Complications and Outcome of Exchange Blood Transfusion in Neonatal Unconjugated Hyperbilirubinemia

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Abstract

Introduction: Neonatal jaundice is a common neonatal problem, usually have a benign course however in certain unmonitored and untreated conditions, unconjugated hyperbilirubinemia can progress to acute bilirubin encephalopathy, exchange blood transfusion although rarely used now in developed countries still commonly used in developing countries.

Aim of the Work: To assess complications of exchange blood transfusion (EBT) for hyperbilirubinemia, also to study its incidence with exploration of cases with Kernicterus in neonatal intensive care unit (NICU), new children hospital Cairo University.

Patient and Method: A retrospective study in the NICU, new children hospital Cairo University, where data of all cases with neonatal hyperbilirubinemia who were underwent (EBT) over one year starting the first of January – end of December 2007 were collected from patients files and analyzed.

Result: EBT accounted for (30.9%) of NICU cases with neonatal jaundice, 43.8% were females and 56.2% were males, 72.6% delivered by NVD with mean gestational age 37.36 ± 1.67 weeks, the mean age at presentation was 5.4 days ± 2.9 (1-20) and the mean body weight was 2.73 ± 0.54kg. ABO incompatibility accounted for 51.9% of causes of jaundice and no cause can be determined in 27.4% of cases, Kernicterus was recorded in 18 cases 8.6%, pre-exchange bilirubin level was the most important determinate factor with (p value 0.000). Complications of EBT included hypoglycaemia (10.09%), hypocalcaemia (25.5%), hyponatremia (6.3%), hypernatremia (3.84%), Hypokalemia (5.3%) and hyperkalemia (5.3%). Thrombocytopenia was recorded in (28.36%), cholestasis in (9.6%). NEC (0.5%), sepsis (18.3%). Mortality was recorded in 14 cases (6.7%) and it was correlated with GA and age at presentation with (p value 0.03) for both, mortality was more common among kernicteric group with (p value 0.02).

Conclusion: Incidence of neonatal jaundice among NICU is high, exchange blood transfusion was done more frequently which could be explained by relative late presentation with high mean bilirubin level causes of severe neonatal hyperbilirubinemia were undetermined in 27.4% complication of EBT included, electrolytes disturbances, thrombocytopenia and cholestasis, major complications included NEC, sepsis and death. Kernicterus still recorded in NICU with bad outcome and the most important determinant factor for it is a pre-exchange bilirubin level.

Key Words: Neonate – Jaundice – Kernicterus – Exchange – Complications.

Introduction

ALTHOUGH the frequency of neonatal exchange transfusions (ETs) has declined markedly in the past 20 years in the United States, newly diagnosed Kernicterus cases are continuing to be reported in different areas of the world [1]. ET is still performed in many countries to prevent the development of Kernicterus, especially in countries with a high incidence of neonatal hyperbilirubinemia Umbilical vessels, especially the umbilical vein (UV), are used in conventional double-volume blood ETs in neonates with hyperbilirubinemia; however, the incidence of adverse events, including death, associated with this method are high [2]. Over 60% of all 3.5 million healthy babies admitted to well baby nurseries in USA will develop jaundice and be diagnosed with hyperbilirubinemia during the first week after birth. In its 2004 guideline on management of neonatal hyperbilirubinemia, the American Academy of Pediatrics (AAP) recommended every newborn be assessed for risk of severe hyperbilirubinemia before hospital discharge, using either pre-discharge bilirubin (PDB) measurement (transcutaneous or serum), assessment of clinical risk factors, or both. The guideline also recommends all bilirubin measurements be interpreted according to the infant’s age in hours, and suggests the use of a published bilirubin 'nomogram' in which the percentile location of a PDB level is used to classify the risk of developing severe hyperbilirubinemia as low (<40th percentile), low-intermediate (40-75th percentile), high-intermediate
These excessively jaundiced but otherwise healthy babies are at risk of bilirubin-related brain damage (Kernicterus) within the first two weeks after birth. As determined in large prospectively studied US and multi-national study populations, severe hyperbilirubinemia occurs in 8.1% to 9% of the healthy and near-term well baby populations who have hour specific TSB values above the 95th percentile (high-risk zone) during the first seven postnatal days [4]. Unmonitored and untreated hyperbilirubinemia can progress to acute bilirubin encephalopathy with invariable post-icteric sequelae. Preventive intervention options include nutrition and lactation support (to decrease the entero-hepatic reabsorption of bilirubin), intensive phototherapy (for an effective reduction of the bilirubin load) or an exchange transfusion (for a dramatic clearance of bilirubin) [5].

Exchange blood transfusion is indicated if the bilirubin concentration does not decrease after adequate hydration and four to six hours of intensive phototherapy, so if phototherapy fails to control the rising bilirubin levels, exchange transfusion is necessary to lower serum bilirubin concentration. Also exchange transfusion is indicated for severe hyperbilirubinemia with hemolysis and signs and symptoms of Kernicterus with different amounts of bilirubin. Small amounts of blood are removed and replace by blood from Umbilical vein catheter so antibody-coated RBCs with uncoated donor RBCs are removed [6]. Because exchange transfusions are now rarely performed, the risks of morbidity and mortality associated with the procedure are difficult to quantify. Death associated with exchange transfusion has been reported in approximately 3 in 1000 procedures, although in otherwise well infants of 35 or more weeks’ gestation, the risk is probably much lower. Significant morbidity (apnea, bradycardia, cyanosis, vasospasm, thrombosis, necrotizing enterocolitis) occurs in as many as 5% of exchange transfusions, and the risks associated with the use of blood products must always be considered. Hypoxic-ischemic encephalopathy and acquired immunodeficiency syndrome have occurred in otherwise healthy infants receiving exchange transfusions [3,7,8].

The aim of this study is to assess complications of exchange blood transfusion (EBT) for hyperbilirubinemia, also to study its incidence with exploration of cases with Kernicterus in neonatal intensive care unit (NICU), new children hospital Cairo University.

**Patients and Methods**

This study is a retrospective study in the NICU, new children hospital Cairo University, data of all cases with neonatal hyperbilirubinemia who were underwent (ETB) over one year starting the first of January – end of December 2007 were collected from patients files and analyzed, these data included the following, gestational age, sex, weight, age at presentation, mode of delivery, type of feeding, presence of maternal illness, data of detailed clinical examination especially those indicating Kernicterus, presence of NEC, haemoglobin % and retics.

EBT was done as per established protocols in the unit according to body weight, age at presentation, and level of bilirubin (total and direct), haemoglobin % and retics.

Detailed laboratory data included bilirubin, pre and post exchange, maternal and baby blood group, complete blood count, reticates, direct coomb’s, glucose, serum electrolytes, Ca, Na, K. and results of blood cultures.

**Exclusion criteria included:**

Exchange transfusion done for other causes rather than hyperbilirubinemia and blood culture positive neonates prior to exchange transfusion.

**The statistical analysis:**

Data were statistically described in terms of range, mean ± standard deviation (± SD), median, frequencies (number of cases) and percentages when appropriate. Comparison of quantitative variables between the study groups was done using Mann Whitney U test for independent samples. For comparing categorical data, Chi square (χ²) test was performed. Exact test was used in stead when the expected frequency is less than 5. A probability value (p value) less than 0.05 was considered statistically significant. All statistical calculations were done using computer programs Microsoft Excel 2003 (Microsoft Corporation, NY, USA) and SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 15 for Microsoft Windows.

**Results**

In this study 208 newborns were recorded to have EBT, they represent 30.1% of the neonates admitted to the NICU with jaundice (671 newborns) and 19.1% of the total NICU admission (1089) the recorded data showed that female/male ratio was
91/117, 27.4% of them were delivered by cesarean section and in 16.8% of them history of maternal illness was present and history of gestational diabetes was present only in 4 cases. The mean gestational age was 37.36 ± 1.67 weeks, the mean age at presentation was 5.4 days ± 2.9 (1-20) and the mean body weight was 2.73 ± 0.54kg, 9.1% of the study populations were less than 37 weeks of gestation as shown in (Table 1) which represent a comparison between neonates less and more than 37 weeks as regards demographic data, pre-exchange bilirubin and clinical complication of EBT.

In (Table 1) there is highly statistical significant difference between weight of neonates more than 37 gestational weeks (2.8 ± 0.450) and weight of neonates less than 37 gestational weeks (1.96 ± 0.485) with \( p = 0.000 \). The difference was statistically significant between bilirubin on admission of neonates more than 37 weeks (32.79 ± 8.15) and neonates less than 37 weeks (26 ± 8.5) with \( p = 0.001 \). Mortality was higher with statistical significant difference in neonates less than 37 weeks (21%) compared to neonates more than 37 weeks (5.2%) with \( p = 0.03 \).

In this study the causes of neonatal jaundice were ABO incompatibility followed by Rh incompatibility and in 27.4% no cause could be determined as shown in Fig. (1).

Kernicterus being a reemerging problem in this study we focused on risk factors associated with Kernicterus, 8.65% in the current study reported to have signs and symptoms indicating acute bilirubin encephalopathy so for diagnosis of acute stage Kernicterus, the minimum eligibility criteria for the registry required documentation of signs of irritability and hypertonia, with early retocolis and opisthotonus, together with any one of the following: drowsiness, poor feeding, alternating tone, high-pitched cry, or a failed auditory brainstem response (ABR) hearing screen [9].

The common presenting symptoms of newborns with Kernicterus were as follow, poor feeding 94.4%, irritability 83.3%, abnormal movements and seizures 50%, opisthotonus and retocolis in 33.3%, hypotonia in 27.7%, abnormal respiration, apnea, progressed to death in 22.2%.

Table (3) shows a highly statistical significant difference between bilirubin on admission in Kernicterus group (45.66 ± 10.65) and non Kernicterus group (30.8 ± 6.9) with \( p = 0.000 \). The difference was statistically significant between causes of jaundice in Kernicterus and non Kernicterus groups with \( p = 0.05 \). 72% of kernicteric group were diagnosed as ABO incompatibility. The presence of cholestasis was higher in Kernicterus group with a high statistical significant difference \( (p = 0.000) \). Positive Coombs test and Retics > 6.5% were higher in Kernicterus group with statistical significant difference \( (p = 0.000) \) and \( (p = 0.012) \) respectively. Mortality in Kernicterus group 4 (22.2%) was a higher than non Kernicterus group 10 (5.35%) with a statistical significant difference \( p = 0.02 \).

As shown in Fig. (2) mean bilirubin on admission was statistically significant different between kernicteric and non kernicteric group.

Fig. (3) showed the difference between mean bilirubin level on admission (32.17 ± 8.39) and the mean bilirubin level after exchange blood transfusion (21.83 ± 7.76).

This high incidence of exchange blood transfusion was accompanied by some complications, some of these complications were laboratory findings and others were life threatening. Table (4) represents the Post Exchange laboratory complications in the study group.

Other complications included presence of cholestasis which is defined as a conjugated bilirubin (CB) greater than 15% of the total bilirubin level [16], in this study 20 neonates 9.6% developed cholestasis and Table (5) represent a comparison between them and the other group with no cholestasis.

Table (5) showed Bilirubin on admission was higher in cholestasis group (42.49 ± 12.72) than non cholestasis group (31.07 ± 7) with a high statistical significant difference \( (p = 0.000) \). Cholestasis was more common among Kernicterus group (40%) than non kernicteric group with \( p \) value= 0.000, however all death were in the non cholestatic groups. NEC as a complication of EBT was recorded in one newborn who was a full term boy, 3 kg, with total bilirubin level 31.8 mg/dL underwent EBT twice his blood culture was positive with no manifestation of Kernicterus, the baby improved on treatment.

Other complication of EBT include development of neonatal sepsis, it was recorded in 38 patients 18.2% and confirmed by blood culture and (Table 6) represent comparison between the patients groups as regards presence of sepsis.
Table (6) shows no statistical significant difference between sepsis and non sepsis groups as regards: gestational age, weight, bilirubin on admission, development of Kernicterus and mortality.

Mortality as a complication of EBT was reported in 14 patients 6.7% in our study group as shown in Fig. (4).

Table (7) represents risk factors for mortality among the studied groups.

Risk factors for mortality with statistically significant difference included gestational age <37 weeks, age at presentation, neonates with coombs positive, hemoglobin % <10g/dL and development of Kernicterus. With p value (0.03, 0.03, 0.001, 0.036 and 0.02) respectively.
Table (2): Pre-exchange laboratory parameter in jaundiced neonates.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Non kernicterus</th>
<th>Kernicterus</th>
<th>$p$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gestational age (wks):</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;37 wks</td>
<td>19 (10%)</td>
<td>0</td>
<td>0.165</td>
</tr>
<tr>
<td>&gt;37 wks</td>
<td>171 (90%)</td>
<td>18 (100%)</td>
<td></td>
</tr>
<tr>
<td><strong>Body weight (kg):</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean±SD</td>
<td>2.73±0.563</td>
<td>2.75±0.340</td>
<td>0.86</td>
</tr>
<tr>
<td>Range</td>
<td>(1.38-4.5)</td>
<td>(2-3.2)</td>
<td></td>
</tr>
<tr>
<td><strong>Age at presentations (days):</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean±SD</td>
<td>5.34±2.8</td>
<td>6.06±3.96</td>
<td>0.4</td>
</tr>
<tr>
<td>Range</td>
<td>(1-17)</td>
<td>(2-20)</td>
<td></td>
</tr>
<tr>
<td><strong>Bilirubin on admission (mg/dl):</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean±SD</td>
<td>30.8±6.9</td>
<td>45.66±10.65</td>
<td>0.000*</td>
</tr>
<tr>
<td>Range</td>
<td>(16.5-57.2)</td>
<td>(27.9-68.7)</td>
<td></td>
</tr>
<tr>
<td><strong>Cause of jaundice:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ABO%</td>
<td>95 (50%)</td>
<td>13 (72.2%)</td>
<td>0.05*</td>
</tr>
<tr>
<td>Rh%</td>
<td>39 (20.5%)</td>
<td>4 (2.2%)</td>
<td></td>
</tr>
<tr>
<td>Not determined %</td>
<td>56 (29.5%)</td>
<td>1 (5.6%)</td>
<td></td>
</tr>
<tr>
<td><strong>Presence of sepsis %:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cholestasis %</td>
<td>32 (16.8%)</td>
<td>6 (33.3%)</td>
<td>0.1</td>
</tr>
<tr>
<td>Not determined %</td>
<td>12 (6.3%)</td>
<td>8 (44.4%)</td>
<td>0.000*</td>
</tr>
<tr>
<td><strong>Positive coombs test %:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hb &lt;10 g/dL, %</td>
<td>11 (5.7%)</td>
<td>7 (38.8%)</td>
<td>0.000*</td>
</tr>
<tr>
<td>Retics &gt;6.5%</td>
<td>37 (19.5%)</td>
<td>4 (22%)</td>
<td></td>
</tr>
<tr>
<td>Mortality %</td>
<td>49 (25.8%)</td>
<td>10 (55.6%)</td>
<td>0.012*</td>
</tr>
<tr>
<td>Not determined %</td>
<td>10 (5.3%)</td>
<td>4 (22.2%)</td>
<td>0.02*</td>
</tr>
</tbody>
</table>

$p$ value <0.05= significant.

Table (3): Comparison between kernicterus and non kernicterus patients.

Table (4): Electrolytes disturbance and thrombocytopenia.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Total number of studied patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrombocytopenia &lt;100.000</td>
<td>59 (28.36%)</td>
</tr>
<tr>
<td>Hypoglycemia ≤50mg/dL [10]</td>
<td>21 (10.09%)</td>
</tr>
<tr>
<td>Hypocalcaemia &lt;7 mg/dL [11]</td>
<td>53 (25.5%)</td>
</tr>
<tr>
<td>Hyponatremia &lt;125mEq/L [12]</td>
<td>13 (6.3%)</td>
</tr>
<tr>
<td>Hypernatremia &gt;150mEq/L [13]</td>
<td>8 (3.84%)</td>
</tr>
<tr>
<td>Hyperkalemia &gt;6mEq/L [14]</td>
<td>11 (5.3%)</td>
</tr>
<tr>
<td>Hypokalemia &lt;3.5mEq/L [15]</td>
<td>11 (5.3%)</td>
</tr>
</tbody>
</table>

Table (5): Comparison between cholestasis and non cholestasis groups.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>No cholestasis</th>
<th>Cholestasis</th>
<th>$p$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gestational age (wks):</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;37 wks</td>
<td>18 (9.57%)</td>
<td>1 (4.52%)</td>
<td>0.7</td>
</tr>
<tr>
<td>&gt;37 wks</td>
<td>170 (90.42%)</td>
<td>19 (9%)</td>
<td></td>
</tr>
<tr>
<td><strong>Body weight (kg):</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean±SD</td>
<td>2.726±0.553</td>
<td>2.806±0.484</td>
<td>0.57</td>
</tr>
<tr>
<td>Range</td>
<td>(1.38-4.5)</td>
<td>(1.5-3.5)</td>
<td></td>
</tr>
<tr>
<td><strong>Bilirubin on admission (mg/dl):</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean±SD</td>
<td>31.07±7</td>
<td>42.49±12.72</td>
<td>0.000*</td>
</tr>
<tr>
<td>Range</td>
<td>(16.5-52)</td>
<td>(23.5-68.7)</td>
<td></td>
</tr>
<tr>
<td><strong>Kernicterus:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deaths</td>
<td>10 (5.31%)</td>
<td>8 (40%)</td>
<td>0.000*</td>
</tr>
<tr>
<td>Mortality %</td>
<td>14 (7.4%)</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

$p$ value <0.05= significant.

Table (6): Comparison between sepsis and non sepsis groups.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>No sepsis</th>
<th>Sepsis</th>
<th>$p$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gestational age (wks):</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;37 wks</td>
<td>14 (8.24%)</td>
<td>5 (13.16%)</td>
<td>0.5</td>
</tr>
<tr>
<td>&gt;37 wks</td>
<td>156 (91.76%)</td>
<td>33 (86.84%)</td>
<td></td>
</tr>
<tr>
<td><strong>Body weight (kg):</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean±SD</td>
<td>2.745±0.502</td>
<td>2.683±0.720</td>
<td>0.6</td>
</tr>
<tr>
<td>Range</td>
<td>(1.51-3.85)</td>
<td>(1.38-4.5)</td>
<td></td>
</tr>
<tr>
<td><strong>Bilirubin on admission (mg/dl):</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean±SD</td>
<td>31.7±7</td>
<td>34.27±10.17</td>
<td>0.09</td>
</tr>
<tr>
<td>Range</td>
<td>(16.5-65.5)</td>
<td>(18.3-68.3)</td>
<td></td>
</tr>
<tr>
<td><strong>Kernicterus:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deaths</td>
<td>12 (7.58%)</td>
<td>6 (15.78%)</td>
<td>0.1</td>
</tr>
<tr>
<td>Mortality %</td>
<td>11 (6.47%)</td>
<td>3 (7.89%)</td>
<td>0.76</td>
</tr>
</tbody>
</table>
Table (7): Risk factors for mortality among studied neonates.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Alive n=194</th>
<th>Deaths n=14</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gestational age (wks):</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;37 wks</td>
<td>15 (7.73%)</td>
<td>4 (28.57%)</td>
<td>0.03 *</td>
</tr>
<tr>
<td>&gt;37 wks</td>
<td>179 (92.26%)</td>
<td>10 (71.42%)</td>
<td></td>
</tr>
<tr>
<td><strong>Body weight (kg):</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean±SD</td>
<td>2.75±0.563</td>
<td>2.68±0.350</td>
<td>0.85</td>
</tr>
<tr>
<td>Range</td>
<td>(1.37-4.4)</td>
<td>(1.9-3.1)</td>
<td></td>
</tr>
<tr>
<td><strong>Age at presentations (days)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean±SD</td>
<td>5.51±2.97</td>
<td>3.93±1.38</td>
<td>0.03 *</td>
</tr>
<tr>
<td>Range</td>
<td>(1-20)</td>
<td>(2-7)</td>
<td></td>
</tr>
<tr>
<td><strong>Bilirubin on admission (mg/dL):</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean±SD</td>
<td>32.2±8.3</td>
<td>31.4±9.99</td>
<td>0.8</td>
</tr>
<tr>
<td>Range</td>
<td>(16.5-68.7)</td>
<td>(16.5-52)</td>
<td></td>
</tr>
<tr>
<td><strong>Cause of jaundice:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ABO%</td>
<td>103 (53.1%)</td>
<td>5 (35.7%)</td>
<td></td>
</tr>
<tr>
<td>Rh</td>
<td>39 (20.1%)</td>
<td>4 (28.6%)</td>
<td>0.4</td>
</tr>
<tr>
<td>Not determined</td>
<td>52 (26.8%)</td>
<td>5 (35.7%)</td>
<td></td>
</tr>
<tr>
<td><strong>Presence of sepsis:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cholestasis</td>
<td>35 (18.04%)</td>
<td>3 (21.4%)</td>
<td>0.2</td>
</tr>
<tr>
<td><strong>Positive coombs test:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hb &lt;10 g/dL</td>
<td>12 (6.81%)</td>
<td>6 (42.8%)</td>
<td>0.001 *</td>
</tr>
<tr>
<td>Retics &gt;6.5%</td>
<td>35 (18%)</td>
<td>6 (42.9%)</td>
<td>0.036*</td>
</tr>
<tr>
<td>Kernicterus</td>
<td>55 (28.4%)</td>
<td>4 (28.6%)</td>
<td></td>
</tr>
<tr>
<td><strong>Kernicterus</strong></td>
<td>14 (7.2%)</td>
<td>4 (28.6%)</td>
<td>0.02 *</td>
</tr>
</tbody>
</table>

*p value <0.05= significant.

Discussion

In this study EBT was done in 208 newborns for neonatal hyperbilirubinemia representing 19.1% of total number of NICU admission (1089) and 30.1% of total number of jaundiced patients 671, this a relatively similar incidence of exchange to the one reported in study of Soud et al. who found that the incidence of neonatal hyperbilirubinemia 38.2% and exchange transfusion was done in 22.5% of the jaundiced babies [17]. Whereas in the study of Joshua and Titus, 1 in every 20 babies admitted to the NICU had exchange blood transfusion they relayed this high incidence of EBT to their inability to carry out intensive phototherapy [18]. In developed countries invasive intervention EBT is thus limited to about 5% of the healthy newborn infants [19]. In the current study high incidence of EBT can be explained by being a referral unit and not a maternity hospital, neonates usually presented to our unit in late stage with the mean pre-exchange bilirubin is higher than other studies as it reached up to 31 ±8.39 and its maximum up to 68.7 mg/dL this may be relayed to late presentation (5.4±2.91) days with maximum 20 days, together with the concept of early neonatal discharge from maternity unit without setting specific follow-up dates being presented late with high level of bilirubin not only increase the incidence of the EBT which is an invasive procedures exposing the neonates to many hazards but also increase risk for Kernicterus. In this study causes underlying severe hyperbilirubinemia included ABO incompatibility in 52%, Rh incompatibility in 20.6% and no cause can be determined in 27.4%, although G6PD deficiency represents a significant importance in cases of neonatal hyperbilirubinemia, we did not get its results from the recorded files. The incidence of ABO incompatibility was 23%, Rh incompatibility 10.9% and G6PD 3.2% and the cause of jaundice was undetermined in more than 40% of cases in the study of Seoud et al. [17]. In another study Joshua and Titus, ABO incompatibility accounted for 30% and G6PD deficiency in 34.4% and other causes like septicemia in 26% [18].

In another study Sgro et al. who prospectively studied cases of severe neonatal jaundice the cause can be identified only in 36% of cases, ABO incompatibility being the main cause [20]. Gestational age <37 weeks was found in 9.13% of cases and it was statistically correlated with the bilirubin level on admission, also other studies revealed that neonates at <37 weeks are four times more likely to have high serum bilirubin than full term babies which could be explained by exaggerated hepatic immaturity and lack of vigorous breast feeding [21]. Kernicterus being the most easily preventable cause of neonatal mortality and brain damage, so in this study we tried to focus on risk factors associated with Kernicterus, 8.65% in the current study reported to have signs and symptoms indicating acute bilirubin encephalopathy. In the study of Seoud et al., 5.2% were diagnosed to have Kernicterus [17]. In comparison to much higher incidence in the study of Joshua, it was 30% [18]. In this study, there was no statistically significant correlation between Kernicterus and gestational age less than 37 weeks, age at presentation, body weight, presence of sepsis on the other hand, bilirubin level on admission was statistically correlated to the development of Kernicterus, also presence of cholestasis, indicator of hemolysis (ABO incompatibility, Coombs positive, retics >6.5%). Mortality was higher among kerneritic group. Other studies revealed that total serum bilirubin level still define the threshold of concern. TSB concentrations >30 mg/dL carry a decidedly higher risk of Kernicterus though some may escape overt injury. More recent data from the Pilot Kernicterus Registry 3 shows that while the median readmission TSB concentration was 35 mg/dL (350 rag/L, 600 lamol/L), seven babies of the 61 infants with classical signs of acute Kernicterus who had peak TSB concentrations <30 mg/dL (300rag/L, 513 lamol/L)
with a range of 21.5 to 29.5 mg/dL at readmission at age 2.5 to 7 days. All of these TSB concentrations, including the seven babies with TSB concentration <30 mg/dL (300μg/L, 513 μmol/L), were well above the high-risk zone and greater than 99.9th percentile for post-natal age in hours [22]. However other studies found that bilirubin level by itself is unprecised indicator of long term neurodevelopment outcome [23]. More recently, the 2004 AAP guidelines specifically stratify the recommendations for intervention based on clinical risk of bilirubin neurotoxicity. Thus, infants at higher risk are identify by their gestational age, hemolysis (used as a surrogate for rise in bilirubin levels) and post natal age in hours (with lower thresholds for concern prior to age 72 hours) [3]. The common presenting symptoms of newborns with Kernicterus were as follow, poor feeding 94.4%, irritability 83.3%, abnormal movements and seizures 50%, opisthotonus and retrocollis in 33.3%, hypotonia in 27.7%, abnormal respiration, apnea, progressed to death in 22.2%. In study of Behjati et al., evidence of bilirubin encephalopathy included fever 24.5%, opisthotonus 18.4%, hypertonia 22.4%, hyperreflexia 2%, high pitched cry 24% and seizures 6% [24]. However, EBT is associated with complications arising from umbilical catheterization like air embolism, lower limb gangrene, necrotizing enterocolitis and cardiac arrythmias. Other complications of EBT include metabolic disorders like hypoglycemia, acidosis, hypocalcaemia and hyperkalemia and transmission of infectious diseases like viral hepatitis, HIV/ AIDS, malaria, and syphilis and blood transfusion reactions [25] Patra K et al. described adverse events of ET during 1992-2002 according to his study, the most common events were thrombocytopenia (44%), hypocalcaemia (29%) and metabolic acidosis (24%) [26]. In this study biochemical adverse effects were in the form of hypocalcaemia in 25.2% compared to 38% reported by Steiner et al. [27]. And 4% in a study of Sh. Behjati et al. [24]. The calcium level may be complicated by the citrate in the exchange transfused blood [27]. Hypoglycemia was reported in 10.09% compared to 4% in the study of Sh. Behjati et al. [24]. This can be explained by rebound hypoglycemia as a reaction to high concentration of glucose in donor’s blood due to use of citrate phosphate dextrose as an anticoagulant and preservatives [28]. Other biochemical changes include hyponatremia in 6.3% and hypernatremia in 3.84% in the current study compared to 4% and 8% respectively in the study of Sh. Behjati et al. [24]. Hypernatremia could be relayed to significant physiological loss of water in neonates in this age and exclusive breast feeding [29].

In our study Hypokalemia was recorded in 5.3% and hyperkalemia in 5.3% while in previous study of Hasiao et al., hyperkalemia was reported in 1.4% of cases [30].

On the other hand cholestasis was documented in 9.6% in our study as a complication of EBT, presence of cholestasis had a significant correlation with the mean level of total bilirubin pre-exchange transfusion and the development of Kernicterus but no statistically significant correlation with mortality, body weight or gestational age. The suggested mechanisms of conjugated hyperbilirubinemia in severe haemolytic anaemia are excessive bilirubin load causing inspissated bile syndrome and rarely functional and/or anatomical liver cell damage secondary to heart failure or anaemia [16].

Another form of complication was thrombocytopenia which was found in 28.36% in our study, non of them required platelet transfusion, thrombocytopenia as a complication of EBT was also documented in previous study of Steiner et al., it was 38% [27]. Other complication related to Umbilical venous catheterization, included dislodge- ment, thrombosis, haemorrhage, arrhythmias, (peri- cardial) effusions, portal hypertension, infection, lower limbs gangrene and blood transfusion reactions even being reported by previous studies were not recorded in the present study [18]. Necrotizing enterocolitis NEC, as a one of severe complication of EBT through UVC was reported in this study in one newborn who was a full term boy, 3 kg, with total bilirubin level 31.8 mg/dL underwent EBT twice his blood culture was positive with no manifestation of Kernicterus and was classified as Bells 2, the baby improved on treatment. In the study of Gauran et al., two neonates out of 248 (UVET) died as a results of NEC and in the study of Jakson, it was reported that one previous stable newborn developed NEC [8,31]. However in the study Behjati et al., non of the studied group developed NEC [24]. Another complication related to EBT was the development of sepsis which was reported in 18.2% in this study and documented by blood culture, however presence of sepsis was not statistically correlated with gestational age, body weight, pre-exchange bilirubin, presence of Kernicterus or mortality, other studies conducted on babies underwent EBT did not document sepsis as a complication of EBT [24,30]. One of the major factors enhancing sepsis in neonates is the ongoing violation of anatomic and mucosal barriers to infection by the intravascular access catheters required for their care [32]. Exchange transfusion related mortality was defined as any death that
was directly related to the exchange transfusion procedure, in this study 6.73% of cases died shortly after or during exchange. Other studies showed mortality up to 10% [18]. And others reported 4.3% mortality [31]. Although no deaths was recorded in other studies [24,30]. In this study mortality showed statistically significant correlation with gestational age less than 37 weeks, age at presentation to NICU and the presence of Kernicterus, neither sepsis or bilirubin level pre-exchange were statistically correlated with mortality. Mortality related to EBT may be caused by air embolism, cardiac arrhythmias, severe metabolic disorders, severe sepsis and acute congestive heart failure [27].

However our study is limited as it was a retrospective study, some of important data were missed in the files like results of G6PD so some cases with undetermined cause of jaundice may be due to G6PD, also serum albumin was not recorded in the files, other important data like detailed maternal illness, exact stay in maternity hospital, onset of jaundice, pre-exchange electrolytes were missed in the files.

**Conclusion:**

Incidence of neonatal jaundice among NICU is high, exchange blood transfusion was done more frequently which could be explained by relative late presentation with high mean bilirubin level causes of severe neonatal hyperbilirubinemia were undetermined in 27.4% complication of EBT included, electrolyte disturbances, thrombocytopenia and cholestasis, major complications included NEC, sepsis and death. Kernicterus still recorded in NICU with bad outcome and the most important determinant factor for it is a pre-exchange bilirubin level.

**Recommendation:**

Improvement of registration programs in the NICU avoiding early discharge from the maternity hospitals especially for newborns with risk factors establishment of applicable guidelines for management of jaundice, follow-up of severe hyperbilirubinemia for early detection of bilirubin induced neurodevelopmental problem.

**References**


19- BHUTANI V.K., JOHNSON L.H., JEFFREY MAISELS


