Original Research Article

Incidence of acute kidney injury in asphyxiated babies in university of Uyo teaching hospital, Uyo, Nigeria

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ABSTRACT

Background: Acute Kidney Injury (AKI) is a consequence of birth asphyxia. In resource poor countries like ours, birth asphyxia still contributes to the high rates of neonatal morbidity and mortality. A few studies have reported the incidence of AKI in birth asphyxia in Nigeria but none from Uyo, south-south region of Nigeria.

Methods: A descriptive cross sectional study carried out in the Newborn Unit of the University of Uyo Teaching hospital, Uyo, Nigeria over a period of eight months. One hundred and four term neonates with provisional diagnosis of birth asphyxia using Apgar scoring were recruited. Blood sample was collected within six hours of life from each subject for serum creatinine estimation using modified Jaffe method. Urine output was assessed by application of plastic collection bag to the skin by adhesive patch. AKI was diagnosed when sCr >1.5mg/dl while oliguria was defined as urinary output <1.5ml/kg/hour.

Results: Of the total of 104 asphyxiated neonates enrolled into the study, 56 (53.8%) were males while 48 (46.2%) were females giving a male/female ratio of 1.2:1. Twenty-eight (26.9%) of the subjects had severe birth asphyxia; 52 (50%) had moderate birth asphyxia while 24 (23.1%) were mildly asphyxiated. Incidence of AKI was 48 (46.1%), twelve (11.5%) had AKI based on serum creatinine criteria while 36 (34.6%) had AKI based on urinary output criteria. The mean urinary output (ml/kg/hr) for the subjects was 1.65±0.68 while the mean serum creatinine (mg/dl) was 0.88±0.46.

Conclusions: The incidence of AKI among asphyxiated neonates in our locale is high at 46.1%.

Keywords: Acute kidney injury, Birth asphyxia, Incidence, Neonates

INTRODUCTION

Acute kidney injury (AKI), the term that has replaced the term Acute Renal Failure (ARF) is defined as an abrupt (within hours) decrease in kidney function, which compasses both injury (structural damage) and impairment (loss of function). It is characterized by a reversible increase in blood concentration of creatinine and nitrogenous waste products and inability of the kidneys to regulate fluid and electrolyte homeostasis appropriately.¹ The Acute Dialysis Quality Initiative (ADQI) group standardized the definition of AKI using the RIFLE criteria, a mnemonic for three levels of severity; Risk, Injury and Failure and two outcomes; Loss of kidney function and End-stage kidney disease.¹²

The Acute Kidney Injury Network (AKIN) devised strata that defined AKI based on time in relation to absolute creatinine increase, percentage increase, or documented oliguria.³ A new consensus definition merging the RIFLE...
criteria and the AKIN network definition has emerged from the Kidney Disease: Improving Global Outcomes (KDIGO). AKIN criteria shows close approximation to RIFLE stratification of patients and both schemes equate specific changes in serum creatinine to specific worsening of oliguria. Increases in RIFLE and AKIN criteria correlate with increased morbidity. The worldwide incidence of AKI in the paediatric population is poorly known because of under-reporting, regional disparities and differences in case definition. Studies from both resource-rich and resource-poor regions of the world have demonstrated high incidence of AKI in children.

Generally, it varies from 1-82%. An incidence of 4.5% and 10% was reported from Canada and USA respectively. In Congo-Brazzaville, AKI represented 13% of childhood renal disorders. In Nigeria, incidence rates have been stated as 3.3% in Ile-Ife, 4.7% in Port-Harcourt, 6.6% in Zaria, 6.7% in Calabar, 7.1% in Enugu, 8.6% in Uyo, 11.5% in Ilorin, and 20% in Lagos.

AKI is a consequence of birth asphyxia. In neonates, the incidence of AKI from birth asphyxia ranges from 30% to 56%. Specific rates outside Nigeria has been reported to be 40% in Turkey, 3.9/1000 live births and 34.5/1000 newborns admitted in neonatal intensive care unit. In Nigeria, 53.4% was reported by Airede et al in Maiduguri, north eastern region and 35.5% by Arochie and Eke in Port-Harcourt, south eastern region of the country. In Uyo, no such reports have been documented despite a high rate of birth asphyxia and its contributions to childhood mortality and so this study was conducted to add to the bulk of knowledge in this field.

METHODS

This was a descriptive cross sectional study carried out in the Newborn Unit of the University of Uyo Teaching Hospital (UUTH), Uyo in Akwa Ibom State (AKS) over a period of eight months (July 2015 to February 2016). Ethical clearance to conduct the study was obtained from the University of Uyo Teaching Hospital Health Research Ethics Committee prior to commencement of the study. Informed consent was obtained from parents/caregivers of eligible neonates before their babies were enrolled in the study.

The study population comprised one hundred and four (104) term neonates (≥37 completed weeks of gestation) with provisional diagnosis of birth asphyxia (Apgar score <7 at 5 minutes) as defined by Ibe. Preterm neonates (<37 completed weeks of gestation), neonates with congenital malformations, neonates at risk for sepsis, decline of consent by parents were excluded from the study.

Complete history was obtained including maternal, obstetric and perinatal history. Gestational age was determined by calculation from date of last menstrual period and/or antenatal ultrasonography and was confirmed by neonatal examination using modified Ballard score. Birth weight, gender, and Apgar score at 1, 5 and 10 minutes were recorded. Apgar scoring was done by the investigator, resident doctors in labour ward and paediatric residents in the neonatal unit. Asphyxiated neonates were categorized into severe (0-3), moderate (4-5) and mild (6) based on Apgar score at five minutes.

Blood sample (5ml) was collected within six hours of life from each subject, was allowed to clot and then subjected to centrifugation at 3000 revolutions per minute. The supernatant serum obtained was transferred to plain tubes and stored at -80°C until analysis. Serum creatinine estimation was done using modified Jaffé method. The test principle involved creatinine reacting with picric acid to form a yellow-red complex. The rate of dye formation (colour intensity) was directly proportional to creatinine concentration in the specimen.

This was determined by measuring the increase in absorbance at 512nm wavelength using the spectrophotometer. AKI was diagnosed when sCr >1.5mg/dl. Urinary output was assessed by application of plastic collection bag to the skin by an adhesive patch. The bag was changed six hourly within the first 24 hours. Oliguria was defined as urinary output <1.5ml/kg/hour.

Statistical analysis was done using Statistical Package for Social Sciences (SPSS) version 20. Data was summarised into tables and graphs as appropriate. Qualitative variables were expressed as numeric values and percentages, while quantitative variables were expressed as mean and standard deviation. Categorical variables were compared using the Chi-square test. A p-value <0.05 was taken to be statistically significant.

RESULTS

Demographic characteristics of study population

A total of 104 asphyxiated neonates were enrolled into the study. Of this number, 56 (53.8%) were males while 48 (46.2%) were females giving a male/female ratio of 1.2:1. The age of the babies at enrolment ranged from 1 to 5 hours with a mean of 3 hours.

A greater percentage of the study population were recruited at 2 hours of life and most of them 58 (55.8%) were delivered vaginally. Most of the neonates studied were delivered at 38 weeks and majority weighed between 3.5-3.9 kilograms as represented in Table 1.

Severity of birth asphyxia

The Apgar scores at five minutes showed that 28 (26.9%) of the subjects had severe birth asphyxia (score of 0 - 3);
52 (50%) had moderate birth asphyxia (score of 4 - 5) while 24 (23.1%) were mildly asphyxiated (score of 6).

Table 1: Demographic characteristics of study population.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Subjects</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>56 (53.8)</td>
<td>54 (51.9)</td>
</tr>
<tr>
<td>Female</td>
<td>48 (46.2)</td>
<td>50 (48.1)</td>
</tr>
<tr>
<td>Age (hours)</td>
<td>1</td>
<td>17 (16.3)</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>36 (34.6)</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>31 (29.8)</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>13 (12.5)</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>7 (6.7)</td>
</tr>
<tr>
<td>Mode of delivery</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vaginal delivery</td>
<td>58 (55.8)</td>
<td>70 (67.3)</td>
</tr>
<tr>
<td>Cesarean section</td>
<td>46 (44.2)</td>
<td>34 (32.7)</td>
</tr>
<tr>
<td>Birth Weight (kg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;2.5</td>
<td>104 (100.0)</td>
<td>104 (100.0)</td>
</tr>
<tr>
<td>2.5-2.9</td>
<td>6 (5.8)</td>
<td>11 (10.6)</td>
</tr>
<tr>
<td>3.0-3.4</td>
<td>37 (35.6)</td>
<td>38 (36.5)</td>
</tr>
<tr>
<td>3.5-3.9</td>
<td>45 (43.3)</td>
<td>39 (37.5)</td>
</tr>
<tr>
<td>&gt;4.0</td>
<td>14 (1.3)</td>
<td>15 (1.4)</td>
</tr>
<tr>
<td>Gestational age (weeks)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>37</td>
<td>104 (100.0)</td>
<td>104 (100.0)</td>
</tr>
<tr>
<td>38</td>
<td>34 (32.7)</td>
<td>37 (35.6)</td>
</tr>
<tr>
<td>39</td>
<td>32 (30.5)</td>
<td>29 (27.9)</td>
</tr>
<tr>
<td>40</td>
<td>20 (19.2)</td>
<td>21 (20.2)</td>
</tr>
<tr>
<td>Total</td>
<td>104 (100.0)</td>
<td>104 (100.0)</td>
</tr>
</tbody>
</table>

Table 2: Number of subjects with AKI using serum creatinine and urinary output criteria.

<table>
<thead>
<tr>
<th>AKI present</th>
<th>No AKI</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (%)</td>
<td>N (%)</td>
</tr>
<tr>
<td>SCr</td>
<td>12 (11.5)</td>
</tr>
<tr>
<td>Urine output</td>
<td>36 (34.6)</td>
</tr>
</tbody>
</table>

Incidence of AKI in the study population

Out of the 104 asphyxiated neonates, 48 (46.1%) had AKI. Twelve of them (11.5%) had AKI based on serum creatinine criteria i.e sCr >1.5mg/dl while 36 (34.6%) had AKI based on urinary output criteria (<1.5ml/kg/hr). The mean urinary output (ml/kg/hr) for the subjects was 1.65±0.68 while the mean serum creatinine (mg/dl) was 0.88±0.46. This is represented in Table 2.

Comparison of the levels of serum creatinine, urinary output with severity of birth asphyxia

Table 3 shows the relationship between levels of serum creatinine and urinary output with the severity of birth asphyxia. Among the subjects, there was a gradual increase in serum creatinine with severity of birth asphyxia with the mean for severe asphyxia as 1.07±0.48; for moderate asphyxia 0.83±0.44 and for mild asphyxia 0.78±0.45. This difference in mean was statistically significant (F=3.44; p=0.04). Urinary output was remarkably reduced in subjects with severe asphyxia (1.27±0.64) compared to those with moderate asphyxia (1.71±0.68) and mild asphyxia (1.96±0.53). The difference in mean was statistically significant (F=7.79; p<0.001).

Table 3: Comparison of the levels of serum NGAL, serum creatinine, urinary output with severity of birth asphyxia.

<table>
<thead>
<tr>
<th>Severity</th>
<th>Mild Mean±SD</th>
<th>Moderate Mean±SD</th>
<th>Severe Mean±SD</th>
<th>F</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum NGAL</td>
<td>68.87±30.73</td>
<td>91.76±48.72</td>
<td>162.96±47.51</td>
<td>33.33</td>
<td>0.001*</td>
</tr>
<tr>
<td>Serum creatinine</td>
<td>0.78±0.45</td>
<td>0.83±0.44</td>
<td>1.07±0.48</td>
<td>3.44</td>
<td>0.04*</td>
</tr>
<tr>
<td>Urinary Output</td>
<td>1.96±0.53</td>
<td>1.71±0.68</td>
<td>1.27±0.64</td>
<td>7.79</td>
<td>0.001*</td>
</tr>
</tbody>
</table>

DISCUSSION

The incidence of AKI among asphyxiated babies of 46.1% obtained in this study falls within the range of 30% to 56% as documented by Durkan et al in their review article.19 It also compares favourably with the report of 40% from Turkey but is lower than the 53.4% obtained from a study in north-east Nigeria.21,22 The index study location is in the south-south region of Nigeria where the incidence of birth asphyxia is not as high as in the north.23,21 A much lower rate of 35.5% was also reported by Anochie et al in Port-Harcourt, south-south Nigeria.24

The urinary output criteria demonstrated AKI in 34.6% of patients in this study. This is comparable to about 35% obtained by El-Farghali et al.25 However, Aggarwal et al, reported that oliguria as a bedside indicator of AKI is an insensitive predictor as over 50% of AKI in neonates is non-oliguric.26 Similarly, Gupta et al, also showed that most AKI in neonates is non-oliguric.33 Interestingly, in contrast, Devarajan reported that following kidney injury,
the only sign may be decreased urinary output, but this does not necessarily correlate with the severity of injury. The same criteria of oliguria was applied by Xia-yu et al in a retrospective staging of AKI in asphyxiated neonates. They suggested oliguria as reliable and a sensitive indicator of AKI in neonates.

Serum creatinine levels obtained in this study within six hours of life showed only 11.5% of the subjects to have AKI. Previous studies reported prevalence rates of 30-56% using diagnostic cut-off of serum creatinine values of 90-133µmol/L at 48 hours of life to define AKI. These higher rates may be explained by the fact that creatinine rises by 24-48 hours after kidney injury whereby 50% of the nephrons may have been lost. This agrees with a report by Devarajan that serum creatinine within the first day of kidney injury in neonates may remain normal. This is because functional change in serum creatinine is a late consequence of kidney injury and not a marker of injury itself. Moreover, serum creatinine concentration may not change until 25-50% of kidney function has already been lost, thus it may take days before a significant rise in serum creatinine is seen.

**CONCLUSION**

The incidence of AKI among asphyxiated neonates in our locale is high. Measures to improve and increase antenatal care thereby reduce the incidence of birth asphyxia in our environment should be intensified. Use of serum creatinine and urine output in the definition of AKI has its drawbacks, hence use of newer novel biomarkers like neutrophil gelatinase associated lipocalin (NGAL) should be explored in further research.

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**Conflict of interest:** None declared

**Ethical approval:** The study was approved by the Institutional Ethics Committee

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