Delayed vitamin k deficiency related bleeding : is it genetically linked ?

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INTRODUCTION

•Hemorrhagic disease of the newborn (HDN) or delayed vitamin K deficiency bleeding (VKDB) is an uncommon disorder with potentially devastating outcomes

•The bleeding is most often intracranial, but can also be mucosal, cutaneous, or gastrointestinal

•Despite administration of vitamin K (VK), some infants show lower activity of VK-dependent coagulation factors

•Exclusive breast feeding with no or inadequate vitamin K prophylaxis, intestinal malabsorption defects (cholestatic jaundice, cystic fibrosis, α-1-antitrypsin deficiency etc.), antibiotics, diarrhea, history of maternal medication are some of the known acquired causes of Vitamin K deficiency in children

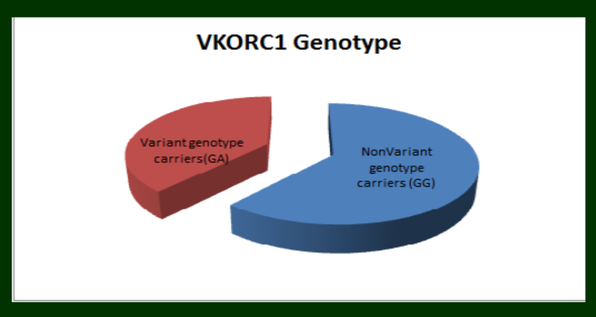
•Genetic polymorphisms involved in VKORC1 and CYP2C9 gene have been known to be linked to excessive bleeding post warfarin (vitamin K antagonist) therapy in some patients. Thus it is reasonable to presume that same polymorphisms will be implicated in bleeding in infants when there is a simultaneous deficiency of vitamin K

Objectives:

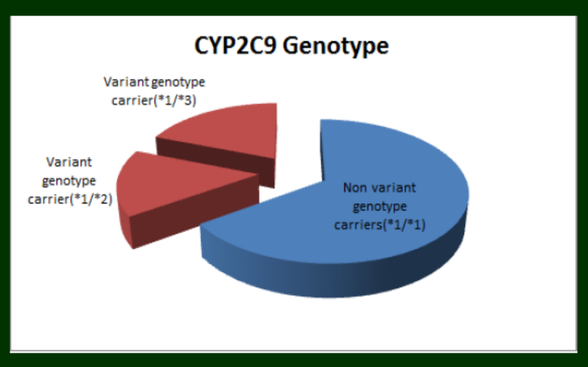
•To determine association of delayed vitamin K deficiency with 3 polymorphisms i.e. VKORC1-1639 G/A, CYP2C9*2 and CYP2C9*3

GRAPHS & TABLES

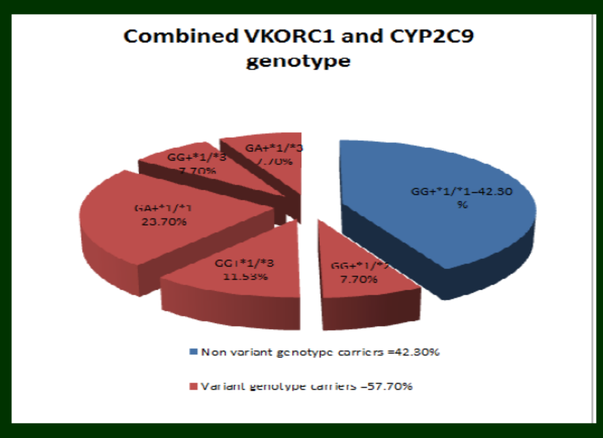
VKORC1 Genotype	
Genotypes	No. of patients (%)
GG	16 (61.5)
GA	10 (38.5)
Total	**26 (100)**



CYP2C9 Genotype	
Genotypes	No. of patients (%)
*1/*1	17 (65.4)
*1/*2	4 (15.4)
*1/*3	5 (19.2)
Total	**26 (100)**



Combined VKORC1 and CYP2C9 Genotype	
Genotypes	No. of patients (%)
Non Variant carriers	
GG+*1/*1	11 (42.30)
Total	**11 (42.30)**
Variant Carriers	
GG+*1/*2	2 (7.70)
GG+*1/*3	3 (11.53)
GA+*1/*1	6 (23.07)
GA+*1/*2	2 (7.70)
GA+*1/*3	2 (7.70)
Total	**15 (57.70)**



RESULTS

We studied 26 infants who presented with vitamin k deficiency related bleeding between 8 weeks to 13 weeks. Ten had IC bleed while 3 had severe epistaxis, 5 had prolonged bleed from the site of injection, 2 had hematuria, 2 had hemoptysis, 3 had bleeding from umbilical stump and one had excessive bleeding from the site of catheter insertion. Analysis of the 3 warfarin sensitive polymorphisms showed that overall, 57.70 % infants had any of the 3 warfarin sensitive allele.

CONCLUSIONS

Present study shows a higher prevalence of warfarin sensitive alleles in delayed vitamin k deficiency group infants, indicating a possible genetic predisposition.

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