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ORIGINAL ARTICLE

Frequency of Acute Kidney Injury with Hypoxic Ischemic Encephalopathy Staging in Neonates with Perinatal Asphyxia: An Observational Study (Descriptive Case Series)

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ABSTRACT

Perinatal asphyxia affects almost all the organs in neonates, kidneys being one of commonly affected organs. Early recognition of disturbances in renal function is important for early intervention to prevent irreversible damage to kidneys.

Objective: In this study we observed the frequency of acute kidney injury (AKI) in neonates with clinical staging of hypoxemic ischemic encephalopathy (HIE) in neonates with perinatal asphyxia.

Methodology: An overall number of 145 term neonates with perinatal asphyxia admitted at nursery of Liaquat University Hospital, Hyderabad from February-2019 to july-2019 were included in this study. Urine output was monitored from day one and serum creatinine was sent on third day of life. Serum creatinine was sent early of those neonates having low urine output.

Results: The average birth weight was 2.72±2.67 kg. There were 106 (73.1%) males and 39 (26.9%) females. Most neonates were born via simple vaginal delivery 100 (68.97%) and few via caesarian section 45 (31.03%). Out of 145 neonates 38 (26.21%) were in stage I, 95 (65.52%) in stage II and 12 (8.28%) in stage III HIE. Frequency of AKI in neonates with perinatal asphyxia was 55 (37.93%). Incidence of AKI was significantly high in stage II 45(81.8%) as compare to stage I 0(0%) and stage III 10(18.2%) (p=0.0005).

Conclusion: AKI is a common complication of perinatal asphyxia. Further multicenter based and studies on large scale need to be done to identify the inter-relationship between maternal factors and perinatal asphyxia associated AKI to prevent neonatal morbidity and mortality.

Keywords: Acute kidney injury, perinatal asphyxia, hypoxic ischemic encephalopathy.

INTRODUCTION

Neonatal mortality is one of the significant causes of mortality in under-five age group. According to WHO estimates in Pakistan 49% deaths in under-five age group occurred in neonatal period, with perinatal asphyxia and birth trauma contributing 23% to neonatal deaths [1]. WHO has described perinatal asphyxia as "failure to initiate and sustain breathing at the time of birth" [2]. The term perinatal asphyxia is applied frequently instead of birth asphyxia, as asphyxia may occur at any time in utero, at birth or in the postnatal period. Perinatal asphyxia affects all the organs in neonates. In term neonates with perinatal asphyxia, renal, central nervous system, heart and lung dysfunction occurring in 50%, 28%, 25% and 25% cases, respectively [3]. The neonatal kidney is anatomically, functionally immature and has been defined as 'halfway to acute kidney failure'. Renal insufficiency may develop as early as 24 hours of life, leading to un-repairable cortical damage when hypoxia is prolonged [4,5,6]. The incidence of perinatal asphyxia and its severity matchup with increasing incidence of acute kidney injury[7]. Asphyxia causes redistribution of cardiac output to maintain cerebral, cardiac, and adrenal perfusion while minimizing skin, renal and gastrointestinal, perfusion making kidneys vulnerable [8]. According to one study conducted on the causes of AKI in neonates, 36.5% patients developed AKI due to perinatal asphyxia showing that it is second most common cause of AKI in neonates [9]. Therefore, timely noticing the renal injury is essential in neonates with hypoxic ischemic encephalopathy (HIE) to maintain a normal biochemical environment and start early proper management [10].

METHODOLOGY

Descriptive case series study conducted at Liaquat University Hospital, Hyderabad, from February-2019 to july-2019 after taking approval from ethical review committee. Total 145 neonates with perinatal asphyxia were enrolled. Full term neonates (37-41 weeks and 6 days confirmed by ultrasound report or last menstrual period), admitted with the history of perinatal asphyxia within 24 hours of delivery were selected, and while newborns with sepsis (if 2 or more of the following findings were present: high erythrocyte sedimentation rate for age, white blood cell count less than 5 × 109/L, immature/total neutrophil count greater than 0.2, and positive serum C-reactive protein), congenital renal malformations, and newborns those parents refused to take part were excluded from study. By taking prevalence of 76%, confidence level of 95% and margin of error 7%, the sample size of the study has been calculated 145 by WHO calculator. Sampling technique was Non-probability consecutive. Neonates admitted in paediatric nursery at Liaquat university hospital Hyderabad with history of perinatal asphyxia meeting inclusion criteria were selected and written consent was taken. The patients enrolled in the study had the right to leave during study, they were not deprived of any benefit and confidentiality was maintained. After giving emergency care, resuscitation and taking anthropometric measurements, all asphyxiated newborns were staged as stated in Sarnat scoring system daily up to third day of life. A predesigned proforma was used and the data such as; gestational age, birth weight and relevant perinatal history was collected. On the first day all the neonates underwent ultrasound abdomen to rule out congenital anomalies of renal system. Urine volume was observed from day one by applying small urine sample collection bag or by catheterizing patients. For collection of urine soft rubber N/G, tubes of appropriate size were used, to prevent any trauma during catheterization. On third day of life serum creatinine sample of all the neonates enrolled in study was sent to laboratory. Because during the first 48 hours of life serum creatinine still reflects the maternal creatinine levels, sample for serum creatinine was sent early of those neonates having low urine output. Final outcome was recorded in predesigned proforma by researcher himself. Statistical analysis was conducted by using SPSS version 20. Mean and standard deviation was calculated for quantitative variables like, age at admission, gestational age, weight, plasma creatinine. If the data is not normally distributed then median was calculated. Frequency and percentage was calculated for qualitative variables like gender, mode of delivery, HIE stages (I, II, III), AKI (anuria, oliguria, non-oliguria). Effect modifiers were controlled through stratification. Frequency of AKI was compared with HIE staging using chi-square test. Post stratification Chi2 for

data {age at admission, gestational age gender, mode of delivery} was applied. p- Value of 0.05 or less was taken as significant.

RESULTS

A total 145 full term delivered neonates admitted within 24 hours of delivery to the nursery with the history of perinatal asphyxia were selected for study. The average birth weight was 2.72±2.67 kg. There were 73.1% male and 26.9% female. The mean age, gestational age at the time of birth and serum creatinine was also reported. Most neonates were born via spontaneous vaginal delivery 100 (68.97%) and few via caesarian section 45 (31.03%). Out of 145 neonates enrolled in study 38 (26.21%) were in stage I, 95 (65.52%) were in stage II and 12 (8.28%) were in stage III HIE (figure 1). Frequency of AKI in neonates with perinatal asphyxia was noted 55 (37.93%). Incidence of AKI was significantly high in stage II 45 (81.8%) as compare to stage I 0 (0%) and stage III 10 (18.2%) (p=0.0005). Stratification analysis was performed and observed that frequency of AKI in neonates with perinatal asphyxia was not statistically significant in age groups (p=0.484). It was also not statistically significant with neonatal gender, gestational age, mode of delivery and place of delivery. Comparing the frequency of AKI with HIE staging in neonates with perinatal asphyxia with respect to age groups was observed and found that rate of AKI was high in stage II cases for below and equal to 30 minutes of age while it was not statistically significant with above 30 minutes. Comparing the frequency of AKI with HIE staging in newborns with perinatal asphyxia with respect to neonatal gender, gestational age at birth, mode of delivery and place of delivery were significant (Table 2).

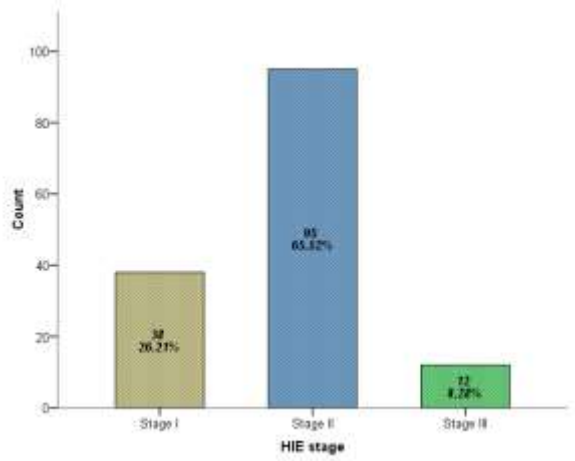

Figure 1: Hypoxic Ischemic Encephalopathy Staging n= 145

Table 1: Compare the Frequency of Acute Kidney Injury with Hypoxic Ischemic Encephalopathy Staging in Neonates with Perinatal Asphyxia

HIE Stage	Acute Kidney Injury		Total	P-Value
	Yes	No		
Stage I	0 (0%)	38 (42.2%)	38	0.0005
Stage II	45 (81.8%)	50 (55.6%)	95	
Stage III	10 (18.2%)	2 (2.2%)	12	

Chi-Square = 37.32

Table 2: Compare the Frequency of AKI with HIE Staging in Neonates with Perinatal Asphyxia by Statistically Significant Variables

Variable Studied		HIE Stage	Acute Kidney Injury		P-Value
			Yes	No	
Age groups	≤ 30 Minutes	Stage I Stage II Stage III Total	0 (0%) 38 (84.4%) 7 (15.6%) 45	33 (41.8%) 45 (57%) 1 (1.3%) 79	0.0005
	31-20 Minutes	Stage I Stage II Stage III Total	0 (0%) 3 (75%) 1 (25%) 4	1 (16.7%) 4 (66.7%) 1 (16.7%) 6	0.679
	>120 Minutes	Stage I Stage II Stage III Total	0 (0%) 4 (66.7%) 2 (33.3%) 6	4 (80%) 1 (20%) 0 (0%) 5	0.021
Gender	Male	Stage I Stage II Stage III Total	0 (0%) 31 (81.6%) 7 (18.4%) 38	27 (39.7%) 39 (57.4%) 2 (2.9%) 68	0.0005
	Female	Stage I Stage II Stage III Total	0 (0%) 14 (82.4%) 3 (17.6%) 17	11 (50%) 11 (50%) 0 (0%) 22	0.001
Mode of delivery	SVD	Stage I Stage II Stage III Total	0 (0%) 31 (83.8%) 6 (16.2%) 37	27 (42.9%) 36 (57.1%) 0 (0%) 63	0.0005
	Caesarean Section	Stage I Stage II Stage III Total	0 (0%) 14 (77.8%) 4 (22.2%) 18	11 (40.7%) 14 (51.9%) 2 (7.4%) 27	0.006
Place of delivery	At Home	Stage I Stage II Stage III Total	0 (0%) 8 (72.7%) 3 (27.3%) 11	13 (46.4%) 15 (53.6%) 0 (0%) 28	0.001
	In Hospital	Stage I Stage II Stage III Total	0 (0%) 37 (84.1%) 7 (15.9%) 44	25 (40.3%) 35 (56.5%) 2 (3.2%) 62	0.0005

DISCUSSION

Neonatal mortality is a serious health problem in developing countries with deficient resources and it accounts for 44% of total under-five mortality globally [11]. Although under-five child mortality has lessened in all regions of low-income countries, but decrease in neonatal mortality in comparison to post-neonatal mortality reduction observed is slow. The global neonatal mortality is reduced from 5.1 million to 2.7 million over the period of 1990-

2015 [12]. Early neonatal deaths are caused by infection (36%), premature birth (28%) and perinatal asphyxia (23%), making perinatal asphyxia the third leading cause of neonatal mortality [13]. A recent publication from Karachi, Pakistan, reported national neonatal death rate (NNDR) 34/1000 live births in which 64% were due to birth asphyxia [14]. In another study Jehan et al revealed a 26% incidence of birth asphyxia in urban Pakistani population [15]. Asphyxia can lead to multiorgan dysfunction and redistribution of cardiac output to maintain cerebral, cardiac, and adrenal perfusion while minimizing renal, gastrointestinal, and dermal perfusion [16]. Acute renal injury in asphyxiated neonates is one of the common complications, which occur in up to 50% of these cases [17, 18]. Early identification of AKI is important in newborns with perinatal asphyxia to start timely and appropriate fluid and electrolyte management, as maintaining a stable biochemical environment is essential in improving the outcomes in these babies. To find out the frequency of AKI in newborns with perinatal asphyxia and to compare the frequency of AKI with HIE staging in neonates with perinatal asphyxia, total 145 full term delivered neonates admitted to the nursery with the history of perinatal asphyxia within 24 hours of delivery were enrolled in this study. Studies by Jayshree [19], and Gupta [20] considered the threshold of 90 µmol / l for serum creatinine at 48 hours of life. Studies by Karlowicz [21] picked the serum creatinine threshold of 133µmol/l at 48 hours to make a diagnosis of AKI. In our study, we considered the threshold of ≥1.5mg/dl for creatinine at 24-48 hours of life in order to increase our possibility of diagnosis as there would be significant reduction in the maternal creatinine level by that time [22]. In our study stage II was most common stage of HIE 95 (65.52%). Our study noted 37.93% (55/145) Rate of AKI was significant in neonates with perinatal asphyxia. Ganavi et al. [23] in their study reported that incidence of ARF in asphyxiated neonates was 75%. Our study noted that the rate of AKI was significantly high in stage II as compare to stage I and stage III of Clinical HIE staging. Our results showed that stage II was most common stage of HIE with 65.5% neonates in stage II while 26.2% and 8.2% neonates were in stage I and II respectively. The higher degree of HIE was also statistically remarkably associated with oliguria type of AKI than non-oliguria type of AKI. This is also in accordance to earlier studies [19, 20].

As serum creatinine is delayed and unreliable marker of AKI and is used as indicator of AKI in this study is a major limitation of this study.

CONCLUSION

Asphyxia during perinatal period is among main causes of neonatal acute kidney injury. Diagnosis of acute kidney injury can be made by monitoring serum creatinine and urine output. Acute kidney injury can also occur in non-oliguric patients with birth asphyxia. Hence, monitoring of biochemical renal parameters is required along with urine output measurement. Neonates with HIE stage II and III had higher incidence of AKI. New urinary biomarkers have been developed and verified for the early detection of renal damage in both adult and pediatric populations. Newer markers like, serum cystatin C (sCysC), NGAL, IL-18, the sodium-hydrogen exchanger-3 and kidney injury molecule-1 should be studied for early detection of kidney injury. Further studies in multi-centers and on large scale need to be done to identify maternal factors associated with perinatal asphyxia related AKI.

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