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A Comparative Study of Renal Parameters and Serum Calcium Levels in Birth Asphyxiated Neonates and Normal Neonates

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Abstract

Background and Objectives: Acute renal failure is a frequent clinical condition in neonatal intensive care units. The leading cause of neonatal acute renal failure is perinatal asphyxia. Early recognition of acute renal failure is particularly important in asphyxiated neonates, in whom a stable biochemical milieu is vital, because it facilitates the administration of appropriate fluid and electrolyte replacement. This study was done to determine the incidence of renal failure and its correlation with severity of asphyxia. **Methods:** 45 term neonates born with Apgar score of < 7 at 5 minutes after the birth are selected as cases and 45 term normal neonates as controls. All asphyxiated neonates (as per World Health Organization definition) with clinical features of Hypoxic ischemic encephalopathy are staged by Sarnat and Sarnat staging. The relevant blood and urine investigations done at 24, 48 and 72 hours of life and urine output was monitored. The babies were managed according to standard protocol. The renal indices were calculated after 48 and 72 hours. **Results:** The incidence of renal failure was significantly higher among cases (66.67%, 30 of 45 cases). All cases had non oliguric (100%) renal failure -11 (24.44%) cases had intrinsic renal failure. The renal parameters were higher among cases and correlated with the severity of asphyxia. Hyponatremia was seen in cases and its severity correlated with asphyxia severity. The serum calcium level was lower among cases and severity of hypocalcaemia correlated with severity of asphyxia. Fractional excretion of sodium (FeNa) was higher among cases and 11 cases had value more than 3. Renal failure Index was higher among cases and 12 cases had value more than 4. **Interpretation and Conclusions:** Perinatal asphyxia is an important cause of renal failure in the neonatal period. Acute renal failure in birth asphyxia is predominantly Pre renal failure and depends on the severity of asphyxia. Renal failure in birth asphyxia is predominantly non-oliguric, monitoring of urine output for renal failure alone does not help to identify renal failure. The renal parameters should be monitored and if possible the renal indices should be calculated to identify pre-renal and intrinsic renal failure.

Keywords: Acute Renal Failure, Birth Asphyxia, Hypoxic Ischemic Encephalopathy, Neonate

1. Introduction

Perinatal asphyxia refers to a condition during first and second stage of labor in which impaired gas exchange leads to fetal hypoxemia and hypercarbia. It is identified by fetal acidosis as measured in umbilical arterial blood. Although the most widely accepted definition of fetal acidosis is a pH of < 7, even with this degree of acidosis, the likelihood of brain injury is low[1]. Asphyxia (as-ffik-se-ah) (Greek: "stopping of the pulse"). Definitions based on Apgar scores may be useful as it can be used for formulating guidelines for post-asphyxial treatment of neonates. Apgar scores are also useful for predicting long term outcome in infants with perinatal asphyxia[2,3]. Almost any organ can be affected but the brain, myocardium, kidneys and bowels appear to be more

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sensitive to hypoxic injury. Kidneys are involved in 50%, brain involvedin 28%, heart in 25% and lungs in 23% of cases[4,5]. Early recognition of renal failure is important in babies with Hypoxic ischemic encephalopathy to facilitate appropriate fluid and electrolyte management as a stable electrical milieu is vital. Diagnosis of renal failure is difficult in this group as many clinical and biochemical parameters are unreliable in this age group. Hence this study was done to determine the incidence of acute renal failure in asphyxiated babies and correlate the severity with Hypoxic ischemic encephalopathy grading with emphasis on early diagnosis of acute renal failure which may be of particular benefit for asphyxiated newborns at risk of developing renal failure[6].

Birth asphyxia is associated frequently with metabolic changes like hypoglycemia, hypocalcaemia, hyponatremia, hyperphosphatemia and metabolic acidosis. Calcium is an important second messenger in our body and also helps out muscle function and acts as a co-factor for several enzymatic activities. During pregnancy, calcium is transferred actively from the maternal circulation to the fetus by a transplacental Ca pump regulated by the parathyroid hormone-related peptide. The majority of fetal Ca accretion occurs in the third trimester. This process results in higher plasma Ca concentration in fetus than in the mother and leads to fetal hypocalcaemia with total and ionized Ca concentration of 10-11 mg/dl and 6 mg/dl in umbilical cord blood at term.

After birth due to the abrupt cessation of placental transfer of calcium hence, levels starts falling to 8-9 mg/dl and ionized calcium to 4.4-5.4 mg/dl at 24 h of age. Serum calcium then starts rising to reach levels comparable to older children and adults by 2 weeks of age[13].

2. Methods

A comparative study of 45 Newborn term, appropriate for gestational age babies born/admitted to NICU of tertiary care centre with birth asphyxia during study period and 45 normal newborn babies without birth asphyxia are included in the study. At the time of enrolment an informed written consent was obtained from the parents. Detailed perinatal history was obtained from hospital records. Detailed clinical examination was done. Newborns identified as appropriate for gestational age by applying Ballard's score and by percentile chart. Diagnosis of birth asphyxia by Apgar score, Gestational age, birth weight, relevant perinatal history, findings on physical examination and systemic examination were recorded on predesigned proforma. Renal function parameters – urine output, urine analysis and urine sodium and creatinine and serum calcium were monitored initially within 24hrs of birth. At 48hrs and 72hrs in addition, blood urea and creatinine were measured. Ultrasonography would be performed to detect congenital renal anomalies. Acute renal failure is defined as serum creatinine of level >1.0 mg/dl on day 3 of life and/or urine output of <1.0ml/kg/hour. On the basis of Apgar score at 5 minutes the asphyxiated babies are grouped into mild (score of 6-7), moderate (score of 4-5) and severe asphyxia (score of 3 or less). Collected data is analyzed by Unpaired and Paired 't' test, Karl Pearson correlational coefficient and by chi square test.

3. Results

Male neonates had a higher incidence of birth asphyxia (Figure 1). In this study, the incidence of renal failure among asphyxiated neonates was 66.67 % (Figure 2) with non oliguric renal failure seen in 100% (Table 3). The fractional excretion of sodium was > 3 in 24.44% of asphyxiated neonates which accounted for 36.67 % of cases with renal failure (Table 1). The incidence of renal failure had a linear correlation with severity of asphyxia and incidence of intrinsic renal failure increased as the severity of asphyxia. The serum sodium was lower among cases than the controls (Table 4). There was no linear correlation between severities of asphyxia with hyponatremia.

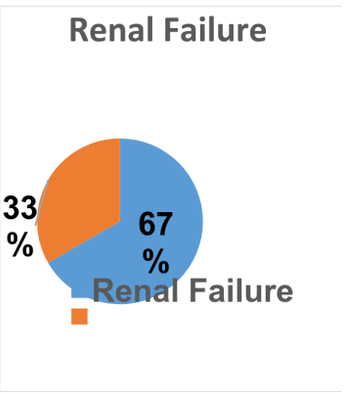

Figure 1. Incidence of Renal Failure in Asphyxiated Neonates.

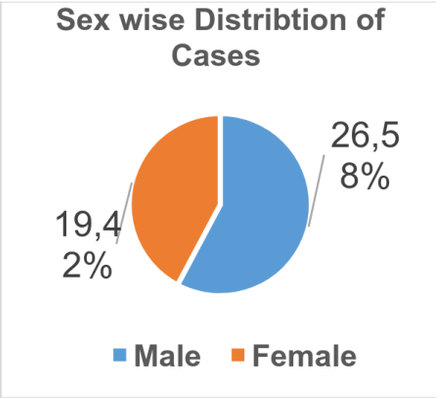

Figure 2. Sex wise Distribution of Cases.

Table 1. Fractional excretion of sodium in patients with Renal failure

Fractional excretion of sodium	Frequency	Percentage
Intrinsic renal Failure(FENA>3)	11	24.44%
No Intrinsic renal Failure(FENA<3)	34	75.56%

Table 2. Incidence of Renal failure in different grades of Asphyxia

Renal Failure	Birth Asphyxia		
	Mild	Moderate	Severe
Renal Failure	4	22	4
No Renal Failure	2	13	0
Total	**6**	**35**	**4**

The serum potassium was higher among cases but none had serum potassium more than 6 (Table 4). The serum calcium was lower among cases and significant difference was noted at 48 and 72 hours of life, none had hypocalcaemia less than 7 mg/dl and serum calcium levels found to be lower with severity of asphyxia (Table 4). The blood urea and creatinine was elevated among cases and higher levels of both values found with severity of asphyxia (Table 4). Proteinuria is the only abnormal finding noted in urine routine examination, seen in 29% of cases and not associated with severity of birth asphyxia. Urine sodium and urine creatinine was higher among cases and not had any correlation with asphyxia. Fractional excretion of sodium (FeNa) was higher among cases. FeNa>3 indicating intrinsic renal failure being more common with severity of asphyxia (Table 1) (Table 4). Renal failure index was higher among cases and their values independent with asphyxia (Table: 4).

4. Discussion

The incidence of renal failure was comparable with the studies done by Gupta et al, Zulfikar Ali Mangietal[12], Aggarwal et al.,[7] and Jayashree et al[8]. In our study serum creatinine of more than 1 mg/dl after 72 hrs is considered as renal failure. 40% of neonates with asphyxia had FeNa > 3 suggestive of intrinsic renal failure which accounted for 24.44% of neonates with renal failure, as like other studies in our study also pre renal failure being more common. This is probably due to majority of our cases belonged to stage II and III Hypoxic ischemic encephalopathy.

Table 3. Incidence of Oliguria in cases and cases with ARF

Urine output >24 hrs	Cases		Cases with ARF	
	Frequency	Percentage	Frequency	Percentage
<=1 ml/kg/hr	9	20.00%	0	0.00%
>1 ml/kg/hr	36	80.00%	30	100.00%

Table 4. Renal parameters and Serum electrolytes levels in Cases and Controls

Parameters	Cases	Controls	P values
Serum Creatinine	1.32±0.12	0.77±0.11	P< 0.0001
Serum Urea	32.73±0.15	21.93±1.13	P< 0.0001
Serum Calcium	8.55±0.58	9.19±0.06	P< 0.0001
Serum Sodium	133.21±0.12	137.91±0.39	P< 0.0001
Serum Potassium	5.17±0.07	4.63±0.03	P<0.0001
Fractional excretion of sodium	8.55±0.58	9.19±0.06	P< 0.0001
Renal failure Index	2.75±0.15	0.78±0.10	P< 0.0001

All studies showed that non-oliguric renal failure being most common in asphyxiated neonates. Non-oliguric renal failure can be explained due to decreased pituitary release of vasopressin or reduced responsiveness of renal to vasopressin and heterogeneous response of individual nephrons to the tubular epithelium that results in anatomical damage in majority of nephrons, leading to reduction in single nephron GFR and decreased tubular fluid. But if damage to tubular epithelium is less severe, there is a decrease in fractional reabsorption which exceeds the decrease in single nephron GFR leading to polyuria in non oliguric renal failure[4]. The mean blood urea levels were higher among cases as compared to controls which were statistically significant but there was no significant difference among groups with severity of asphyxia. The results of our study are comparable to other studies. In our study we found that serum creatinine levels were higher in cases as compared to controls and the difference between the groups was statistically significant both at 48 and 72 hrs. But however the serum creatinine value was higher in cases with severe asphyxia, the difference among the groups was not statistically significant. The observations in our study are comparable with other studies.

In our study the mean serum sodium concentration was lower among the cases as compared to controls which were comparable with other studies which was statistically significant. The serum sodium levels were lower in neonates with severe birth asphyxia; the mean serum sodium is higher in our study as compared to Misra et al.,[10] study in which the study population is small with most neonates belonging to either stage II or stage III which indicates either moderate or severe degree of asphyxia. Pallab Basu and colleagues[11] study does not mention the distribution of cases in with different severity of asphyxia. The mean serum potassium level was higher in cases than the controls which is comparable with other studies. In Misra et al.,[10] study the mean serum potassium level was higher than the other studies in which only 7 neonates have been studied and majority had severe birth asphyxia.

The mean serum calcium level in our study was lower as compared to controls, which was noticed after 24-48 hrs, as only few patients belong to severe birth asphyxia. The mean serum calcium level is not reduced to as low as in Pallab Basu[11] study in which they have not considered regarding the distribution of cases. As most neonates were on calcium supplementation, hypocalcaemia of < 7 was not seen in any neonates.

In our study the mean FeNa was higher in cases than the controls which were statistically significant. The FeNa increased as the severity of asphyxia increased or as there is progression in Hypoxic ischemic encephalopathystaging. The results of our study is comparable with Misra et al.,[10] study, but in this study the mean value of FeNa is higher than our study because it studied only 7 neonates, with majority in stage II and III Hypoxic ischemic encephalopathy which reflects the severity of asphyxia being moderate to severe. B D Gupta[9] had a lower FeNa as compared to our study as 32 of 70 neonates they studied had no Hypoxic ischemic encephalopathy which reflects a milder degree of asphyxia.

The mean renal failure index was higher among case as compared to controls which was statistically significant. The Renal Failure Index (RFI index) was higher in neonates with severe asphyxia. The mean Renal failure index in our study is lower as compared to Misra et al.,[10] study as it included only neonates with stage II or stage III HIE in their study population, reflecting moderate or severe degree of asphyxia as compared to our study which included majority of neonates with mild to moderate asphyxia.

5. Conclusion

Perinatal asphyxia is an important cause of neonatal renal failure. Monitoring of blood levels of urea, serum creatinine, serum calcium and urine output helps in the early diagnosis and management of renal failure in birth asphyxia. However, in birth asphyxia, since non oliguric renal failure is common, monitoring only urine output does not help in the diagnosis of acute renal failure, the biochemical parameters in both blood and urine should be monitored. The renal indices should be calculated, as fractional excretion of sodium is preferred to classify the renal failure into pre renal or intrinsic renal failure as management differs for both entity.

It can be concluded from the present study that with perinatal asphyxia, develops hypocalcaemia (when serum calcium levels<7 mg/dl) after birth in proportion to severity of asphyxia and severely asphyxiated babies develop hypocalcaemia which may require medical interventions.

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