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Original Article

Paediatrics Section

# Incidence of Acute Renal Failure (ARF) in Birth Asphyxia and its Correlation with Hypoxic Ischemic Encephalopathy (HIE) Staging

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## ABSTRACT

**Introduction:** Acute kidney injury (AKI) previously known as Acute renal failure is a recognized complication of neonates with perinatal asphyxia. In all asphyxiated neonates emphasis must be laid on early recognition of AKF, so that it paves a way for timely and appropriately management thereby preventing consequences of irreversible renal failure.

**Aim:** To determine the incidence of Acute renal failure in birth asphyxia and to correlate the severity of renal failure with and HIE grading of asphyxiated neonates.

**Materials and Methods:** A case control study was conducted for a period of 1 year, where 100 term (37-42 wks) neonates born with Apgar score of 7/<7 at 5 minutes after birth were selected as cases and 50 normal term (37-42 wks) neonates as controls. Sarnat and Sarnat staging was used for HIE. After 72 hrs and before 96 hrs of life blood was collected and sent for relevant investigations and clinical condition of the baby and urine output was monitored and data was collected in predesigned proforma after informed consent.

**Results:** Incidence of ARF is significantly more in cases (75.0% vs. 4.0%) 18.4 times more likely when compared to controls. Among the 75 cases which had acute renal failure , 64 (85.3%) had pre-renal ARF and 11(14.6%) had intrinsic ARF , and based on urine output 24 (32.0%) had oliguric ARF and 51 (68.0%) had non oliguric ARF and among the 50 controls 2 neonates had pre-renal and non-oliguric type of ARF. Incidence of ARF had a strong correlation with HIE staging.

**Conclusion:** ARF in birth asphyxia is predominantly pre-renal ARF and responds to fluid challenge and it is of non oliguric type. ARF in birth asphyxia correlates well with HIE staging. Mortality is more in intrinsic ARF. Early diagnosis and management of renal failure helps in prevention of intrinsic renal failure and its consequences.

**Keywords:** Hypoxia, Kidneys, Neonates, Oliguria

## INTRODUCTION

Birth asphyxia is an eventuality with consequences in the neonatal period and beyond. So far, in general, incidence of asphyxia is found to be reported as 1 to 1.5% at various centers and has strong correlation with birth weight and gestational age of the baby. Almost every tissue and every organ of the body suffers damage due to hypoxia and ischemia and the most affected are the kidneys in 50% followed by Central nervous system (CNS) in 28%, cardiovascular system (CVS) in 25% and lungs in 23% cases. As Kidneys are very sensitive to hypoxia, renal insufficiency occurs within 24 hours of a hypoxic ischemic episode, on prolongation, hypoxic ischemic insult causes irreversible cortical necrosis. A stable biochemical milieu is vital for all neonates exposed to hypoxic ischemic episode, so to facilitate appropriate fluid and electrolyte management early recognition of renal failure is important in babies with HIE. In neonates diagnosis and early recognition of renal failure is very difficult as many of the clinical and biochemical parameters are very unreliable and not well established in this age group [1].

We performed this study to determine the incidence of renal failure in birth asphyxia and to correlate the severity of renal failure with and HIE grading of asphyxiated neonates to mainly emphasize on continuous monitoring of the renal function in asphyxiated neonates as early diagnosis of disturbed neonatal kidney function in asphyxiated newborns can prevent these high risk group from developing irreversible cortical necrosis and hence the mortality.

## MATERIALS AND METHODS

A prospective case control study was conducted for a period of 1 year, Vanivilas Hospital Bangalore, from January-2009, January-2010, where100 term (37-42 wks) neonates born with APGAR score of 7/< 7 at 5

minutes after birth were selected as cases and 50 normal term (37-42 wks) neonates were selected as controls by using stratified random sampling as one new born per week. Neonates with confounding factor believed to alter renal functions such as septicemia, Respiratory distress syndrome, Necrotizing enterocolitis, major congenital anomalies, on IV nephrotoxic drugs, h/o maternal drug intake, h/o maternal fever, gestational age < 37 wks / > 42 wks are excluded from the study. All asphyxiated (as per WHO definition) neonates were selected as cases [2], variables such as Gestational age, birth weight were recorded. Perinatal history was taken in detail. Examinations findings are recorded in predesigned proforma. The post asphyxiated neonates were managed according to standard protocol. All neonates who have suffered asphyxia were closely monitored clinically including Sarnat and Sarnat staging for HIE. Vital parameters were monitored round the clock for early detection of complications so that they can be managed effectively. After 72 hrs of birth and before 96 hrs of birth after obtaining informed written consent from the parents, under aseptic precautions 3 ml blood is drawn and is evaluated for blood urea (Berthelot method), serum creatinine (Jaffe's test), Serum electrolytes (Calorimetric method) after 72 hrs and before 96 hrs of birth and 24 hr urine output (U.O) is monitored by applying plastic collection bag (minicom) and clinical condition of the baby was monitored.

Criteria adopted for defining Acute renal failure in neonates is oliguria <0.5ml/kg/hr or serum creatinine of > 2 standard deviation (SD) above of mean value for gestational age i.e. equal to 1.19 mg/dl [1]. Those neonates which fulfilled the above criteria were diagnosed as ARF, and were first given a fluid challenge 20 ml/kg of normal saline monitored for urine output and clinical parameters if U.O < 1ml/kg/hr it was followed by diuretic injection lasix 1mg/kg and still if urine output < 1ml/kg/hr were diagnosed as intrinsic renal ARF and peritoneal dialysis was planned. The results were analyzed using following statistical methods: Descriptive statistical analysis has been used in the present study. Results are presented on Mean ± SD (Min-Max) on continuous measurements and results are presented in Number (%) on categorical measurements. Significance is assessed at 5% level of significance. To find the significance of study parameters on continuous scale between two groups Student-'t'-test (two tailed, independent) has been used and Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more group. Student-'t'-test has been used to find the homogeneity of parameters on continuous scale and Chi-square /Fisher exact test has been used to find the homogeneity of samples on categorical scale. The Statistical software namely SPSS 15.0, Stata 8.0, MedCalc 9.0.1 and Systat 11.0 were used for the analysis of the data and Microsoft word and Excel have been used to generate tables.

## RESULTS

In our study, incidence of ARF is significantly more in cases (75.0% v/s. 4.0%) 18.4 times more likely when compared to with 2=50.049; p<0.001** as in [Table/Fig-1].

Among the 75 cases which had acute renal failure , 64 (85.3%) had pre-renal ARF , 11(14.6%) had intrinsic ARF , 24 (32.0%) had oliguric ARF and 51 (68.0%) had non oliguric ARF and among the controls 2 neonates had pre-renal and non-oliguric type of ARF as in [Table/Fig-2].

Our study shows, that 21 (52.5%) HIE I cases had ARF, 44 (88%)%) HIE II cases had ARF and 10 cases of HIE III all 10 (100%) had ARF. Incidence of ARF has a strong correlation with the staging of HIE as in [Table/Fig-3,4].

Distribution of type of ARF shows, all cases of HIE I had pre- renal ARF and 14 (66.6%) of non – oliguric type of ARF, 43(97.72%) cases of HIEII had pre-renal and 31 (70.45%) of non– oliguric type of ARF, All 10 cases of HIE III had intrinsic ARF and 6 (60%) of non - oliguric ARF. Outcome of neonates as in [Table/Fig-5], 64 (85.4%) had pre renal ARF, 11 (14.6%) had intrinsic ARF, 9 neonates died.

## DISCUSSION

Ambar Bhatnagar, in his study with 60 asphyxiated and 50 healthy neonates, showed that 37/60 cases had AKI (61.6%) and among them 18.3% were oliguric and 81.6% were non-oliguric. 83.7% had pre renal failure

| ARF | Controls (n=50) | | Cases (n=100) | |
|---|---|---|---|---|
| | No | % | No | % |
| Present | 2 | 4.0 | 75 | 75.0 |
| Absent | 48 | 96.0 | 25 | 25.0 |

**[Table/Fig-1]:** Incidence of ARF.

| | Total | Pre-Renal | Intrinsic Renal | Oliguric | Non-Oliguric |
|---|---|---|---|---|---|
| Cases with ARF | 75 | 64(85.3%) | 11(14.6%) | 24(32%) | 51(68.0%) |
| Controls with ARF | 2 | 2(100%) | 0(0%) | 0 (0%) | 2(100%) |

**[Table/Fig-2]:** Type of ARF in cases and controls.

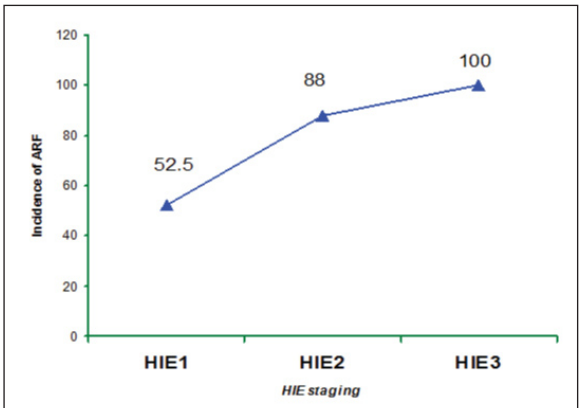
and 16.2% had renal AKI. Incidence of AKI significantly increased with HIE staging from 38.7% among HIE I Group had AKI to 100% in HIE III group [3].

Girish Gopal conducted a study with 50 asphyxiated neonates and 25 normal neonates and showed 64% of the asphyxiated neonates had AKI. There was increase in the levels of blood urea and serum creatinine as HIE staging progressed and majority had pre renal failure. Mortality was more in oliguric AKI [4].

Gupta et al., in his study showed that the incidence of ARF in asphyxiated neonates was 47.14% as he had studied 70 asphyxiated neonates of them 32

| HIE staging | Total number of neonates | No. of ARF | No.of cases of Pre-renal ARF | No.of cases of intrinsic ARF | No. of oliguric | No-of non-oliguric |
|---|---|---|---|---|---|---|
| HIE1 | 40 | 21(52.5%) | 21 100%) | 0(0%) | 7(33.3%) | 14(66.6%) |
| HIE2 | 50 | 44(88%) | 43(97.72%) | 1(2.2%) | 13(29.45%) | 31(70.45%) |
| HIE3 | 10 | 10 (100%) | 0(0%) | 10(100%) | 4(40%) | 6(60%) |
| Total | 100 | 75 (75%) | 65(85.4%) | 11(14.6%) | 24 (32%) | 51(68%) |
| p-value | | < 0.001 ** | | | | |

**[Table/Fig-3]:** Incidence ARF and Type of ARF and its correlation among different stages of HIE.




**[Table/Fig-4]:** Curve showing correlation of incidence of ARF with HIE staging.

| Out Come of Cases with ARF | Number of neonates | Percentage |
|---|---|---|
| Clinically improved after fluid therapy (PRE RENAL) | 64 | 85% |
| Clinically did not improve after fluid therapy (INTRINSIC RENAL FAILURE) | 11 | 14.6% |
| • Neonates who underwent peritoneal dialysis and died | 2 | 2.6% |
| • Neonates in whom peritoneal dialysis was planned but went DAMA (Discharge against medical advice) | 2 | 2.6% |
| • Number of Neonates who had associated morbidities and refused peritoneal dialysis and who died. | 7 | 9.33% |
| Total number of neonates who died | 9 | 12% |

**[Table/Fig-5]:** Outcome among the cases.

cases had no HIE features, and criteria adopted for labeling an asphyxiated neonate as having renal failure were urine output< 0.5 ml/kg/hr, blood urea >40 mg/dl, serum creatinine > 1 mg/dl, presence of significant hematuria or proteinuria, 3 out 4 criteria when fulfilled were considered as indication of renal failure. Non oliguric renal failure was more common [5].

Aggarwal et al., studied 25 cases and showed that incidence of ARF was 56%, less as compared to our study , this is because those neonates who died within four days were excluded from the study, and these are the neonates who might have suffered severe asphyxia and logically should have had ARF, and also he 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 his study [6].

Pammi V Mohan in his study with 50 neonates with birth asphyxia showed that the incidence of ARF as defined in his study as blood urea nitrogen greater than 20 mg/dl on at least 2 blood samples was 72%. And oliguria was defined urine output< 1 ml/kg /hr and study showed that non-oliguric was more common [7].

Karlowicz et al., showed that the incidence of ARF in asphyxiated neonates was 61% and Non oliguric ARF was more common. He had selected the neonates based on asphyxia morbidity score and also has not mentioned about the distribution of neonates according to HIE staging [8].

Pejović B, et al., performed a prospective survey of 31 term neonates with Perinatal asphyxia and but without congenital malformations or sepsis in NICU and concluded that in term neonates with severe perinatal asphyxia oliguric ARF was the predominant type of ARF [9]. Airede A et al., did a prospective evaluation from a referral hospital, Showed that perinatal asphyxia was the commonest etiology for acute renal failure in neonates [10].

In our study the incidence of ARF in asphyxiated neonates was found to be 75% and is higher compared to other studies. Because first, all asphyxiated neonates with features of HIE in all 3 stages were studied, second the Criteria adopted for defining Acute renal failure in neonates is oliguria <0.5ml/kg/hr or serum creatinine of > 2 SD above of mean value for gestational age [1] i.e. equal to 1.19 mg/dl which no other previous studies had used, 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 highlighting that in HIE kidney despite being the best oxygenated organ, it is the most susceptible to ischemic –hypoxic injury because of redistribution of the blood flow to other vital organs and unique vascular supply of renal medulla and results in transient loss of renal concentrating capacity. More prolonged injury produces wide spread tubular dysfunction and progress to intrinsic renal failure. The asphyxiated neonates have to pick up when they are in stage of pre renal failure and managed with adequate fluids and i.v. frusemide so that they don't progress to intrinsic renal failure as they have high mortality.

Nouri S et al., conducted a prospective study including 87 full-term neonates and found that transient renal failure is commonly observed in perinatal asphyxia and renal failure correlated with neurologic severity [11].

The mortality pattern of our study were compared. To studies of Pammi PV who showed the mortalilty was 36.1% as most of them had associated morbidity and among them 46.15% non- oliguric type [7]. Gupta et al., showed that in his study oliguric ARF was more common [5].

In our study mortality was 12%, all cases of HIE III and 1 case of HIE II (in all total 11 Cases) did not show improvement after fluid therapy and had intrinsic ARF. Peritoneal dialysis was planned for them but only for 2 cases peritoneal dialysis was done and they succumbed to death, other 2 cases went discharge against medical advice (DAMA) and remaining seven died as they had associated co morbid condition, shock, Multi organ dysfunction syndrome (MODS). The asphyxiated neonates has to be screened for ARF at the earliest so that they can be managed at the pre renal failure stage only without letting them to progress to intrinsic renal failure as they have high mortality.

Gupta et al., studied 70 asphyxiated neonates, 38(54.25%) cases had HIE features with 12.8% HIE I, 28.5% HIE II and 12.8% HIE III and found that as HIE staging progressed, concentration of blood urea and serum creatinine were on the increasing trend, and the difference was statistically significant between babies with no HIE and HIE III [5] very similar results were also found in studies conducted by Ambar Bhatnagar and Girish gopal [3,4].

In our study also, it was found that the incidence of ARF increased as the HIE staging progressed .as in [Table/Fig-8].

## CONCLUSION

Perinatal asphyxia is an important cause of neonatal renal failure. Monitoring of blood levels of blood urea and serum creatinine helps in the early diagnosis and management of renal failure. ARF in birth asphyxia is predominantly non oliguric so monitoring only urine output does not help in the diagnosis of ARF. ARF in asphyxiated neonates is predominantly pre renal and responds to fluid administration with 100% recovery. Shock is important predisposing factor and a clinical marker associated with ARF in birth asphyxia. ARF in birth asphyxia shows a strong correlation with HIE staging. Prevention of intrinsic renal failure is better than managing as it has 100% mortality.

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