Acute Kidney Injury in Neonates with Perinatal Asphyxia in a Tertiary Care Hospital of Nepal: a cross-sectional study

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ABSTRACT

Background

Renal involvement is the most common form of systemic complication in neonates with perinatal asphyxia. Acute Kidney Injury (AKI) can be oliguric or non oliguric. There is no consensus on the definition of acute kidney injury in neonates, which makes early diagnosis and management difficult. Acute kidney injury leads to significant morbidity and mortality in neonates.

Objective

Current study aims to explore the prevalence of Acute Kidney Injury in Neonates with perinatal asphyxia and its relation to the severity of Hypoxic Ischemic Encephalopathy (HIE).

Method

A single-center, retrospective, cross-sectional study was carried out to analyze the cases of perinatal asphyxia in the Neonatal Intensive Care Unit (NICU) and Neonatal Ward (NNW) for a period of three years (September 2020 to August 2023) in a tertiary care center. The study analyzed 195 neonates with perinatal asphyxia and Hypoxic Ischemic Encephalopathy (HIE). Data analysis was done using Statistical Package for Social Sciences (SPSS) version 25. Descriptive statistics(mean ± SD for continuous variables; percentages for categorical variables) and chi-square test (to compare categorical associations) were applied. The prevalence of acute kidney injury and its relation to grades of HIE were determined using a chi-square test.

Result

The prevalence of acute kidney injury among cases of perinatal asphyxia was 17.4%. The prevalence of acute kidney injury increased with an increase in the grading of hypoxic ischemic encephalopathy. Acute kidney injury was predominant among males with a male-to-female ratio being 3.2:1. Oliguric acute kidney injury was more common than non-oliguric acute kidney injury. 8.8% of cases had mortality, with the majority of cases being hypoxic ischemic encephalopathy grade II. The Chi-square test found a statistically significant association between hypoxic ischemic encephalopathy grades and acute kidney injury (p value=0.0113, i.e., $p < 0.05$)

Conclusion

Acute kidney injury remains one of the common complications of Perinatal Asphyxia (PA). There was a significant association between acute kidney injury cases and grades of Hypoxic Ischemic Encephalopathy (HIE), with HIE II being the most common type. Screening for acute kidney injury in case of hypoxic ischemic encephalopathy should be prioritized.

KEY WORDS

Acute kidney injury, Birth asphyxia, Oliguria, Perinatal asphyxia

INTRODUCTION

Perinatal Asphyxia (PA) is defined by the World Health Organization as the failure to establish breathing at birth, often leading to a cascade of pathophysiological events that can result in significant neonatal morbidity and mortality.[1] In situations of acute hypoxia, the diving reflex is engaged and blood is redirected to essential organs such as the brain, bypassing organs such as the kidney and the liver.[2] This results in Acute Kidney Injury (AKI), the commonest consequence of Hypoxic Ischemic Encephalopathy (HIE). Kidney Disease: Improving Global Outcomes (KDIGO) defined AKI as any of the following (Not Graded): "increase in SCr by ≥ 0.3 mg/dl (≥ 26.5 micromol/l) within 48 hours; or increase in SCr to 1.5 times baseline, which is known or presumed to have occurred within the prior 7 days; or Urine volume < 0.5 ml/kg/h for 6 hours".[3] The presence and severity of AKI have been found to correlate with the severity of HIE.[4]

Ellis and Manandhar, based on a literature search of published studies from 20 developing countries in the previous 15 years, estimate that 24% to 61% of perinatal mortality was attributable to asphyxia.[5] Past studies in Nepal showed a prevalence of 6 cases of PA per thousand live births.[4] Although perinatal asphyxia is a leading cause of neonatal morbidity and mortality globally, the burden of its renal complications, such as acute kidney injury, remains understudied in low-resource settings. In Nepal, where neonatal mortality rates are high and healthcare resources are constrained, understanding the prevalence and outcomes of AKI in neonates with PA is crucial for improving neonatal care and outcomes.

In this study, we aim to study the prevalence of Acute Kidney Injury in Neonates with perinatal asphyxia in a tertiary care hospital of Nepal and to assess its association with the severity of HIE.

METHODS

A single-center, retrospective, cross-sectional study was done to analyze cases of perinatal asphyxia in the Neonatal Intensive Care Unit (NICU) and Neonatal Ward (NNW) for a period of three years (September 2020 to August 2023) in a tertiary care center. Ethical approval was obtained from the institutional review board of Kathmandu University School of Medical Sciences (KUSMS-IRC) with approval number 165/23. Patient confidentiality was maintained by anonymizing data during analysis.

Neonates were diagnosed with Perinatal Asphyxia based on i) Apgar score < 5 at 5 minutes ii) clinical features of HIE, and (iii) profound acidosis (pH < 7.00) in umbilical artery blood sample Cases were included irrespective of the period of gestation (including preterm, term and post-term neonates) were included. Neonates born with birth defects, those with prenatal diagnosis of renal and urinary tract malformations and those with absent hospital records were excluded from the study. The study analyzed a total of 195 neonates diagnosed with perinatal asphyxia. Total population sampling was done, where all eligible cases admitted during the study period were included. Detailed history, examination, and relevant laboratory investigations were done for all the cases. HIE was graded based on the Sarnat and Sarnat classification system.[6] AKI was diagnosed using the neonatal modified Kidney Disease: Improving Global Outcomes (KDIGO) criteria. An absolute creatinine value of ≥ 1.5 mg/dL at 48-72 hours was also taken as a case of AKI.

The data was extracted from the hospital records, including maternal history, neonatal clinical data, and laboratory tests. Serum creatinine levels were measured for 48-72 hours of life and then every day until they returned to normal, and urine output was recorded hourly. SPSS version 25 was used for the data analysis process. For continuous variables, descriptive data were shown as: mean ± standard deviation and for categorical variables as percentages. Categorical data were compared using chi-square tests.

RESULTS

There were 195 cases of perinatal asphyxia fulfilling the inclusion criteria admitted during the study period of three years, 63% were male, and 27% were female neonates. The mean gestational age was 37.9 ± 1.9 weeks of gestation. The average birth weight was 2.7 ± 0.6 kg. The variability in modes of delivery is summarized in figure 1. Based on the Sarnat and Sarnat classification, 35.8% of cases were graded as HIE grade I, 58.4% as HIE grade II, and 5.6% of cases as HIE grade III. The mean APGAR at one minute was 3.8 ± 1.6 and at five minutes was 6.1 ± 1.2.

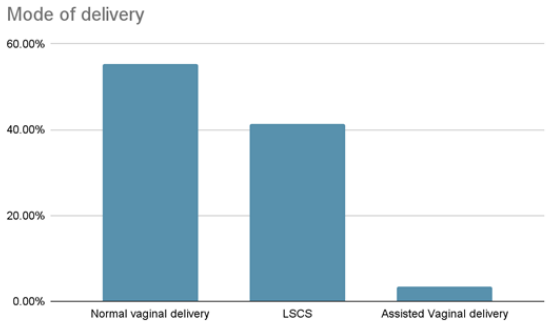

Figure 1. **Bar diagram showing modes of delivery**

Table 1. **Showing the gender-wise distribution of AKI**

Gender	AKI present	AKI absent	Total
Male	26	97	123
Female	8	64	72

AKI was diagnosed in 34 of 195 neonates (17.4%) in our study. Among these, oliguric AKI accounted for 19 cases (55.8%) with a mean urine output of 0.37 ± 0.11 ml/kg/hr, while non-oliguric AKI was observed in 15 cases (44.2%) with a mean urine output of 1.9 ± 1.1 ml/kg/hr. No pregnancy and labor complications were seen in 20 (58.8%) AKI cases; however, in the remaining cases, complications like the prolonged second stage of labor, nonprogress of labor, breech presentation, antepartum hemorrhage, preterm premature rupture of membrane, post-dated pregnancy, and fetal distress were seen.

Table 2. Showing the relationship of HIE grades with AKI

HIE	AKI present	AKI absent	Total
I	7(10%)	63(90%)	70(100%)
II	22(19.3%)	92(80.7%)	114(100%)
III	5(45.45%)	6(54.6%)	11(100%)
Total	34	161	195

Among AKI cases, 79.4% cases had various conditions associated with AKI. Neonatal sepsis was the commonest one seen in 41.1% of AKI cases followed by meconium aspiration syndrome seen in 26.4% of cases.

Table 3. Showing mean urine output and Mean creatinine levels

Type of AKI	Mean Urine Output (ml/kg/hr)	Mean Creatinine	Mean Creatinine (mg/dL)
Oliguric AKI	0.37	1.09	
Non-oliguric AKI	1.92	1.79	

The Chi-square test found a statistically significant association between HIE grades and AKI (p value = 0.0113, i.e., $p < 0.05$). This means that the distribution of AKI presence varies significantly across the different HIE grades. Kruskal-Wallis test done using spss 25 revealed statistically significant differences in AKI occurrence across HIE grades ($\chi^2(2) = 8.58$, $p = 0.014$). Post-hoc Dunn tests showed this was driven by the contrast between Grade I (10% AKI) and Grade III (45.5% AKI) ($p = 0.012$).

Table 4. Showing the Chi-Square test result for HIE-AKI association

Test	χ^2 value	df	p-value
Chi-Square test	8.58	2	0.011

Among the AKI cases, the condition of 64.7% of cases improved, 20.6% of cases went on LAMA and 8.8% of cases had mortality. Among the mortality, 66.6% cases were cases of HIE grade II and the remaining 33.3% were cases of HIE grade I. No mortality was seen in cases of grade III HIE.

DISCUSSION

Our study was done to determine the prevalence of Acute Kidney Injury (AKI) in cases of perinatal asphyxia (PA), its correlation with the degree of hypoxic-ischemic encephalopathy (HIE) as well to determine short-term outcomes. According to our research, the prevalence of AKI in asphyxiated neonates lies at 17.4%, with an increasing prevalence with an increase in severity of HIE. From the sample that developed AKI, 8.8% died, most of whom were neonates with HIE Grade II.

The result of our study demonstrates that birth asphyxia was more in males than females, which is consistent with the other studies.[4,7,8] The Male gender has been identified as a risk factor of birth asphyxia.[9,10] The mean gestational age was 37.9 ± weeks of gestation which was similar to the study done by Memon et al. and Laeeq et al.[8,11] Our study showed that 55.3% of cases were delivered via normal vaginal delivery similar to the study done by Memon et al. (50%) and Medani et al. (56.4%).[7,11] The cases born via LSCS were 41.3% which is similar to studies by Alaro et al. and Memon et al.[11,12] However it is higher in comparison to the study by Laeeq et al.[8] In our study, a significant number of cases had LSCS because of pregnancy and labor complications like fetal distress, prolonged labor, nonprogress of labor and post-dated pregnancy. Out of 195 cases of PA with HIE, HIE grade II was the most common (58.4%) with HIE grade III being the least common (5.6%). This type of variation was seen in most of the studies.[4,7,13]

AKI was seen in 17.4% cases of perinatal asphyxia. This is consistent with other studies.[11,14,15] The Prevalence of AKI in our study is less than in other studies because of the fact that we didn't consider BUN as a diagnostic criterion for AKI in contrast to most of the studies.[4,16] Our study witnessed lower occurrences of AKI compared to Mohan et al. findings (72%), which was due to the use of different diagnostic criteria favoring an increased number of AKI cases.[16] In the same manner, they discovered a higher incidence rate (47.14%) in the case of Gupta et al., who used a lower creatinine threshold (1 mg/dL). This confirms the flexibility of AKI definitions across different research. This points out the need for fully standardized diagnostic criteria, which can then be reliably used for comparison studies. Oliguric AKI was the commonest type of AKI in our study, similar to the study by Jayashree et al.[17] However, many studies have nonoliguric AKI as the commonest type of AKI.[7,16,18] With increasing HIE severity, the prevalence of AKI increased in our case. A significant association was seen between HIE grade and AKI. The chi-square test employed here highlighted the proportional differences in AKI by HIE grades ($p = 0.0113$), and the Krushkal-Wallis test further confirmed an ordinal trend of HIE ($p = 0.014$). The use of both non-parametric test has reinforced the credibility of results.

Mortality was observed in 8.8% of AKI cases, with two cases from HIE Grade II and one case from HIE Grade I, while no mortality was reported in HIE Grade III. This variation, different from other studies, could be attributed to the low number of HIE III cases with AKI.

Our study is one among few articles focusing on the prevalence and outcome of AKI in cases of perinatal asphyxia in a setting of a resource-poor country like Nepal. The rarity of articles on such a common problem seen in neonatal life emphasized the need for articles like ours. The findings seen in our cases highlight the need for urine output monitoring and serial renal biochemical monitoring for early diagnosis and appropriate intervention which eventually helps in reducing perinatal morbidity and mortality. Additionally, prior research suggests that neonates who experience AKI are at a higher risk of developing chronic kidney disease (CKD) later in life, underscoring the need for long-term follow-up of renal function, possibly incorporating advanced imaging techniques like MRI.[19,20]

Though this study provides insightful data and information on AKI and its outcome, there are some limitations to this study. This study has a single-centric, cross-sectional, and retrospective study design. Due to the research being done in a single center (in a tertiary care center), It may not be applicable in all the other settings, esp. resource-poor areas. Due to the relatively small sample size, the outcomes of this study might not represent the whole neonatal population. Since the study is retrospective and cross-sectional, there can be missing information, and causality cannot be established. Measurement of urine output might not have been accurate since all neonates were not under urinary catheters. To validate the findings in our articles, there is a need for research with prospective design with long-term follow-up to find the long-term outcome and complications of AKI.

CONCLUSION

In conclusion, AKI remains one of the common complications of Perinatal Asphyxia (PA). There was a significant association between AKI cases and grades of Hypoxic Ischemic Encephalopathy (HIE) with HIE II being the most common type. Urine output and serial renal biochemical parameters monitoring can help in the early diagnosis of AKI, hence preventing further morbidity and mortality.

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