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Original Research Article

Study on clinical presentations, risk factors and short term outcome of hemorrhagic disease of newborn

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Abstract: Haemorrhagic Disease of Newborn (HDN), also called vitamin K deficiency bleeding (VKDB), is an acquired coagulopathy secondary to reduction of vitamin K dependent coagulation factors below hemostatic levels. It is a preventable disease with prophylactic administration of vitamin K at birth. Aim of this study was to identify clinical presentations, risk factors and short term outcome of infants with hemolytic disease of newborn. A total of 62 patients with hemorrhagic disease of newborn (aged from birth to 6 month) randomly selected to participate in this cross sectional analytical study. In this study 13% babies presented as early HDN, 35% presented as classical HDN and 51% as late HDN In this study, 87% babies were on exclusive breast feeding. The high incidence of HDN in breast-fed babies is due to its low content of vitamin K. Vitamin k was not given in home delivered babies illustrates that traditional birth attendants are unaware about the importance of administration of vitamin K at birth. The most common presentation of HDN was intracranial haemorrhage noted in 41.9% of cases. In this study, majority of babies (87.09%) recovered and discharged. This shows that HDN has good prognosis when adequately treated and not associated with intracranial haemorrhage.
Keywords: Vitamin k deficiency ,hemorrhagic disease of newborn ,intracranial hemorrhage.

INTRODUCTION

The term 'hemorrhagic disease of newborn' was first used in 1894 by Charles Townsend [1]. He reported a series of breast-fed infants who presented with self limiting bleeding, usually from gastrointestinal tract, on the second or third day of life with subsequently normal hemostasis in the survivors [2].

Hemorrhagic disease of new born also called vitamin K deficiency bleeding (VKDB), is the name given to the occurrence of spontaneous bleeding in early days of life [2] .Bleeding can occur from birth up to six months of life [3].

Haemorrhagic disease of newborn is more common in certain group of babies like breast-fed infants, preterm babies, malabsorption, cystic fibrosis and neonatal cholestasis etc[4].Late onset disease occurs primarily in exclusively breast-fed infants and is associated with intracranial hemorrhage in about 50% of the cases[1].There are a number of factors which contribute to a transient reduction in the availability of vitamin K to the infant in the newborn period: reduced stores of vitamin K , absence of the bacterial flora which normally synthesize vitamin K ,functional immaturity of the liver (where the vitamin- K-dependent factors are synthesized).

Vitamin K facilitates the post-transcription gamma carboxylation of glutamic acid residues on Factors II, VII, IX, and X [5]. In premature infants, the degree and duration of factor deficiency may increase resulting in a more severe and prolonged bleeding tendency [5]. Incidence of vitamin K deficiency bleeding in babies not receiving vitamin K at birth is 0.25% to 1.7%. in united state[6] .Late vitamin K deficiency bleeding has fallen from 4.4-7.2 cases per 100,000 births to 1.4-6.4 cases per 100,000 births in reports from Asia and Europe after regimens for prophylaxis were instituted [7-9].

The disease is classified according to the age of onset; Early (first 24 hours of life), Classic (2-7 days of life) and Late onset (8 days to 6 months of life) disease [4]. Outcome of HDN depends upon type of HDN, site and severity of bleeding, and presence or absence of underlying risk factors. In the absence of intracranial hemorrhage, prognosis is good [1] .So HDN is an important cause of mortality and morbidity in developing countries where vitamin K prophylaxis is

not routinely practiced; it can be prevented by providing vitamin K prophylaxis to all newborn [10] .Aim of this study was to identify clinical presentation, risk factors and short term outcome of infants with hemolytic disease of newborn

MATERIAL AND METHODS

Study type, institutional ethical committee permission and patient consent**:**

This cross sectional analytical study was carried out after obtaining ethical committee clearance from the institute. A written consent from the parents of all enrolled patients was taken prior to the study and the parents were briefed about the study in the language they understood.

A total of 62 patients with hemorrhagic disease of newborn (aged from birth to 6 month) admitted in SPMCHI, SMS Medical College, Jaipur, randomly selected to participate in this cross sectional analytical study during the period from march 2013to april 2014. Infants with vitamin K deficiency bleeding typically have a prolonged prothrombin time (PT) with platelet counts and fibrinogen levels within the normal range for newborns. Thrombocytopenia or a prolonged Activated Partial Thromboplastin Time (APTT) should prompt workup for other causes of bleeding during the neonatal period.

Infants with obvious predisposing causes of bleeding e.g. sepsis, thrombocytopenia, neonatal hepatitis and biliary atresia were excluded.

A proforma was used to record the details of history including age at onset of bleeding, gender, place of delivery, mode of delivery, history of vitamin K given at birth or not, feeding history, history of jaundice in baby, family history of bleeding disorder, presenting complaints and acute outcome during hospital stay like cure of symptoms or death. Detailed clinical and neurological examination was also done in all babies. Hemoglobin level, total and differential leukocyte count, platelet count, Bleeding Time (BT), Prothrombin Time (PT) and Activated Partial Thromboplastin Time (APTT) were determined in all babies. Cranial Ultrasonography done in all patients to rule out intracranial bleed. Computed tomogram (CT scan) was done for confirmation in whom clinical suspicion and Ultrasonography suggestive of intracranial haemorrhage.

On the basis of age at onset of symptoms babies were divided into 3 groups: early onset disease (first 24 hours of life), classic onset disease (2 to 7 days of life) and late onset disease (8 days to 6 months of life). After taking sample for investigations, vitamin K (5 mg) was given to all babies. Fresh blood (10 ml/kg) was given to those babies who were anemic (hemoglobin < 10 gm/dl) or in shock (hypotension, poor peripheral pulses, and tachycardia). Fresh frozen plasma (10 ml/kg) was given to those babies who were not anemic. Babies were monitored daily during hospital stay for acute outcome. Prothrombin time and activated partial thromboplastin time was repeated after 24 hours in every baby. Those babies having no active bleeding, no residual deficit and normal PT and APTT were called cured.

Statistical analysis

Data were analyzed statistically .Qualitative data expressed in the form of percentage and proportions. Quantitative data expressed in the form of means and standard deviation . Difference in proportions inferred by Chi-square Test. Difference in Means inferred by unpaired 't' Test/ANOVA. Risk factors was assessed by Odd's Ratio.

Chi-square test was applied to determine the significance of difference in measurement of these variables and relationship between these variables and outcome. P-value of less than 0.05 was considered significant.

RESULTS

Demographic data

In present study out of 62 enrolled patients, 40(64.5%) are male and 22(35.5%) are female. In present study among 62 children ,8(12.9%) presented as early HDN (within 24 hours of birth), 22(35.48%) presented as classical HDN (2^{nd} to 7^{th} day of life) and 32(51.61%) as late HDN(more than 7 days).Mean age for late HDN was 39.7±1.5 days so in our study most common type is late HDN.

Clinical data

In our study among 62 children, 44(70.96%) presented with visible bleeding in form of cutaneous bleeding in 12(19.35%), per rectal in 20(32.25%), prick site bleeding in 6(9.68%) and cutaneous with prick site bleed in 6(9.68%) children (Table no.1). In study all enrolled 62 children had neurological features presented as convulsion in 22(35.48%), excessive cry in 14(22.58%) and refusal to feed in 26(41.93%).

In our study out of 8 children of early HDN, 6(75%) presented as per rectal bleeding and 2(25%) as cutaneous bleed (echymotic patches).In classical HDN among 22 children ,12(54.5%) presented as cutaneous bleed (echymotic patches and hematomas), 6(27.2%) as per rectal bleeding and 4(18.2%) children as intra cranial hemorrhage . So in classical HDN common presentation was cutaneous bleeding. In late HDN out of 32 children, 22(68.7%) presented as ICH, 12(37.5%) as cutaneous bleed (echymotic patches and hematomas) and 4(12.5%) as per rectal bleeding. ICH was the most common presentation of late HDN followed by cutaneous bleeding.

Table-1: Clinical presentation

Presenting symptoms	Numbers	(%)
Visible bleeding	44	70.96
Cutaneous	12	19.53
Per rectum	20	32.45
Prick site	6	9.68
Cutaneous+prick site	6	9.68
Neurological features	62	100
Convulsions	22	35.48
Excessive cry	14	22.58
Refusal to feed	26	41.94
Pallor	40	64.51

Table-2: Presentation according to type of HDN

Presentation	Early HDN	Classic HDN	Late HDN
Per rectal bleeding	6(75%)	6(27.2%)	4(12.5%)
Echymotic patches	2(25%)	12(54.5%)	12(37.5%)
ICH	0(0%)	4(18.2%)	22(68.7%)
Prick site bleeding	0(0%)	4(18.2%)	6(18.7%)

Risk Factor Analysis

In our study 46 babies were delivered by spontaneous vaginal delivery while 16 by caesarean section and the difference was significant (p=0.002). 40(64.5%) babies were home delivered none of them were given vitamin k prophylactic dose. 22 children had institutional delivery and out of them 8(13%) babies had history of vitamin K given at birth and the difference was significant (p=0.02).

In our study exclusive breastfeeding was noted in 54 (87%) babies while 8 (13%) babies received mixed (bottle and breast) feeding and the difference was significant (p=0.001). Vitamin K was given to all 50 babies after taking samples for investigations in hospital. Blood transfusion was given to 18 (29%) babies due to low hemoglobin level. Fresh frozen plasma was given to 28 (45.1%) babies in our study.

Table-3: Various risk factors for HDN

FACTOR			CHI SQUARE VALUE	P VALUE
Sex	22(female)	40(male)	5.226	0.02
Place of delivery	22(institutional)	40(home)	5.226	0.02
Mode of delivery	16(lscs)	40(ND)	14.516	0.001
Gestational age	4(Pre-Term)	58(Full-term)	47.032	0.001
Feeding	8(breast+top feed)	54(Exclusive breast feed)	34.129	0.001
Prophylactic vitamin K	8(vitamin K given)	54(vitamin K not given)	34.129	0.001

Outcome of the study

In present study 54 babies (87.09%) recovered and discharged and 8(12.9%) children died. In our study death occurred in 8 children out of them 6(75%) are of late onset disease. All of them were male and home delivered and none of them were received prophylactic vitamin K, and cause of death was intra cranial hemorrhage in all children. In our study, majority of babies (87.09%) recovered and got discharged. This showed that HDN has good prognosis when adequately treated and not associated with intracranial haemorrhage so Vitamin K deficiency bleeding is a preventable problem and prevention can be done by prophylactic administration of vitamin K to all newborns.

DISCUSSION

Haemorrhagic Disease of Newborn (HDN), also called vitamin K deficiency bleeding (VKDB), is an acquired coagulopathy secondary to reduction of vitamin K dependent coagulation factors below haemostatic levels. It is a preventable disease with prophylactic administration of vitamin K at birth.

In our study most common type of HDN was late onset disease noted in 32(51.61%) of cases. This finding does not correspond with western studies, where classic onset disease is found to be the commonest type [2,11] . This discrepancy may be due to the fact that late onset disease is confined to exclusive breast-fed babies and the practice of breastfeeding is more frequent in Asians [11-14]. In our study, 54(87%) of babies were on exclusive breastfeeding. The high incidence of HDN in breast-fed babies is due to its low content of vitamin K. Breastfeeding is an important risk factor for HDN especially for late onset disease. McNinch et al., Bor O et al ., and D'Souza et al., described that late onset VKDB remains virtually confined to breast-fed infants

[15-17]. Males were affected more than females in our study. Male gender was found as risk factor for HDN by Nakagawa et al., too [10].

Most of babies 40(64.5%) were delivered at home in our study. Vitamin K was not given to those babies who delivered at home. This showed that traditional birth attendants are unaware about the importance of administration of vitamin K at birth. Out of 62 patient presenting with HDN In our study 8 (12%) had history of vitamin K given at birth and all were presented as late HDN. This showed that single IM dose of vitamin K might be not sufficient against the prevention of late HDN. Solves et al ., and Ciantelli et al ., also suggest that a potential risk is still present with a single dose of intramuscular vitamin K at birth [18,19]. They conclude that 1 mg IM vitamin K at birth may be insufficient to prevent late vitamin k deficiency bleeding. Kasatkar et al., also reported VKDB cases despite receiving appropriate dosage of parenteral vitamin K at birth [20]. Pirinccioglu et al., indicate that it may be questionable whether single dose vitamin K at birth is adequate for the prevention of late vitamin k deficiency bleeding [21].

The most common presentation of late HDN was intracranial haemorrhage noted in 41.9% of cases. While McNinch et al., described 37% incidence of intracranial haemorrhage in their study [22] .Zengin et al , and Hubbard et al , mentioned that late HDN frequently presents with intracranial haemorrhage leading to high morbidity and mortality [12,13].

The next common presentation was bleeding into the skin (echymotic patches, bruising and hematomas) noted in 26 (41.9%) patients in our study. Skin bleeding was most commonly noted in classical onset disease in 12 out of 22(54.5%) patients. In late HDN skin bleeding noted in 37.5% of cases. Skin bleeding was also noted in 30% of patients in late onset disease by Flood et al., [3].

In our study, majority of babies (87.09%) recovered and discharged. This showed that HDN has good prognosis when adequately treated and not associated with intracranial haemorrhage. This can be correlated with Aydinli et al., study in which no case fatality was noted [23] .Death occurred in 8 (12.9%) babies in our study. Mortality was observed in 26% by Lulseged et al., and 32% of patients by Demiroren et al., [24,25] .

In our study, the cause of death was intracranial haemorrhage in all babies and all were of late onset disease. This finding correlates with other studies mentioning late onset disease as major factor for mortality and morbidity. Hubbard D et al ., Studied about Intracerebral hemorrhage due to hemorrhagic disease of the newborn and failure to administer vitamin K at birth[12]. They illustrated that hemorrhagic disease of the newborn can occur when prophylactic vitamin K is not administered and that it can have devastating consequences. Given these issues, the routine administration of vitamin K to all infants is mandatory and should not be considered optional.

Per H, Kumandaş S *et al.* studied about Intracranial hemorrhage due to late hemorrhagic disease found that late HDN may be associated with serious and life-threatening intracranial hemorrhage [14]. Late HDN is characterized by intracranial bleeding in infants aged 1 week to 6 months due to severe vitamin K deficiency, occurring particularly in exclusively breastfed infants.

Pooni PA *et al. s*tudied about Intracranial hemorrhage in late hemorrhagic disease of the newborn [26]. They concluded that Late HDN is still an important cause of mortality and morbidity in developing countries where vitamin K prophylaxis is not routinely practiced. Isolated intracranial hemorrhage is a common mode of presentation. Vitamin K deficiency bleeding is a preventable problem and prevention can be done by prophylactic administration of vitamin K to all newborns [27,28,29].Therefore vitamin k prophylaxis is necessary, at least for breastfed infants.

CONCLUSION

Haemorrhagic disease of newborn is more common in certain group of babies like breast-fed infants, preterm babies, mal-absorption, cystic fibrosis and neonatal cholestasis etc. Late onset disease occurs primarily in exclusively breast-fed infants and is associated with intracranial hemorrhage in about 50% of the cases. Late HDN is still an important cause of mortality and morbidity in developing countries where vitamin K prophylaxis is not routinely practiced. Isolated intracranial hemorrhage is a common mode of presentation. Vitamin K deficiency bleeding is a preventable problem and prevention can be done by prophylactic administration of vitamin K to all newborns. Therefore vitamin K prophylaxis is necessary, at least for breastfed infants.

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