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Late Haemorrhagic Disease of Newborn: Can It be Prevented by Changing Prophylaxis Policy?

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background: Vitamin K deficiency can cause severe haemorrhage in the newborn and is an important cause of infant morbidity and mortality. HDN can be classified according to the time of presentation after birth into early (0–24 hours), classical (1–14 days) and late (2–12 weeks) HDN. Late HDN, which presents after the first week of life, mainly manifests as intracranial haemorrhage, depending upon the site and amount of bleeding, it either results in mortality or life long sequelae in the form of cerebral palsy and scar epilepsy with or without cognitive impairment.
Objective: To determine the frequency of ICH about vitamin K deficiency and outcome in infants aged 2 to 24 weeks.
Materials and Methods: From 1 September 2017 to 30 September 2019 we retrieved the retrospective data of 8 patients with late HDN admitted to Bapuji Child Health Institute and Chigateri Government General Hospital, Davangere.
Results: Six of eight cases with late HDN had an intracranial haemorrhage, of whom 5 patients died (62%), one ended up with neurological sequelae (12%) and 2 cases had an extracranial bleed. Out of these 8 cases, 5 had not received vitamin K at birth.
Conclusion: For neonates on strict breastfeeding, despite some with vitamin K prophylaxis, some patients still may suffer from intracranial and extracranial bleeding due to late HDN. Therefore, a

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change in strategy in the form of making the paediatricians and Anganwadi workers working in subcenters to give vitamin K, who have been vaccinating the babies after birth, would increase the vitamin K coverage.

Keywords: Late haemorrhagic disease; newborn; prevalence; prophylaxis.

1. INTRODUCTION

Vitamin K deficiency can cause severe haemorrhage in the newborn and is an important cause of infant morbidity and mortality. HDN can be classified according to the time of presentation after birth into early (0–24 hours), classical (1–14 days) and late (2–12 weeks) HDN [1,2].

Newborn infants are at risk for HDN for the following reasons [2,3]:

(1) Reduced bioavailability because of poor placental transfer of vitamin K and the relatively short half-life of the K1 liver stores;
(2) Reduced vitamin K content in breast milk compared with fortified cow's milk-based formula; and
(3) Reduced production of vitamin K because of immature or altered gut flora.

Because dietary intake is an infant's main source of vitamin K, exclusively breastfed infants have a higher risk for HDN than formula-fed infants. In infants, the plasma concentrations of all vitamin K dependent clotting factors are 40-60% of the adult values and slowly rise during infancy but can take up to 90 days to completely normalize even with adequate vitamin K stores. Late HDN, which presents after the first week of life, mainly manifests as intracranial haemorrhage, depending upon the site and amount of bleeding, it either results in mortality or life long sequelae in the form of cerebral palsy and scar epilepsy with or without cognitive impairment [4,5].

Hemorrhagic Disease of Newborn (HDN) was first described by Townsend in 1894. In a definitive study published in 1944, prophylactic vitamin K given at birth was shown to reduce HDN associated death by greater than fivefold in the first 2 weeks of life [2]. With evidence mounting over the next two decades, the American Academy of Pediatrics [6] stated in 1961 recommending that a single dose of vitamin K be given to all neonates shortly after birth, either 0.5-1 mg intramuscular (IM) or 1-2 mg oral. In the era of prophylaxis, HDN has become rare, with most reported cases being classical or late-onset and occurring in infants who either did not receive adequate vitamin K prophylaxis at birth and are exclusively breastfed or who had an undiagnosed malabsorptive or hepatobiliary disorder [5]. Early HDN is mainly because of the effect of maternal medications and can be effectively prevented by vitamin K at birth; when no prophylaxis is given, the rate of early HDN is 6-12% [7]. Without prophylaxis, the incidence of classical HDN is as high as 1.7% of live births [8] whereas the incidence of late HDN ranges from 4.4 to 7.2 per 100,000 live births [9]. When IM vitamin K prophylaxis is given at birth, the rate of late HDN ranges from 0.24 to 3.2 cases per 100,000 live births [10-14]. ICH occurs frequently in cases of late HDN and can lead to significant morbidity and mortality. In a pooled analysis of 131 cases, 63% of late HDN presented with ICH, with 14% mortality and 40% long-term neurological morbidity among surviving infants [15].

2. MATERIALS AND METHODS

From 1 September 2017 to 30 September 2019, we retrieved the retrospective data of 8 patients with late HDN admitted to Bapuji Child Health Institute and Chigateri Government General Hospital, Davangere.

Patients with prematurity and perinatal asphyxia were all excluded from the study. The details regarding pregnancy and delivery such as the timing of presentation, place of birth (hospital or home), signs and symptoms, bleeding sites, underlying illness of the baby, laboratory results, management, outcomes, route of vitamin K administration at birth, types of feeding were all recorded.

The diagnostic criteria of late HDN were established by the following criteria:

(a) Bleeding in an infant after seven days of life;
(b) Normal levels of fibrinogen and platelet counts;

(c) Returning to normal levels of prothrombin time (PT) and activated partial thromboplastin time (aPTT) after vitamin K administrations which were both elevated before vitamin K administration.

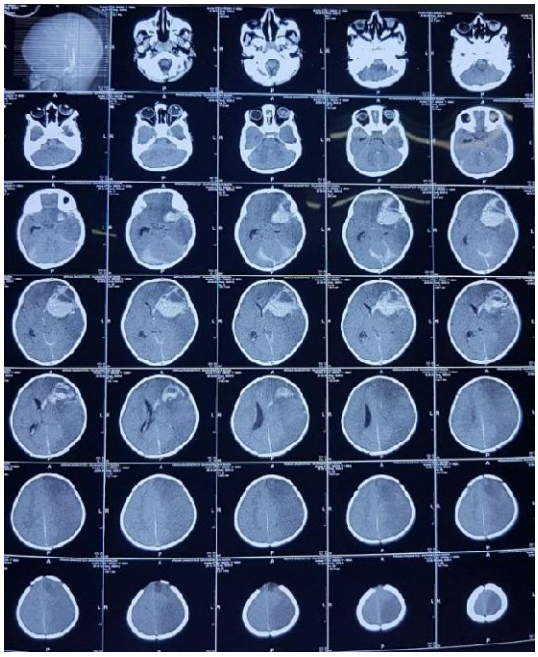

Fig. 1. CT brain showing hyperdense lesion in left frontal lobe with intraorbital extension

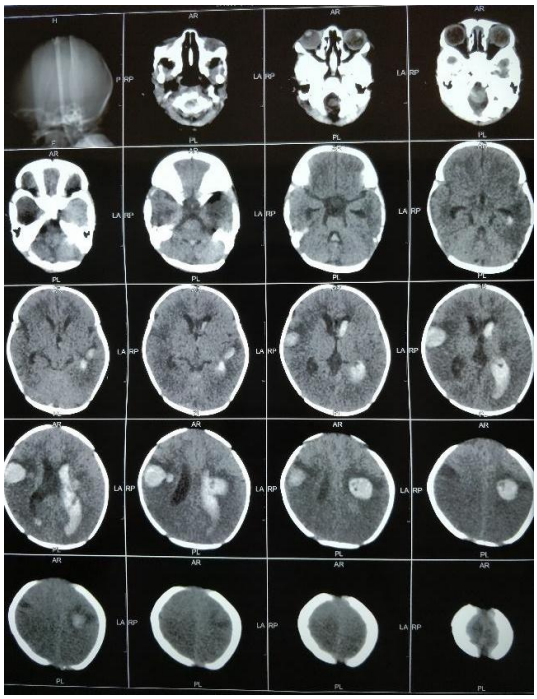

Fig. 2. CT brain showing multiple foci of acute haemorrhages in bilateral frontal, left parietal and left temporal lobes with interventricular extension along with diffuse cerebral oedema noted

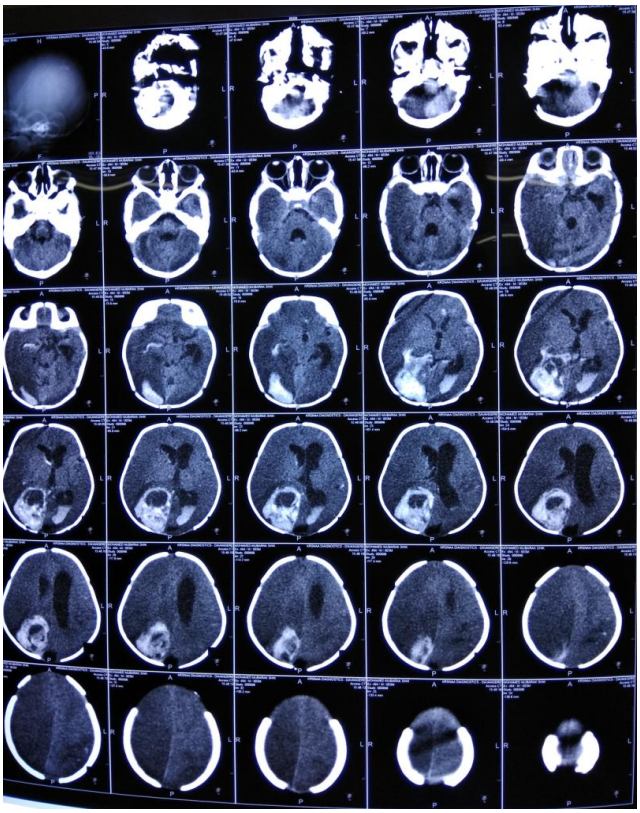

Fig. 3. CT brain showing hyperdense lesion in right occipital lobe with intraventricular extension

Laboratory results included complete blood count, clotting profile, liver function tests and urine analysis. Cranial computerised tomography and/ or magnetic resonance imaging was performed to whom suspected with ICH. All cases were evaluated for possible complications for ICH. During the follow-up period; psychomotor assessments and neurological examinations were done in all patients.

3. RESULTS AND DISCUSSION

The frequency of ICH due to late HDN in infants aged two to 24 weeks of age was six times more than reported in a study by Visser et al. in 2011 [11]. The rate of late HDN ranges from 4.4 to 7.2 cases per 100 000 births, based on reports from Europe and Asia [6-8,12-15]. The higher frequency of late HDN found by this study suggests the need to confirm these data and to check the efficiency of the prophylaxis programme.

European studies prove that intramuscular vitamin K1 prophylaxis (1 mg) is highly effective in preventing late HDN and demonstrated higher incidence of late HDN in babies who received oral vitamin K compared with those with parenteral vitamin K at birth [14,16-19]. Most patients were presented at the fifth week, with a male-to-female ratio of 1.8:1, and this was comparable with other studies [17-20]. The high percentage of exclusive breastfeeding reported in our patients raised the possibility that exclusive breastfeeding could be a predisposing factor for HDN [21,22]. This raises the problem of low concentration of vitamin K in human breast milk [4]. The predisposition to vitamin K deficiency bleeding following exclusive breastfeeding is emerging as a matter of concern, especially in developing countries where exclusive breastfeeding is vigorously advocated to promote optimal health in the infant.

Other studies reported that 88% and 97% of their studied patients with late HDN were exclusively breastfed [11-15]. On the one hand, several studies revealed that vitamin K deficiency is seen following prolonged antibiotic therapy and during severe diarrhoeal diseases, especially infectious ones and despite prophylaxis [23,24]. On the

Table 1. Demographic status, prophylaxis and outcome of patients included in the study

Sex	Age	Feeding	Vitamin K prophylaxis	Delivery place	Additional morbidity	Outcome
F	6 months	EBF	No	Home	No	Died
F	1 month	EBF	No	Ambulance	No	Died
M	2 months	EBF	No	Ambulance	No	Quadriparesis
M	1 month, 15 days	EBF	Don't know	PHC	No	Died
M	1 month, 20 days	EBF	No	Home	No	DAMA
M	3 months	EBF	No	PHC	Biliary atresia	Died
F	2 months	EBF	Yes	District hospital	Biliary atresia	No sequelae
M	2 months	EBF	Yes	District hospital	Cholestasis	No sequelae

other hand, antibiotic use and infections before the onset of the bleeding were not detailed in the reports that included a large series of patients with HDN [25,26]. Despite the national guidelines, the ground reality is that vitamin K is not given to all babies and late HDN continues to be a problem in India. The possible reasons could be lack of availability of injections, lack of trained adequate staff in health facilities, accountability and still 20% rate of home deliveries (NFHS -4, 2015 -16).

Table 2. Natural course of disease in 1-year analysis

Total duration	1 year
No of cases in 1-year analysis	8 (100.00%)
No of cases expired	5 (62.50%)
Neurological sequelae	1 (12.50%)
Recovered	2 (25.00%)
Not received Vitamin K at birth	5 (62.50%)

4. CONCLUSION

There should be a serious discussion as to how to improve the coverage of vitamin K at birth to prevent late HDN. With the rate of institutional delivery is 78.9%, the rate of BCG vaccination is 92% (NFHS -4, 2015 -16).

For neonates on strict breastfeeding, despite some with vitamin K prophylaxis, some patients still may suffer from intracranial and extracranial bleeding due to late HDN. Therefore, a change in strategy in the form of making the pediatricians and Anganwadi workers working in subcenters to give vitamin K, who have been vaccinating the babies after birth, would increase the vitamin K coverage of vitamin K prophylaxis specially among those born at home and those born at institutes but for the same reason missed the dose.

CONSENT AND ETHICAL APPROVAL

As per university standard guideline participant consent and Human Research Ethics Committee approval has been collected and preserved by the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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