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Research Article

Hemorrhagic Disease of Newborn: A Prospective Study of Clinical Features and Outcome.

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Abstract:

Background: Majority of the neonates have a transient deficiency of vitamin K dependant coagulation factors like II, VII, IX and X by 48-72 hours of life. This transient deficiency is resolved by the age of 7-10 days. This transient Vit K dependant coagulation factor deficiency may cause spontaneous bleeding in neonates such bleeding if occurs in between 2nd to 7th day of life is called classical HDN. The other 2 forms of HDN are early onset HDN (Manifesting within 24 hours) and late onset HDN (Occurring between 1-6 months of life). We conducted a prospective study of neonates admitted to our neonatology unit with hemorrhagic disease of newborn to know risk factors and outcome in neonates with HDN.

Aims and Objectives: To study the clinical features and outcome of neonates with hemorrhagic disease of newborn.

Materials and Methods: This was a prospective cohort study comprising of 30 neonates admitted in NICU with the diagnosis of hemorrhagic disease of newborn. HDN associated risk factors, age at presentation, Demographic profile, clinical features, complications and outcomes were studied. Appropriate statistical analysis was done. P-Value less than 0.05 was taken as statistically significant.

Results: In this study out of 30 neonates diagnosed with hemorrhagic disease of newborn there were 18 (60%) males and 12 (40 %) females with a M:F ratio of 1:0.66. The most common type of HDN was found to be classical type (53.33 %) followed by early onset (12 %) and late HDN (34.77 %). Majority of the infants (83.33%) with HDN were exclusively breastfed and most common site of bleeding were intracranial (23.33 %) and GI bleeding (23.33%). Outcome of neonates showed that 43.33 % babies recovered without any sequele, 13.33 % infants expired and remaining 43.34 % infants had some sequele at the time of discharge.

Conclusion: Hemorrhagic disease of newborn is a common cause of bleeding in a well looking baby. Any well looking baby with bleeding manifestations should be considered to be having HDN (early onset, classical or late onset) unless proved otherwise. Appropriate treatment has an excellent outcome in these babies.

Keywords : Hemorrhagic Disease of Newborn, Vitamin K Dependent Coagulation Factors, Intracranial Hemorrhage, Neonatal Seizures.

Introduction:

Newborn babies are at increased risk of coagulation abnormalities secondary to transient deficiency of vitamin K dependant clotting factors like factor II, VII, IX and X[1]. There is a very limited transplacental transfer of vitamin K from mother to fetus in utero consequently there is very little storage of vitamin K in neonatal liver making a neonate vulnerable for development of vitamin K deficiency and its consequences unless exogenous vitamin K is administered to the baby immediately after birth[2].

The incidence of HDN in newborn baby differs depending upon whether or not prophylactic vitamin K was administered or not. In babies who have not received prophylactic vitamin K the incidence of HDN is reported to be 0.5 – 2%[3]. This incidence is reported to drastically decrease (1 per 1000,000 infants) in infants who were given prophylactic vitamin K. With the widespread use of prophylactic vitamin K in developing countries including India the incidence of HDN is declining[4]. Nonetheless in our country especially in rural and semiurban areas many deliveries occur at home and these neonates generally do not receive prophylactic vitamin K making them vulnerable for developing HDN. Males and females both are affected equally. Though no racial predisposition communities in which exclusive breast feeding is common seem to have more incidence of HDN5. Age of presentation usually depend upon whether it's early (within 24 hours), classical (2-7 days) or late onset (1-6 months) HDN.

The causes of vitamin K deficiency in neonates may include physiological deficiency of vitamin K in newborns, maternal medications like antiepileptic, cephalosporins, Rifampicin and warfarin amongst others[6]. In addition to these infants having diarrhea, hepatitis, cystic fibrosis and celiac disease are more prone for development of HDN. Babies exclusively fed on breastfeeding are more prone to develop HDN due to relatively vitamin K deficient breastmilk[7].

Most babies with HDN are "well looking" in contrast to bleeding due to other causes (Sepsis, DIC and NEC) in which the baby appears sick[8]. The severity of the symptoms depends upon the site of bleeding. The baby may present as hemetamesis, malena, soft tissue swelling or epistaxis. Neonates with intracranial hemorrhage may present as subtle or focal convulsions. The differential diagnosis may include bleeding secondary to sepsis, DIC or NEC (Sick baby), alloimmune thrombocytopenia (Prolonged bleeding time and normal clotting time) pediatric Von Willebrand and some other uncommon coagulopathies[9]. The diagnosis is usually made on the basis of full coagulation profile and complete blood count. A prolonged PT, normal fibrinogen concentration, normal or prolonged PTT and normal platelet count in a well looking baby is almost confirmatory of HDN. The specific test to diagnose vitamin K deficiency is elevated levels of des-gamma-carboxy prothrombin (DCP) also known as protein induced by vitamin K absence/Antagonist-II (PIVKA II). Neurosonography or MRI should be done in neonates in whom intracranial hemorrhage secondary to HDN is suspected. The management consists of treatment of underlying cause if any. Vitamin K supplementation is given in appropriate doses. Supportive care, blood transfusions and Fresh frozen plasma maybe required if severe bleeding is present. If there are features suggestive of intracranial bleeding the infant should be transferred to an appropriate level III NICU and appropriate intensive care must be provided[10].

Materials and Methods:

This was a prospective cohort study comprising of 30 newborns babies admitted to our hospital with a diagnosis of hemorrhagic disease of newborn during the study period. Diagnosis of HDN was made in infants up to 6 months of age with bleeding from any site on the basis of coagulation abnormalities (raised PT, Raised or normal PTT, normal platelet count and normal fibrinogen levels) in absence of any other obvious cause of bleeding. Detailed antenatal, natal and post natal history was taken with special attention towards factors predisposing the infants for HDN like h/o maternal intake of antiepileptic, antitubercular drugs or warfarin. Complete blood count, sepsis screen, CRP, Pt, aPTT and fibrinogen levels were done in all cases. Neuroimaging was done in infants who presented with seizures or in whom intracranial hemorrhage was clinically suspected. The infants were divided into 3 groups on the basis of age at presentation early onset HDN (within 24 hours of birth), classical HDN (2-7 days) and late onset HDN (8 days-6 months of life). A detailed clinical and neurological examination was done. Site of bleeding and presence of any complication was noted. Baby was managed and discharged as per NICU protocol. Outcome was noted and follow up was adviced. The data was tabulated and analyzed using SPSS 16.0 version software.

Inclusión Criteria:

1. All newborn babies admitted with the diagnosis of HDN.

Exclusion Criteria:

A. Infants whose parents refused informed consent.

B. Infants with coexisting morbidities like sepsis and NEC.

C. Infants with alloimmune thrombocytopenia.

Results:

In this prospective cohort study 30 patients with hemorrhagic disease of newborn either early, classical or late onset was studied. Out of 30 studied infants there were 18 (60%) males and 12 (40%) female babies with a M:F ratio of 1:0.66 .

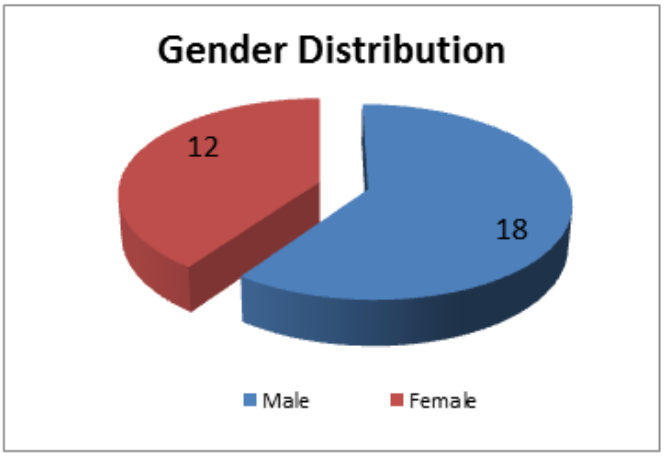

Figure 1: Gender Distribution of the infants with HDN.

The most common type of HDN was found to be classical HDN (53.33 %), followed by early onset HDN (12%) and only 2 (6.66%) babies presented with early onset HDN.

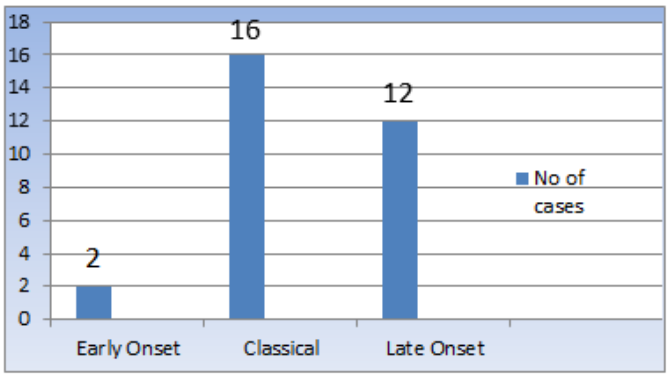

Figure 2 : Distribution of cases on the basis of age of presentation.

The analysis of neonates on the basis of place of delivery revealed that 12 (40 %) babies were born at home. 8 (26.66 %) babies were born at government Primary health centres and 10 (33.33 %) babies were born at private hospitals. Out of 18 institutional deliveries there were 4 LSCS and 14 (46.66 %) normal deliveries.

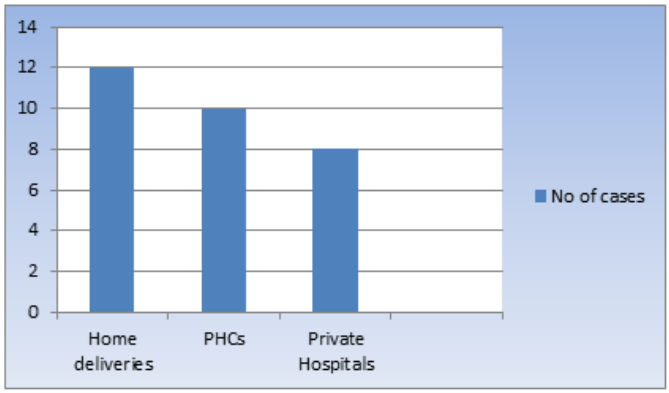

Figure 3 : Distribution of the cases on the basis of place of birth.

Out of 30 cases 25 (83.33 %) infants were exclusively breastfed while 5 babies were being given mixed feeding. Out of the 5 (16.66 %) babies receiving mixed feeding 2 (6.66 %) babies were being formula fed and 3 (10 %) babies were being given cows milk with sugar along with breast feeding.

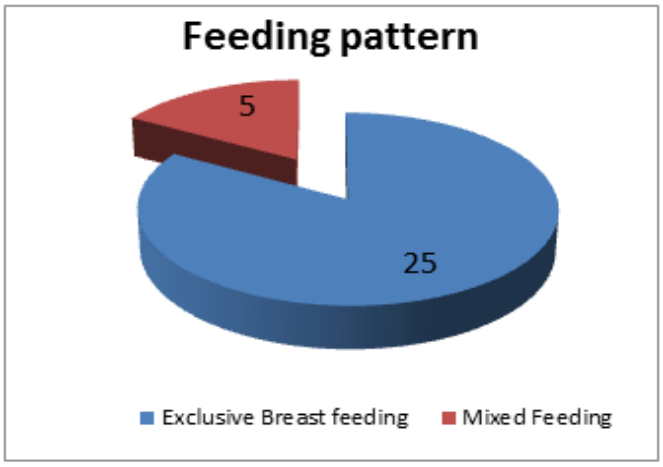

Figure 4 : Feeding Pattern in the studied Cases.

The study of clinical features of the studied cases revealed that the most common sites for bleeding in neonates presenting with HDN were either intracranial hemorrhage (23.33 %) or GI bleeding in the form of hematemesis or malena (23.33 %). The other sites from where bleeding was seen included bleeding from injection site (13.33 %), superficial bleeding (10 %), bleeding from umbilicus(10 %), nose or hematuria(10 %).

	Type Of HDN			Total
	Early Onset	Classical	Late Onset	
Intracranial	0	2 (6.66 %)	5 (16.66 %)	7 (23.33 %)
Superficial	0	3 (10 %)	0	3 (10 %)
Umbilicus	1 (3.33%)	2 (6.66 %)	0	3 (10%)
Hematemesis/Malena	1 (3.33 %)	4 (13.3 %)	2 (6.66 %)	7 (23.33 %)
Hematuria	0	2 (6.66 %)	1 (3.33 %)	3 (10 %)
Nasal Bleeding	0	1 (3.33 %)	2 (6.66 %)	3 (10%)
Bleeding From injection site	0	2 (6.66 %)	2 (6.66 %)	4 (13.33 %)
Tota;	2 (6.66%)	16 (53.3 %)	12 (30 %)	30 (100 %)

All 30 babies were given vitamin K in the appropriate doses depending upon gestational age and weight. 26 (86.66 %) babies were given blood transfusion and 12 (40 %) babies were given Blood transfusion as well as fresh frozern plasma. 4 (13.33 %) babies needed FFP on multiple occassions. Out of 26 (86.66 %) babies who were given blood transfusion 8 (26.66 %) babies needed blood transfusions on multiple occasions.

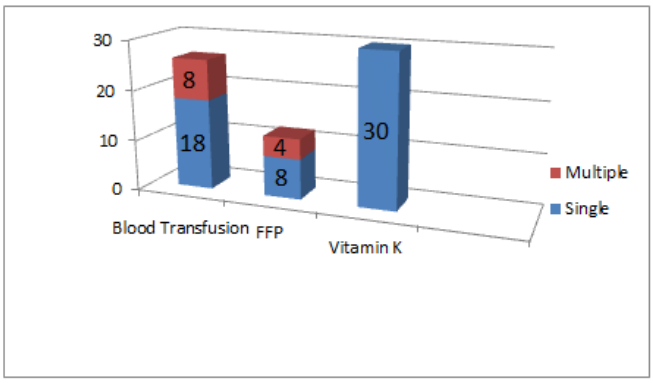

Figure 5 : Mnagament of HDN by Vitamin K, FFP and Blood transfusions.

Finally the analysis of the outcome showed that out of 30 patients 26 (86.66 %) patient survived. 4 (13.33 %) infants died. All infants who dies had intracranial hemorrhage. Out of the 26 patients who had recovered 3 (10 %) patients had seizures so there were put on oral anticonvulsants and parents were adviced follow up after 2 weeks. 2 (6.66 %) baies had focal neurological deficit at the time of discharge, 5 (16.66 %) babies had some kind of feeding problem and 3 (10 %) babies were having weight less than 1 SD of expected.

Outcome	No Of Cases	Percentage
Fully Recovered	13	43.33 %
On ANticonvulsants	3	10 %
Focal Neurological Deficit	2	6.66 %
Feeding problems	5	16.66 %
Underweight	3	10 %
Expired	4	13.33 %
Total	30	100 %

Table 2 : Outcome Of the babies with HDN.

Discussion:

This was a prospective study of infants presenting with hemorrhagic disease of newborn. The incidence of HDN was more in male children than females and most common type of HDN was found to be classical HDN presenting between 2nd to 7th day of life (53.33 %). Various studies have found classical HDN to be the most common type of HDN. Choo K E et al in their retrospective study of the epidemiology, clinical features, laboratory findings, treatment and outcome of hemorrhagic disease in 42 infants reported classical HDN to be the most common type of HDN. In this study all the infants had prolonged a prothrombin and partial thromboplastin time

which was corrected by vitamin K administration. Subdural hemorrhage was the commonest form of intracranial hemorrhage, followed by subarachnoid hemorrhage. The overall case fatality rate was 14%. The authors concluded that all neonates should be given prophylactic Via K to prevent mortality secondary to intracranial haemorrhage[11].

In our study a substantial number of infants with HDN were born at home. Because of the home delivery they didn't receive vitamin K prophylaxis. It was found in our study that home delivery was one of the important causes of HDN. Similar findings were reported by many authors who found that home delivery was one of the important risk factors for development of hemorrhagic disease of newborn[12]. RG Holla reported a case of infant with HDN who presented with subdural hematoma[13]. The infant was delivered by spontaneous vaginal delivery at home (did not receive vitamin K at birth) and was on exclusive breast feeds. Similar cases of infants delivered at home and presenting with HDN were also reported by D Hubbard et al[14].

Breast milk is relatively deficient in vitamin K and babies who are exclusively breastfed are at the risk of developing hemorrhagic disease of newborn. Out of 30 cases in this study 25 cases (83.33 %) were exclusively breastfed. Exclusive breastfeeding as a risk factor for development of HDN has been reported by many investigators. Rana MT et al in their study of fifty patients with hemorrhagic disease of newborn reported that 90% of the affected babies were being fed exclusive on breastmilk15. The authors concluded that hemorrhagic disease of newborn was common in male gender, breast-fed infants and spontaneous vaginal deliveries. Similar findings were seen in studies conducted by MM IJland et al[16].

In our studies intracranial hemorrhage and GI bleeding were the most common form of bleeding seen in infants with HDN. A study of 42 infants with hemorrhagic disease of newborn conducted by Pooni PA et al showed that 71% patients presented with intracranial hemorrhage and the most common site of ICH was found to be intracerebral and multiple ICH[17]. In contrast to 70% infants having ICH only 33.33 % infants were found to have some kind of external bleeding. Similar findings were reported by Bör O et al who in their study of 15 infants with idiopathic late HDN found that the most common manifestation in these infants was intracranial hemorrhage which was seen in 73 % patients[18].

Finally the neonatal or infant mortality in our study was found to be 13.33 %. 43.33 % of the patients had fully recovered before discharge and in rest of the infants there was some or the other kind of morbidity which was present at the time of discharge. These findings were similar to the studies conducted by Lippi G et al and Isarangkura PB et al who found the mortality due to HDN to be 21% and 22 % respectively[19, 20.]

Conclusion:

Hemorrhagic disease of newborn is a preventable cause of hemorrhage in a newborn. Any well looking baby with bleeding manifestations should be considered to be having HDN (early onset, classical or late onset) unless proved otherwise. Prophylactic dose of vitamin K immediately after birth can reduce the incidence of HDN and its complications.

Conflict Of Interest: None

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