

## PREVALENCE AND OUTCOME OF ACUTE KIDNEY INJURY AMONG TERM NEONATES WITH ASPHYXIA ADMITTED IN A TERTIARY CARE HOSPITAL

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### Abstract

**Background:** Acute kidney injury (AKI) is commonly seen in asphyxiated neonates, accounting 56% of these cases. Early diagnosis of AKI is important in neonates with hypoxic ischemic encephalopathy (HIE) for appropriate fluid and electrolyte management. Clinical prediction of outcome of perinatal asphyxia is important in guiding management decisions and instituting timely rehabilitative measures. The present study was performed to estimate the prevalence of renal failure among asphyxiated neonates and also to determine the severity and type of Acute kidney injury with APGAR score and HIE. **Materials and Methods:** A hospital based prospective cohort study was conducted among term neonates with H/O Perinatal Asphyxia admitted in Neonatal Intensive Care Unit. Sarnat and Sarnat scoring system was used for hypoxic ischemic encephalopathy (HIE) staging. Criteria for defining AKI was oliguria (urine output <0.5ml/kg/hr) and/or serum creatinine level more than 1.5mg/dl. Epi-Info Software Version 7.1.4.0. was used for statistical analysis. **Results:** The prevalence of AKI among neonates with perinatal asphyxia was found to be 36% (97) with 40% being males and 30% females. Acute kidney injury was found to be highest among neonates with stage III HIE (87%) on 3rd day of life. The mortality rate among neonates with asphyxia and AKI was 76%. **Conclusion:** One among every 3 asphyxiated neonates is likely to develop AKI. It is recommended to diagnose AKI early and institute appropriate measures from 3rd day of life as late diagnosis leads to more severe AKI with poor prognosis.

## INTRODUCTION

Perinatal asphyxia is a significant problem globally resulting in neonatal morbidity and mortality.<sup>[1]</sup> Hypoxia and ischemia can cause damage to any tissue and organ of the body with common involvement of kidneys, brain, heart and lungs.<sup>[2]</sup> The most frequently involved systems are renal (50%) followed by central nervous system (28%), cardiovascular (25%) and pulmonary system (23%).<sup>[3]</sup>

Acute kidney injury is commonly seen in asphyxiated neonates, accounting for 56% of these cases.<sup>[4]</sup> Renal insufficiency can occur within 24 hours of a hypoxic ischemic episode as kidneys are highly sensitive to hypoxia, which if prolonged may lead to irreversible cortical necrosis.<sup>[5]</sup> AKI affects 8-24% of critically ill neonates and mortality ranges

between 10 - 61% and 40% of survivors suffers residual kidney dysfunction.<sup>[6]</sup>

Early recognition of AKI is important in neonates with hypoxic ischemic encephalopathy (HIE) for appropriate fluid and electrolyte management, as maintaining a stable biochemical parameters is vital in improving the outcomes in these babies.<sup>[7]</sup> Clinical prediction of outcome of neonates with perinatal asphyxia is important in guiding management decisions and instituting timely rehabilitative measures especially for those projected to have acute kidney injury. Awareness on perinatal asphyxia associated-AKI among the clinicians makes them more alert in suspecting the condition. Against this background the present study was conducted to ascertain the contribution of perinatal asphyxia to acute kidney injury thereby neonates at risk of renal damage could be identified for prompt treatment.

## Objectives

To estimate the prevalence of acute kidney injury in term asphyxiated neonates with hypoxic ischemic encephalopathy and assess the outcome.

## MATERIALS AND METHODS

Study design: A hospital based prospective study.

Study setting: Neonatal Intensive Care Unit (NICU), Sri Venkateswara Ramnarayan Ruia Government General Hospital, Tirupati.

Study population: Term newborns with perinatal asphyxia admitted in NICU in one year.

Inclusion criteria: Term neonates with failure to initiate and sustain breathing at birth with APGAR less than 7 and clinical evidence of HIE as per Sarnat&Sarnat staging.

Exclusion criteria: Neonatal sepsis, respiratory distress syndrome, necrotisingentero-colitis, major congenital anomalies of the kidney & urinary tract, neonates on intravenous nephrotoxic drugs, or born to mothers with significant drug intake/ antepartum fever and neonates died within 3 days of admission were excluded.

Sample size: At 95% confidence interval, a sample size of 267 was estimated with the prevalence of AKI at 60% and 10% allowable error.

### Study Method

A predesigned and pretested proforma was used to collect maternal and neonatal data. After performing general physical examination, systemic signs were recorded. The APGAR score was noted at 5 min after birth. Sarnat and Sarnat scoring system was used to classify neonates with clinical features of HIE.<sup>[8,9]</sup> Ultrasonography was done within 24 hours of birth to rule out congenital malformations of the urinary tract if any. Renal function testss – blood urea, serum creatinine, serum electrolytes, urinalysis including urinary creatinine and sodium were monitored twice: initially within first 24 hours of birth and on 3rd day of life. Laboratory parameters of neonates with abnormal renal functions 72 hrs after birth were monitored every day till recovery or death. Urine output was monitored with the help of plastic collection bag or by catheterization if required. Criteria to define AKI was presence of oliguria (urine output <0.5ml/kg/hr.) and/or serum creatinine level more than 1.5mg/dl. Neonates with urine output persistently <1ml/kg/hr despite the above treatment, were diagnosed to have intrinsic AKI. Epi-Info Software Version 7.1.4.0. by CDC,

WHO, Atlanta, USA was used for statistical analysis.

## RESULTS

Among 2030 newborns, 270 neonates who satisfied inclusion criteria were taken into the study. Among them, 154 were males (57%) and 116 were females (43%). Birth weight ranged from 2500 to3200 gm with a mean weightof 2756 ± 196 gm; mean length was 48 ± 1.48 cm. Nearly 224 neonates had moderate APGAR score (83%) and only 46 (17%) of them had a very low score. Majority of the neonates (167; 62%) were in stage II HIE followed by stages I (57; 21%) and III (46; 17%).

The prevalence of AKI among asphyxiated neonates was found to be 36% (97) with 40% being males and 60% females. Majority of AKI secondary to perinatal asphyxia were non oliguric type (79; 81%) compared to oliguric type (18; 19%). On day 3 of life, majority of the neonates with stage III HIE had AKI (87%) compared to neonates with stage I HIE (10.5%). But there is no statistically significant difference in between any of the neonatal characteristics and AKI.

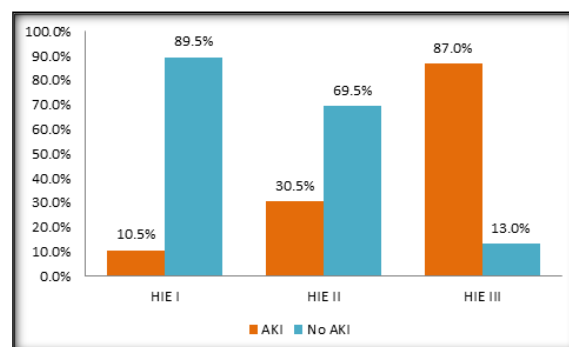


Figure 1: Relation between HIE and AKI among neonates

High mortality rate was seen in perinatal asphyxia with AKI (76%). The risk of development of AKI in HIE stage III is 6 fold higher compared to HIE stage I [95% CI (2.6 – 16.5); p<0.0001]. The risk of death in AKI in HIE III is 12 folds higher compared to HIE I [p<0.0001 at 95% CI (6.9-23)]. The median day of death among neonates with AKI was found to be 4.5 days. Only 23 (24%)newbornswithAKI were discharged when compared to those without AKI (80%).

Table 1: Outcome of the neonates with AKI

Outcome	AKI (n=97)	No AKI (n=173)
Discharged	23 (24%)	138 (80%)
Died	74 (76%)	35 (20%)

## DISCUSSION

Perinatal asphyxia is an insult to the fetus or the newborn due to hypoxia and/or ischemia which can lead to fleeting biochemical and/or functional

changes in various organs in the body. Renal injury is a consequence of adaptive mechanism in perinatal asphyxia. Among renal complications i.e. acute tubular necrosis, renal vein thrombosis and AKI, AKI is the most common with poor prognosis.<sup>[5]</sup>

The current study noted that no significant association was found between mentioned (maternal and neonatal) characteristics and development of AKI. This can be attributed to the lesser sample size in this study.

The serum creatinine threshold at 48 hours of life was chosen to be 90  $\mu\text{mol/l}$  in some studies.<sup>[5,10,11]</sup> A threshold of 133  $\mu\text{mol/l}$  at 48 hours was chosen Studies by Karłowicz.<sup>[12]</sup> and Kaur.<sup>[13]</sup> for diagnosing AKI. The present study also considered the creatinine threshold of 133  $\mu\text{mol/l}$  at 72 hours of life so as to increase the possibility of diagnosis of AKI due to marked reduction in the maternal creatinine level by that time.

Incidence of AKI was found to be highest in the asphyxiated term infants ranging from 7% to 72%.<sup>[5,13]</sup> The present study reported a prevalence rate of AKI to be 36%. Slightly higher rates have been reported in the studies by Gopal et al (64%), Ambar et al (62%) and Varma et al (54%). In contrast, lower rates were reported by Nouri et al (17.2 %), and Alaro et al (11.7%).<sup>[15,17,16,10,14]</sup> The prevalence rates in the available studies were similar in various settings stating that AKI in perinatal asphyxia is a universal problem.

This study noted that AKI was observed in 10.5% of neonates with HIE I and in 87% with HIE III which amounted for six fold increased risk of development of AKI in stage III HIE when compared to stage I HIE. With increase in the incidence of AKI, the perinatal asphyxia and its severity tend to increase.<sup>[5]</sup> A study by Nouri et al. showed that two-thirds of babies with AKI had HIE of grade II and one-third with AKI had HIE of grade III but renal impairment was not seen among neonates with grade I HIE.<sup>[19]</sup> However Gupta et al. study revealed that serum creatinine and blood urea were significantly higher among asphyxiated neonates with HIE when compared to the control group thereby suggesting the correlation between AKI and HIE.<sup>[5]</sup> Kaur et al. study reported that AKI developed among 56% and 9% of neonates with severe and moderate asphyxia respectively.<sup>[13]</sup> Whereas Alaro et al study observed that it was common in neonates with HIE III (42.9%) compared to HIE I (4.6%).<sup>[14]</sup> Another study by Gopal et al. revealed that AKI was seen in 25% and 100 % of HIE stage I and III cases respectively.<sup>[15]</sup>

A study done by Nouri et al. had reported a significant association between AKI and low APGAR score at 5 min.<sup>[10]</sup> In the present study, all the babies with severe score developed AKI while the majority of babies with moderate score had AKI. However, this study found no significant association between AKI and APGAR score. Most of the newborns with severe asphyxia died before day 3 of life and were not included in the study which might be the reason for the lower rate of AKI in severe asphyxia cases. Gopal et al study reported that among asphyxiated neonates with AKI, 62.5% were non-oliguric, while the remaining 37.5% were oliguric.<sup>[15]</sup> The present study reported that 81% of

cases were non oliguric type and 19% of cases were oliguric type.

The outcome of AKI in critically ill neonates is poor; however, independent risk factors have not been identified. Variable rates of mortality had been reported in asphyxiated newborns with AKI ranging from 2% to 75 %.<sup>[5,10,11,22,14]</sup> This study reported a 76% mortality rate by one week of life in neonates with AKI compared to only 20% among neonates without AKI. This high mortality rate could be attributed to the small sample size.

#### **Study Limitations**

Inability to get a good representation of less severely asphyxiated babies as this is a tertiary hospital and one third of the neonates had been referred due to the severity of their illness. The moderate and severely asphyxiated newborns are not common and the study would have needed to be conducted over a longer period to get a larger sample size. The study was unable to generate correlates and risk factors due to sample size being small.

## **CONCLUSION**

Perinatal asphyxia is most common cause of AKI in neonates. One among every 3 asphyxiated neonates is likely to develop AKI with a prevalence of 36%. AKI with asphyxia is associated with poor outcome with a mortality rate of 76%, dying by 4th day of life. The risk of development of AKI and risk of mortality is higher with increasing severity of HIE. Hence it is recommended to diagnose AKI as early as possible and institute appropriate measures from 3rd day of life as late diagnosis leads to a severe AKI with poor prognosis. Larger studies are required to find out risk factors and to assess the long term outcome of asphyxiated babies with AKI discharged from the newborn unit.

Ethical consideration: IEC clearance was obtained prior to the start of the study. ( )

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