Incidence of Acute Kidney Injury in Asphyxiated Neonates and Its Relationship with Severity of Hypoxic-Ischemic Encephalopathy: Experience from a Medical College Hospital, Bangladesh.

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Abstract:

Background: *Perinatal asphyxia (PNA) is one of the leading causes of neonatal morbidity and mortality in Bangladesh. Among others, hypoxic-ischemic encephalopathy and acute kidney injury are two common complications of perinatal asphyxia. Morbidity and mortality increases when PNA is associated with these two complications.*

Objective: *The objectives of the study were to determine the incidence of acute kidney injury (AKI) among asphyxiated neonates associated with various stages of hypoxic-ischemic encephalopathy (HIE) and to find out the relationship between AKI and HIE stages.*

Materials and Methods: *This cross-sectional study was conducted in the neonatal unit of Jalalabad Ragib-Rabeya Medical College Hospital, Sylhet, between the periods of January 2018 and June 2018. A total of 130 newborns admitted in the neonatal ward within 24 hours of age with perinatal asphyxia and hypoxic-ischemic encephalopathy were included in the study by the consecutive sampling method. Serum creatinine level was measured at 24 hours after birth. AKI was considered if serum creatinine level was ≥1.5 mg/dL.*

Result: *Among 130 neonates, 35.4% had HIE stage-I, 56.1% had HIE stage-II and 8.5% had HIE stage-III. AKI was present in 12.3% of the asphyxiated neonates. There were no significant relationship between AKI and demographic variables like gender, birth weight, and place of delivery, mode of delivery and parity of the mothers. AKI was significantly associated with HIE stage-II and stage-III compared to HIE stage-I (p=0.02). The mean serum creatinine level was significantly higher in HIE stage-II and stage-III than HIE stage-I (p=0.001). Among the study neonates, 28.5% died. There was no significant relationship between death and AKI (p=0.74). The Pearson correlation test revealed no statistically significant relationship between serum creatinine levels and hospital stay.*

Conclusion: *The incidence of acute kidney injury was 12.3% among asphyxiated newborn associated with HIE. Frequency of AKI significantly associated with severity of HIE.*

Keywords: *Perinatal asphyxia, Hypoxic-ischemic encephalopathy, Acute kidney injury.*

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Introduction

Bangladesh still has a high newborn mortality rate. Perinatal asphyxia, which accounts for 22.9% of newborn deaths, is the second most frequent cause of newborn mortality[1]. Perinatal asphyxia (PNA) is an injury to the foetus or newborn caused by hypoxia and/or ischemia to numerous organs. It manifests as a challenge in establishing spontaneous respiration, which is apparent by a delayed cry after birth[2]. Inability to initiate and maintain breathing at birth is referred to as perinatal asphyxia (PNA) by the World Health Organization (WHO)[3]. The incidences of PNA in term

neonates in developed countries are ranges from 4.3 to 8.5%, which is around 23% in developing countries[4].

Asphyxia in the newborn may damage all organ system of the body including brain and kidney. In severely asphyxiated neonates, the brain damage leads to hypoxic-ischemic encephalopathy (HIE). HIE categorized into stage one to three by sernat and sernat staging method[5]. The severity of hypoxic-ischemic encephalopathy increases mortality in asphyxiated newborns. It has been responsible for as high as 50% of fatalities. In the first month of life, most of these deaths take place[5].

During asphyxia, cardiac output redistributes to brain, heart, and adrenal glands to maintain perfusion to these vital organs. As a result, blood supply compromises to other organs including kidney, gastrointestinal tract and skin, which occasionally may leads to multiorgans failure. Additionally, the renal parenchymal cells are very susceptible to reperfusion injury and have a low capacity for anaerobic respiration, all of which lead to acute kidney injury (AKI)[6]. In asphyxiated baby, acute kidney injury is a common complication that adversely affects the overall morbidity and mortality of the newborn. The incidence of AKI among asphyxiated neonate ranges from 11.7% to 75% in various studies in Africa and India[6,7,8]. In a hospital based study among asphyxiated neonates in Bangladesh, it was found that the incidence of AKI was 68.7%[9].

AKI has been linked to a longer length of stay in the hospital[10]. Children who survive AKI are also prone to have persistent renal abnormalities[11]. Identification of newborns at high risk and early AKI detection are the initial steps in the prevention and treatment of neonatal AKI, allowing for the mitigation of further harm.

One of the most common causes of renal failure in neonatal population is birth asphyxia. This is due to the fact that when a patient develops oliguria, we typically suspect renal failure, whereas up to 33% of instances of AKI in newborns are nonoliguric[12].

Since AKI is a frequent complication of perinatal asphyxia with hypoxic-ischemic encephalopathy, we performed this study to determine the incidence of AKI among asphyxiated neonates associated with HIE admitted to the neonatal ward of Jalalabad Ragib-Rabeya Medical College Hospital, Sylhet and to find out the relationship between AKI and HIE staging.

Materials and Methods

This cross-sectional study was carried out in the neonatal unit of the department of paediatrics, Jalalabad Ragib-Rabeya Medical College Hospital, Sylhet, between the periods of January 1st, 2018 andJune 30th, 2018. A total of 130 term newborns (e"37 completed weeks of gestation) admitted within 24 hours of birth to the neonatal unit due to perinatal asphyxia and different stages of hypoxic-ischemic encephalopathy (HIE) were included in the study by the consecutive sampling method. Perinatal asphyxia was defined as the inability to initiate and sustain breathing at birth[3], clinical evidence of HIE[12] and/or an APGAR score ≤7 at 5 minutes[2]. Premature neonates (<37 weeks of gestational age), septicaemia, multiple congenital anomalies, anomalies of kidney or urinary tract, admitted after 24 hours of age, maternal kidney disease, and those guardian refused to participate in the study were excluded. Informed consent was obtained from the parents or caregivers of every patient. Ethical clearance was obtained from the institutional review board. After enrolment, antenatal and natal histories (including parity of mothers, place of delivery, mode of delivery, residence, gender of the newborn) were recorded. A digital weighing scale was used to determine weight. The APGAR score was obtained from the referral note of the department of obstetrics in inborn cases. In outborn cases, a history of delayed crying after birth was obtained. Every patient was then examined and assessed for hypoxic-ischemic encephalopathy (HIE) by modified sarnat and sarnat staging for HIE[12] and classified as stage-I, stage-II and stage-III. All patients were treated according to institutional guidelines. A blood sample was sent to the hospital laboratory at 24 hours after birth to be tested for serum creatinine levels. AKI was diagnosed when serum creatinine level was ≥1.5 mg/dL. After receiving the report, all newborns were divided into two groups. Neonates with AKI were included in group-I and those without AKI were included in group-II. The outcome of the patient was recorded as either discharged or death and the lengths of their hospital stay were noted at the same time.A pre-designed questionnaire was used to collect data. Data were then analysed by using Statistical Package for Social Science V21 (SPSS V21). Numerical data were presented as mean and standard deviation and categorical data were presented as frequency and

percentage. A Chi-square test, an Independent Sample T test, a one-way Anova test, and a Pearson correlation test were done to determine the association between the variables. A p-value <0.05 was considered statistically significant.

Results

A total of 130 neonates admitted due to perinatal asphyxia and having different stages of HIE enrolled for the study. Among them, male were 90 (69.2%) and 40 (30.8%) were female. In 35.4%, 56.1%, and 8.5% of the neonates, respectively, HIE stage-I, stage-II and stage-III were present. AKI was present in 16 (12.3%) of the asphyxiated neonates with HIE (Figure-1). Mean birth weight was 2850±417.73 grams in the AKI group and 2819.74±438.09 grams in the without AKI group. Majority (83.8%) of the respondents were coming from rural area. Most of the babies born outside the study hospital (56.2%), and most of them were delivered vaginally (56.2%). Majority (63.8%) of the mothers were primi. Mean hospital stay in the AKI group was 7.562±5.988 days and 5.701±4.460 days in the without AKI group. There was no significant relationship between AKI and demographic and other variables like gender, mean birth weight, residence, place of delivery, mode of delivery, parity of mother and mean hospital stay (p>0.05) (Table-I). AKI was significantly higher in HIE stage-II and stage-III in relation to HIE stage-I (p=0.02) (Table-II). One-way Anova test showed that the mean creatinine level was significantly higher in HIE stage-II and stage-III than HIE stage-I (p=0.001) (Table-III). Among the asphyxiated neonates, 93 (71.5%) patients were discharged and 37 (28.5%) were died. There was no significant relationship between death and AKI (p=0.74) (Table-IV). Pearson correlation test showed that there was no statistically signification relation between mean serum creatinine levels and hospital stay, though a negligible positive correlation was present (r=0.149, p=0.09) (Figure-2).

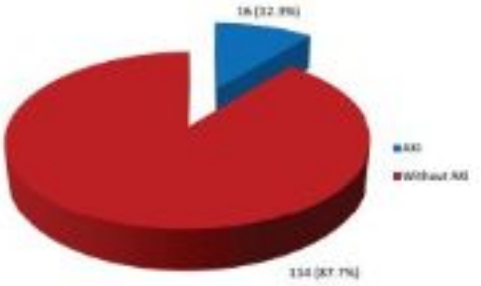

Fig.-1: *Acute kidney injury in the study neonates, N=130*

Table-I

Comparison of demographic and other variables between two groups, N=130

Variables		Acute kidney injury		Total	p-value
		Present	Absent		
Gender	Male	13 (14.4)	77 (856)	90 (100)	0.26
	Female	3 (7.5)	37 (92.5)	40 (100)	
Birth weight (Grams)	Mean±SD	2850±417.73	2819.74±438.09	—	0.79*
Residence	Urban	2 (9.5)	19 (90.5)	21 (100)	0.67
	Rural	14 (12.8)	95 (87.2)	109 (100)	
Place of delivery	Inborn	6 (10.5)	51 (89.5)	57 (100)	0.58
	Outborn	10 (13.7)	63 (86.3)	73 (100)	
Mode of delivery	Vaginal	7 (9.6)	66 (90.4)	73 (100)	0.28
	LSCS	9 (15.8)	48 (84.2)	57 (100)	
Parity of mother	Primi	13 (15.7)	70 (84.3)	83 (100)	0.12
	Multi	3 (6.4)	44 (93.6)	47 (100)	
Hospital stay (Days)	Mean±SD	7.562±5.988	5.701±4.460	—	0.138*

*Indipendent Sample T test

Table-II: *Relationship between hypoxic ischemic encephalopathy staging and acute kidney injury, N=130*

Stages of HIE	AKI		Total	p-value
	Present	Absent		
Stage-I	1 (2.2)	45 (97.8)	46 (100)	0.02
Stage-II	12 (16.4)	61 (83.6)	73 (100)	
Stage-III	3 (27.3)	8 (76.3)	11 (100)	

Table-III

Association between creatinine level and HIE staging by One-Way Anova test, N=130

HIE	n	Creatinine level	p-value
Stage 1	46	0.829±0.253	0.001
Stage 2	73	1.103±0.485	
Stage 3	11	1.185±0.429	

Table-IV

Association between death and AKI, n=130

Variables		Death		p-value
		Yes	No	
AKI	Present	4 (25)	12 (75)	0.74
	Absent	33 (28.9)	82 (71.1)	

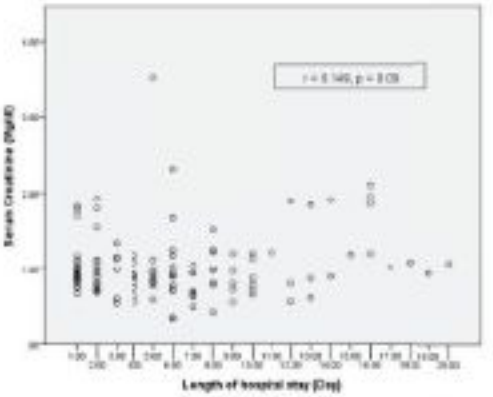

Fig.-2: *Pearson correlation between serum creatinine level and length of hospital stay*

Discussion

Perinatal asphyxia occurs when there is lack of oxygen (hypoxia) and/or lack of perfusion (ischemia) of sufficient magnitude and duration to produce more than transient functional and/or biochemical changes to various organs in the body. Renal insufficiency may develop within 24 hours of a hypoxic-ischemic episode because kidneys are extremely sensitive to oxygen deprivation; if it persists, it may potentially result in irreversible cortical necrosis[14]. In our study we determined the incidence of acute kidney injury in asphyxiated neonates with hypoxic-ischemic injury, and find out the association between AKI and HIE staging. A total of 130 newborns with PNA and different stages of HIE were included. Among them, majority of the patients were male (69.2%). Male predominance was found in different studies conducted by Alaro et al.[6], Amardiyanto et al.[8], Emina et al.[15] and Medani et al[16]. It may be that males are more prone to develop asphyxia at birth due to biological plausibility, or because of socioeconomic reasons, the rates of hospital admissions for boys are higher. Mean birth weight in the AKI group was 2850±417 grams and without AKI group was 2819.74±438 grams. Gopal G in his study found that mean birth weight of asphyxiated neonates with AKI was 2860±280 grams, which is nearly similar to our study[14].

Aslam et al. in a study found that the risk of experiencing birth asphyxia was higher for vaginal deliveries conducted by untrained traditional midwives[17]. Other studies also discovered that vaginal deliveries had a higher risk of perinatal asphyxia[8,14,15]. In our study, majority (56.2%) of the asphyxiated neonates delivered vaginally.

Reddy et al.[18] discovered in their study that the majority of the asphyxiated babies (70.7%) were outborn, which is consistent with our findings. In the current study, 56.2% of the participants were not born in the study hospital.

The incidence of AKI reported in various researches varies greatly. In their investigations, Agarwal et al.[7] and Reddy et al.[18] discovered that 75.6% and 70.7% of asphyxiated neonates, respectively, had AKI, whereas Alaro et al.[6] discovered that 11.7% of the neonates in their study had the condition. This variation in incidence rate can be the result of the

researcher using different diagnostic standards for AKI and also the inclusion criteria of the study sample. Vasudevan and Phadke[10] stated in an editorial that the absence of a clear description of childhood AKI has made it difficult to comprehend the burden of the condition and its implications. Wide variations in incidence and results have been reported using more than 30 definitions from the literature. In several studies, serum creatinine levels >1.5 mg/dl, rising serum creatinine levels, oliguria (<0.5 ml/kg/min) and high blood urea levels, are utilised to identify neonatal AKI. Some authors diagnosed AKI using just one criterion, whereas others used two or more[7,14,16,19]. In the present study, acute kidney injury was present in 12.3% of the asphyxiated neonates based on serum creatinine level ≥1.5 mg/dl.

The frequency of acute kidney injury increased along with the severity of prenatal asphyxia[15]. In our study, neonates with HIE stage-III had the highest incidence of AKI (27.3%) while those with stage-I had the lowest incidence (2.2%). This difference was statistically significant. Strong correlation between incidence of AKI and staging of HIE also found by Agarwal et al.[7] in their study. Ferdaus et al. in a study found that the most frequent cause of AKI was perinatal asphyxia with HIE stage-II or stage-III. But no patient with HIE stage-I developed AKI[20]. In another study, Saha et al.[9] found that AKI was present in 41.94%, 73.47%, 95.5% newborns with HIE stage-I, stage-II and stage-III, respectively. They used pRIFLE criteria for the diagnosis of AKI, which may be the reason of high incidence of AKI in their study.

Numerous studies have demonstrated increasing trends in the mean serum creatinine level with increasing severity of HIE[14,15]. Our study also found the similar findings. The neonates with HIE stage-II and HIE stage-III compared to stage-I had a significantly higher mean serum creatinine level. There was no significant relationship between mean serum creatinine level and length of hospital stay on Pearson correlation in this study. Vasudevan et al.[10] stated that AKI in children is associated with prolonged hospital stay, which didn't support our study.

Death rate was 28.5%in our study. Death was not significantly associated with AKI. Death rate was varying in different studies. In a study at Dhaka Medical College Hospital, Ferdaus et al. found that death rate was 27.27% in newborns suffering from AKI, which is similar to our study[20]. Reddy et al.[18] in their study found that death rate was 5.3%, which was 8.7% in the study done by Medani et al[16]. These rates are lower than our study. Death rate was found 18.75% in another study conducted by Gopal G that is nearly similar to our study[14].

Limitations

The study had several flaws, such as the lack of laboratory tests to confirm asphyxia, the single evaluation of serum creatinine levels 24 hours after birth, and the lack of additional research into the aetiology of AKI.

Conclusion

The incidence of acute kidney injury in our study was 12.3% among newborn having perinatal asphyxia associated with hypoxic-ischemic encephalopathy. Newborn with HIE stage-II and stage-III had significantly higher possibilities to develop acute kidney injury.

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