Effectiveness of early clinical assessment and bilirubin estimation for prediction of neonatal hyperbilirubinemia

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ABSTRACT

Background: Neonatal hyperbilirubinemia is common cause of neonatal morbidity seen in 60% term and 80% preterm neonate. Early clinical assessment and bilirubin estimation is important in preventing long term sequale of hyperbilirubinemia, preventable cause of neurological sequale (kernticterus).

Methods: Clinical assessments of all Preterm and term neonate born in our medical college were studied for effectiveness of early clinical assessment (Kramer’s index) compared to it gold standard test serum bilirubin (TB).

Results: A total of 500 neonates were studied in which 11.4 % developed significant hyperbilirubinemia. Cord blood bilirubin has a PPV-63.9% and specificity-99.1%. Kramer’s index is less effective clinically if serum bilirubin is in lower range, comparatively kramer’s index effectiveness increases as serum bilirubin increases with p value 0.001.

Conclusions: 11.4% of neonates had significant hyperbilirubinemia requiring treatment. Umbilical cord bilirubin >3 mg/dl showed a good predictor for early detection of hyperbilirubinemia. Kramer’s index at 48 hours correlates significantly with higher levels of serum bilirubin with p value of 0.001.

Keywords: Neonatal hyperbilirubinemia, Total bilirubin, Direct bilirubin, PPV

INTRODUCTION

The common cause of neonatal morbidity is hyperbilirubinemia. It is observed in 1st week of life around 60% of term & 80% of preterm neonates.

It is the visible manifestation of elevated serum concentration of bilirubin.1 Neonates may not appear jaundiced until the serum total bilirubin exceeds 5 to 7 mg/dl (86 to 119 micromol/L).2

Neonatal hyperbilirubinemia is a cause of concern for the parents as well as for paediatrician. Early discharge of healthy new borns after delivery has become a common practice because of social reasons, medical and economic constraints.3

However decreased length of hospital stay is found to increase the risk of readmission to the hospital.4, 5

This necessitates a study to identify the incidence of neonatal hyperbilirubinemia in the present day community.

The most common cause for readmission during the early neonatal period is hyperbilirubinemia.6 Thus recognition of new born jaundice early and giving early therapy will reduce the risk of neonatal hyperbilirubinemia and its complications and also the risk of readmission.
To ensure early treatment there is a need for an early indicator of neonatal hyperbilirubinemia which can predict later development of jaundice in an apparently healthy baby.

The recognition, follow up and early treatment of jaundice has become more difficult in recent days as a result of earlier discharge from the hospital.

Severe jaundice and even kernicterus can occur later in new borns discharged early with no apparent finding of hemolysis at birth. Hence the new born discharged within 48hrs should have a follow up visit after 2-3 days to detect significant jaundice.6

A reliable clinical method for assessment of the risk of bilirubin dependant brain damage is still lacking.

Physical examination as a measure of serum bilirubin still remains questionable. However Kramer’s index is said to be a reliable evaluation of serum bilirubin though subjective.7

Under these circumstances it would be desirable to identify simple methods in order to identify the risk of jaundice early enough so as to implement early treatment and there by minimize the risk of bilirubin dependant brain damage.

METHODS

- All babies fulfilling the above criteria, born in Dr. SMCSI medical college and hospital, Karakonam and a total of 500 new borns will be taken for study.
- Informed consent will be obtained from all mothers.

Cord blood sample of all babies born are collected and sent to laboratory for total bilirubin, and direct bilirubin estimation by Jendrassik method. This method uses, wavelength for Total bilirubin-576 (560-600 nm) and direct bilirubin-546.9

- The normal value of cord blood bilirubin is 1-3mg/dl.
- Cord blood Total bilirubin of more than 3 mg/dl is said to be abnormal.10
- It is taken as a reliable parameter for prediction of development of neonatal hyperbilirubinemia.
- A complete physical examination of the baby is done immediately after birth by a postgraduate and kramer’s index at birth as well is documented in all new borns included in study.

Follow up of all these babies every 24th hourly for physical assessment of development of jaundice by Kramer’s index and in clinically very significant babies like Rh and ABO incompatibility serum bilirubin is sent earlier.12,13

- All babies kramer’s index will be assessed at 48 hours by a postgraduate who is blinded about serum bilirubin value and document than the serum bilirubin sent at 48 hours (only after assessment of Kramer’s index).
- “Serum total bilirubin of ≥8 or and ≥12 mg/dl on day 2, ≥12 and or ≥15 mg/dl on day 3 for birth weight of 2000 to 2500 gms and more than 2500 gms were defined as significant hyperbilirubinemia”.
- Indication for phototherpy in new born at 48 hours of life (Total bilirubin).
- Healthy term new born with medium risk ≥12 mg/dl. Term babies with high risk factors >11 mg/dl. Preterm ≥10 mg/dl.
- Comparison of clinical assessment (Kramer’s index) and laboratory parameters are done.

RESULTS

A total of 500 new borns were recruited into the study.

Percentage distribution according to cord blood bilirubin

Table 1: Percentage distribution according to cord blood Bilirubin - TB.

<table>
<thead>
<tr>
<th>Cord blood bilirubin-TB</th>
<th>Count</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;3</td>
<td>11</td>
<td>2.2</td>
</tr>
<tr>
<td>&lt;=3</td>
<td>489</td>
<td>97.8</td>
</tr>
</tbody>
</table>

Figure 1: Percentage distribution according to cord blood bilirubin-TB.

Figure 1 shows distributions of new born according to cord bilirubin about 2.2% have cord blood bilirubin more than 3 mg/dl.

Percentage distribution according to Kramer’s index at birth

Table 2: Percentage distribution according to Kramer’s Index-at birth.

<table>
<thead>
<tr>
<th>Kramer’s index-at birth</th>
<th>Count</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 6</td>
<td>500</td>
<td>100.0</td>
</tr>
</tbody>
</table>
Table 2 shows all new born is assessed by Kramer’s index at birth.

**Percentage distribution according Kramer’s index at 48 hours**

Table 3: Percentage distribution according to Kramer's index at 48 hours.

<table>
<thead>
<tr>
<th>Kramer's index at 48 hours</th>
<th>Count</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;6</td>
<td>251</td>
<td>50.2</td>
</tr>
<tr>
<td>6-9</td>
<td>120</td>
<td>24.0</td>
</tr>
<tr>
<td>9-12</td>
<td>77</td>
<td>15.4</td>
</tr>
<tr>
<td>12-15</td>
<td>35</td>
<td>7.0</td>
</tr>
<tr>
<td>&gt;15</td>
<td>17</td>
<td>3.4</td>
</tr>
</tbody>
</table>

Figure 2 shows at 48 hours all the new borns included in the study were assessed clinically by Kramer’s index and documented. 50.2% showed KI <6, 24.0% were between 6-9, around 15.4% were between 9-12 and 7% were 12-15 and 3.4% new borns values is suspected to be >15 since according to Kramer’s index clinically significance was involving both palns and soles.

**Percentage distribution according to hyperbilirubinemia at 48 hours**

Table 4: Percentage distribution according to hyperbilirubinemia at 48 hours.

<table>
<thead>
<tr>
<th>Hyperbilirubinemia at 48 hours</th>
<th>Count</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>57</td>
<td>11.4</td>
</tr>
<tr>
<td>No</td>
<td>443</td>
<td>88.6</td>
</tr>
</tbody>
</table>

Figure 3 shows about 11.4% among 500 new borns at 48 hours developed significant hyperbilirubinemia required phototherapy.

**Percentage distribution according to gestational age**

Table 5: Percentage distribution according to gestational age.

<table>
<thead>
<tr>
<th>Gestational age</th>
<th>Count</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Term</td>
<td>462</td>
<td>92.4</td>
</tr>
<tr>
<td>Pre term</td>
<td>38</td>
<td>7.6</td>
</tr>
</tbody>
</table>

Figure 4 shows that among 500 new borns included in study around 7.6% were preterm and rest 92.4% were term babies, no post-term babies was included in this study.

**Percentage distribution according to phototherapy**

Table 6: Percentage distribution according to phototherapy.

<table>
<thead>
<tr>
<th>Phototherapy</th>
<th>Count</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Received</td>
<td>81</td>
<td>16.2</td>
</tr>
<tr>
<td>No phototherapy</td>
<td>419</td>
<td>83.8</td>
</tr>
</tbody>
</table>

Figure 5 shows out of total 500 new borns included in study 16.2% of new born i.e. total of 81 new born required phototherapy treatment alone.
Percentage distribution according to exchange transfusion

![Percentage distribution according to exchange transfusion](image)

**Figure 5: Percentage distribution according to phototherapy.**

Table 7: Percentage distribution according to exchange transfusion.

<table>
<thead>
<tr>
<th>Exchange transfusion</th>
<th>Count</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not required</td>
<td>500</td>
<td>100.0</td>
</tr>
<tr>
<td>Required</td>
<td>0</td>
<td>0.0</td>
</tr>
</tbody>
</table>

Exchange transfusion was not required for any of the babies included in this study.

**Predictive power of cord blood bilirubin in hyperbilirubinemia**

Table 8A: Cord blood bilirubin-TB in predicting hyperbilirubinemia is gold standard.

<table>
<thead>
<tr>
<th>Cord Blood Bilirubin-TB</th>
<th>Hyperbilirubinemia</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>&gt;3</td>
<td>24</td>
<td>24</td>
</tr>
<tr>
<td>&lt;=3</td>
<td>33</td>
<td>439</td>
</tr>
<tr>
<td>Total</td>
<td>57</td>
<td>443</td>
</tr>
</tbody>
</table>

Kappa = 0.18**, p = 0, Fair agreement.

In our study cord blood bilirubin >3 mg/dl as a predictor of hyperbilirubinemia showed a kappa=0.18, p=0 showed a fair agreement with positive predictive value of 63.6%, specificity of 99.1%, sensitivity of 12.3%.

![ROC Curve](image)

Area under curve = 0.676 (fair prediction)

**Figure 5: ROC curve for the prediction of hyperbilirubinemia using cord blood bilirubin.**

Sensitivity and specificity at different cut off point for Cord Blood Bilirubin in prediction of hyperbilirubinemia.

Table 8B: Sensitivity and specificity at different cut off point for cord blood bilirubin in prediction of hyperbilirubinemia.

<table>
<thead>
<tr>
<th>Positive if greater than or equal To</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.70</td>
<td>0.98</td>
<td>0.00</td>
</tr>
<tr>
<td>1.05</td>
<td>0.98</td>
<td>0.02</td>
</tr>
<tr>
<td>1.15</td>
<td>0.95</td>
<td>0.04</td>
</tr>
<tr>
<td>1.25</td>
<td>0.86</td>
<td>0.14</td>
</tr>
<tr>
<td>1.35</td>
<td>0.82</td>
<td>0.23</td>
</tr>
<tr>
<td>1.45</td>
<td>0.79</td>
<td>0.36</td>
</tr>
<tr>
<td>1.55</td>
<td>0.72</td>
<td>0.46</td>
</tr>
<tr>
<td>1.63</td>
<td>0.68</td>
<td>0.55</td>
</tr>
<tr>
<td>1.68</td>
<td>0.68</td>
<td>0.56</td>
</tr>
<tr>
<td>1.75</td>
<td>0.60</td>
<td>0.66</td>
</tr>
<tr>
<td>1.85</td>
<td>0.54</td>
<td>0.76</td>
</tr>
<tr>
<td>1.95</td>
<td>0.49</td>
<td>0.86</td>
</tr>
<tr>
<td>2.05</td>
<td>0.42</td>
<td>0.91</td>
</tr>
<tr>
<td>2.15</td>
<td>0.30</td>
<td>0.95</td>
</tr>
<tr>
<td>2.25</td>
<td>0.26</td>
<td>0.96</td>
</tr>
<tr>
<td>2.35</td>
<td>0.23</td>
<td>0.98</td>
</tr>
<tr>
<td>2.45</td>
<td>0.18</td>
<td>0.98</td>
</tr>
<tr>
<td>2.55</td>
<td>0.18</td>
<td>0.99</td>
</tr>
<tr>
<td>2.70</td>
<td>0.14</td>
<td>0.99</td>
</tr>
<tr>
<td>2.95</td>
<td>0.12</td>
<td>0.99</td>
</tr>
<tr>
<td>3.15</td>
<td>0.07</td>
<td>1.00</td>
</tr>
<tr>
<td>3.30</td>
<td>0.04</td>
<td>1.00</td>
</tr>
<tr>
<td>4.40</td>
<td>0.0</td>
<td>1.0</td>
</tr>
</tbody>
</table>

Table 8C: Sensitivity, specificity, PPV and NPV of cord blood bilirubin in predicting hyperbilirubinemia.

<table>
<thead>
<tr>
<th>Gestational age</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>12.3</td>
</tr>
<tr>
<td>Specificity</td>
<td>99.1</td>
</tr>
<tr>
<td>False negative</td>
<td>87.7</td>
</tr>
<tr>
<td>False positive</td>
<td>0.9</td>
</tr>
<tr>
<td>Predictive value of positive test</td>
<td>63.6</td>
</tr>
<tr>
<td>Predictive value of negative test</td>
<td>89.8</td>
</tr>
<tr>
<td>Positive likelihood ratio</td>
<td>13.6</td>
</tr>
<tr>
<td>Negative likelihood ratio</td>
<td>0.9</td>
</tr>
<tr>
<td>Accuracy</td>
<td>89.2</td>
</tr>
</tbody>
</table>

Table 8D: Cord blood bilirubin cut-off 2 mg/dl as predicting hyperbilirubinemia.

<table>
<thead>
<tr>
<th>Cord blood Bilirubin – TB</th>
<th>Hyperbilirubinemia</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>&gt;2</td>
<td>24</td>
<td>24</td>
</tr>
<tr>
<td>&lt;=2</td>
<td>33</td>
<td>33</td>
</tr>
<tr>
<td>Total</td>
<td>57</td>
<td>Total</td>
</tr>
</tbody>
</table>
Table 9: Cord blood bilirubin-TB in predicting hyperbilirubinemia is gold standard.

<table>
<thead>
<tr>
<th>Percentage</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>False negative</th>
<th>False positive</th>
<th>Predictive value of positive test</th>
<th>Predictive value of negative test</th>
<th>Positive likelihood ratio</th>
<th>Negative likelihood ratio</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;6</td>
<td>42.1</td>
<td>91.2</td>
<td>57.9</td>
<td>8.8</td>
<td>38.1</td>
<td>92.4</td>
<td>4.8</td>
<td>0.6</td>
<td>85.6</td>
</tr>
</tbody>
</table>

Kappa = 0.32**, p = 0, Fair agreement.

Cord blood bilirubin >1.95 mg/dl showed a much better results than cord blood bilirubin>3 mg/dl in prediction of hyperbilirubinemia with sensitivity of 49%, specificity of 86% and positive predictive value of 92.4%.

Association between hyperbilirubinemia at 48 hours and selected variables

Table 9A: Comparison of sr. bilirubin-TB at 48 hrs. based on kramer’s index-at 48 hours.

<table>
<thead>
<tr>
<th>Kramer’s index-at 48 hours</th>
<th>Mean</th>
<th>SD</th>
<th>N</th>
<th>F</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;6</td>
<td>7.3</td>
<td>1.6</td>
<td>251</td>
<td>83.71</td>
<td>0.001</td>
</tr>
<tr>
<td>6-9</td>
<td>9.0</td>
<td>1.3</td>
<td>120</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9-12</td>
<td>9.7</td>
<td>1.8</td>
<td>77</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12-15</td>
<td>10.8</td>
<td>1.9</td>
<td>35</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;15</td>
<td>11.8</td>
<td>2.7</td>
<td>17</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Figure 6: Comparison of sr. bilirubin - TB at 48 hrs. based on kramer’s index-at 48 hours.

Comparison of serum total bilirubin at 48 hours on Kramer’s index at 48 hours done by an ANOVA test shows significant variation that as serum bilirubin increases the clinical effectiveness of kramer’s index increases in clinical prediction, with p value being showing significance level p=0.001 (Significance p<0.005).

Kramer’s index is less effective clinically if serum bilirubin is in lower range, comparatively Kramer’s index effectiveness increases as serum bilirubin increases.

Table 9B: Comparison of sr. bilirubin-TB at 48 hrs pair wise comparison (Scheffe multiple comparisons)-post hoc test.

<table>
<thead>
<tr>
<th>Pair</th>
<th>df</th>
<th>F</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;6 &amp; 6-9</td>
<td>(4,495)</td>
<td>22.72</td>
<td>0.000</td>
</tr>
<tr>
<td>&lt;6 &amp; 9-12</td>
<td>(4,495)</td>
<td>32.89</td>
<td>0.000</td>
</tr>
<tr>
<td>&lt;6 &amp; 12-15</td>
<td>(4,495)</td>
<td>35.89</td>
<td>0.000</td>
</tr>
<tr>
<td>&lt;6 &amp; &gt;15</td>
<td>(4,495)</td>
<td>30.76</td>
<td>0.000</td>
</tr>
<tr>
<td>6-9 &amp; 9-12</td>
<td>(4,495)</td>
<td>2.23</td>
<td>0.064</td>
</tr>
<tr>
<td>6-9 &amp; 12-15</td>
<td>(4,495)</td>
<td>8.26</td>
<td>0.000</td>
</tr>
<tr>
<td>6-9 &amp; &gt;15</td>
<td>(4,495)</td>
<td>11.04</td>
<td>0.000</td>
</tr>
<tr>
<td>9-12 &amp; 12-15</td>
<td>(4,495)</td>
<td>2.68</td>
<td>0.031</td>
</tr>
<tr>
<td>9-12 &amp; &gt;15</td>
<td>(4,495)</td>
<td>5.75</td>
<td>0.000</td>
</tr>
<tr>
<td>12-15 &amp; &gt;15</td>
<td>(4,495)</td>
<td>1.09</td>
<td>0.360</td>
</tr>
</tbody>
</table>

Table 9C: Comparison of Sr. Bilirubin - TB at 48 hrs based on Kramer’s index-at 48 hours – for term.

<table>
<thead>
<tr>
<th>Kramer’s index-at 48 hours</th>
<th>Mean</th>
<th>SD</th>
<th>N</th>
<th>F</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;6</td>
<td>7.3</td>
<td>1.5</td>
<td>245</td>
<td></td>
<td>73.96**</td>
</tr>
<tr>
<td>6-9</td>
<td>9.0</td>
<td>1.3</td>
<td>111</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9-12</td>
<td>9.5</td>
<td>1.8</td>
<td>63</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12-15</td>
<td>10.8</td>
<td>2.0</td>
<td>31</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;15</td>
<td>12.0</td>
<td>3.1</td>
<td>12</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 9D: Comparison of sr. bilirubin-TB at 48 hrs pair wise comparison (Scheffe multiple comparisons) - post hoc test - for term.

<table>
<thead>
<tr>
<th>Pair</th>
<th>DF</th>
<th>F</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;6 &amp; 6-9</td>
<td>(4,457)</td>
<td>21.68</td>
<td>0.000</td>
</tr>
<tr>
<td>&lt;6 &amp; 9-12</td>
<td>(4,457)</td>
<td>24.25</td>
<td>0.000</td>
</tr>
<tr>
<td>&lt;6 &amp; 12-15</td>
<td>(4,457)</td>
<td>33.16</td>
<td>0.000</td>
</tr>
<tr>
<td>&lt;6 &amp; &gt;15</td>
<td>(4,457)</td>
<td>25.26</td>
<td>0.000</td>
</tr>
<tr>
<td>6-9 &amp; 9-12</td>
<td>(4,457)</td>
<td>1.07</td>
<td>0.373</td>
</tr>
<tr>
<td>6-9 &amp; 12-15</td>
<td>(4,457)</td>
<td>7.74</td>
<td>0.000</td>
</tr>
<tr>
<td>6-9 &amp; &gt;15</td>
<td>(4,457)</td>
<td>9.84</td>
<td>0.000</td>
</tr>
<tr>
<td>9-12 &amp; 12-15</td>
<td>(4,457)</td>
<td>3.36</td>
<td>0.010</td>
</tr>
<tr>
<td>9-12 &amp; &gt;15</td>
<td>(4,457)</td>
<td>6.3</td>
<td>0.000</td>
</tr>
<tr>
<td>12-15 &amp; &gt;15</td>
<td>(4,457)</td>
<td>1.3</td>
<td>0.268</td>
</tr>
</tbody>
</table>

Table 9 (c) (d) & Figure 10 - Comparison of serum total bilirubin at 48 hours with kramer’s index for term newborns in Indian babies analysis done by ANOVA (c) & Scheffe multiple comparison(d) showed significant association with higher the serum bilirubin value higher the clinical effectiveness of kramer’s index with p<0.001.
Figure 7: Comparison of sr. bilirubin-TB at 48 hrs based on kramer’s index-at 48 hours for Term.

Table 9 (c): Comparison of sr. bilirubin - TB at 48 hrs based on kramer’s index-at 48 hours for pre-term.

<table>
<thead>
<tr>
<th>Kramer’s index-at 48 hours</th>
<th>Mean</th>
<th>SD</th>
<th>N</th>
<th>F</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;6</td>
<td>8.7</td>
<td>1.9</td>
<td>6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6-9</td>
<td>9.2</td>
<td>1.2</td>
<td>9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9-12</td>
<td>10.6</td>
<td>1.2</td>
<td>14</td>
<td>3.63*</td>
<td>0.015</td>
</tr>
<tr>
<td>12-15</td>
<td>10.5</td>
<td>1.0</td>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;15</td>
<td>11.1</td>
<td>1.5</td>
<td>5</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 9 (f): Comparison of sr. bilirubin-TB At 48 hrs pair wise comparison (Scheffe multiple comparisons) post hoc test for – Preterm.

<table>
<thead>
<tr>
<th>Pair</th>
<th>DF</th>
<th>F</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;6 &amp; 6-9</td>
<td>(4,495)</td>
<td>0.12</td>
<td>0.974</td>
</tr>
<tr>
<td>&lt;6 &amp; 9-12</td>
<td>(4,495)</td>
<td>1.95</td>
<td>0.126</td>
</tr>
<tr>
<td>&lt;6 &amp; 12-15</td>
<td>(4,495)</td>
<td>1.07</td>
<td>0.385</td>
</tr>
<tr>
<td>&lt;6 &amp; &gt;15</td>
<td>(4,495)</td>
<td>2.04</td>
<td>0.111</td>
</tr>
<tr>
<td>6-9 &amp; 9-12</td>
<td>(4,495)</td>
<td>1.36</td>
<td>0.270</td>
</tr>
<tr>
<td>6-9 &amp; 12-15</td>
<td>(4,495)</td>
<td>0.65</td>
<td>0.628</td>
</tr>
<tr>
<td>6-9 &amp; &gt;15</td>
<td>(4,495)</td>
<td>1.5</td>
<td>0.226</td>
</tr>
<tr>
<td>9-12 &amp; 12-15</td>
<td>(4,495)</td>
<td>0</td>
<td>1.000</td>
</tr>
<tr>
<td>9-12 &amp; &gt;15</td>
<td>(4,495)</td>
<td>0.13</td>
<td>0.972</td>
</tr>
<tr>
<td>12-15 &amp; &gt;15</td>
<td>(4,495)</td>
<td>0.09</td>
<td>0.986</td>
</tr>
</tbody>
</table>

Figure 8 (e) (f) & Figure 11- comparison of STB at 48 hours with KI at 48 hours for preterm done by ANOVA(e) and scheffe multiple comparison (f) has significant variation with p=0.015 (Significance p<0.005).

**Significant at 0.01 levels.

**

Association between hyperbilirubinemia at 48 hours and gestational age

Table 10: Association between hyperbilirubinemia at 48 hours and gestational age.

<table>
<thead>
<tr>
<th>Gestational Age</th>
<th>Yes Count</th>
<th>Yes %</th>
<th>No Count</th>
<th>No %</th>
<th>$\chi^2$</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Term</td>
<td>34</td>
<td>7.4</td>
<td>428</td>
<td>92.6</td>
<td>98.3**</td>
<td>p&lt;0.01</td>
</tr>
<tr>
<td>Pre term</td>
<td>23</td>
<td>60.5</td>
<td>15</td>
<td>39.5</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Figure 9: Association between hyperbilirubinemia at 48 hours and gestational age.

DISCUSSION

Since hyperbilirubinemia is common cause of neonatal morbidity which is seen in approximately 60% term and 80% preterm newborns.²

A descriptive study was done with a total 500 new born born in our medical college after considering exclusion criteria.

In concert to the higher incidence of hyperbilirubinemia early prediction by assessing clinically as well comparing it with cord bilirubin at birth and clinically new born were assessed by Kramer’s index and subsequently serum
bilirubin at 48 hours is done to compare the effectiveness of clinical assessment and cord blood TB, 48 hours serum bilirubin.

Kanchamabat S, Boonyarittpong P, Kreinghirum O from Department of pediatrics, Vajira Medical College, University of Bangkok Metropolis conducted study on predictive value of hyperbilirubinemia by cord blood bilirubin. Published in Vajira medical journal Vol.54 no.2 May August 2010.14

Table 11: Cord blood bilirubin cut-off in various studies with sensitivity and specificity.

<table>
<thead>
<tr>
<th>Author</th>
<th>CBB cut-off</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive predictive value</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kanchanabat et al</td>
<td>&gt;2.3 mg/dl</td>
<td>14.6%</td>
<td>91.3%</td>
<td>25%</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Sun et al 42 (2007)</td>
<td>&gt;2</td>
<td>45.08%</td>
<td>68%</td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Knudsen 33 (1989)</td>
<td>&gt;2.35</td>
<td>13%</td>
<td>99%</td>
<td>85%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Amar Taksande et al 3 (2005)</td>
<td>&gt;2</td>
<td>38.8%</td>
<td>85%</td>
<td>89.5%</td>
<td>0.000</td>
</tr>
<tr>
<td>Our study</td>
<td>&gt;3 mg/dl</td>
<td>12.3%</td>
<td>99.1%</td>
<td>63.6%</td>
<td>0.001</td>
</tr>
</tbody>
</table>

In our study comprising 500 new borns cord blood bilirubin was collected and cut off value of ≥3mg/dl was taken and nearly 2.2% of those new born cord bilirubin was ≥3 mg/dl developed significantly peribilirubinemia requiring phototherapy with Positive predictive value of 63.6%, specificity of 99.1% sensitivity of 12.3%. Analysis is done by kappa correlation.

Kappa = 0.18, p=0.Fair agreement.

Acosta-Torres TM et al in 2012 studied usefulness of Kramer’s index in diagnosis of hyperbilirubinemia a total of 50 new born value serum total bilirubin 12.02 ± 3.41mg/dl and 62.8% of neonates were at kramers level 3 correlation bilirubin/Kramer’s index r=0.93 (p<0.005).

Our study in 500 new born about 50.2% were in Kramer’s level 1, 24.9% in level 2, 15.4% in level 3, 7 % in level 4, 3.4% in level 5.

Association between clinical assessment done by kramer’s index at 48 hours and serum bilirubin at 48 hours is assessed & analysis is done by X², ANOVA and Scheffe multiple comparison showed a significant variation-clinical effectiveness of Kramer’s index increase significantly as serum bilirubin increase, means at higher serum bilirubin value, Kramer’s index is more effective than compared to lower serum bilirubin value with p=0.001 which is a significant variation.

Carbonell Estrany X, Botet Mussons F et al from Department of Neonatology, university of Barcelona, Spain studied 169 new born in April 1999 and published in Espanol paediatric journal in April 1999 and reported that A significant hyperbilirubinemia was present in 2.95% of the new borns. Umbilical cord blood bilirubin with a cut-off point of 2.2 mg/dl was not a useful predictor of neonatal jaundice.15

In this study predictive value of umbilical cord blood bilirubin value ≥2.3mg/dl showed a positive predictive value of 25%, negative predictive value 84.3%, sensitivity 14.6% & specificity of 91.3%. Various studies showed a similar range of cord bilirubin in prediction of subsequent hyperbiliruinemia.14

At 24 and 48 hours of life serum bilirubin levels ≥6 mg/dl and ≥9 mg/dl, respectively, predicted a Subsequent hyperbilirubinemia with a sensitivity of 100% at both time-points, specificity of 47.5% and 64.3%, positive predictive value of 7.3% and 16.4%, respectively, and a negative predictive value of 100% for both.

Almost similarly in our study of 500 new born. A significant hyperbilirubinemia was present in 11.4% of new born. Umbilical cord cut-off of ≥3 mg/dl showed kappa correlation of kappa=0.18**, p=0 Fair agreement, with positive predictive value of 63.6%, specificity of 99.1%, sensitivity of 12.3%.

Detailed analysis of 500 new born cord blood bilirubin in our study showed a cord blood bilirubin of ≥1.95 mg/dl showed a better prediction than ≥3 mg/dl with sensitivity of 49% & specificity of 86%.

Association between serum bilirubin at 48 hours and kramer’s index at 48 hours showed good clinical significance out of which 11.2 % required phototherapy for hyperbilirubinemia with p=0.001.

CONCLUSIONS

In the present study out of 500 new born studied, 81 new born developed significant hyperbilirubinemia requiring phototherapy while 444 did not require phototherapy. Hence in this study incidence of significant hyperbilirubinemia is 11.4%. 


Umbilical cord bilirubin ≥3 mg/dl is a fair predictor of subsequent hyperbilirubinemia whereas cord blood bilirubin ≥1.95 mg/dl has a good prediction.

Incidence of hyperbilirubinemia is greater in Preterm compared to term babies.

Kramer’s index at 48 hours correlates significantly with higher level of serum bilirubin at 48 hours with significance p value of 0.001.

Kramer’s index at 48 hours has a poor correlation with lower levels of serum bilirubin at 48 hours.

Also an association was found between hyperbilirubinemia at 48 hours and gestational age - among term babies 7.4% and preterm 60.5% and this variation is clinically significant.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES
