

A STUDY TO COMPARE THE SEVERITY AND OUTCOME OF NEONATAL BLEEDING AND ANALYSIS OF VARIOUS CAUSES OF NEONATAL BLEEDING AND THEIR CORRELATION WITH MATERNAL FACTORS

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Abstract

Introduction: Bleeding in neonates is a significant cause of morbidity and mortality in the neonatal period. The early identification of bleeding and its cause (bleeding or clotting disorder) is very important for the appropriate management and for prognostication.

Material & Methods: After obtaining institutional ethics committee approval, 21 patients with diagnosis of onset of hemorrhagic disorder were recruited from 550 patients admitted to the Neonatal Intensive Care Unit (NICU) after obtaining written informed consent from their parents/guardians. A detailed history including family history, maternal history and perinatal history was recorded. Thorough assessment and relevant investigations were done for all 21 patients diagnosed with bleeding disorder out of 550 patients. Duration of hospital stay and immediate outcome i.e.-Morbidity and mortality in such neonates were noted.

Results: The incidence of bleeding in neonates was 3.8%. Thrombocytopenia was major cause for bleeding [8(38.1%)] followed by VKDB [5 (24%)]. VLBW babies (19.04%) and preterm babies (11.1%) had a statistically significant risk of bleeding. 71.4% (15/21) of neonates had bleeding in the first week of life. 14.3% (3/21) of NICU deaths were in the neonates with bleeding which indicates that bleeding constituted a significant risk factor for mortality in NICU. The outcome in the VKDB was dismal (67% mortality and 33% neurologic sequelae) A statistically significant correlation was found between maternal factors such as Gestational Age<34 weeks, History of Instrumental delivery, history of maternal fever and Anaemia

Conclusion: Early and prompt diagnosis of hemorrhagic disease of the newborn can alleviate the devastating consequences.

Keywords: Vitamin K deficiency, bleeding neonates, DIC, coagulation disorders

INTRODUCTION

The human haemostatic system is dynamic and is profoundly influenced by age. [1,2] In neonates, there is decreased activity of several clotting factors, diminished platelet function, and suboptimal defence against clot formation. [3,4] Bleeding disorders are scarcely reported in the overall neonatal population, but, as commonly observed among hospitalized neonates, they pose a great challenge to the treating physician. Neonatal hemorrhage either localized or generalized has significant morbidity and mortality. [5]

The presence of a bleeding or clotting disorder can be suspected by following symptoms: Cephalhematomas, hematoma at the injection site, bleeding-following invasive procedures, facial purpura following birth associated with severe platelet dysfunction or thrombocytopenia, delayed cord separation and persistent oozing from the umbilical stump: defective fibrinogen production or function and FXIII deficiency. [2] Intracranial Hemorrhage (ICH) may be the clinical presenting symptom of a severe coagulation factor deficiency like hemophilia.[2]

A positive family history could be indicative of congenital coagulation factor deficiency, obstetric complications and events during labor may affect the fetal hemostatic system resulting in coagulation activation and DIC. Medications administered to the mother may interfere with vitamin K metabolism leading to bleeding events in the neonatal period. [6] Thus, it is imperative to rule out the etiological background of the bleeding in neonates to establish a correct diagnosis and provide the most optimal treatment.

The present study aimed to describe and evaluate the various causes of bleeding (due to bleeding and clotting disorders) in neonates and their association with maternal factors at a tertiary care Centre.

MATERIAL AND METHODS

The prospective observational study was conducted at the Department of Pediatrics at a tertiary care hospital in Department of IMCHRC, Indore from August 2022 to March 2023 after obtaining ethical clearance from the institutional Ethics committee. A written informed consent was taken from all the patients qualifying the inclusion criteria.

Study Design: Prospective Observational Study.

Sample Size: 21 patients with diagnosis of onset of hemorrhagic disorder were recruited from 550 patients admitted to the Neonatal Intensive Care Unit (NICU) after obtaining written informed consent from their parents/guardians.

Inclusion criteria: Neonates under 1 months of age presenting with bleeding, anaemia, hematoma, ecchymosis admitted to the Neonatal Intensive Care Unit (NICU) and patients whose Parent/Guardian consented for the study were recruited into the study

Exclusion criteria: Neonates more than 1 months of age, Children with hemorrhagic disease who are partially treated outside IMCHRC and patient whose parent did not consent for the study were excluded from the study.

Method:

After obtaining institutional ethics committee approval, 21 patients admitted in NICU at Tertiary care Centre, IMCHRC, Indore with clinical features suggestive of hemorrhagic disorder were enrolled after taking an informed written consent. A detailed history including family history, maternal history and perinatal history was recorded. Thorough assessment and relevant investigations were done for all 21 patients diagnosed with bleeding disorder out of

550 patients. Duration of hospital stay and immediate outcome i.e.-Morbidity and mortality in such neonates were noted.

Statistical Analysis

Data were analyzed using SPSS 25.0 version software. Continuous variables are expressed in mean \pm standard deviation (mean \pm SD), while categorical variables are expressed as percentage and frequency. The data was statistically analyzed using Chi-square test for nonparametric data and analysis of variance for parametric data. $P \leq 0.05$ was considered significant.

RESULTS

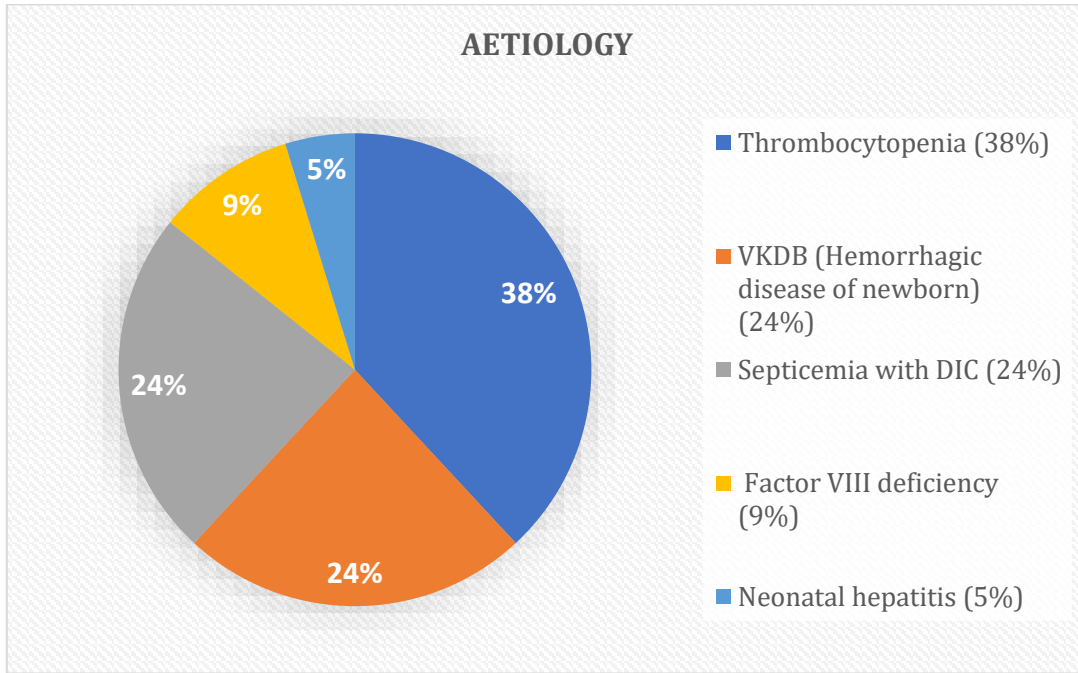
The incidence of bleeding in neonates was 3.8%. (21 out of 550).

Thrombocytopenia constituted the major cause for bleeding [8 (38.1%)]- 6 cases out of which were secondary to sepsis and 2 cases were suspected to be due to NAIT (neonatal alloimmune thrombocytopenia) Vitamin K deficiency bleeding (VKDB) constituted [5 (24%)]. Nearly 2/3rd cases of Vitamin K deficiency bleeding (VKDB) were classic Vitamin K deficiency bleeding (VKDB).

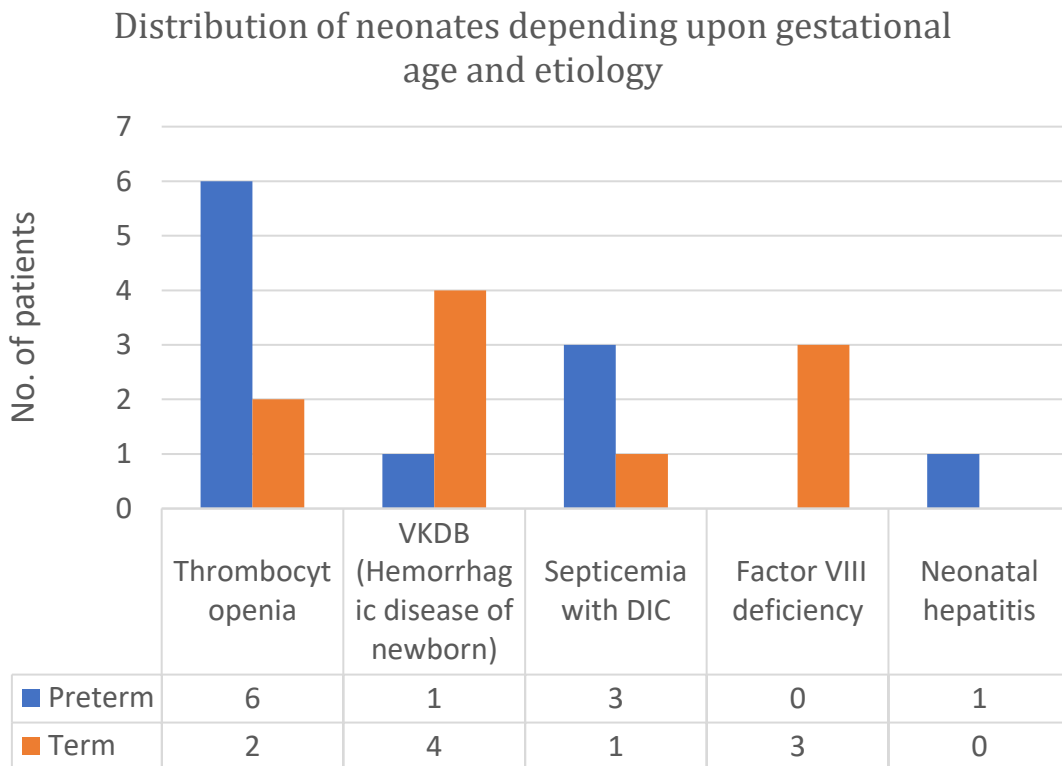
VLBW (very low birth weight) babies (19.04%) and preterm babies (11.1%) had a statistically significant risk of bleeding. 71.4% (15/21) of neonates had bleeding in the first week of life.

14.3% (3/21) of NICU deaths were in the neonates with bleeding which indicates that bleeding constituted a significant risk factor for mortality in NICU. The outcome in the Vitamin K deficiency bleeding (VKDB) was dismal (67% mortality and 33% neurologic sequelae)

A statistically significant correlation was found between maternal factors such as **Gestational Age < 34 weeks, History of Instrumental delivery, history of maternal fever and Anaemia**



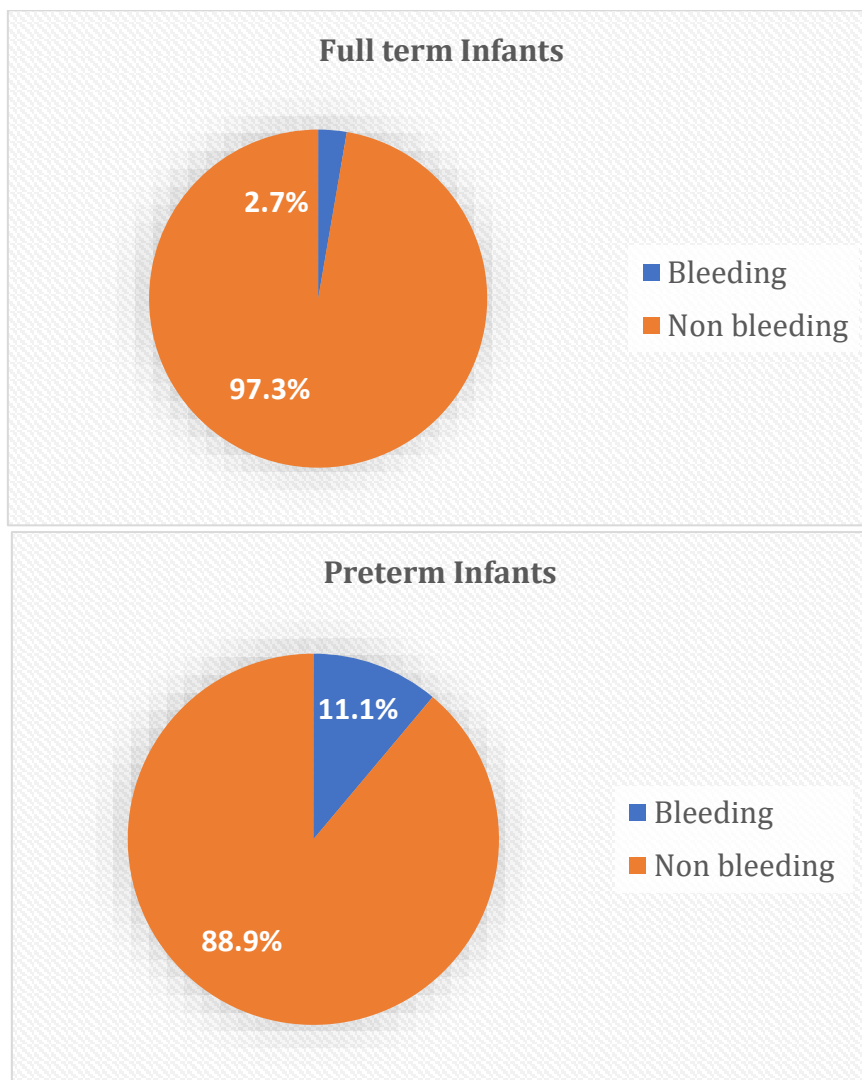
Graph 1. Distribution of patients depending upon the etiology of bleeding disorder in neonates



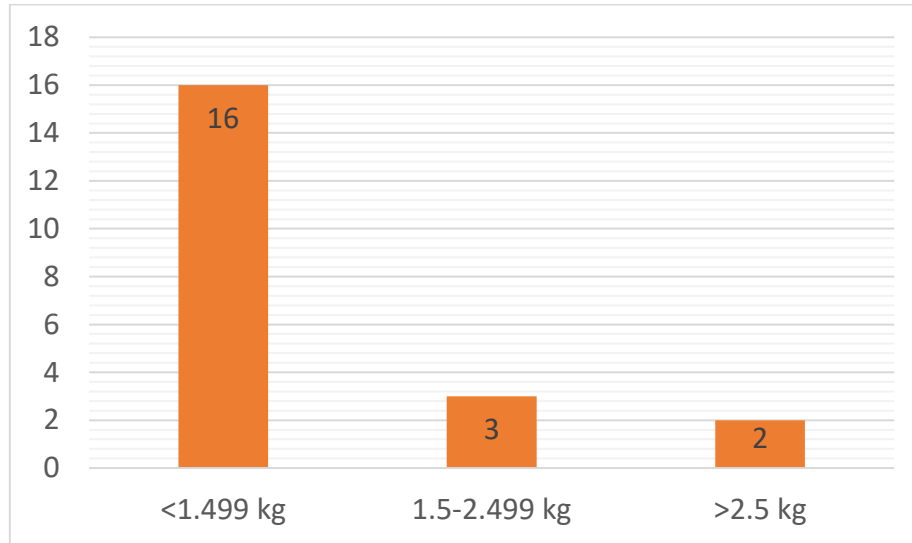
Graph 2. Distribution of neonates depending upon gestational age and etiology

Gestational Age Category	Total Neonates	Bleeding Neonates	Percentage	p-value
Preterm	72	8	11.1	<0.001
Term	478	13	2.7	
Total	550	21	3.8	

Table 1. Distribution of neonates depending upon gestational age



Graph 3. Bleeding in neonates related to gestational age



Graph 4. Bleeding neonates and birth weight

Maternal factors	Total	P value
Maternal Age<20 years	11	0.1345 NS
Gestational Age<34 weeks	8	<0.05*
History of Instrumental delivery	5	<0.05*
History of maternal fever	2	< 0.05*
PIH	8	0.1859 NS
Eclampsia	10	0.1658 NS
PROM	5	0.1673 NS
Anaemia	13	< 0.05*

Table 2. Bleeding in neonates related to maternal factors

DISCUSSION

Bleeding in neonates is a significant cause of morbidity and mortality in the neonatal period. The early identification of bleeding and its cause (bleeding or clotting disorder) is very important for the appropriate management and for prognostication. The relative paucity of Indian studies on bleeding in newborns prompted us to do this study looking at clinical Presentation, aetiological Profile and immediate Outcome of bleeding Neonates

Incidence of bleeding: In our study, the incidence of bleeding was 3.8%. Similar results were obtained by Swarnim S et al. and Arutsivasakthi et al. with an incidence of 3.88% and 5.2% respectively. [2,7]. Contrasting results were reported by Hathway et al. with an incidence of 1%, which is much lower than ours, which shows that various factors like geography, cultural practices, good obstetric practices, low incidence of sepsis, artificial feeding which is known to prevent VKDB, better quality of neonatal care, contributes to lower mortality in advanced countries. [5]

Factors influencing incidence of bleeding: Gender had no effect on the incidence of bleeding among the neonate ($p>0.05$). Similar results were reported by Swarnim S et al. [2] However, gestational age showed statistically significant correlation Preterm infants had a higher incidence of bleeding ($p<0.05$). This is similar to the findings of Swarnim S et al. & Hathaway et al. that sick preterm do bleed excessively owing to many pathological conditions that may complicate easily. [2,5] The reason could be immaturity of hemopoietic system and capillaries as well as their susceptibility to various insults like hypoxia, hypothermia, and infections.

Factors influencing incidence of bleeding: For birth weight a statistically significant increased risk of bleeding was observed especially in Very low birth weight babies ($p<0.05$). This was similar to study done Perlman et al. and Swarnim S et al. in their study also had a similar finding that preterm and VLBW babies and IUGR neonates are highly susceptible to coagulation abnormalities. [2,8] For Onset of bleeding, in our study, 71.4% of the neonates had bleeding manifestation between the second and seventh day of life. This finding can be explained by the immaturity of the neonatal haemostatic system and their vulnerability to perinatal factors. In our study, we also assessed the correlation between etiology and bleeding. Thrombocytopenia constituted the major cause for bleeding [8(38.1%)] and VKDB constituted [5(24%)]. Nearly 2/3rd cases of VKDB were classic VKDB. This was in contrast to study done by Swarnim S et al. who reported DIC as the major cause of bleeding with an incidence of 55.7%. [2] Septicemia with DIC was reported in 4(19%) patients. Most of the septicaemic babies had Gram negative sepsis (75%). This is similar to findings of Tallur et al. and Mishra et al., where Klebsiella was found to be the commonest organism followed by Pseudomonas. [9,10] The sick neonates are more prone to develop DIC because of decreased synthesis of coagulation factors, underdeveloped reticuloendothelial system and tendency to develop hypoxia, acidosis and shock. Vitamin K deficiency bleeding (VKDB) is another important cause of neonatal bleeding and constituted 24% of bleeding neonates in our study. Among patients with Vitamin K deficiency bleeding (VKDB), Classic Vitamin K deficiency bleeding (VKDB) was seen in 2/3rd of cases. Hereditary coagulation disorders can also present during the neonatal period, though they are less commonly seen. One case had a family history of hemophilia and presented with subgaleal hemorrhage after vacuum extraction. The other case with factor XIII deficiency had umbilical bleeding. Lack of prophylactic administration of vitamin K was an important risk factor for VKDB.

A good clinical assessment, coupled with a screening test (CBC, PT, aPTT, FDP) can help in arriving at a proper diagnosis in most of the cases. The coagulation parameters should be interpreted based on the normal values for gestational and postnatal age. Mortality rate of

14.3% (3/21) was seen in our study for the neonates with bleeding. Bleeding constituted a significant risk factor for mortality in NICU. It was found that when bleeding was a clinical manifestation, the mortality was statistically significant ($p < 0.01$). Septicemia with DIC was the commonest cause of mortality, contributing to 66.66% of death. Tallur et al., Swarnim S et al. and Mishra et al. have observed that septicemia was responsible for death in bleeding neonates in 47.52%, 65.1% and 61.7% of cases respectively. [2,9,10]

In our study, there were 3 cases of late VKDB and of them, 2 presented with intracranial hemorrhage and 1 of them died (33.3%). In other studies, in contrast to late VKDB, the outcome of early and classic VKDB was excellent. Out of 3 cases of late VKDB, 1 died giving a mortality of 33.3% and the one who survived had developmental delay. Hence routine vitamin K prophylaxis should be administered to all new-borns at birth.

We also found that most of the early and classic VKDB had a normal outcome, whereas, patients with late VKDB had significant mortality and morbidity. A statistically significant correlation ($P < 0.05$) was found between neonatal bleeding and maternal factors like gestational age, history of maternal fever and anaemia.

CONCLUSION

Preterm, IUGR, out born babies, sick neonates have a higher incidence of bleeding. Bleeding is more commonly seen in the first week of life. Late VKDB had a bad prognosis. Vitamin K prophylaxis has a significant role in Vitamin K deficiency bleeding (VKDB) prevention. We, therefore, conclude that early recognition and rapid intervention can significantly improve outcome in bleeding neonates.

IMPLICATIONS

Hemorrhagic disease of the newborn is a life-threatening condition associated with high mortality and morbidity. But it can easily be prevented by administering 1 mg IM of vitamin K within 1 hour of birth.

Early and prompt diagnosis of hemorrhagic disease of the newborn can alleviate the devastating consequences. Strong interprofessional communication and care coordination by clinicians, nurses, and pharmacists can help improve outcomes and ensure patient safety. Parents should be counselled regarding the condition, and the severity and follow-up routine with the clinician should be scheduled on a regular basis to check the well-being of the patient.

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