



ORIGINAL ARTICLE

Clinical profile and outcome of neonates presenting with hemorrhagic disease at a tertiary care hospital in Karachi, Pakistan.

Syeda Shamama Zehravi¹, Mashal Khan², Mehmood Sheikh³, Sulman Javaid⁴, Mohammad Hanif⁵

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ABSTRACT... Objective: To identify the clinical presentations and outcomes of infant with Hemorrhagic Disease of Newborn (HDN). **Study Design:** Descriptive Cross-sectional study. **Setting:** Department of Neonatology, National Institute of Child Health (NICH), Karachi, **Period:** July to December 2021. **Material & Methods:** The babies diagnosed with HDN were included in the study. Age at onset of symptoms, gender, feeding pattern, place of delivery, site of bleeding and outcome were recorded. The outcome was compared with the chi-square test and the p-value <0.05 is considered significant. **Results:** Ninety five babies were included in the study. Male to female ratio was 1.87:1 and mean age of admission was 6.31 ± 5.98 days. The type of HDN was Early in 21 (22.1%), Classic in 55 (57.9%) and Late in 19 (20%) babies. In this study, 77.9 % babies were on exclusive breast feeding. Fifty four (56.8%) were delivered at homes, 9 (9.5%) at private clinics and 32 (33.7%) at government hospitals. In our country most babies are delivered at home where vitamin K is not given prophylactic to the newborn, leading to HDN. The site of bleeding were gastrointestinal, superficial, umbilicus and intracranial in 36 (37.9%), 24 (25.3 %), 21 (22.1%) and 12 (12.6%) neonates respectively. In this study, majority of babies (88.4 %) discharged. **Conclusion:** HDN was common in male gender, home deliveries, vaginal deliveries and breast fed.

Key words: Coagulation Factors, Hemorrhagic Disease of Newborn, Intracranial Bleed, Neonate, Vitamin K.

INTRODUCTION

Hemorrhagic disease of the newborn (HDN) is one of the most common cause of acquired hemostatic disorder in first few weeks of life secondary to vitamin K deficiency, therefore commonly known as vitamin K deficiency bleeding (VKDB).¹ Vitamin K is essential for the synthesis and activation of clotting factors by the liver, namely Factors 2, 7, 9, 10, Protein C and S.² The term, vitamin K deficiency bleeding, was introduced by Charles Townsend in 1894 reporting self-limited bleeding in new born infants mostly from gastrointestinal tract.³ HDN is categorized into three categories depending upon the age at disease presentation i.e., early, classic, and late onset. Early HDN occurs within first 24 hours, classic HDN occurs within 2 to seven days, whereas late onset presents between one week and six months of life.⁴⁻⁷ Incidence of early, classical and late onset of HDN were noted in 6-12%, 0.01-0.4% and

1/15000-20000 babies respectively.⁸ In a previous study done in the National Institute of Child Health (NICH), Karachi, it was found to be 0.4% in normal birth weight and 1.5% in low birth weight infants.⁹

Children with HDN presented with visible bleeding either at the site of pricking, skin, umbilical cord, nose, in urine or stool. On physical examination pallor, bruises, jaundice may be present; whereas parents may report about convulsion, excessive cry, poor feeding, malena and hematemesis. In most of the cases prognosis is good, however, children can also present with potentially fatal bleeding including intracranial bleeding in that case prognosis is poor.^{4,9,10} HDN is associated with different risk factors such as male gender, place of delivery, gestational age, type of feeding (mother milk does not contain enough vitamin K to fulfill the needs of baby), history of maternal drug (anti-epileptics, anti-tuberculosis,

1. MBBS, Postgraduate Trainee Pediatric, National Institute of Child Health, Karachi.
2. MBBS, FCPS, Professor Pediatric Medicine, National Institute of Child Health, Karachi.
3. MBBS, FCPS (Peds Medicine), FCPS (Neonatology), Assistant Professor Pediatric Medicine, National Institute of Child Health, Karachi.
4. MBBS, FCPS (Peds Medicine), Assistant Professor Pediatric Medicine, The Children Hospital and Institute of Child Health, Faisalabad.
5. MBBS, FCPS (Peds Medicine), Assistant Professor Pediatric Medicine, National Institute of Child Health, Karachi.

Correspondence Address:
Dr. Syeda Shamama Zehravi
B-61, Bloc1-1, Gulistan-e-johar, Karachi.
shamama.zehravi@hotmail.com

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warfarin) use during pregnancy and who did not receive prophylactic vitamin K supplementation at birth.^{4,7,9} In order to prevent hemorrhagic disease of newborn it has been recommended by the American Academy of Pediatrics that all newborns should be administered prophylactic vitamin K 0.5 or 1 mg soon after birth.¹¹⁻¹³

Pakistan is among the developing countries, where level of education and health care facilities are poor, as a result most of the babies are delivered pre-term and at home, where vitamin K is not given prophylactically.¹⁴ Therefore, newborn children are at a higher risk of developing life-threatening bleeding due vitamin k deficiency. Studies from all over world have reported common sign and symptoms and outcome associated with hemorrhagic disease of the newborn, but local data is in dearth. Therefore, this study was planned to identify the common sign and symptoms of HDN in term neonates and their outcome at a tertiary care Pediatric hospital in Karachi.

MATERIAL & METHODS

It was a cross sectional descriptive study carried out at Neonatology Department, NICH, Karachi, for a period of 6 months from July to December 2021. The study was carried out after obtaining clearance from the Institutional Review Board (03/2021) and informed consent from the parents/guardian. All babies from birth to 6-months of life with history of bleeding from any site along with prolonged prothrombin Time (PT), activated partial thromboplastin time (APTT) and normal platelets were eligible to be included in the study by consecutive non-probability sampling; until the desired number of patients was completed.

Babies with obvious predisposing causes of bleeding e.g. sepsis, thrombocytopenia, neonatal hepatitis and biliary atresia were excluded from the study. Data including history, examination and outcome was collected on specially designed proforma. Investigations included CBC, CRP, PT and APTT was done. Ultrasound was done for confirmation in whom clinical suspicion of intracranial hemorrhage was present by a consultant radiologist at the Department

of Radiology, National Institute of Child Health, Karachi. According to the age of onset of symptoms, the children 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 (from 8 days to 6 months of life). After taking sample for investigations, vitamin K (5 mg) was given to all babies. Anemic neonates (hemoglobin <10 g/dl) or in shock (hypotension, weak peripheral pulse and tachycardia) received fresh blood (20 ml/kg). Fresh frozen plasma (10 ml/kg) was administered to the non-anemic neonates.

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 recovered. Short-term outcomes of the neonate were measured in terms of discharge and death.

Results were analyzed using SPSS-20. Qualitative variable were presented as mean and standard deviation, while quantitative variables presented in frequency and percentages. The chi-square test was used to compare the variables. The value of P 0.05 was considered statistically significant.

RESULTS

A total of 97 babies were enrolled in the study, however, two neonates were excluded due to insufficient data. There were 62 (65.3%) males and 33 (34.7%) females. Mean age of study population was 6.31 ± 5.98 days. The mode of delivery was SVD in 79 (83.2%) and Caesarean section in 16 (16.8%) cases. Out of the 95 cases, 54 (56.8%) babies were delivered at home while 32 (33.7%) babies were delivered at government hospital and 9 (9.5%) were delivered in private hospital. Exclusive breast feeding was observed in 74 (77.9%) babies while top feeding and mixed feeding were noted in 5(5.3%) and 16 (16.8%) babies respectively. There was history of Vitamin K prophylaxis in 39 (41.1%) while 56 (58.9%) did not receive vitamin k at birth. Profile of Babies having HDN are summarized in Table-I.

The type of HDN was Early in 21 (22.1%), Classic

in 55 (57.9%) and Late in 19 (20%) babies. The site of bleeding was intracranial in 12 (12.6%), superficial in 24 (25.3%), umbilicus in 21 (22.1%), gastrointestinal in 36 (37.9%), 2 (2.1%) babies.

Regarding the outcome of study, 72 (75.8%) babies, were cured, 12 (12.6%) were discharged with deficit and 11 (11.6%) expired. Spectrum of Presentation of HDN are summarized in Table-II.

		No. of Babies (%)
Gender	Male	62 (65.3%)
	Female	33 (34.7%)
Mode of Delivery	Spontaneous Vaginal Delivery	79 (83.2%)
	Caesarean Section	16 (16.8%)
Place of Delivery	Home	54 (56.8%)
	Government Hospital	32 (33.7%)
	Private Hospital	9 (9.5%)
Feeding Type	Breast Feeding	74 (77.9%)
	Top Feeding	5 (5.3%)
	Mix Feeding	16 (16.8%)
Vitamin K Prophylaxis	Yes	39 (41.1%)
	No	56 (58.9%)
Outcome	Cured	72 (75.8%)
	Discharged With Deficit	12 (12.6%)
	Expired	11 (11.6%)

Table-I. Profile of babies having HDN

		Type of HDN				
		Early	Classic	Late	Total	Percentage
Site of Bleeding	Intracranial	3	6	1	12	12.6
	Superficial	3	14	7	24	25.3
	Umbilicus	3	16	2	21	22.1
	Gastrointestinal	10	18	8	36	37.9
	Nasal	0	1	1	2	2.1
	Total	21	55	19	95	100

Table-II. Spectrum of presentation of HDN

DISCUSSION

Vitamin k plays a vital role in the physiology of clotting.¹⁴ It is essential for carboxylation of clotting factors 2, 7 9 10 protein C and protein S.¹⁵ Vitamin k deficiency is seldom seen in adults due to its availability in plants, other dietary sources and its synthesis from the gut flora. Newborns are vulnerable to vitamin k deficiency as there is very limited transport of vitamin k across the placenta and inadequate production of vitamin K from the relatively sterile neonatal gut flora.² Similarly, breast feed contains trace amounts of vitamin k in contrast to formula feed, predisposing the exclusively breastfed babies to Vitamin K bleeding disorder (VDKB).^{2,8}

The male:female ratio in our study was 1.8:1, which is similar to local studies.^{9,10} Most of the

babies in our study were exclusively breastfeed (77.9%), which is similar to the observations of Rana MT and Gopchade.^{3,10} The breastfeed, owing to its low vitamin K amount, is a risk factor for HDN as noticed by the studies performed by McNich and D'souza.^{16,17}

We noted that 41.4% babies received vitamin K prophylaxis at birth, while 57% of the babies were delivered at home, where prophylactic vitamin K was not given. On the contrary, all the babies received vitamin k injection at birth in an Indian study.¹⁰ It may be due to lack of awareness of health care workers or birth attendants regarding the importance of vitamin K at birth. According to literature search there is low prevalence of HDN in countries that emphasize the need for intramuscular vitamin k shortly after birth.¹⁸

Classic HDN presenting between 2nd to 7th day of life, was the commonest type in our study observed in 57.8% of cases, which is similar to the results of Choo et al (48%) and Gopchade (53.3%).^{10,19}

Gastrointestinal bleed was the most common site of bleed seen in 37.9% of babies in our study. Farid had a similar finding in 77.4% neonates.⁹ An Indian study, however, observed intracranial bleed (23.3%) and GI bleeding (23.3%) to be the major modes of presentation.¹⁰ Rana noticed the intracranial hemorrhage to be the leading presentation with a frequency of 52%.³ Bor O et al found that intracranial hemorrhage (73.3%) is the leading presentation.²⁰

As we look at the outcomes, the pattern of recovery (75.8%), death (11.8%), and discharge with disabilities (12.6%) was similar to Choo Et al study in which (78.5%), (7.14%) and (7.14%) participants got recovery, death and discharge with disability respectively.¹⁹ The rate of recovery was 56% in a local study whereas, 24% babies were discharged with deficit and 20% babies expired which are twice as much as compared to our results.³

CONCLUSION

Hemorrhagic disease is a common cause of bleeding in healthy infants. Appropriate treatment gives excellent results in these infants. Hemorrhagic disease of the newborn was common in home births and breastfed births. It is recommended that vitamin K1 be administered to all newborns in a single intramuscular dose of 0.5 to 1 mg.

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AUTHORSHIP AND CONTRIBUTION DECLARATION

No.	Author(s) Full Name	Contribution to the paper	Author(s) Signature
1	Syeda Shamama Zehravi	Data collection, Data analysis, manuscript writing.	
2	Mashal Khan	Proof reading.	
3	Mehmood Sheikh	Data analysis and interpretation.	
4	Sulman Javaid	Manuscript writing.	
5	Mohammad Hanif	Manuscript writing.	