INTRODUCTION

Haemorrhagic Disease of Newborn (HDN), also called vitamin K deficiency bleeding (VKDB), is the name given to the occurrence of spontaneous bleeding in early days of life.1 Bleeding can occur from birth up to six months of life.2

The term ‘haemorrhagic disease of newborn’ was first used in 1894 by Charles Townsend, when he reported a series of breast-fed infants who presented with self-limiting bleeding, usually from gastrointestinal tract, on the second or third day of life with subsequently normal hemostasis in the survivors.3

Incidence of vitamin K deficiency bleeding in babies not receiving vitamin K at birth is 0.25% to 1.7%.4 Vitamin K is essential for normal function of hemostasis.5 It is needed for the synthesis of coagulation factors II, VII, IX, and X.6 At birth, vitamin K dependent factors are reduced to about 50% of normal adult values.7

Results: The mean age at onset of symptoms was 51.65±39.49 days. Male to female ratio was 2.1:1 (p=0.047). Late onset disease (8 days to 6 months of life) was noted in 32 (72%) babies (p=0.094). Exclusive breastfeeding was noted in 45 (90%) babies (p <0.001). Thirty babies (60%) were delivered at homes (p=0.025), 13 (26%) at private clinics and 7 (14%) at government hospitals. Intracranial haemorrhage was noted in 26 (52%) babies, skin bleeding in 09 (18%) babies, gastrointestinal in 08 (16%), bleeding from injection site in 04 (8%), hematuria in 02 (4%) and bleeding from umbilicus in 01 (2%) baby. Forty babies recovered, whereas death occurred in 10 babies. The cause of death was intracranial haemorrhage in all babies (p=0.059) and all were of late onset disease (p=0.088).

Conclusion: Haemorrhagic disease of newborn was common in male gender, breast-fed infants and spontaneous vaginal deliveries. Intracranial haemorrhage and late onset disease were the causes of mortality in all cases.

Key words: Haemorrhagic disease of newborn. Intracranial haemorrhage. Vitamin K. Late onset disease.

METHODOLOGY

This cross-sectional analytical study was conducted in Paediatric Medicine Unit II, Nishtar Hospital, Multan, from June 2004 to May 2006.

The disease is classified according to the age of onset; early (first 24 hours of life), classic (2-7 days of life) and late onset (8 days to 6 months of life) disease.8 Late onset disease occurs primarily in exclusively breast-fed infants and is associated with intracranial haemorrhage in about 50% of the cases.3

Haemorrhagic disease of newborn is more common in certain group of babies like breast-fed infants, preterm babies, malabsorption, cystic fibrosis and neonatal cholestasis etc.9

Breast milk is insufficient as the source of vitamin K which contains only 1/5th of recommended daily allowance (RDA) of vitamin K (2 µg/ml) compared with formula (50 µg/ml) and cow milk (60 µg/ml).8

Outcome of HDN depends upon type of HDN, site and severity of bleeding, and presence or absence of underlying risk factors. In the absence of intracranial haemorrhage, prognosis is good.3

Haemorrhagic disease of newborn is a preventable disease with prophylactic administration of vitamin K at birth. This study was planned to find out the risk factors, presentation and outcome of this disease.
Fifty patients diagnosed as haemorrhagic disease of newborn during the study period were included in the study. Diagnosis of haemorrhagic disease of newborn was made on the basis of history of bleeding from any site without an obvious cause or predisposing factor in a baby from birth to 6-month of life along with prolonged Prothrombin Time (PT), Activated Partial Thromboplastin Time (APTT) and normal bleeding time and platelets.

Infants with obvious predisposing causes of bleeding e.g. sepsis, thrombocytopenia, neonatal hepatitis and biliary atresia were excluded.

A proforma was used to record the details of history including age at onset of bleeding, gender, place of delivery, mode of delivery, history of vitamin K given at birth or not, feeding history, history of jaundice in baby, family history of bleeding disorder, presenting complaints and acute outcome during hospital stay like cure of symptoms or death.

Detailed clinical and neurological examination was also done in all babies.

Hemoglobin level, total and differential leukocyte count, platelet count, Bleeding Time (BT), Prothrombin Time (PT) and Activated Partial Thromboplastin Time (APTT) were determined in all babies.

Computed tomogram (CT scan) was done for confirmation in whom clinical suspicion of intracranial haemorrhage was present. On the basis of age at onset of symptoms babies 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 (8 days to 6 months of life). All babies were assessed in detail for presentation (site and extent of bleeding) and risk factors like gestational age, place of delivery, mode of delivery, vitamin K given at birth or not, feeding history etc.

After taking sample for investigations, vitamin K (5 mg) was given to all babies. Fresh blood (20 ml/kg) was given to those babies who were anemic (hemoglobin < 10 gm/dl) or in shock (hypotension, poor peripheral pulses, and tachycardia). Fresh frozen plasma (10 ml/kg) was given to those babies who were not anemic. Babies were monitored daily during hospital stay for acute outcome. 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 cured.

Data was analyzed statistically by SPSS 10, to determine the frequencies and percentage of different variables including age at onset of symptoms, gender, feeding pattern, presentation (site of bleeding), mode and place of delivery, history of vitamin K given at birth or not and shortcoming outcome. Chi-square test was applied to determine the significance of difference in measurement of these variables and relationship between these variables and outcome. P-value of less than 0.05 was considered significant.

RESULTS

Fifty patients having haemorrhagic disease of newborn were studied. Out of whom 34 babies (68%) were males and 16 (32%) were females (p=0.047). Thirty six (72%) babies were of late onset disease (p=0.094). Mean age at presentation of late onset disease was 2.36±0.96 months with range of 1-4 months. Twelve (24%) babies were of classic onset disease and mean age at presentation was 2.75±1.14 days. Two (4%) babies were of early onset disease. Overall mean age at onset of symptoms was 51.65±39.49 days.

Forty two (84%) babies were delivered by spontaneous vaginal delivery while 8 (16%) by caesarean section (p=0.020). Thirty (60%) babies were delivered at homes, 13 (26%) babies at private clinics and 7 (14%) at government hospitals (p=0.025). No baby had history of vitamin K given at birth.

Exclusive breastfeeding was noted in 45 (90%) babies, while 5 (10%) babies received mixed (bottle and breast) feeding (p <0.001). Sites of bleeding are shown in Table I.

Vitamin K was given to all 50 babies after taking samples for investigations in hospital. Blood transfusion was given to 45 (90%) babies due to low hemoglobin level. Fresh frozen plasma was given to 5 (10%) babies in this study.

Forty babies (80%) recovered (p=0.045). Among those, 28 (56%) were cured (p=0.016), while 12 (24%) were discharged with focal deficit, feeding problems or low conscious level.

Death occurred in 10 (20%) babies. The cause of death was intracranial haemorrhage in all babies.

The different factors associated with the occurrence of haemorrhagic disease of newborn are shown in Table II.

Table I: Site of bleeding (total number=50).

<table>
<thead>
<tr>
<th>Site of bleeding</th>
<th>Early onset</th>
<th>Classic onset</th>
<th>Late onset</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intracranial</td>
<td>0</td>
<td>2 (4%)</td>
<td>24 (48%)</td>
<td>26 (52%)</td>
</tr>
<tr>
<td>Skin</td>
<td>0</td>
<td>1 (2%)</td>
<td>8 (16%)</td>
<td>9 (18%)</td>
</tr>
<tr>
<td>Umbilicus</td>
<td>0</td>
<td>0</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>2 (4%)</td>
<td>5 (10%)</td>
<td>1 (2%)</td>
<td>8 (16%)</td>
</tr>
<tr>
<td>Injection site</td>
<td>0</td>
<td>2 (4%)</td>
<td>2 (4%)</td>
<td>4 (8%)</td>
</tr>
<tr>
<td>Haematuria</td>
<td>0</td>
<td>2 (4%)</td>
<td>0</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>Total</td>
<td>2 (4%)</td>
<td>12 (24%)</td>
<td>36 (72%)</td>
<td>50 (100%)</td>
</tr>
</tbody>
</table>

Table II: Factors associated with haemorrhagic disease of newborn (n=50).

<table>
<thead>
<tr>
<th>Variables</th>
<th>Number of patients (%</th>
<th>Chi-square value</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male gender</td>
<td>34 (68%)</td>
<td>6.480</td>
<td>0.047</td>
</tr>
<tr>
<td>Breastfeeding</td>
<td>45 (90%)</td>
<td>32.000</td>
<td>0.001</td>
</tr>
<tr>
<td>Home delivery</td>
<td>30 (60%)</td>
<td>11.127</td>
<td>0.025</td>
</tr>
<tr>
<td>SVD*</td>
<td>42 (84%)</td>
<td>7.837</td>
<td>0.020</td>
</tr>
</tbody>
</table>

*Spontaneous vaginal delivery
Different variables were also assessed for their contribution to mortality and are shown in Table III.

### Table III: Factors associated with mortality (n=10).

<table>
<thead>
<tr>
<th>Factors</th>
<th>Number of patients (%)</th>
<th>Chi-square value</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Late onset disease</td>
<td>10 (100%)</td>
<td>4.861</td>
<td>0.088</td>
</tr>
<tr>
<td>Male gender</td>
<td>6 (60%)</td>
<td>0.483</td>
<td>0.786</td>
</tr>
<tr>
<td>Intracranial haemorrhage</td>
<td>10 (100%)</td>
<td>10.648</td>
<td>0.059</td>
</tr>
<tr>
<td>Spontaneous vaginal delivery</td>
<td>5 (50%)</td>
<td>0.893</td>
<td>0.640</td>
</tr>
<tr>
<td>Home delivery</td>
<td>6 (60%)</td>
<td>0.825</td>
<td>0.935</td>
</tr>
<tr>
<td>Breastfeeding</td>
<td>7 (70%)</td>
<td>0.278</td>
<td>0.87</td>
</tr>
</tbody>
</table>

DISCUSSION

In this study, the most common type of HDN was late onset disease noted in 72% of cases. This finding does not correspond with western studies, where classic onset disease is found to be the commonest type. This discrepancy may be due to the fact that late onset disease is confined to breast-fed babies and the practice of breastfeeding is more frequent in Asians.

In this study, 90% of babies were on exclusive breastfeeding. The high incidence of HDN in breast-fed babies is due to its low content of vitamin K. Breastfeeding is an important risk factor for HDN especially for late onset disease. McNinch, Bor O and D’Souza described that late onset VKDB remains virtually confined to breast-fed infants.

Males were affected more than females in this study. Male gender was found as risk factor for HDN by Nakagawa et al. as well.

Most of babies were delivered at home in this study. Vitamin K was not given to those babies who delivered at home. None of the patient presenting with HDN in this study had history of vitamin K given at birth. This showed that our traditional birth attendants are unaware about the importance of administration of vitamin K at birth.

The most common presentation of HDN was intracranial haemorrhage noted in 52% of cases.

Most of those patients (24 out of 26) were of late onset HDN, showing that the intracranial haemorrhage is the common presentation of late onset disease. Pooni et al. mentioned 71% incidence of intracranial haemorrhage in late onset disease. McNinch and Tripp described 37% incidence of intracranial haemorrhage in their study. Zengin and Hubbard mentioned that late HDN frequently presents with intracranial haemorrhage leading to high morbidity and mortality. Intracranial haemorrhage is the major determinant of outcome of HDN.

The next common presentation was bleeding into the skin noted in 9 (18%) patients in this study. Skin bleeding was noted in late onset disease in most of patients (8 out of 9), in association with intracranial haemorrhage. Skin bleeding was noted in 30% of patients in late onset disease by Flood et al. Visible external bleeding was noted in 1/3rd of patients with intracranial haemorrhage by Pooni and is considered as warning sign in late onset disease for intracranial haemorrhage.

Gastrointestinal bleeding was noted in 8 (16%) patients in this study. This finding correlates with Ijland et al. study mentioning gastrointestinal bleeding in 17% of patients with late onset disease. Gastrointestinal bleeding was noted in 62% of patients in classic onset disease in this study. Gastrointestinal bleeding is a common presentation of classic onset disease.

In this study, majority of babies (80%) recovered and got discharged. This showed that HDN has good prognosis when adequately treated and not associated with intracranial haemorrhage. This can be correlated with Aydinli study in which no case fatality was noted.

Death occurred in 10 (20%) babies in this study. Mortality was observed in 26% by Lulseged and 32% of patients by Demiroren.

In this study, the cause of death was intracranial haemorrhage in all babies and all were of late onset disease. This finding correlates with other studies mentioning late onset disease as major factor for mortality and morbidity. Late HDN may be associated with serious and life-threatening intracranial haemorrhage leading to high mortality and morbidity in developing countries, where vitamin K prophylaxis is not routinely practiced.

Vitamin K deficiency bleeding is a preventable problem and prevention can be done by prophylactic administration of vitamin K to all newborns.

Small sample size was a major limitation of this study, limiting the generalization of results, still it provides a data-base from local perspective. Further large-scale studies are required.

CONCLUSION

Haemorrhagic disease of newborn was more common in male infant, breast-fed infants, spontaneous vaginal delivery and home delivery. The most common type was the late onset disease. Late onset disease and intracranial haemorrhage showed a trend towards higher mortality.

Vitamin K deficiency bleeding is a preventable disease, which can lead to death or permanent brain damage so vitamin K needs to be administrated to every newborn as a prophylaxis against haemorrhagic disease of newborn.
REFERENCES


