 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. Satistical 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. Gestational Age showed a significant association with thrombocytopenia in preterm neonates with moderated diagnostic accuracy.

Keywords: gestational age, preterm neonates, thrombocytopenia

1. Introduction

Thrombocytopenia is a common haematological problem in neonates, especially in preterms. It is defined as platelet count of less than 150×10^9/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 and mortality associated with thrombocytopenia in a preterm neonate identification of risk factors are important early in the course of treatment so that preventive measures can be initiated early. This study was hence done with the aim to evaluate gestational age as a risk factor for thrombocytopenia in preterm neonates.

2. 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 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 Leishmen's stain. Platelet Count of less than150×10^9/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.

3. 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 150×10^9/L-100×10^9/L), 20 (35.7%) had moderate thrombocytopenia (Platelet count 100×10^9/L-50×10^9/L) and 12 (21.4%) had severe thrombocytopenia (Platelet count $<50\times10^9$/L).

Baseline demographic characteristics of the thrombocytopenic preterm neonates are depicted in table 1.

Table 1: Description of baseline demographic characteristics of thrombocytopenic preterm neonates

Characteristics	Mean ± SD
Gestational age(in weeks)	34.3 ± 1.54
Birth weight in grams	1707.3 ± .445
Sex; n (%)	31(55.4)
Male	25(44.6)
Female	
Growth status; n (%)	
AGA	52(92.9)
SGA	4 (7.1)

Baseline maternal demographic information of thrombocytopenic neonates is depicted in table 2.

Table 2: Description of baseline maternal demographic characteristics of thrombocytopenic preterm neonates

Characteristics	Values N (%)
Maternal Age (In years) Mean ± SD	24.54 ± 4.173
Gravida - Primigravida	28(50.0)
Maternal medical problems	
Hypertension	7(12.5%)
AIDS	1(1.8%)
Gestational hypertension	7(12.5%)
Evidence of maternal infection	
Maternal fever	5(8.9)
Foul smelling liquor	4(7.1)
PROM>24hrs	8(14.3)

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

Table 3: Description of baseline perinatal characteristics of thrombocytopenic preterm neonates (n=56)

Characteristics	Values N (%)
Maternal medication	
Antenatal steroid	11(19.6%)
Antibiotic	5(8.9%)
Pitocin	6(10.7%)
Mode of delivery	
Vaginal Delivery	45(80.3)
LSCS (Emergency)	9(16.1)
LSCS (Elective)	2(3.6)
Resuscitation	
Required	14(25)
Not Required	42(75)
Delayed cry	20(35.7)
Apgar Score at 5 min.	
≤7	20(35.7)
>7	36(64.3)

Neonates with lower gestational age had a statistically significant association with thrombocytopenia as compared to neonates without thrombocytopenia (33.46±1.81 versus 34.72 ± 1.19, p<.001). On logistic regression analysis gestational age was found to have an Odds Ratio of 4.537 with a 95% CI of 1.274-16.2 hence found to be an independent risk factor for thrombocytopenia in preterm neonates.

The optimal cut off point for gestational age was further analysed by constructing a Receiver-Operating Characteristics (ROC) curve (figure 1). For optimal cut off value of gestational age, a value of 33.5 weeks was identified to have a maximum sensitivity of 89.3% for a lowest false positive rate (1-specificity) of 48.2%. Gestational age had an Area Under ROC curve of 0.706 (95% of CI 0.616-0.797, p=<.001).

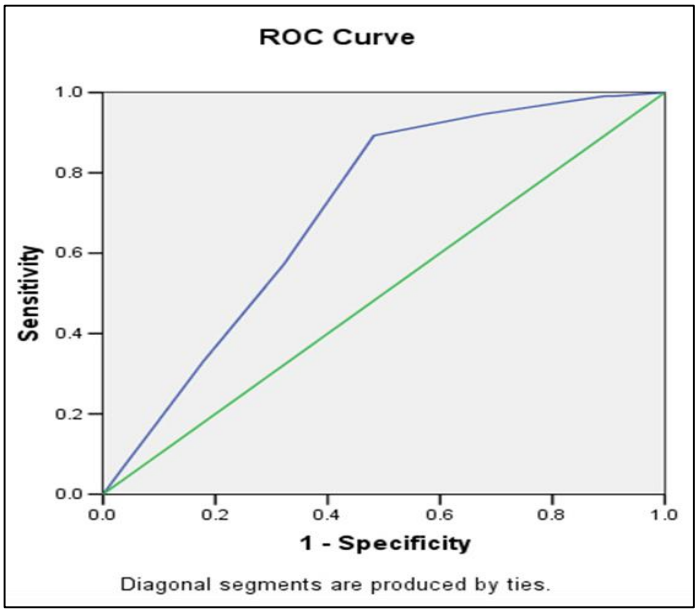

Fig 1: ROC curve for thrombocytopenia associated with gestational age

The sensitivity, specificity, positive and negative predictive value of having thrombocytopenia in preterm neonates if their gestational age is less than 33.5 weeks is presented in Table 4.

Table 4: Predictive accuracy of gestational age <33.5 weeks for thrombocytopenia in preterm neonates

INDEX	Value in %
Sensitivity	89.3%
Specificity	51.8%
Positive Predictive Value	78.7%
Negative Predictive Value	70.7%

4. Discussion

Neonatal thrombocytopenia frequently occurs in the preterm sick neonates admitted to neonatal intensive care unit, and it can contribute to high mortality. 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, this study was planned to evaluate the outcome of thrombocytopenic preterm neonates. There are limited prospective Indian studies till date conducted to evaluate clinical outcome of thrombocytopenia 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 al* [9] found that 93 (31%) preterm neonates were thrombocytopenic out of 305 babies (gestational age between 27-35 weeks). Bonifacio L [3] studied 1054 preterm neonates, out of which 94 (8.9%) had at least one episode of thrombocytopenia.

In our study, neonates with lower gestational age had a statistically highly significant association with thrombocytopenia as compared to neonates without thrombocytopenia (33.46±1.81 versus 34.72 ± 1.19, p=<.001). Beiner ME *et al* [9] 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 al* [3] revealed that mean gestational age of < 28 weeks or less had significant association with thrombocytopenia on preterm neonates.

The optimal cut off point achieving the top and left most position in the ROC curve was for gestational age 33.5 weeks had a sensitivity of 89.3% for a corresponding false positive rate of 48.2%. Gestational age had an AUROC curve of 0.706 (95% of CI 0.616-0.797, p=<.001). The diagnostic accuracy of gestational age was analyzed by calculating the area under the ROC curve (AUROC). In the current study, the AUROC curve for gestational age was 0.706 indicating a moderate accuracy.

Gestational age had a positive predictive value (PPV) of 78.7% meaning that 78.7% chances of having thrombocytopenia in the study preterm neonates if their gestational age less than 33.5 weeks. Gestational age had a negative predictive value (NPV) of 70.7% meaning that 70.7% of the study neonates will not have thrombocytopenia if their gestational age more than 33.5 weeks.

5. Conclusion

56 preterm out of 168 (33.3%) were found to be thrombocytopenic. 20.8% had early onset of thrombocytopenia and 12.5% had late onset of thrombocytopenia.

Lower gestational age was associated with thrombocytopenia in preterm neonates. On statistical analysis an optimal cut off of 33.5 was calculated. The sensitivity, specificity, positive and negative predictive value of having thrombocytopenia in preterm neonates if their gestational age is less than 33.5 weeks are 89.3%, 51.8%, 78.7% and 70.7% respectively. With an AUROC curve of 0.706 gestational age has moderated diagnostic accuracy for thrombocytopenia in preterm neonates.

6. References

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