

# Intracranial Hemorrhage Caused by Vitamin K Deficiency Beyond Neonatal Period

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## Abstract

Vitamin K deficiency bleeding (VKDB) can manifest as intracranial hemorrhage (ICH) and is still prevalent in poor resource countries. Infants aged one to twelve months with the diagnosis of ICH from 1<sup>st</sup> July 2011 to 30<sup>th</sup> June 2016 were included. There were 16 cases of ICH attributed to vitamin K deficiency. Clinical presentations were anemia 16 (100%), bulged fontanel 13(81.3%), seizures 10(62.5%), vomiting 8(50%) and fever 9(56.3%). Mean INR at admission was 8.575±7.267 and 1.868±0.838 after three doses of vitamin K administration. Sites of intracranial bleed were parenchymal 5(31.3%), subdural 4(25%), extradural 2(12.5%), ventricular 2(12.5%). In 3(18.8%) of cases bleeding was more extensive involving more than one site. Mortality was 4(25%) and 3(18.8%) had abnormal neurological findings at discharge. There is an urgent need for national policy for vitamin K prophylaxis at birth.

**Key words:** Intracranial haemorrhage-Late onset haemorrhagic disease of newborn -Vitamin K

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## Introduction

Deficiency of vitamin K predisposes to bleeding and it can be divided into early, classical, or late vitamin K deficiency bleeding (VKDB) according to their onset, early (<24 h), classical (days 1-7) and late (>1 week <6 months), and by etiology into idiopathic and secondary. In secondary VKDB, in addition to breast feeding, other predisposing factors are apparent, such as poor intake or absorption of vitamin K<sup>1</sup>.

Late onset VKDB occurs after 7<sup>th</sup> day of life at neonatal period and is most commonly associated with intracranial bleeding, serious neurological sequelae and death<sup>2,3</sup>. Other common bleeding sites are gastrointestinal and umbilical. Late onset VKDB can be incidental finding in 6.6% cases without signs of any bleeding<sup>3</sup>. Administration of Vitamin K (1mg, IM) at birth can prevent these severe complications especially hemorrhage in the central nervous system<sup>4</sup>.

The median (interquartile range) burden of late VKDB is 35 (10.5 to 80) per 100 000 live births in infants who do not receive prophylaxis at birth; the burden is much higher in low- and middle-income countries as compared with high-income countries 80 (72 to

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80) vs 8.8 (5.8 to 17.8) per 100 000 live births<sup>5</sup>. A study from south western Uganda has shown high prevalence of vitamin K deficiency in mothers and newborns<sup>6</sup>.

Evidences show use of parenteral vitamin K prophylaxis can significantly reduce the risk of VKDB when compared with no prophylaxis<sup>5</sup>. Multiple oral doses are also used but parenteral vitamin K is preferred<sup>7</sup>. Authors regard the effectiveness oral route inconclusive because most of the studies used biochemical indicators which lack correlation and scientific evidence<sup>8</sup>. In view of high burden of VKDB additional dose of vitamin K is suggested for all infants<sup>2,9</sup>. In breast fed infants, infants with liver disease, antibiotic uses and diarrhoea there is definitive role of additional doses<sup>10</sup>. In many developing countries vitamin K prophylaxis is not routinely administered<sup>11</sup>. There is limited information about spectrum of VKDB and lack of uniform policy regarding vitamin K prophylaxis from the developing countries.

## Material and Methods

A retrospective study was conducted in the Manipal Teaching Hospital, Pokhara, Nepal from the data retrieved from the hospital records maintained in the medical records department. All infants in the age group 1 to 12 months with the discharge diagnosis of ICH during the period of 1st July 2011 to 30th June 2016 were eligible. Other causes of ICH including trauma, vascular malformations, other bleeding disorders (haemophilia, liver disease, thrombocytopenia, DIC) were excluded. Patient details including age, sex, presenting complaints, physical signs, laboratory parameters haemoglobin levels coagulation profile, international normalized ratio (INR) at admission and at 72 hours were also retrieved. CT scan reports were collected to note site of intracranial bleed. Final outcome, discharge with

or without neurological deficit, left against medical advice (LAMA) or death were recorded. Infants had received 5 mg daily doses of vitamin K for minimum of 5 days or till INR was normalized. Supportive treatment was given for features of raised intracranial pressure and seizures were treated with phenobarbitone, phenytoin and benzodiazepines.

Data analysis was done using SAS University Edition and Microsoft Excel 2008. Continuous data was presented as mean and S.D. and categorical data expressed as frequency, percentage and 95% confidence interval.

## Results

There were 16 cases of ICH attributed to vitamin K deficiency in the age group 1 month to 12 months during the study period of 5 years. Mean age of presentation was  $2.36 \pm 1.97$  months. (Table 1) Clinical presentations were anemia in 16 (100 %), bulged anterior fontanel 13 (81.3%), seizures 10 (62.5%) vomiting in 8 (50%), fever 9 (56.3%). Altered sensorium was universal finding with Glasgow Coma Scale (GCS)  $6.56 \pm 2.966$  at admission. Mean INR at admission was  $8.575 \pm 7.267$  and  $1.868 \pm 0.838$  after 72 hours following 3 doses of vitamin K administration. Only 3 (18.7%) out of 16 infants had received vitamin K at birth. (Table 2)

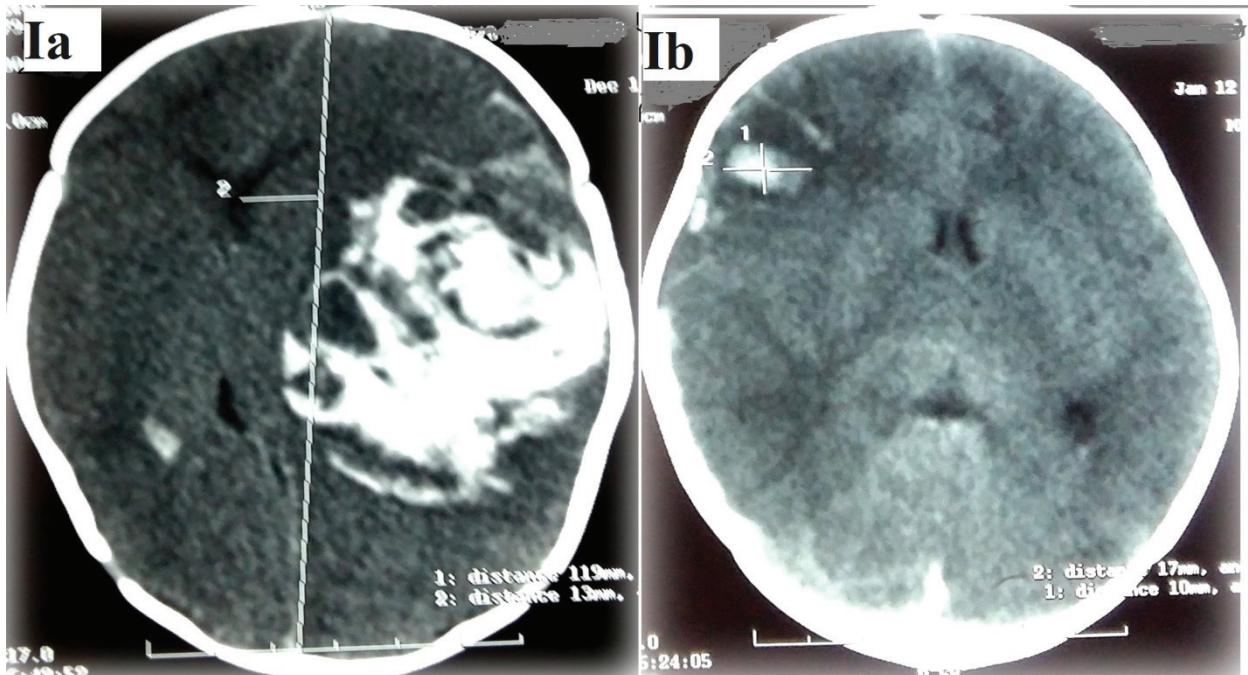
Site of intracranial bleed were parenchymal 5 (31.3%), subdural 4 (25%), extradural 2 (12.5%), ventricular 2 (12.5%). In 3 (18.8%) of cases bleeding was more extensive involving more than one site. (Image 1a and Image 1b). Six (37.5%) of patients were discharged without any neurological deficits and 3 (18.8%) had abnormal neurological findings at discharge. Hospital mortality was 4 (25%) and 3 (18.8%) of patients had left against medical advice.

**Table 1:** Clinical presentations seen in the series.

	Number (N)	Percentage (%)
Sex		
Male	10	62.5
Female	6	37.5
Received Vitamin K at birth	3	18.75
Bulged fontanel	13	81.3
Seizures	10	62.5
Fever	9	56.3
Vomiting	8	50

**Table 2:** Laboratory finding of patients with Intracranial bleed.

	Mean ± S.D.	95% C.I.
Age in months	2.363 (1.9772)	1.309-3.416
GCS	6.56±2.966	4.98-8.14
Hemoglobin (gram/DL)	5.781 (1.5437)	4,959-6.604
INR initial	8.575 (7.267)	4.702-12.447
INR repeat (72 hours)	1.868 (0.838)	1.475-2.262



**Fig. 1:** Image 1a – Parenchymal bleed in left temporo-parietal region with subdural and subarachnoid extension and midline shift. Image 1b Parenchymal bleed in right frontal regional with perifocal edema and subarachnoid and subdural extension.

**Discussion**

VKDB especially classic form can be prevented by prophylaxis at birth. Intracranial haemorrhage due to VKDB causes significant mortality and morbidity<sup>3,9,10</sup>. Neurological deficits including developmental delay, epilepsy, blindness, strabismus, spastic paresis, growth retardation and hydrocephaly have been described in surviving infants<sup>10</sup>.

Mean age of presentation was 2.36± 1.97 months and ICH was more common in males (62.5%) compared to females (37.5%). Most of the infants 13 (81.25%) had not received prophylaxis at birth. Altered sensorium and pallor were universal presentation. Low haemoglobin concentration with mean haemoglobin concentration of 5.78± 1.5 gm/dl was correlated with clinical finding and one feature suspicious of ICH. Coma is most common symptom and Demiroren et al reported coma in 74% of patients. Bulged fontanel in infants was reliable sign and present in 81.25% of ICH. Earlier studies described bulged fontanel in 60-70% of infants with ICH<sup>10,13,14</sup>.

Seizures were present in 62.5% of patient in this study slightly higher than earlier studies by 58% Demiroren et al and 49% by Özdemir et al<sup>10,13</sup>. Half of the infants had vomiting earlier studies noted vomiting in 45% patients<sup>10,13</sup>. Nine (56.3%) children were febrile on admission. Fever is common symptom even in the absence of sepsis and Yılmaz et al had also described 40% patients with ICH febrile<sup>12</sup>.

In a bleeding infant a prolonged PT together with a normal fibrinogen level and platelet count is almost diagnostic of VKDB; rapid correction of the PT and/or cessation of bleeding after VK administration are confirmative<sup>1</sup>. There was prompt response to parenteral vitamin K and INR declined from baseline 8.57±7.2 to 1.86±8 after 48 hours. Parenchymal bleed was most common followed by subdural, multiple intracranial sites, extradural, ventricular in the present study. Earlier studies also mentioned parenchymal as most common ICH site<sup>1,10,12</sup>. However, another study described subdural as commonest bleed site<sup>13</sup>.

Mortality was noted in 25% in patients with in ICH due to VKDB in this study. Demiroren et al and Yilmaz et al described mortality of 32 % and 32 % respectively<sup>10,12</sup>. In another study from Bastent university hospital mortality was higher 50%, however, in their cohort 58.33% had undergone surgery<sup>13</sup>. A One third of patients (37.5%) were discharged without frank neurological deficit while 18.8% patients had neurological deficient including hemiparesis, monoparesis, and cranial nerve palsy. Outcome of 18.8 % patient was unknown as they were discharged against medical advice. Finding from current study highlights urgent necessity for steps in prevention of VKDB.

## Conclusion

Intracranial hemorrhage due to VKDB causes significant mortality and morbidity. Diagnosis of ICH can be easily established with clinical features, neuroimaging with the supplementation of laboratory findings. Parenchymal bleed is the most common bleeding site. We recommend large prospective multicenter study to know disease burden in Nepal. There is an urgent need for a national policy for vitamin K prophylaxis at birth.

## References

1. Sutor AH, von Kries R, Cornelissen EA, McNinch AW, Andrew M. Vitamin K deficiency bleeding (VKDB) in infancy. ISTH pediatric/perinatal subcommittee. International society on thrombosis and haemostasis. *Thromb Haemost* 1999;81:456-61.
2. Karaci M, Toroslu E, Karsli T, Kanber Y, Uysal S, Albayrak D. Intracranial haemorrhage due to late-onset vitamin k deficiency. *HK J Paediatr (new series)* 2015;20:80-5.
3. Unal E, Ozsoylu S, Bayram A, Ozdemir MA, Yilmaz E, Canpolat M et al. Intracranial hemorrhage in infants as a serious, and preventable consequence of late form of vitamin K deficiency: a selfie picture of Turkey, strategies for tomorrow. *Childs Nerv Syst* 2014;30:1375-82. doi: 10.1007/s00381-014-2419-2.
4. Majeed R, Memon Y, Majeed F. Clinical presentation of late haemorrhagic disease of newborn. *Pak J Med Sci* 2008;24:52-5
5. Sankar MJ, Chandrasekaran A, Kumar P, Thukral A, Agarwal R and Paul VK. Vitamin K prophylaxis for prevention of vitamin k deficiency bleeding: a systematic review. *J Perinatal* 2016;36,Suppl:29–35 doi: 10.1038/jp.2016.30.
6. Santorino D, Siedner MJ, Mwanga-Amumpaire J, Shearer MJ, Harrington DJ, Wariyar U. Prevalence and Predictors of Functional Vitamin K Insufficiency in Mothers and Newborns in Uganda. *Nutrients* 2015;7(10):8545-552. doi:10.3390/nu7105408.
7. American Academy of Pediatrics Committee on Fetus and Newborn. Controversies concerning vitamin K and the newborn. *Pediatrics* 2003;112:191-2.
8. Martín-López JE, Carlos-Gil AM, Rodríguez-López R, Villegas-Portero R, Luque-Romero L, Flores-Moreno S. Prophylactic vitamin k for vitamin k deficiency bleeding of the newborn. *Farm Hosp* 2011;35:148-55. doi:10.1016/j.farmae.2010.05.001.
9. Cekinmez M, Cemil T, Cekinmez EK, Altinörs N. Intracranial hemorrhages due to late-type vitamin K deficiency bleeding. *Childs Nerv Syst* 2008;24:821-25.
10. Demiroren K, Yavuz H, Cam L. Intracranial hemorrhage due to vitamin k deficiency after the newborn period. *Pediatr Hematol Oncol* 2004;21:585-92.
11. Danielsson N, Hoa D, Thang N, Vos T, Loughnan P. Intracranial haemorrhage due to late onset vitamin K deficiency bleeding in Hanoi province, Vietnam. *Arch Dis Child (Fetal and Neonatal Ed)* 2004;89(6):F546-F550. doi:10.1136/adc.2003.047837.
12. Yilmaz C, Yuca SA, N, Bektaş MS, Caksen H. Intracranial hemorrhage due to vitamin k deficiency in infants: a clinical study. *Int J Neurosci* 2009;119:2250-56. doi: 10.3109/00207450903170437.
13. Özdemir MA, Karakucukcu M, Per H, Unal E, Gumus H, Patiroglu T. Late-type vitamin K deficiency bleeding: experience from 120 patients. *Childs Nerv Syst* 2012;28:247-51.
14. Misirloglu ED, Aliefendioğlu D, Bademci G, Baydar Z, Kose G, Cakmak FN. Intracranial hemorrhage due to Vitamin K deficiency in infancy: clinical and radiological findings. *J Neurol Sci* 2009; 18:18-25.