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Original Article

Incidence of acute renal failure in birth asphyxia and its correlation with hypoxic-ischemic encephalopathy staging

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ABSTRACT

Introduction: Acute renal failure (ARF) is a recognized complication of birth asphyxia and it carries a poor prognosis. Early recognition of ARF is particularly important in asphyxiated neonates with hypoxic-ischemic encephalopathy (HIE). **Objectives:** To determine the incidence of ARF in term asphyxiated neonates and to correlate it with HIE staging. **Methods:** A total of 50 term (37-42 weeks) neonates born with Apgar score of <7 at 5 min after birth were selected as cases and 50 normal term (37-42 weeks) neonates as controls. All asphyxiated neonates with clinical features of HIE are staged by Sarnat and Sarnat staging. Gestational age, birth weight, relevant perinatal history, and examination findings are recorded in predesigned pro forma. After 72 h and before 96 h of life, blood was collected and sent for relevant investigations, and clinical condition of the neonate and urine output were monitored and neonates were managed according to the standard protocol. **Results:** Incidence of ARF is significantly more in cases (76.0% vs. 4.0%) than the controls. Among 38 cases with ARF, 32 (84.2%) had pre-renal ARF and 6 (15.8%) had intrinsic ARF. On the basis of urine output, 12 (24.0%) had oliguric ARF and 38 cases (76.0%) had non-oliguric ARF while out of 50 controls, 2 (4%) neonates had pre-renal and non-oliguric type of ARF. Incidence of ARF correlated well with HIE staging. Among the 50 cases, 32 (84.3%) improved clinically after fluid therapy, while 6 (15.7%) did not improve. **Conclusion:** Perinatal asphyxia is an important cause of neonatal renal failure. ARF in birth asphyxia is predominantly pre-renal and non-oliguric type and it responds to fluid challenge. ARF in birth asphyxia correlates well with HIE staging.

Key words: *Acute renal failure, Birth asphyxia, Hypoxic-ischemic encephalopathy, Neonates*

Birth asphyxia is a detrimental condition that has consequences both in natal period and beyond that. Total incidence of asphyxia ranges from 1 to 1.5% at various centers and is correlated with birth weight and gestational age of the neonate. Every tissue and organ is affected by hypoxia and ischemia. Renal insufficiency is the most common manifestation that occurs within 24 h of a hypoxic-ischemic episode as kidneys are most sensitive to hypoxia. Prolonged ischemic episode may lead to irreversible cortical necrosis [1]. Maintaining a stable biochemical milieu is vital in neonates with hypoxic-ischemic encephalopathy (HIE). This can be done by early identification of renal failure that facilitates appropriate fluid and electrolyte management. Renal failure diagnosis is extremely difficult in neonates as biochemical and clinical parameters are unreliable in this age group.

The early diagnosis of the disturbed kidney function in asphyxiated neonates and an early therapy may be of great benefit to newborns that have a high risk of acute renal failure (ARF) development [2]. The main aim of the study was to assess the incidence of ARF in term asphyxiated neonates and also to correlate the severity of ARF with HIE staging.

MATERIALS AND METHODS

A prospective study was conducted in an urban setting of Raichur between July 2015 and June 2016 after getting approval from the Institutional Ethics Committee. A total of 50 term (37-42 weeks) neonates born with Apgar score of 7/<7 at 5 min after birth were selected as cases, and 50 normal term (37-42 weeks) neonates were selected as controls. Neonates with confounding factor believed to alter renal functions such as septicemia, respiratory distress syndrome, necrotizing enterocolitis, major congenital anomalies, antenatally diagnosed hydronephrosis (unilateral or bilateral), neonates on IV nephrotoxic drugs, neonates with history of maternal drug intake or maternal fever, and gestational age <37 weeks/>42 weeks were excluded from the study.

All asphyxiated neonates (as per WHO definition) [3,4] with clinical features of HIE were staged by Sarnat and Sarnat staging. Gestational age, gender, birth weight, relevant perinatal history, and examination findings were recorded in a predesigned pro forma. After 72 h and before 96 h of life, blood was collected and sent for estimation of blood urea (enzymatic kinetic method), serum creatinine (Jaffe's method), serum electrolytes (ion selective electrode dilution). Creatinine clearance was calculated

by Cockraft-Gault equation. Criteria adopted for defining ARF in neonates were oliguria <0.5 ml/kg/h or serum creatinine of >2 standard deviation (SD) above of mean value for gestational age which is >1.19 mg/dl. The clinical condition of the neonate and urine output were monitored and neonates were classified as pre-renal (who respond to fluid challenge of 20 ml/kg), renal, and post-renal failures (not responding to fluid challenge) and depending on urine output into oliguric (<0.5 ml/kg/h) and non-oliguric renal failure. These neonates were managed according to the standard protocol [2], and duration of hospital stay was noted.

RESULTS

Demographic details of the study population are given in Tables 1-4. Gender distribution of neonates was statistically similar in both the groups (p=0.633). Postnatal age of the neonates was statistically similar in both the groups (p=0.496). Birth weight was statistically similar in both the groups (p=0.498). There was a significant increase in the mean values of the blood urea and serum creatinine as the HIE staging progressed. Creatinine clearance significantly decreased as the HIE staging progressed. Duration of stay showed HIE III stayed for only 3-7 days and died HIE II stayed for 11-15 days and HIE I for 5-9 days (Table 2).

DISCUSSION

In this study, we determined the incidence of renal failure, renal parameters, and type of ARF in birth asphyxia and correlated the severity of renal failure with HIE grading of asphyxiated neonates. In our study, the incidence of ARF was 76% among cases and 24% among them had oliguric and 52% had non-oliguric ARF. Ganavi et al. in their study showed that incidence of ARF in asphyxiated neonate was 75% [5]. Gupta et al. showed that the incidence of ARF in asphyxiated neonates was 47.14% in 70 asphyxiated neonates. They considered renal failure in an asphyxiated neonate when 3 out of following 4 criteria were fulfilled: Urine output <0.5 ml/kg/h, blood urea> 40 mg/dl, serum creatinine >1 mg/dl, and presence of significant hematuria or proteinuria [6]. Aggarwal et al. studied 25 cases and showed that incidence of ARF was 56%, less than that of our study [7]. This may be because those neonates who died within 4 days were excluded from their study, and these are the neonates who might have suffered the severe asphyxia and logically should have had ARF. Furthermore, they considered neonates with serum creatinine value >1.5 mg/dl as having ARF and not mentioned about distribution of neonates according to HIE staging. Non-oliguric ARF was more common in their study [7].

Medani et al. showed that Acute kidney injury was a common consequence among asphyxiated neonates in 46 (54.1%) neonates, and it was most common in HIE II [8]. Mean blood urea nitrogen level of severely asphyxiated neonates on day 1 and day 3 was significantly higher than that of moderately and mildly asphyxiated neonates (p<0.01); mean urinary output (UOP) in severely asphyxiated neonates on day 1 of life was significantly lower as compared to mean UOP in mildly and moderately asphyxiated neonates [9].

In our study, the incidence of ARF in asphyxiated neonates was found to be 76% and is higher compared to other studies because first, all asphyxiated neonates with features of HIE, in all 3 stages, were studied and second, the criteria adopted for defining ARF in neonates are oliguria <0.5 ml/Kg/h or serum creatinine of >2 SD above of mean value for gestational age which is >1.19 mg/dl. These criteria were not used by other previous studies, which helped in the management of the neonates at the early stages where the neonates had pre-renal failure and responded well to the fluid challenge and had 100% recovery. This highlights the fact that in HIE, the asphyxiated neonates have to be picked up when they are in stage of pre-renal failure and managed with adequate fluids so that they do not progress to intrinsic renal failure as they have high mortality.

Ganavi et al. [5] showed that the mortality was 12%. Gupta et al. showed that oliguric ARF was more common in their study. Jayashree et al., in her study, showed that the mortality

Table 1: Demographic profile of the study population

Parameters	Control (n=50)	Cases (n=50)
	n (%)	n (%)
Gender		
Male	30 (60.0)	32 (64.0)
Female	20 (40.0)	18 (36.0)
Age (h)		
72-84 h	30 (60.0)	45 (90)
85-96 h	20 (40.0)	05 (10)
Mean	81.22 h	78 h
Birth weight (kg)		
<2.5	0 (0.0)	0 (0)
>2.5	50 (100)	50 (100)
Mean	2.83±0.27	2.86±0.28

Table 2: Renal parameters and duration of hospital stay in different stages of HIE

HIE staging	Mean creatinine	Mean blood urea	Mean creatinine clearance	Mean NA+levels	Mean K+levels	Mean chloride levels	Duration of stay days
HIE I	1.15	68.77	16.25	138.72	4.64	99.6	7±2
HIE II	1.87	85.05	14.09	140.30	4.30	100.55	13±2
HIE III	2.36	107.4	9.16	130.56	4.78	99.24	5±2
Total	1.55	76.78	15.89	139.14	4.41	100.16	10±2
p value	<0.001**	<0.002**	<0.001**	0.053	0.235	0.820	

HIE: Hypoxic-ischemic encephalopathy, **p<0.05

Table 3: Incidence of ARF

Urine output	Control (n=50)	Cases (n=50)
	n (%)	n (%)
< 0.5 ml/kg/h	2 (4.0)	38 (76)*
>0.5 ml/kg/h	48 (96.0)	12 (24)

Incidence of ARF is significantly more in cases (76.0% vs. 4.0%) 19 times more likely when compared to with χ^2=50.049; p<0.001*, ARF: Acute renal failure

Table 4: Incidence ARF and type of ARF and its correlation among different stages of HIE

HIE staging	Number of neonates	ARF (%)	Pre-renal ARF (%)	Intrinsic ARF (%)	Oliguric ARF (%)	Non-oliguric ARF (%)
HIE I	20	11 (55)	11 (100)	0 (0)	3 (27.3)	8 (72.7)
HIE II	25	22 (88)	21 (98.4)	1 (4.5)	7 (31.2)	15 (68.2)
HIE III	05	5 (100)	0 (0)	5 (100)	2 (40)	3 (60)
Total cases	50	38 (75)	32 (85.4)	06 (14.6)	12 (32)	26 (68)
p value		<0.001				
Controls	50	2	2 (100)	0	0 (0)	2 (100)

HIE: Hypoxic-ischemic encephalopathy, ARF: Acute renal failure

was 61.5% and most of them (87.5%) were oliguric and deaths were attributed to HIE, shock, and renal failure [6]. In our study, mortality was 13.1% and all cases of HIE III and 1 case of HIE II, i.e., a total of 6 cases did not improve with fluid therapy and had intrinsic ARF. A total of 5 neonates died among them 2 despite peritoneal dialysis due to multiorgan dysfunction syndrome.

Furthermore, in our study, we had 12 cases with oliguric ARF and 2 (16.6%) of them succumbed and 6 (15.8%) cases with non-oliguric ARF died, thus highlighting that even though urine output is good, they can have ARF which should not be missed. Limitations of the study included renal parameters which were not monitored daily from day 1 of life, maternal creatinine values were not considered, and urinary indices were not done.

CONCLUSION

Birth asphyxia during perinatal period is an important cause of neonatal renal failure. Early diagnosis of renal failure can be made by monitoring serum creatinine and urine output. Renal failure can occur in non-oliguric patients with birth asphyxia. Hence, monitoring of biochemical renal parameters is required along with urine output measurement.

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