Incidence and causes of neonatal hyperbilirubinemia in a center of Catania

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Aim and scope: We conducted this study to estimate the incidence of hyperbilirubinemia in a small neonatal care unit in Catania, Italy, and to determine the underlying causes, which would be of value in identifying and implementing strategies to prevent morbidity from this condition.

Background: Management of hyperbilirubinemia remains a challenge for neonatal medicine because of the risk for serious neurological complications related to the toxicity of bilirubin.

Methods: From January 2006 to January 2007, we screened 525 newborns born at the Neonatal Care Unit of Valsalva Hospital in Catania, Italy. Infants aged 3–5 days and with unconjugated hyperbilirubinemia were included for assessment if they had a peak serum total bilirubin level exceeding 6 mg/dl (102 μmol/L). Sex, birth weight, gestational age, breast feeding, type of birth, presence of facial bruising (including cephalohematoma) and ABO group were noted. Patients with Toxoplasma or Cytomegalovirus infection, hepatic insufficiency, or suspected drug-induced hyperbilirubinemia were excluded from more detailed analysis.

Results: Our year-long nursery sample examined otherwise healthy-appearing term infants for the prevalence of hyperbilirubinemia (defined as bilirubin levels exceeding 6 mg/dL [11 mol/L]). We found hyperbilirubinemia in 19% (100/525). Among the patients with hyperbilirubinemia, almost all (99%) had peak levels of bilirubin >20 mg/dL, levels which are generally considered to be potentially neurotoxic.

Conclusions: In our clinic experience, hyperbilirubinemia was generally a serious medical issue and one whose etiology can usually be well defined.

Keywords: hyperbilirubinemia, newborns, incidence, breastfeeding

Introduction

Severe hyperbilirubinemia continues to be the most common cause of neonatal readmission for hospitals in North America. This pattern continues despite attempts to identify newborns at risk of clinically important hyperbilirubinemia before they are discharged from hospital. Long-term results of severe hyperbilirubinemia, including bilirubin encephalopathy and kernicterus, were thought to be rare since the advent of exchange transfusion, maternal Rh immunoglobulin prophylaxis, and phototherapy. However, cases of kernicterus have been reported recently in healthy near-term and term infants without evidence of hemolytic disease or other risk factors.

We begin our study of this problem with a survey of a single clinic experience over a year with respective to severity and probable causes of hyperbilirubinemia.

Background

Management of hyperbilirubinemia remains a challenge for neonatal medicine because of the risk for serious neurological complications related to the toxicity of bilirubin. The neonatal hyperbilirubinemia practice guidelines published in 2004 by the American Academy of Pediatrics (AAP) expresses the pediatric community’s concern regarding bilirubin-induced neurological pathology. Risk factors recognized...
to be associated with severe hyperbilirubinemia in newborns have included jaundice in the first 24 hours of life, jaundice noted before discharge from hospital, a sibling who had jaundice treated with phototherapy, near-term gestational age of 35–36 weeks, and the presence of infant with bruising or cephalohematoma.

Materials and methods
From January 2006 to January 2007, we screened 525 newborns born at the Neonatal Care Unit of Valsalva Hospital in Catania, Italy. Infants aged 3–5 days and with unconjugated hyperbilirubinemia were included for assessment if they had a peak serum total bilirubin level exceeding 6 mg/dl (102 μmol/L). Sex, birth weight, gestational age, breast feeding, type of birth, presence of facial bruising (including cephalohematoma), and ABO group were noted. Patients with *Toxoplasma* or *Cytomegalovirus* infection, hepatic insufficiency, or suspected drug-induced hyperbilirubinemia were excluded from more detailed analysis.

We focused on healthy term infants without risk factors. Infants who had known Rh iso-immunization were excluded since antenatal and postnatal strategies already exist to prevent the occurrence of severe neonatal hyperbilirubinemia from this cause. Infants who were born at less than 36 weeks’ gestational age were also excluded as well as newborn with severe facial bruising or cephalohematoma from more detailed analysis.

Data were summarized using descriptive statistics. Continuous variables were analyzed using the independent Student’s t-test and Fisher’s exact test. A chi square test was used to test associations between all other categorical variables.

Results
We found 100 children with unconjugated hyperbilirubinemia. Causes identified by laboratory investigations include Rh and ABO incompatibility, as well as glucose-6-phosphate dehydrogenase (G6PD) deficiency. We found potentially neurotoxic levels of hyperbilirubinemia in only one case, with value of peak bilirubin of 20 mg/dL (342 mmol/L), treated with phototherapy. The other 99 cases had milder hyperbilirubinemia and did not receive any treatment.

In our series, we found breastfeeding in 65 cases, cesarean section in 61, and mild facial bruising in 16. Medicaments during the pregnancy were used in 39 cases and post-pregnancy in 35 (Table 1). A single case showed evidence of liver disease (Gilbert disease). *Cytomegalovirus* and toxoplasmosis infection were found in 2% and 6% of the cases, respectively (Table 1). Maternal microcytosis was found in two cases.

We also evaluated the ABO group in the mothers and in the newborns (Table 2). No significant differences were found in the examined group. No other risk factors were found in those patients.

We tried to analyze the characteristics of neonatal jaundice. We took in consideration over 525 children, 100 infants with a value of bilirubin level of more than 6 mg/dl (102 μmol/L) (Table 3).

Discussion

Hyperbilirubinemia is felt to be a benign condition for infants born at term or near-term gestation. In around 5% of healthy term infants, however, serum bilirubin values exceed 17 mg/dL (291 mmol/L), a value which the AAP deems significant. Levels exceeding 20 mg/dL (342 mmol/L) occur in 1.2% of healthy newborn infants. The vast majority of infants with serum bilirubin values of 20 mg/dL remain well; mostly need minimal care other the occasional use of phototherapy and careful monitoring of serum levels. Before 1990, kernicterus in the previously healthy-term infant was extraordinarily rare and for most pediatricians, it was a

<table>
<thead>
<tr>
<th>Table 1 Pregnancy factors</th>
<th>Yes</th>
<th>No</th>
<th>Total</th>
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</thead>
<tbody>
<tr>
<td>Breastfeeding</td>
<td>65</td>
<td>35</td>
<td>100</td>
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<tr>
<td>Cesarian section</td>
<td>61</td>
<td>39</td>
<td>100</td>
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<td>Spontaneous delivery</td>
<td>39</td>
<td>61</td>
<td>100</td>
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<tr>
<td>Bruising face</td>
<td>16</td>
<td>84</td>
<td>100</td>
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<tr>
<td>Drugs in pregnancy</td>
<td>39</td>
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<td>Drugs after pregnancy</td>
<td>35</td>
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<tr>
<td>Liver disease</td>
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<td>99</td>
<td>100</td>
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<tr>
<td><em>Cytomegalovirus</em> in pregnancy</td>
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<td>98</td>
<td>100</td>
</tr>
<tr>
<td>Microcytemic mother</td>
<td>2</td>
<td>98</td>
<td>100</td>
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<table>
<thead>
<tr>
<th>Table 2 Blood groups</th>
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<th>Children group</th>
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<tr>
<td>0−</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>0+</td>
<td>52</td>
<td>48</td>
</tr>
<tr>
<td>A−</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>A+</td>
<td>17</td>
<td>29</td>
</tr>
<tr>
<td>B−</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>B+</td>
<td>16</td>
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<tr>
<td>AB−</td>
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<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>
Our series comes from a small center in Catania, Italy. Catania is one of the sunniest spots on Earth, with approximately 225 sunny days per year (which does not include partly cloudy days). It is possible that this plays some role in the relatively low incidence of hyperbilirubinemia in our studies as compared to previous studies. Furthermore, future studies should investigate the presence of individual susceptibility, environmental factors, especially environmental climate (daylight), and genetic factors to explain the different incidences of the disease, and the frequency of such findings in infants with moderate degrees of hyperbilirubinemia and possible modes of prevention and new therapeutic strategies.

### Table 3 Characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Value</th>
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<tbody>
<tr>
<td>No (%) of infants</td>
<td>100</td>
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<tr>
<td>Gestational age, wk, mean (SD)</td>
<td>38.5 (1.4)</td>
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<tr>
<td>Sex: male and female</td>
<td>42 and 68</td>
</tr>
<tr>
<td>Birth weight, g, mean (SD)</td>
<td>3250 (± 489)</td>
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<tr>
<td>Age at presentation of jaundice, h, mean (SD)</td>
<td>78.5</td>
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<tr>
<td>Breast-feeding</td>
<td>65</td>
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<tr>
<td>Peak total bilirubin level, μmol/L, mean (SD)</td>
<td>186 (± 76)</td>
</tr>
</tbody>
</table>

### Disclosure

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### References