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Evaluation of Renal Function Test in Birth Asphyxia in Term Neonates

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Abstract

Background: Acute renal failure is recognized complication of birth asphyxia. It carries a poor immediate prognosis and may result in permanent renal damage in upto 40% of survivors. Early recognition of acute renal failure is particularly important in asphyxiated neonates with HIE, in whom a stable biochemical milieu is vital, because it facilitates the administration of appropriate fluid and electrolyte replacement. *Aim:* To determine the incidence of renal failure in birth asphyxia and to correlate the severity of renal failure with HIE grading of asphyxiated neonates. *Materials and Methods:* 100 term (37-42 wks) neonates born with Apgar score of < 7 at 5 minutes after birth were selected as cases. All asphyxiated neonates (as per WHO definition) with clinical features of HIE are staged by Sarnat & Sarnat staging. Gestational age, birth weight relevant perinatal history examination findings are recorded in predesigned proforma. 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 out put was monitored and were managed accordingly. *Results:* Incidence of ARF in our study is 50 (50.0%) Among the 50 cases which had acute renal failure, 40 (80%) had pre-renal ARF and 10 (20%) had intrinsic ARF, and based on urine out put 15 (30.0%) had oliguric ARF and 35 (70.0%) had non oliguric ARF. Comparison of blood parameters among the cases with and without ARF showed that the renal parameters were raised in cases with ARF. Incidence of ARF correlated well with HIE staging. Among the 50 ARF cases 35 improved clinically after fluid therapy, 15 did not improve clinically after fluid therapy, 10 neonates died. Among the 10 neonates who died all 10 (10.0%) had oliguric ARF. *Conclusions:* Perinatal asphyxia is an important cause of neonatal renal failure. 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. A simple procedure like measuring urineoutput in birth asphyxia helps to detect intrinsic renal failure thereby preventing & reducing mortality.

Keywords: Neonates; Birth Asphyxia; Hypoxic Ischemic Encephalopathy; Acute Renal Failure.

Introduction

Birth asphyxia is an eventuality having far reaching consequences in the neonatal period. According to 2000 report of National Neonatal Perinatal Database of India, perinatal asphyxia occurred in 9% of institutional deliveries & is related to birth weight & gestational age of baby.

Hypoxia and ischemia can cause damage to almost every tissue and organ ofthe body and various target organs involved have been reported to be kidneys in 50% followed by CNS in 28%, CVS in 25% and lungs in 23% cases. As kidneys are very sensitive to oxygen deprivation, renal insufficiency may occur within 24 hours of a hypoxic ischemic episode, which if prolonged, may even lead to irreversible cortical necrosis. Early recognition of renal failure is important in babies with HIE to facilitate appropriate fluid and electrolyte management as a stable biochemical milieu is vital. Diagnosis of renal failure is difficult in neonates as many of the established clinical and biochemical parameters are unreliable in this age group.

We performed this study to determine the incidence of Acute renal failure in birth asphyxia and to correlate the severity of renal failure with HIE grading of asphyxiated neonates to mainly emphasize on early diagnosis of disturbed neonatal kidney function and also on monitoring & therapeutical aspects which may be of benefit for asphyxiated newborns at high risk for developing acute renal failure [1].

Acute renal failure occurred in 61% of infants with severe asphyxia, acute renal failure associated with severe asphyxia was predominantly nonoliguric. The renal functions glomerular filtration rate (GFR) and fractional sodium excretion (FENa) were found significantly impaired up to 60% in the asphyxic babies especially those whose clinical presentation was expected to be severe [1,2]. Hence, our aim is to evaluation of renal functions in birth asphyxia in term neonates.

Materials and Methods

It is a Prospective cohort study in 100 term asphyxiated neonates admitted in NICU, Depatment of Pediatrics, Niloufer Institue of child & woman health, during the study period Jan 2012 – Jan 2013.

Inclusion Criteria: The term neonates with 5 min APGAR < 7, the term neonates who needed resuscitation – IPPV, h/o delayed cry with neurological manifestations. Uniformity in neonatal resuscitation protocol & grading of asphyxia according to Apgar at 5 min was assured by eliminating observer bias.

Exclusion Criteria: 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.

Ethical scientific committee approval was taken & 100 asphyxiated [as per WHO definition] neonates were selected as cases, Gestational age, birth weight relevant perinatal history, examination findings are recorded in predesigned proforma. The post asphyxiated neonates were managed according to protocol.

The initial management of all such neonates consisted of with additional allowance of 20 ml/kg/day for radiant warmer. First 48 hrs fluid given was 10% dextrose and then Isolyte p was started. Injection vitamin K 1mg was administered to all these babies. A stomach wash was performed if there was meconium staining.

All neonates who have suffered asphyxia were closely monitored clinically. This monitoring aims to detect derangements in the clinical, metabolic and hemodynamic milieu so as to ensure prompt management. The respiratory status was monitored by meticulous record of the RR, B/Ladequate chest expansion & air entry. The CVS status was assessed by monitoring pulse volume, HR, color, CFT, Pulse oximetry, & temperature. Assessment of the neurologic status should include Sarnat & Sarnat staging for HIE along with assessment of anterior fontanel, tone, seizures, pupillary size & reaction every 12 hrly. Seizures was treated energetically. Continuous monitoring of vital parameters was done for early detection of derangements and complications and their timely management.

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 out put 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 mote than 2 SD above of mean value for

gestational age [3] which is more than 1.19 mg/dl & blood urea more than 40 mg/dl.

Those neonates which fulfilled any 2 of the above 3 criteria were diagnosed as ARF & first given afluid challenge 20 ml/kg of normal saline monitored for urine out put and clinical parameters. if u.o < 0.5ml/kg/hr it was followed by diuretic inj lasix 1mg/kg and still if urine out put < 0.5ml/kg/hr were diagnosed as intrinsic renal ARF.

The results were analysed using following statistical methods: Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5% level of significance. Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale. Chi square & Fischer test are used to find homogeneity of samples.

Results

The rate of deaths among neonates with ARF was significantly higher (p value = 0.001) than neonates without ARF.

The rate of death among neonates with intrinsic renal disease was significantly higher (p value <0.001) when compared to infants with pre renal disease.

The rate of deaths amongst neonates with oliguria was significantly higher (p value <0.001) when compared to neonates without oliguria.

The rate of deaths among neonates with stage 3 HIE was significantly higher (p value <0.001) when compared to neonates with either stage 1 or stage 2 HIE.

Table 1: Demographic details in study

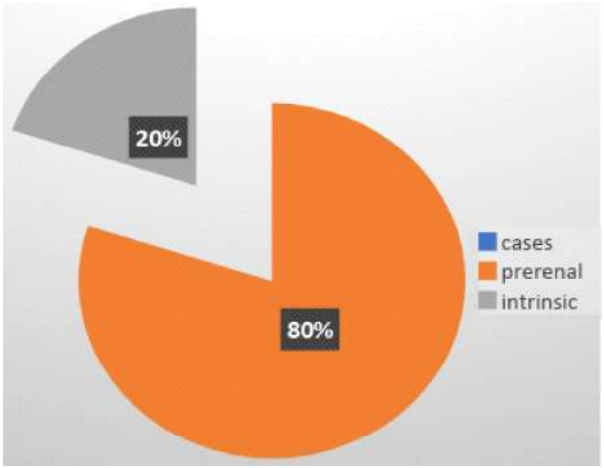
	Cases (n=100)	
Gender	**Number of cases**	**percentages**
Male	47	47
Female	53	53
Age in{hrs}		
72-84 hrs	98	98%
85-96 hrs	2	2%
Mean	78 hrs	
Birth weight in kgs		
<2.5	0	0
>2.5	100	100
Mean ± SD	2.69±0.27	
Perinatal risk factors for birth asphyxia		
MSAF {meconium stained amniotic fluid}	55	55%
Prolonged Second stage	22	22%
LOC {loop of cord around the neck}	10	10%
MSAF+LOC+Prolonged Stage	10	10%
APH	2	2%
Cord prolapse	1	1%
Total	100	100%
Urine Output(ml/kg/hr)		
Without ARF		
<0.5	15	24
>0.5	85	85
With ARF		
<0.5	15	100%
>0.5	35	35%

Table 2: Stages of HIE with urine output in babies with ARF

Urine output in babies with ARF	Stage of HIE 1	2	3	Total
Oliguria	0(0%)	5 (16.7%)	10 (10%)	15 (30%)
Non oliguria	10 (100%)	25 (83.3%)	0 (0%)	35 (70%)
Total	10(100%)	30(100%)	10(100%)	50(100%)

1=oliguria, 2=non-oliguric, 3 stage of HIE Crosstabulation

50% of babies with HIE were diagnosed as having ARF (p value <0.001)



Among the 50 cases which had acute renal failure, 40 (60.0%) had pre-renal ARF, 10(20.0%) had intrinsic ARF, 15 (30.0%) had oliguric ARF and 35 (70.0%) had non oliguric ARF

Table 3: Comparison of blood parameters with and without ARF in cases

Blood chemistry	Without ARF	With ARF	P value
Blood urea	28.96±10.28	71.6.±20.8	<0.001**
S creatinine	0.91±0.14	1.74±0.37	<0.001**
Na+[sodium]	130.68±6.0	132.91±4.57	0.661
K+[potassium]	4.17±0.56	4.5±0.78	0.827

Comparison of blood parameters among the cases with and without ARF Showed that Blood urea, Serum creatinine urea was significantly higher in cases with ARF.

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

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	10(25.0%)	10 (100%)	0(0%)	0(0%)	40(100%)
HIE2	50	30(60%)	25(83.40%)	5(16..5%)	5(29.45%)	45(90 %)
HIE3	10	10 (100%)	0(0%)	10(100%)	10(40%)	0(0%)
Total	100	50 (50%)	35(60%)	15(30%)	15(15%)	85(85%)
P value	<0.001* < 0.001 **					

10 (25%) HIE I cases had ARF, 30 (60%)%) HIE II cases had ARF and 10 cases of HIE III all 10 (100%) had ARF Distribution of type of ARF shows all cases of HIE I had pre- renal ARF and non oligurit type of ARF, 25 (83.4%) cases of HIE II had pre-renaland 45 (90%) of non – oliguric type of ARF, All 10 cases of HIE III had intrinsic ARF and oliguric ARF.

Table 5: Distribution of renal parameters and duration of stay in the hospital among different stages of HIE

HIE Staging	Mean Creatinine	Mean Blood urea	Mean NA+	Mean K+	Duration of stay
HIE1	1.51	53.6	137.33	4.18	7±2 days
HIE2	1.65	65.71	138	4.08	13±2 days
HIE3	2.27	107.7	131.7	4.37	5±2 days
Mean	1.74	71.69	132.9	4.5	10±2 days
P value	<0.001**	<0.002**	0.053	0.235	

There was a significant increase in mean values blood urea and serum creatinine as the HIE Staging progressed. Duration of stay showed HIE III stayed for only 5±2 days and died, HIE II stayed for 2±13 days and HIE I for 2±7 days.

Table 6: Outcome among the cases

Out come of cases with ARF	Number of Neonates	Percentage
Clinically improved after fluid therapy (Pre Renal)	35	70
Clinically did not improve after fluid therapy (Intrinsic Renal Failure)	15	30
Total number of neonates who died	10	20

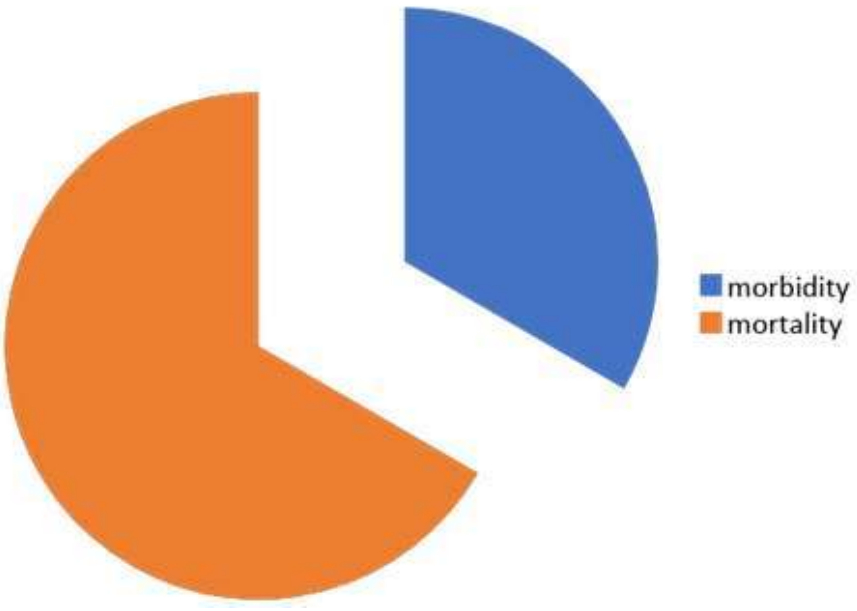


Fig. 2: Outcome of cases with intrinsic renal failure

Discussion

Perinatal asphyxia is an insult to the fetus or the newborn due to lack of oxygen (hypoxia) and/or a lack of perfusion (ischemia) to various organs of sufficient magnitude and duration to produce more than fleeting functional and /or biochemical changes. Hypoxia and ischemia can cause damage to almost every tissue and organ of the body and various target organs involved have been reported to be kidneys in 50% followed by CNS in 28%, CVS in 25% and lungs in 23% cases. As kidneys are very sensitive to oxygen deprivation, renal insufficiency may occur within 24 hours of a hypoxic ischemic episode, which if prolonged, may even lead to irreversible cortical necrosis.

In this study we determined the incidence of renal failure, renal parameters, type of ARF in birth asphyxia and correlated the severity of renal failure with HIE grading of asphyxiated neonates. The results obtained in our study were compared with other studies and discussed as follows.

The Incidence of ARF among the cases in our study was 50% and among them 30% were oliguric and 70% were non-oliguric. Gupta etal 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 cases had no HIE features, and criteria adopted for labeling an asphyxiated neonate as having renal failure were urine out put < 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.

Aggarwal et al. [5] 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.

Karlowicz et al. [2] 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. Jayshree etal showed that the incidence of ARF in asphyxiated neonates was only 43.3% as compared to our study of 75% and oliguric ARF is more common in her study, this is because criteria adopted was any neonate presenting with oliguria (u.o<1 ml/kg/hr), blood urea > 40 mg/dl or serum creatinine > 1 mg/dl was subjected to an intravenous fluid challenge of 20 ml/kg after 30 min if oliguria persisted it was followed by inj frusemide 2mg/kg, if oliguria still persisted then the infant was diagnosed as ARF.

Pammi V Mohan [7] 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 u.o < 1 ml/kg/hr and study showed that non-oliguric was more common.

In our study the incidence of ARF in asphyxiated neonates was found to be 50% and is higher compared to other studies because first, all asphyxiated neonate 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 more than 2 SD above of mean value for gestational age [3] which is more than 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

Table 7: studies showing the incidence of ARF among the cases

Studies	Year	ARF	Oliguric ARF	Non oliguric ARF
Gupta et al.[4]	2005	47.14%	21.21%	78.78%
Aggarwal et al.[2]	2005	56%	42%	58%
Karlowicz et al.[5]	1995	61%	40%	60%
Jayashree et al.[6]	1991	43.30%	69.20%	30.80%
Pammi v mohan [7]	2000	72%	44%	56%
Present study	2012	50%	30%	70%

concentrating capacity, More prolonged injury produces wide spread tubular dysfunction and progress to intrinsic renal failure. The asphyxiated neonates have to picked up when they are in stage of pre renal failure and managed with adequate fluids, so that they don't progress to intrinsic renal failure as they have high mortality.

In our study the most common type was non-oliguric this can be explained as due to pituitary release of vasopressin or renal responsiveness to vasopressin is decreased and heterogeneous response of individual nephron and variable damage to the tubular epithelium that results in anatomical damage in majority of nephrons leading to the reduction in single nephron GFR and decreased tubular fluid flow and subsequent decrease in fractional reabsorption from tubules. So, only oliguria will not determine ARF even neonates who are non oliguric will have ARF which is more common presentation in Birth asphyxia and should not be missed. None of our neonates had features of fluid overload.

Gupta et al. [4] studied 70 asphyxiated neonates of them 32 cases had no HIE features so the mean value was only 35.72 ± 17.87 among the cases, Aggarwal et al. [5] in his study with 25 cases and 25 controls showed the mean value was 33.6±11.5 among the cases, in his study he has not mentioned about the distribution of cases according to HIE grading and he has excluded those neonates who died within 4 days.

Jayashree et al. [6] showed in her study the mean value of blood urea among the cases was 94±32.7, as she studied 30 neonates among them 55.5% were HIE III. The mean blood urea levels among the cases in our study showed that it was significantly high in cases. The results of our study are comparable to studies of Gupta et al. [4], Aggarwal et al. [5], Jayashree et al. [6] and other studies [8,9,10].

The mean blood urea levels among the cases in our study was 71.69±20.82 mg/dl The mean serum creatinine levels among the cases in our study was 1.74±0.37 mg/dl Gupta et al. [4] studied 70 asphyxiated neonates of them 32 cases had no HIE features so the mean value was only 1.08±0.49 among the cases,Aggarwal etal studied 25 cases and 25 controls showed the mean value was 1.0±0.5 among the cases and no mention about the biochemical method for estimation of creatinine is made, he has not mentioned about the distribution of cases according to HIE grading and he has excluded those neonates who died within 4 days.

Jayashree et al. [6] showed in her study the mean value of blood urea among the cases was1.58±0.58 as she studied 30 neonates among them 55.5% were HIE III. The mean serum creatinine levels among the cases in our study showed that it was significantly high. The results of our study are comparable to studies of Gupta et al., [4] Aggarwal et al. [5], and Jayashree et al. [6].

Table 8: studies showing the mean blood urea values among the cases

Studies	Year	Cases
Mean blood urea		
Gupta et al [4]	2005	35.72± 17.87
Aggarwal et al [5]	2005	33.6±11.5
Jayashree et al [6]	1991	94±32.7
Present study	2012	71.69±20.82
Mean serum creatinine		
Gupta et al [4]	2005	1.08±0.49
Aggarwal et al [5]	2005	1.0±0.5
Jayashree et al [6]	1991	1.58±0.58
Present study	2012	1.74±0.37
Serum Sodium		
Gupta et al [4]	2005	133.7±40.1
Present study	2012	132.90±4.76
Serum Potassium		
Gupta et al [4]	2005	4.5±0.5
Present study	2012	4.50±0.70

In our study the mean serum sodium levels among the cases was 132.90±4.76 and mean serum potassium levels among the cases was 4.50±0.7 there was no statistical significance for the mean serum sodium levels, mean serum potassium levels among the cases. Gupta et al. [4] studied 70 asphxiated 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 there was a rising trend in concentration of blood urea and serum creatinine as HIE staging progreesed and the difference was statistically significant between babies without HIE and HIE III.

In our study, correlation of incidence of ARF with HIE staging it was found that the incidence of ARF increased as the HIE staging progressed, and those all neonates with HIE I and 15 HIE II had prerenal failure and responded well to fluid challenge, where as remaining 5 cases of HIE II, 10 cases of HIE III did not respond to fluid challenge the results of our study were compared to Gupta et al. [4] showed that in his study oliguric ARF wasmore common. Jayashree et al [6] in her study showed that the mortality was 61. In our study mortality was 10%, all cases of HIE III and 5 case of HIE II ie total 15 cases did not improve with fluid therapy and had intrinsic ARF. 10 neonates died among them. Which is in accordance with study of Ravindra LM [11].

The asphyxiated neonates has to be screened for ARF at the earliest so that they can be managed at the pre renal failure stage onlywith out letting them to progress to intrinsic renal failure as they have high mortality. Also in our study we had 15 cases who were oliguric, all (100%) had ARF 10 (67%) of them succumbed and 85 cases who were non-oliguric 35 (29.7%) had ARF thus highlighting that though urine output is good till they can have ARF which should not be missed & measuring urine output is an important tool to identify intrinsic ARF in birth asphyxia.

Conclusion

Perinatal asphyxia is an important cause of neonatal renal failure. Monitoring of blood levels of blood urea, serum creatinine and urine output helps in the early diagnosis and management of renal failure. In birth asphyxia even nonoliguric neonates had ARF hence monitoring only urine out put does not help in the diagnosis of ARF, renal biochemical parameters should be monitored.

ARF in asphyxiated neonates is predominatly pre renal and responds to fluid resuscitation with 100% recovery. ARF in birth asphyxia shows a strong positive correlation with HIE staging.

In HIE prevention of intrinsic renal failure by its early recognition by measuring urineoutput is better than managing as it isassociated with MODS and has 100% mortality.

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