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STUDY TO REVEAL FREQUENCY OF VITAMIN K DEFICIENCY IN NEONATES WITH ABNORMAL BLEEDING PRESENTING TO THE NEONATAL UNIT

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Abstract:

Introduction: *The term vitamin K comes from the German language Koagulations - vitamin. Vitamin K is a fat-soluble vitamin that is absorbed from the gastrointestinal tract in the presence of bile salts. Vitamin K is needed for the synthesis of coagulation factors II, VII, IX, X by the liver2. Due to the short half-life of these factors and the small amounts of vitamin K stored in the body, insufficient vitamin K intake may result in its deficiency in a short time. In the past, all neonatal bleeding disorders were grouped together under the diagnosis of neonatal hemorrhagic disease (HDN).*

Aim: *The objective of this study was to determine the prevalence of vitamin K deficiency in newborns presenting with abnormal bleeding to the neonatal unit.*

Methods: *A total of 375 infants with bleeding were excluded from the study, while those with an obvious cause of a bleeding disorder, eg, with anticoagulation therapy, were excluded from the study. It was a cross-sectional study conducted at the Department of Hematology and Transfusion Medicine of Nishtar Hospital Multan for one-year duration from March 2019 to March 2020.*

Results: *In an age distribution study, 45 (12%) were found to be 1-24 hours old, 185 (49.3%) were 2-7 days old and 145 (38.6%) were found. at 1-2 weeks of age, 237 (63.2%) are male and 36.8% are female. Discussed by geographical area (urban and rural). Out of a total of 375 cases, 168 (44.8%) were from cities, and 207 (55.2%) from rural areas. Incidence of abnormal clotting profiles in cases, 369 (98.4%) patients had an abnormal clotting profile, and 6 (0.01%) had a normal clotting profile. Incidence of platelet abnormalities in newborns reporting bleeding 362 (96.5%) had normal platelet counts and 13 (0.03%) had abnormal platelet counts. 352 (93.8%) had vitamin K deficiency bleeding and 23 (0.06%) had a bleeding disorder other than vitamin K deficiency bleeding.*

Conclusion: *Vitamin K deficiency bleeding is a very important cause of bleeding in the first month of life. It is more common in men and in the countryside. Vitamin K deficiency bleeding is an avoidable cause of bleeding, therefore vitamin K prophylaxis should be mandatory after birth in all newborns.*

Key words: *Prevalence, vitamin K deficiency bleeding.*

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INTRODUCTION:

The term vitamin K comes from the German Koagulations vitamin. Vitamin K is a fat-soluble vitamin that is absorbed from the gastrointestinal tract in the presence of bile salts. Vitamin K is needed for the liver synthesis of clotting factors II, VII, IX, X. In the past, all neonatal bleeding disorders were grouped together under the diagnosis of neonatal hemorrhagic disease (HDN) [1-2]. The new term for neonatal hemorrhagic disease is Vitamin K Deficiency Bleeding (VKDB). Currently, there are methods available for the accurate diagnosis of factor deficiency states and immune thrombocytopenia. Vitamin K deficiency Bleeding can be distinguished from other disorders by excluding and observing the patient's response to a 1 mg I / M injection of vitamin K. Vitamin K deficiency may cause bleeding in the infant during the first weeks of life [3-4]. This is known as neonatal hemorrhagic disease (HDN). Vitamin K is commonly administered postnatal prophylactic to prevent HDN, but the preferred route is uncertain. The classic onset of vitamin K deficiency bleeding in a breastfed infant occurs 2-7 days after birth. Classic VKDB is defined as bleeding that occurs 2 to 7 days postpartum [5-6]. This is more commonly seen in infants whose feeding is delayed in the first few days of life, either because for some reason their feeding is infrequent (for example, they are drowsy due to the effects of an injection of pethidine given to the mother to ease the pain of labor) or because feeding is not possible because the child feels unwell in intensive care. If a child develops classic VKDB, excessive bleeding may occur around the baby's umbilical cord (although a small amount of bleeding is not uncommon when the umbilical cord separates).

Bleeding in a child's brain is a major concern of VKDB, as it can lead to varying degrees of brain damage and, in rare cases, death of the child [7-8]. The prevalence of classical VKBB is believed to range from about 0.44% in healthy children to 1.5% if the child is sick. Administration of vitamin K after birth will obviously reduce bleeding incidence and complications in this age group [9-10]. However, parental refusal of prophylaxis and increasing frequency of breastfeeding may result in recurrence of vitamin K deficiency bleeding. We planned this study to determine the prevalence of vitamin K deficiency in newborns presenting with abnormal bleeding to the neonatal unit.

MATERIALS AND METHODS:

A total of 375 infants with bleeding were excluded from the study, while those with an obvious cause of a bleeding disorder, e.g, with anticoagulation therapy, were excluded from the study. It was a cross-sectional study conducted at the Department of Hematology and Transfusion Medicine of Nishtar Hospital Multan for one-year duration from March 2019 to March 2020. The study was approved by the ethics committee. In this study, 375 cases of bleeding infants who met the inclusion and exclusion criteria were collected over a 6-month period from both the neonatal, inpatient and outpatient neonatal units. After informed consent was obtained, mandatory tests were performed, including CBC (complete blood count) for platelet counts and PT (partial thromboplastin), APTT (activated partial thromboplastin time) to determine coagulopathy. Informed consent was obtained from the parents of all study patients. CBC was performed by collecting 3 ml of blood by venipuncture and EDTA anticoagulation using strict aseptic techniques. The samples were then processed by the sysmex kx-21, while the PT and APTT were done manually according to the SOP (Standard Operating Procedures) of the laboratory. Neonatal bleeding time was determined by capillary puncture using the Ivy's method, using strict aseptic techniques. A blood pressure cuff was placed around the upper arm of the patients and inflated to 40 mm Hg. The palmar part of the forearm was cleaned with a spirit swab and three small stab wounds were made with a lancet. Blood that leaked from these small stab wounds was removed with filter paper every 30 seconds. The time to stop bleeding was recorded with a stopwatch.

Patients with abnormal bleeding, prolonged PT and APTT, and normal platelet counts and bleeding time were administered vitamin K injection of 1 mg I / M. The response to vitamin K therapy was assessed by reducing the intensity or complete cessation of bleeding after 24 hours. The data was entered into a computer and statistically analyzed using SPSS-12.

RESULTS:

A total of 375 newborns meeting the inclusion and exclusion criteria were enrolled in the study to determine the frequency of vitamin K deficiency bleeding in neonates presenting to the neonatal unit. The data was collected by a specially designed proforma. The distribution of cases by age is calculated in Table No. 1 and it was found that 45 (12%) were 1-24 hours of age, 185 (49.3%) were 2-7 days of age, and 145 (38.6%) were 1-2 weeks of age. The mean age was 8.52 +/- 2.14.

The gender distribution of the subjects was calculated in Table 2, where 237 (63.2%) were men and 36.8% were women, with a male to female ratio of 1:05. Table No. 3. It was shown that between the ages of 1

and 24 hours, 29 (64.4%) were men and 170 (37.7%) were women, with a male-to-female ratio of 1.7: 1. the age of 2-7 days was as follows. 110 (59.4%) were male and 75 (40.5%) female with a male to female ratio of 1.4: 1 The gender distribution at 1-2 weeks of age was as follows, 97 (66.8%) were male, 48 (33.1%)) were women with a male-to-female ratio of 2.02: 1. The table shows the distribution of cases by geographical area (city and village). Out of a total of 375 cases, 168 (44.8%) were from cities, and 207 (55.2%) from rural areas. Table 5 showed the frequency of reductions in PT and APTT of cases, 369 (98.4%) patients had reduced PT and APTT, and 6 (0.01%) had a normal clotting profile. Table 6 shows the incidence of a reduced platelet count in bleeding neonates. 362 (96.5%) had a normal platelet count and 13 (0.03%) had a reduced platelet count. Table 7 presents the frequency of vitamin K deficiency bleeding in newborns presenting with abnormal bleeding to the neonatal unit of a grade III hospital. 352 (93.8%) had vitamin K deficiency bleeding and 23 (0.06%) had a bleeding disorder other than vitamin K deficiency bleeding.

Table 1: Distribution of cases according to different age groups. (n=375)

Age Groups	**n**	**%age**
1-24 hrs Early VKDB	45	12
2-7 days Classic VKDB	185	49.3
1-2 wks Late VKDB	145	38.6

Mean age+ S.D 8.52 + 2.14

Table 2: Distribution of data according to gender.

Gender	**n**	**%age**
Male		63.2
Female	138	36.8

Male: Female ratio=1:0.5

Table 3: Male to female ratios in different age groups

Gender	**1-24 hrs**	**2-7 Days**	**1-2 Weeks**
Male	29(64.4%)	110(59.4%)	97(66.8%)
Female	17(37.7%)	75(40.5%)	48(33.1%)
Male: Female	1.7:1	1.4:1	2.02:1

Table 4: Distribution of cases according to the geographical areas.

Geographical Area	**n**	**%age**
Urban	168	44.8
Rural	207	55.2
Total	**375**	**100**

Table 5: Frequency of increased and normal PT and APPT in children presenting in the neonatal unit with complaint of bleeding.

PT & APPT	**n**	**%age**
Yes (Increased)	369	98.4
No (normal)	06	0.01

Table 6: Frequency of normal and decreased platelet count in neonates presenting with bleeding.

Platelet count	n	%age
Normal	362	96.5
Decreased	13	0.03
Total	375	100

Table 7: Frequency of VKDB in neonates.

Vitamin K Deficiency	n	%age
Yes	352	93.8
No	23	0.06
Total	**375**	**100**

DISCUSSION:

Vitamin K deficiency can cause unexplained bleeding in the first week of life in healthy, previously born babies. Late VKDB, a syndrome defined as unexplained bleeding that can be attributed to severe vitamin K deficiency in infants 2-6 weeks of age, occurs predominantly in exclusively breastfed infants who have not received any vitamin K prophylaxis in newborns or have received insufficient prophylaxis [9-10]. The age at the presentation of the VKDB varies according to different reports. It was found that in one report it was 34 days. The result of the present study shows that the age of onset of VKDB was 8.52 days, which is the mean age for all three types of VKDB i.e. Early (1-24 hours) Classic (1-7 days) and Late VKDB (1-2 weeks). The mean age of onset was 51.65 days in the local study. Similarly, another study found an age of 20.4 +/- 4.9 days. Another research study found that the average age was 30 days. Studies by Van Hasselt PM, de Koning TJ et al. Have shown that the female gender is more exposed to VKDB. However, the current study found that men were at greater risk. Men are 237 (63.2%) and women 138 (36.8%), and the ratio among women was 1:05 [11-12]. The same association with male dominance was also shown by another study in Hanoi, Vietnam. A study in Ethiopia in Adis Ababa found a male-to-female ratio of 1.8: 1. The Pediatric Medicine Department of the Nishtar Hospital in Multan conducted a 2004-2006 study that found male predominance, as did the current study in which male-to-female ratios for females was 2.1: 1. A German study also found that the male gender impact was greater than that of female. Previous research on VKDB noted that the rural population suffered more from VKDB, possibly from home deliveries and an inability to take vitamin K at birth [13-14]. The same result was observed in this study. A study in Kelantan Malaysia also found the same effect of having more patients from rural areas, which is due to the trend of home deliveries among the rural population. PT and APTT of patients suffering from VKDB are usually elevated, an Egyptian study in 2004 also found that PT and APTT were elevated prior to injection of vitamin K and returned to the normal reference range after I / M injection of vitamin K7. The same results were also seen in the present study. In 369 (98.4%) cases, PT and APTT were increased, and in 6 (0.01%) cases, PT and APTT were normal.

VKDB platelet counts are almost always within the normal reference ranges of 150-450x109 / L Three studies that conducted VKDB studies all had normal platelet counts of 150-450x109 / L in the inclusion criteria7,10,12 Conducted this study. 362 (96.5%) patients had a normal platelet count and 13 (0.03%) had a reduced platelet count. The prevalence of VKDB was 2.21% in a local Pakistani research paper published in 2001, but the incidence was calculated based on general patterns of neonatal admission to the neonatal unit[15]. Another study that calculated only the incidence of early VKDB, which occurs in the first week of life, found the incidence to be 0.25-1.7%. In this study, the frequency of VKDB was calculated to be 352 (93.8%), but it is slightly higher than in all other studies, therefore the frequency was calculated among children with bleeding disorders. Note, however, that in this study, the frequency of VKDB was calculated in all three VKDB subtypes, and not separately in all three subtypes.

CONCLUSION:

Bleeding from vitamin K deficiency is a very important cause of bleeding in the first month of life. It is more common in men (63.2%) and rural population (55.2%). In the present study, the incidence of vitamin K deficiency bleeding is 93.8% in newborns with bleeding, and the mean age is 8.5 days. Vitamin K deficiency bleeding is an avoidable cause of bleeding; therefore, vitamin K prophylaxis should be mandatory after birth in all newborns.

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