

INCIDENCE AND OUTCOME OF ACUTE RENAL FAILURE IN NEONATES WITH PERINATAL ASPHYXIA AND ITS CORRELATION WITH APGAR SCORE AND HYPOXIC ISCHEMIC ENCEPHALOPATHY GRADING**¹Sandeep Banga, ²Mukhtiar Singh Pannu, ³Sahab Ram, ⁴Palveen, ⁵Showkat Hussain Talli and ⁶Harijot Singh Bhattal**¹Assistant Professor, Aimsr Bathinda.²Professor, Gmc Amritsar.³Physician.⁴Junior Resident, Aimsr Bathinda.⁵Assistant Professor, Aimsr Bathinda.⁶Associate Professor, Aimsr Bathinda.***Corresponding Author: Dr. Sandeep Banga**

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ABSTRACT

Background: World Health Organization has defined perinatal asphyxia (PNA) as a “failure to initiate and sustain breathing at birth.” Acute renal failure a recognized complication of birth asphyxia, carries poor immediate prognosis and may result in permanent renal damage in survivors. **Objectives:** To determine the incidence of Acute Renal Failure in cases of Perinatal Asphyxia and to correlate it with severity of Apgar score and Hypoxic Ischemic Encephalopathy grading. **Methods:** this study is done on newborns with gestational age >34 weeks having evidence of birth asphyxia based on APGAR scores and renal function assessment done at day 3 of life. **Results:** among 50 newborns studied, 46 Forty six percent patients had mild PNA where as 42 % patients & 12% patients were having moderate & severe PNA based on APGAR score. ARF was found in 24% cases of PNA with oliguric renal failure (ORF) in 42% and non oliguric renal failure (NORF) in 58% cases. All cases of ARF (100%) had raised blood urea while it was raised only in 8% of non ARF cases. All patients of severe PNA (100%) had ARF whereas only 28% patients of moderate PNA had ARF. None of patients with mild PNA had ARF. Renal USG showed abnormalities in only 2 (4%) asphyxiated newborns. **Conclusions:** Our results showed a strong relation between severity of PNA and ARF, with no ARF seen in mild PNA. This study showed a linear relationship between incidence of ARF and staging of HIE. Mortality occurred in ORF cases only.

KEYWORDS: Acute Renal failure in newborns, HIE, PNA.**INTRODUCTION**

As per the AAP (American Academy of Paediatrics) and ACOG (American College of Obstetrics and Gynaecology), all the following must be present for designation of asphyxia (a) profound metabolic or mixed acidemia (pH < 7.00) in cord blood (b) Persistence of Apgar score 0-3 for longer than 5 minutes. (c) Neonatal neurologic sequelae (e.g. seizures, coma, hypotonia). (d) Multiple organ involvement (e.g. Kidney, lungs, liver, heart, intestine). The overall incidence of PNA varies from 1.0-1.5% at various centres and is related to gestational age and birth weight.^[1]

Hypoxia can cause damage to almost every tissue and organ. In a term infant with PNA renal, neurologic, cardiac and lung dysfunction occur in 50%, 28%, 25% and 23% cases respectively.^[2] Brain hypoxia and ischemia due to systemic hypoxemia, reduced cerebral blood flow (CBF), or both are the primary physiological

processes that lead to hypoxic-ischemic encephalopathy. As kidney is very sensitive to oxygen deprivation, renal insufficiency may occur within 24 hrs of an ischemic episode, which if prolonged, may even lead to irreversible cortical or medullary necrosis.^[3]

ARF and renal vein thrombosis are recognized complications of birth asphyxia, out of these ARF is commonest and carries poor immediate prognosis and may result in permanent renal damage in survivors. ARF is characterized by a sudden deterioration of renal function which leads to the accumulation of nitrogenous end products. Renal response to an acute hypoxic injury is reduction of GFR and paralysis of tubular functions. The site of the disorder can be localized as prerenal, renal or post-renal.^[4]

The RIFLE criteria for classification of acute kidney injury consists of three graded levels of injury (Risk,

Injury, and Failure) based upon either the magnitude of elevation in serum creatinine or urine output, and two outcome measures (Loss and End-stage renal disease).^[5]

The early recognition of renal dysfunction is important in asphyxiated neonates with HIE, in whom stable biochemical milieu is vital, because it facilitates the administration of appropriate fluid and electrolyte replacement. With improved survival of sick asphyxiated neonates due to advances in medical care, clinical entity of renal function is of concern.

Thus this prospective study was planned with following aims and objectives:

AIMS AND OBJECTIVES

1) To determine the incidence of Acute Renal Failure in cases of Perinatal Asphyxia. 2) To correlate incidence and outcome of Acute Renal Failure with severity of Apgar score and Hypoxic Ischemic Encephalopathy grading.

MATERIALS AND METHODS

The study was carried out in the Department of Pediatrics, Govt. Medical College, and Amritsar. Neonates with PNA (fulfilling the criteria of perinatal asphyxia) were enrolled in this study, using non probability convenience sampling method. The neonates were delivered in the Department of Obstetrics & Gynaecology.

Inclusion Criteria

1. All newborns having gestational age ≥ 34 weeks (as per Ballard scoring method with history of birth asphyxia).
2. Evidence of neurological abnormalities suggestive of HIE (altered tone, seizures, depressed level of consciousness).
3. Apgar score of 6 or less at 5 minutes in non-intubated babies and 7 or less in intubated babies.

Exclusion Criteria

1. Neonates who have received aminoglycoside antibiotics.
2. Congenital abnormalities of kidneys and / or urinary tract.
3. Cardiovascular pathology not related to PNA.
4. Patients who died within 48 hours of admission were excluded because of incomplete investigations.
5. Neonates with severe respiratory distress syndrome, necrotizing enterocolitis, severe septicemia.

On the basis of Apgar score at 5 minutes the asphyxia was further grouped into mild (score of 6 or 7), moderate (score 5 or 4) and severe asphyxia (score 3 or less). All neonates with clinical features of HIE were staged by Sarnat and Sarnat grading system^[6] as under:

Grade I-HIE: Hyper alert (irritable), tone normal, weak suck, strong Moro's reflex, mydriasis and tachycardia.

Grade II-HIE: Lethargic, seizures, differential tone legs more than arms, weak Moro's reflex, absent or weak suck miosis and bradycardia.

Grade III-HIE: Comatose, flaccid, no suck, no Moro reflex, prolonged and frequent seizures, unequal pupils and variable heart rate.

The criteria of acute renal failure (ARF) in an asphyxiated neonate as having renal failure were:

1. Urine output less than 0.5 ml/kg/hr
2. Blood urea more than 40mg/dl
3. Serum creatinine more than 1.5 mg/dl
4. Presence of significant hematuria or proteinuria

These criteria were applied on day 3 of life and any three of four when fulfilled were considered as indication of renal failure. Urine was collected in the pediatrics urine collecting bag to maintain strict input output chart. The 24 hours fluid intake and daily body weight was recorded. Collected urine was analyzed for blood, glucose, protein by multistix method and microscopically for pus cells and casts. The renal function parameters were monitored within 24 hours of birth and then on day 3 of life. After three days those babies having abnormal renal functions (i.e. having ARF) were further monitored for laboratory parameters every alternate day till recovery, discharge or death during hospital stay. Neonates with renal failure were followed at 3 months of age to detect any residual abnormalities. USG imaging of kidneys was carried out at the beginning of study and on the day of discharge and at 3 months from the Department of Radiology. Kidney size, echotexture and corticomedullary differentiation were noted.

RESULTS

Fifty neonates with PNA were enrolled in this study with following base line characteristics.

Table 1: Baseline Characteristics.

Variable		Number of cases
Gestational age (weeks)	34-36(Preterm)	11(22%)
	≥ 37 (Term)	39(78%)
Sex	Male	34(68%)
	Female	16(32%)
Mode of delivery	NVD	28(56%)

	LSCS	22(44%)
Weight (kg)	<2.5	14(28%)
	≥ 2.5	36(72%)

Table 2: Severity of PNA on the Basis of Apgar Score at 5 Minutes.

Apgar score	Number of subjects having Apgar score at 5 min	Severity of PNA
6-7	23(46%)	Mild
4-5	21(42%)	Moderate
0-3	6(12%)	Severe

Table 3: Severity of HIE Grading in Asphyxiated Neonates.

Severity of HIE	Number of cases
Normal	21(42%)
HIE-1	13(26%)
HIE-2	9(18%)
HIE-3	7(14%)

Table 4: Abnormal Biochemical Parameter & Incidence of arf.

Abnormal biochemical parameters on day 3 rd	Number of cases with ARF	Number of cases with no ARF
Oliguria(< 0.5ml/kg/hr)	5	7
Increased Blood urea(>40mg/dl)	12	3
Increased serum creatinine (> 1.5 mg/dl)	11	—
Urinary abnormalities (Proteinuria or hematuria)	12	3

Oliguria was found in 24% cases of PNA. Its incidence was higher in ARF cases(42%) than non ARF cases (19%). Fifty eight percent of ARF cases were non oliguric and 58 % of cases had oliguria but no ARF.

Table 5: Corelation of Incidence of Arf with Severity of PNA.

Severity of Apgar score(PNA)	Number of patients who had PNA	Number of patients who had ARF
6-7 (Mild)	23	0
4-5 (Moderate)	21	6(28 %)
0-3 (Severe)	6	6(100 %)

Table 6: Outcome of arf.

S. No.	Case No.	Type of ARF	Day on which babies expired	Day on which babies recovered from ARF	USG finding		Day of discharge	Follow up at 3 months	
					At beginning	At discharge		Renal function	USG
1	2	NORF	—	5 th	N	N	9th	N	N
2	6	ORF	—	9 th	Abn	Abn	15th	N	N
3	9	NORF	—	7 th	N	N	9th	N	N
4	17	NORF	—	5 th	N	N	15th	N	N
5	18	NORF	—	5 th	N	N	9th	N	N
6	26	NORF	—	7 th	N	N	11th	N	N
7	30	ORF	3rd	—	—	—	—	—	—
8	34	ORF	—	9 th	Abn	Abn	15th	N	N
9	43	ORF	—	7 th	N	N	15th	N	N
10	46	NORF	—	7 th	N	N	11th	N	N
11	47	ORF	3rd	—	—	—	—	—	—
12	49	NORF	—	9 th	N	N	11th	N	N

ORF— Oliguric renal failure

NORF— Non oliguric renal failure

Abn—Abnormal

N— Normal

DISCUSSION

Among Fifty neonates in current study, Male & female ratio was 2:1. Forty six percent patients had mild PNA (Apgar score at 5 minutes between 6-7) where as 42%

patients & 12% patients were having moderate & severe PNA (Apgar scores 4 to 5 & between 0-3 respectively). Only 58% had clinical evidence of HIE in PNA. Twenty six percent of the asphyxiated patients were graded into having HIE-1 while 18% patients & 14% patients were graded into having HIE-2 & HIE-3 respectively as per Sarnat & Sarnat staging.

While reduced urine output is a hallmark of renal impairment, some patient may develop acute loss of renal functions without oliguria. Nonoliguric renal failure (NORF) is a recognized entity secondary to PNA. Moreover, patients recovered from oliguria earlier in non ARF cases (on day 5) than ARF cases (on day 7). Oliguria has been reported by many authors in a high percentage of patients. Perlman et al reported oliguria in 40% of their study cohort of PNA. Tach Eric et al reported normal urine output in 77% and oliguria in 23%. Our study also showed oliguria in 24% PNA cases.

All cases of ARF (100%) had raised blood urea in our study while it was raised only in 8% of non ARF cases. Hence, our study showed 100% sensitivity and 92% specificity to diagnose ARF in all PNA cases by taking

Account of raised blood urea on day 3 of life. Eleven Cases of ARF had raised serum creatinine and only one case of ARF had serum creatinine 1.4 mg/dl, which was also near higher range, though it did not fulfil the b criteria of ARF (i.e.1.5mg/dl). None of the case had raised serum creatinine in non ARF cases. Hence this study showed 92% sensitivity and 100% specificity to diagnose ARF in all PNA cases by taking account of raised serum creatinine. Similar significantly higher levels of blood urea and serum creatinine in asphyxiated neonates were reported by Jeffery et al. Higher serum creatinine levels were reported in asphyxiated babies by Perlman et al, Martin et al, Jayshree et al⁴², Mangi and colleagues and Gupta BD et al.

Thirty percent cases of PNA had significant urinary abnormalities in the form of proteinuria, hematuria or both. All cases (100%) of ARF had urinary abnormalities while these were present only in 8% cases of non ARF cases. Martin et al reported proteinuria in 31% of ARF cases in their study. Polito et al and Mishra et al showed that 100% and 50% respectively of asphyxiated newborns had urinary abnormalities

We found incidence of ARF in 24% cases of PNA. Gupta B D et al had reported ARF in 47% cases while Perlman et al & Aldena et al both reported renal involvement in 50% asphyxiated newborns in their study. We found oliguric renal failure (ORF) in 42% and non oliguric renal failure (NORF) in 58% cases. Jayshree et al observed ORF in 69.2% and NORF in 30% of all cases of ARF in neonates with severe asphyxia. Gupta BD et al showed ORF in 21% cases and NORF in 78% cases in all asphyxiated neonates. Though blood urea & serum creatinine were higher in ORF than that of NORF

but the observed differences were not significant statistically ($p=0.42$ & $p=0.68$). Our results have shown a strong relation between severity of PNA and ARF, which was in accordance with the results of Gupta BD et al, Jayshree G et al & Mangi ZA and colleagues.

Table 7: Corelation Of Incidence Of Arf With Severity Of HIE Staging.

Staging of HIE	Number of cases with HIE	Number of patients had ARF
HIE-1	13	2(15%)
HIE-2	9	4(44%)
HIE-3	7	6(86%)
Total	29	12 (41%)

Fifty eight percent of PNA cases developed HIE. Out of these HIE cases, 41% patients had ARF. Fifteen percent in HIE stage 1, 44% in stage 2 & 86% in HIE stage 3 had ARF. This shows a linear relationship between incidence of ARF and staging of HIE. Mangi ZA & colleagues showed 41% ARF in HIE-II & 100% ARF in HIE-III which is similar to present study.

Renal USG showed abnormalities in only 2 (4%) asphyxiated newborns in the form of increased size, altered echo texture and loss of corticomedullary differentiation. Both had altered renal functions and were oliguric but showed normal USG at 3rd month of follow up.

Twenty four percent asphyxiated neonates in our study who had ARF on day 3 were managed conservatively and as a result, 10/12 (83%) showed improvement whereas 2/12 (17%) newborns expired within 3 days of life. Newborns who suffered ARF in neonatal period following asphyxia were followed till recovery and at 3 months for detection of any residual impairment or progression of renal dysfunction. No neonate remained oliguric after 7 days of life. All ten newborns that had ARF returned for follow up at 3 months and showed biochemical parameters i.e. blood urea, serum creatinine within normal limits. Renal ultrasound was also found to be normal in all follow up cases.

PNA insult induced a reduction in number of functional nephrons resulting in ARF. However, compensatory hypertrophy of their residual nephrons was able to improve renal functions in early months of life. Whether it brings them to normal range or not, can only be said after long term follow up. Therefore, one must be cautious in stating the long term prognosis of neonates who suffered neonatal ARF. Hence, there is need for continuous long term follow up of neonates with ARF.

The limitations of our study have been our inability to check for serum electrolytes, BP monitoring, urinary concentrating ability and evidence of renal tubular acidosis.

SUMMARY AND CONCLUSION

- ❖ ARF is seen in 24% asphyxiated neonates. Out of these, 58% had non oliguric renal failure (NORF) while 42% had oliguric renal failure (ORF). So majority had NORF in PNA.
- ❖ Newborns with ORF had statistically significantly lower urine output than those with NORF.
- ❖ Our results showed a strong relation between severity of PNA and ARF, with no ARF seen in mild PNA.
- ❖ This study showed a linear relationship between incidence of ARF and staging of HIE.
- ❖ Mortality occurred in ORF cases only.
- ❖ Renal USG scan showed abnormalities in 4% asphyxiated neonat

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