Stress Induced Hyperbilirubinemia; Biochemical Changes in Some Neonates

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ABSTRACT

Cases of neonatal jaundice due to Hyperbilirubinemia abound with some resulting in mortality especially arising from complications in Cesarean Section. We studied biochemical patterns of some enzymes, hormones and other parameters in 1 - 4 days old neonates. Using spectrophotometric and radioimmunoassay techniques we measured biochemical liver function parameters bilirubin, transaminases and gammaglutamyltransferase. Hormonal evaluation included cortisol, glucagon and adrenocortical hormone. Using SPSS version 23, paired sample test at 95% confidence intervals of difference shows 2 tail significance for bilirubin, transaminase; glucagon, cortisol and ACTH. Paired sample correlation also showed strong negative pattern with days. We conclude that the interplay of nervous system and self-regulating influence of stress hormones coupled with an immature liver triggers the formation of excess bilirubin.

Keyword
Stress, induced, Hyperbilirubinemia, Biochemical, Neonates.

Introduction

The production of bilirubin may be affected due to several factors which has a nexus with the metabolism, storage, uptake or excretion. Jaundice as a result of bilirubinemia could be an outcome of dysfunction in these processes. Classified in various ways, the condition may be due to hemolysis or defective erythropoiesis, reduced bilirubin excretion as in obstruction and hepatitis and abnormal bilirubin metabolism arising from hereditary factors and neonatal jaundice.

A common form of hyperbilirubinemia is unconjugated bilirubinemia which may result in brain damage (Kernicterus) while the rare known genetic disorders such as criggar-Nijjar syndromes arise as a result of reduced or absolute lack of activity of bilirubin UDP glucuronoyitransferase enzymes [1]. The understanding that bilirubin is a potentially toxic substance is now known supporting the need to constantly identify through monitoring those who may become victims of Hyperbilirubinemia.

For most neonates the emerging neonatal jaundice may become apparent within the first three days of birth as earlier reported in the National Neonatal Perinatal Database 2002-2003 [2].

For the fetal life, the liver main function revolves around production of blood and synthesis of protein. The support from maternal liver provides route for the removal of metabolic waste and site for biotransformation of phase 1 and 11 reactions [3].

Most synthetic processes become spontaneous after birth and the newborn is able to commence the process of production, usage, storage and metaboism of nutrients such as production of enzymes and biliary excretion. There is however reason to believe that in the event that this physiological process is altered, biliary excretion can be affected [4].

Hormone act on cells or tissue but occur in the nervous system as neurotransmitters. However, taking into consideration their two major functions as self-regulation and influence on the nervous system, hormones use the influence of the nervous system over the endocrine system to make inefficient the self-regulatory operation, initiate new hormonal response and /or set new base line for
hormone production and action. A target cell may be responsive to different hormones. These hormones can work against each other or produce effects that are additive or complimentary, synergistic or antagonistic. Studies have elucidated the fact that when there is hormonal disorder liver function may be derailed. The pattern secondary to hormone defect such as hypocortisolism could vary causing Indirect hyperbilirubinemia that may result in raised transaminases [5]. The neonatal liver is susceptible to endocrine, metabolic or infections disease. Some cases of severe cortisol imbalance have been-reported [6,7]. We have investigated the interplay of some enzymes, hormones and other biochemical parameters in neonatal jaundice in this research.

Materials and Methods
This study was carried out at the Niger Delta University Teaching Hospital Okolobiri and Federal Medical Centre Yenagoa in Bayelsa State, Nigeria. The subjects for this study were 1–4-day old neonates who were delivered through Cesarean Section.

Serum bilirubin concentration was determined by the Jen drassik - Grof method which utilized diazotized sulphanilic acid and caffeine (a product of QCA/ Spain) to produce azopigment for Total bilirubin in the presence of caffeine measured at 600nm and conjugated bilirubin in the absence of caffeine measured at 540nm.

The transaminases (AST, ALT) and gammaglutamyltransferase (YGT) were all measured by Vitros DT Dry chemical Analyzer (Johnson and Johnson, USA). To determine and evaluate cortisol and glucagon we used (EQUILA/ Roch Diagnostics, GMBH, Manheim, Germany) and ACTH (EQUILA, Immulite 2000, Siemen. Germany). Glucagon in plasma was determined by the competitive radioimmunoassay using a rabit antiserum raised against glucagon albumin conjugate.

Result
We analyzed some liver enzymes especially the Transminases, Alkaline Phophatase and gammaglutamyltransferase. We observed a consistent increase in AST and ALT among cases investigated and the concentration was time dependent. A similar pattern was also seen in alkaline phosphate. Gamma GT levels were however not similarly elevated when compared with normal reference value (Table 1).

### Table 1: Level of liver enzymes assay among the neonates.

<table>
<thead>
<tr>
<th>Age (Days)</th>
<th>AST (U/L)</th>
<th>ALT (U/L)</th>
<th>AKLPOHS (iu/L)</th>
<th>Y-GT (U/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>34.3</td>
<td>30.0</td>
<td>24.0</td>
<td>11.6</td>
</tr>
<tr>
<td>2</td>
<td>55.0</td>
<td>57.4</td>
<td>30.2</td>
<td>25.4</td>
</tr>
<tr>
<td>3</td>
<td>53.4</td>
<td>60.0</td>
<td>43.4</td>
<td>30.0</td>
</tr>
<tr>
<td>4</td>
<td>60.2</td>
<td>58.1</td>
<td>48.1</td>
<td>37.2</td>
</tr>
<tr>
<td>(Normal delivery Day 4)</td>
<td>15.3</td>
<td>14.7</td>
<td>25.2</td>
<td>34.5</td>
</tr>
</tbody>
</table>


### Table 2: Hormone Levels among the neonates.

<table>
<thead>
<tr>
<th>Age (Days)</th>
<th>Cortisol (nmol/l)</th>
<th>ACTH (pmol/l)</th>
<th>Glucagon (Ng/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>11.5</td>
<td>4.8</td>
<td>54.0</td>
</tr>
<tr>
<td>2</td>
<td>11.7</td>
<td>3.2</td>
<td>30.2</td>
</tr>
<tr>
<td>3</td>
<td>24.5</td>
<td>4.0</td>
<td>43.4</td>
</tr>
<tr>
<td>4</td>
<td>30.3</td>
<td>4.7</td>
<td>46.1</td>
</tr>
<tr>
<td>(Normal delivery Day 4)</td>
<td>23.4</td>
<td>12.2</td>
<td>23.7</td>
</tr>
</tbody>
</table>

### Table 3: Some other Biochemical Parameter, among neonates.

<table>
<thead>
<tr>
<th>Age (Days)</th>
<th>TB (umol/l)</th>
<th>CB (umol/l)</th>
<th>Glucose (mmol/l)</th>
<th>Cholesterol (mmol/l)</th>
<th>Albumin (g/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>140.3</td>
<td>15.3</td>
<td>2.7</td>
<td>3.1</td>
<td>3.6</td>
</tr>
<tr>
<td>2</td>
<td>122.5</td>
<td>20.5</td>
<td>3.3</td>
<td>4.4</td>
<td>4.2</td>
</tr>
<tr>
<td>3</td>
<td>205.2</td>
<td>18.7</td>
<td>3.8</td>
<td>4.6</td>
<td>2.3</td>
</tr>
<tr>
<td>4</td>
<td>307.8</td>
<td>33.0</td>
<td>4.0</td>
<td>4.8</td>
<td>4.1</td>
</tr>
<tr>
<td>(Normal delivery Day 4)</td>
<td>23.2</td>
<td>3.3</td>
<td>4.2</td>
<td>3.8</td>
<td>3.6</td>
</tr>
</tbody>
</table>

TB: Total Bilirubin, CB: Conjugated Bilirubin.

Paired sample test for AST on day 1 and 2 gave a significance of 0.000 (at P<0.05) while ALT for the same period gave a significance of 0.001. This was same for Glucagon Day 1 and 2 while glucagon day 3 and 4 was 0.001.

Discussion
Bilirubin has the capacity to accumulate in neonates and this can cause irreversible central nervous system derangement especially in those who are premature or are in a state of distress. Essentially, bilirubin is synthesized by the action of microsomal enzyme known as heme oxygenase on heme which comes from hemoglobin catabolism and non-erythroid hemo proteins which are predominantly in the liver. It has been known that hepatic heme oxygenase (HO) develop in new born rats and that this development is enhanced by fasting, hypoglycemic condition, glucagon and epinephrine which are stress hormones [8,9].

Conditions that could predispose the haemoglobin to breakdown as a result of some catabolic action that encourages formation of large quantity of pigments may result in a push back of these pigments into the blood circulation due to undeveloped pigment conjugation mechanism. In this study we have observed marked elevation of bilirubin. While one would not be categorical on the source of this bilirubin, we would advance the argument in favour of the fact that the release of glucagon and ACTH can enhance release of bilirubin in infants.

The fasting Glucose level in our study for day 1 was within hypoglycemic range (Table 3). Previous literature has opined that process that enhances pigment formation by hormones from non-erythroid hemes and exchange of pigment between liver and the circulation may contribute when hypoglycemia exist [10,11]. Glucose and glucagon are known to play counter regulatory roles. Elevated glucagon would imply a reduced glucose as seen in this study on the first day. It is known that raised glucagon level occurring in the first week of birth appear not to be suppressed by glucose. On the other hand, secretion of this hormone is elicited by a decrease in plasma blood glucose and a facilitated
decline in glycogen store [12]. It is known from previous study that some newborns are oligosymptomatic. In the circumstance if the detection of an underlying endocrine disease is delayed, the patient stands the risk of increased morbidity or mortality due to the possibility of recurrent hypoglycemia, hypothyroidism and acute adrenal insufficiency [13-15].

Comparison of gamma Glutamyltransferase show a consistent increase with days. Serum level of YGT may usually be normal, slightly or moderately elevated or markedly elevated. It is a maker for differentiation or differential diagnosis of extrahepatic disease from primary liver disease. Our findings in this research reveal the facts that factors favouring the formation of bilirubin in neonates include the release of stress hormones and some other biochemical variables.

References