Renal involvement in term neonates with Hypoxic-Ischemic Encephalopathy: A frequency-based study.

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ABSTRACT:

Objective: The objective of this study was to determine the frequency of acute renal failure in term neonates presenting with hypoxic ischemic encephalopathy.

Methodology: This cross-sectional study conducted at PAF Hospital Mushaf Sargodha from 01-01-2025 to 31-06-2025. During study period 159 full term neonates of both gender having APGAR score <7 at 5 minutes after birth were recruited. A written informed consent was taken from parents of every patient. All grades of birth asphyxia were included. Serum creatinine was acquired after 72 hours of birth and acute renal failure was diagnosed if it was ≥1.5mg/dl.

Results: The mean gestational age of the neonates was 39.54±1.83 weeks. 85 (53.5%). The male to female ratio was 1.8:1. Majority (n=110,69.2%) of the neonates were delivered by spontaneous vaginal delivery (SVD) while 49 (30.8%) were delivered by C-section. The mean weight of the neonates was 2.62±0.52 kg. 50 (31.5%) neonates had mild, 90 (56.6%) neonates had moderate and 19 (11.9%) neonates had severe birth asphyxia. Mean blood urea level was 29.6±5.8 mg/dl while mean serum creatinine level was 1.77±0.53 mg/dl. Acute renal failure was observed in 101 (63.5%) neonates. The frequency of ARF increased significantly with increasing severity of birth asphyxia, mild vs moderate vs severe (20% vs 76.7% vs 100%; p<0.001). However, there was no significant difference across gestational age, gender, mode of delivery and birth weight.

Conclusion: A significant percentage of asphyxiated newborns experienced acute renal failure, which was linked to the severity of birth asphyxia. This calls for routine monitoring of asphyxiated neonates in order to promptly detect and treat this problem in future practice to improve the result.

Keywords: Birth Asphyxia, Sarnat Grading, Acute Renal failure.

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Introduction:

Hypoxic ischemic encephalopathy continues to be a leading cause of perinatal morbidity and mortality (23%) with long term disabilities.[1,2] Birth asphyxia results in redistribution of blood flow towards the brain, heart and adrenals and away from kidneys, skin and the gastrointestinal tract.[3,4] The newborn kidney has a very low glomerular filtration rate (GFR) approximately 1ml/min/kg of body weight that is maintained by a delicate balance between vasoconstriction and vasodilation forces. Although sufficient for growth and development under normal conditions, the low GFR of the newborn kidney limits postnatal renal function adaptation to endogenous and exogenous stress.[5,6] This redistribution of blood flow in birth asphyxiated newborns therefore frequently leads to acute renal failure which worsen the course of illness and is associated with increased mortality among such neonates.[7,8]

Tounsa et al. reported that 18.02% of term neonates with birth asphyxia presenting at Bahawal Victoria Hospital, India developed acute renal failure.[9] Among the American asphyxiated neonates Bitar et al. reported the frequency of ARF to be 44%.[10] In Pakistan a study conducted in Karachi declared that AKI was observed in 40.9% babies with HIE,[11] A similar study in a territory care hospital in Khyber Pakhtunkhwa stated its frequency to be 10.5% in asphyxiated neonates.[12]

Thus, acute renal failure is a frequent complication encountered in neonates with birth asphyxia. The reported frequency varies not only among various populations (from as low as 10.5%,[12] to as high as 44%,[10] but within a single population as well (from as low as 10.5%,[12] to as high 40.9%,[11] in Pakistani population). Considering this variation among the existing studies and lack of local such published material, there is need to conduct a similar research in the local context to further validate the evidence. The results of the present study will give an insight into the magnitude of problem and will enable routine screening, early identification and thus timely management of ARF decreasing the morbidity and mortality associated with this complication in asphyxiated neonates.

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Objective:

The objective of this study was to determine the frequency of acute renal failure in term neonates presenting with birth asphyxia.

Operational Definition:

Term Neonates: Infant born between 37-42 completed weeks of gestation calculated from LMP (Last menstrual period).

Birth Asphyxia: It was labeled in neonates having APGAR score <7 at 5 minutes after birth. It was graded clinically by consultant in charge of the unit according to Sarnat & Sarnat staging as mild, moderate and severe

Acute Renal Failure: Serum creatinine was acquired on 3rd day (72 hours of life) and level >1.5mg/dl was considered as ARF.

Methodology:

This cross-sectional study was conducted in the department of Pediatrics at Pakistan Air force Hospital Mushaf, Sargodha over a period of 6 months (01-01-2025 to 31-06-2025) after the approval of hospital ethical committee. A sample size of 159 was calculated using the WHO calculator with 95% confidence level and 5% margin of error while taking expected frequency of ARF to be 11.7% in asphyxiated neonates. Patients were selected by non-probability consecutive sampling. Neonates of either gender aged ≤3 days presenting with birth asphyxia were included. However patients who died within 72 hours of life where labs couldn't be acquired to diagnose ARF, patients with congenital anomalies of the kidney and urinary tract (On antenatal ultrasound), patients who had received aminoglycoside antibiotic (as per history and clinical record) were excluded. As per required sample size,159 patients who presented in the emergency, indoor or outdoor pediatric department, fulfilling the criteria were enrolled in study after taking the informed consent from the parents. Detailed history was taken from the parents of each patient including mode of delivery. Severity of birth asphyxia was established according to Sernat & Sernat staging as mild, moderate and severe. All the patients received routine management as per department protocol comprising of radiant warmer, intravenous line and IV fluids started as 10% dextrose at 60ml/kg/day on Day 1, 75ml/kg/day on Day 2, 90ml/kg/day on Day 3. For first 48 hours dextrose 10%, Injection Vitamin K 1mg was administered to all these babies. A stomach wash was performed if there was history of meconium-stained liquor. Serum urea and creatinine levels were done on 3rd day (72 hours of life) by drawing 3ml of venous blood under aseptic measures and ARF was labeled as per operational definition. All the clinical grading of asphyxia were done by a single consultant and all the labs were done from the same hospital labs to minimize bias. Confounding variables were controlled by exclusion. Statistical analysis was done by SPSS 21. Mean ± SD has been calculated for gestational age at delivery, weight, serum urea and creatinine while frequency and percentage have been calculated for gender, mode of delivery, severity of birth asphyxia and ARF. Data has been stratified for gestational age at delivery, weight, mode of delivery, gender and severity of birth asphyxia to address effect modifiers. Post stratification chi-square test has been applied taking p value <0.05 as statistically significant.

Results:

The gestational age of the neonates ranged from 37 weeks to 42 weeks with a mean of 39.54±1.83 weeks, 85 (53.5%) neonates were delivered between 37- 39 weeks while 74 (46.5%) were delivered between 40-42 weeks. These were 103 (64.8%) male and 56 (35.2%) female patients with a male to female ratio of 1.8:1. Majority (n=110, 69.2%) of the neonates were delivered by SVD while 49 (30.8%) were delivered by C-section. the weight of the neonates ranged from 1.6kg to 3.8kg with a mean of 2.62±0.52 kg.25 (15.8%) neonates weighed between 1.5-2kg. 95 (59.7%) neonates weighed between 2-3 kg while 39 (24.5%) weighed above 3 kg at birth. 50 (31.5%) neonates had mild, 90 (56.6%) neonates had moderate and 19 (11.9%) neonates had severe birth asphyxia as shown in Table No. 1

Blood urea level ranged from 22 mg/dl to 42mg/dl with a mean of 29.6±5.8mg/dl while serum creatinine level ranged from 0.6mg/dl to 2.8mg/dl with a mean of 1.77±0.53 mg/dl as shown in Table No. 1

Acute renal failure was observed in 101 (63.5%) neonates as shown in table No. 2. The frequency of ARF increased significantly with increasing severity of birth asphyxia; mild vs moderate vs severe (26% vs 76.7% vs 100%; p<0.001). however, there was no significant difference across gestational age, gender, mode of delivery and birth weight as shown in Table No.3.

Table No.1: Demography of Study Participants.

Characteristics	Participants n=159
Gestational age (weeks)	
Mean Gestational Age	39.54±1.83
37-39 weeks	85 (53.5%)
40-42 weeks	74 (46.5%)
Gender	
Male	103 (64.8%)
Female	56 (35.2%)
Mode of delivery	
Spontaneous vaginal delivery	110 (69.2%)
C-section	49 (30.8%)
Body weight (kg)	
Mean Body weight	2.62±0.52
1.5-2 kg	25 (15.8%)
2-3 kg	95 (59.7%)
>3 kg	39 (24.5%)
Severity of Hypoxic-Ischemic Encephalopathy	
Mild	50 (31.5%)
Moderate	90 (56.6%)
Severe	19 (11.9%)
Laboratory Investigation	
Blood Urea (mg/dl)	29.6±5.80
Serum Creatinine (mg/dl)	1.77±0.53

Table No. 2: Frequency of Acute Renal Failure in Birth ASPHYXIC Neonates.

Acute renal failure	Frequency (n)	Percentage (%)
Yes	101	63.5
No	58	36.5
Total	159	100

Table No. 3: Stratification of Frequency of Acute Renal Failure in Hypoxic-Ischemic Encephalopathy Neonates

Characteristics	Acute renal failure (n %)	P value
Gestational age		
37-39 weeks	55/85 (64.7%)	0.740
40-42 weeks	46/74 (62.2%)	
Gender		
Male	66/103 (64.1%)	0.844
Female	35/56 (62.5%)	
Mode of delivery		
Spontaneous vaginal delivery	70/110 (63.6%)	0.964
C-section	35/56 (63.3%)	
Body weight (kg)		
1.5-2 kg	16/25 (64%)	0.882
2-3 kg	59/95 (62.1%)	
>3kg	26/39 (66.7%)	
Severity		
Mild	13/50 (26%)	<0.001
Moderate	69/90 (76.7%)	
Severe	19/19 (100%)	

Discussion:

Hypoxic ischemic encephalopathy continues to be a leading cause of perinatal morbidity and mortality (23%) with long term disabilities[2,13] Birth asphyxia results in redistribution of blood flow towards the brain, heart and adrenals and away from kidneys, skin and the gastrointestinal tract.[14] This redistribution of blood flow in birth asphyxiated newborns therefore frequently leads to acute renal failure which worsen the course of illness and is associated with increased mortality among such neonates.[15,16] The reported frequency of acute renal failure among asphyxiated newborns varied not only among populations but within subgroups of same population while there was no such local published material which necessitated the present study. In the present study, the mean gestational age of the neonates was 39.54±1.83 weeks. 85 (53.5%) neonates were delivered between 37-39 weeks while 74 (46.5%) were delivered between 40-42 weeks. Memon et al. reported similar mean gestational age of 38.05±1.22 weeks among neonates with birth asphyxia at CMH Hyderabad.[17] Indra et al.[11] also reported 19.5% <37 weeks and 80.5% ≥37 weeks in Karachi whereas Atta et al revealed mean gestational age as 39.55±1.48 weeks in KPK.

In the present study, there were 103 (64.8%) male and 56 (35.2%) female patients almost similar to Memon et al. With 56.7% males and 43.3% females.[17] Indra et al. reported similar male predominance with 59.1% males to 40.9% females in Sindh[11] while Atta et al. reported it to be 46.66% males to 53.33% females in KPK. [12.] Zainab et al. observed similar male predominance with 56.2% males to 43.7% females in Indian asphyxia neonates.[15] Bitar et al. observed it to be 56% males with 44% females in USA. We observed that majority (69.2%) of the neonates delivered by SVD while 49 (30.8%) were delivered by C-section. A relatively similar frequency of cesarean delivery has been observed among asphyxia neonates by Memon et al who reported it to be 35% at Combined Military Hospital, Hyderabad.[17] Atta et al. reported this frequency to be 43.8% among such neonates at a tertiary care hospital, KPK [12] Whereas Zainab et al reported 60.7% cesarean delivery in India [18] and Bitar et al also 70% in USA neonates.[10]

We observed that the mean weight of the neonates was 2.62±0.52 kg. 25 (15.8%) neonates weighed between 1.5-2 kg, 95 (59.7%) neonates weighed between 2-3kg while 39 (24.5%) weighed above 3 kg at birth. A similar mean birth weight of 2.48±0.52 kg has been reported by Atta et al. among asphyxic neonates in Khyber Pakhtunkhwa.[12] Indra et al. reported slightly higher mean birth weight of 2.60±0.19 kg among such neonates at National Institute of Child Health, Karachi.[11] However Memon et al, Bitar et al and Tounsa et al. Reported a much higher mean birth weight in asphyxiated neonates I.e. 3.60±0.57 kg, 3.23±0.35kg and 3.08±0.31kg respectively.[9,10,17]

In the present study, 50 (31.5%) neonates had mild, 90 (56.6%) neonates had moderate and 19 (11.9%) neonates had severe birth asphyxia. Indra et al. also reported similar frequency of mild (36.5%), moderate (52.2%) and severe (11.3%) birth asphyxia at NICH, Karachi.[11] Memon et al. observed similar frequency of mild, moderate and severe asphyxia and reported it to be 37.5% and 62.5% for moderate to severe HIE in KPK.[17] A slightly higher frequency of mild (34.6%), moderate (14.3%%) and severe (50.9%) birth asphyxia has also been reported by Zainab et al. in Indian population.[18] Bitar et al. Stated it to be 41% mild and 59% moderate to severe HIE in USA.[10]

In the present study acute renal failure was observed in 101 (63.5% neonates) Our results are much higher as compared to those of Indra et al. (40.9%) in NICH, Karachi.[11] Atta et al (10.5%) in KPK.[12] Incidence of AKI in various asphyxiated neonates are 45.36% in Ethopia.[19] Bitar et al. (41%) from USA and Tounsa et al. (18.02%) in Indian population.[9,10]

The frequency of ARF increased significantly with increasing severity of birth asphyxia, mild vs moderate vs severe (26% vs 76.7% vs 100%; p<0.001). however there was no significant difference across gestational age, gender, mode of delivery and birth weight. Zainab et al. reported that there was around 39 fold increase risk of developing AKI in HIE stage III versus HIE stage I.[18] Another study in Bangladesh revealed 10.1% incidence of AKI in HIE II and 45.4% in HIE III, stating that the higher the HIE stage the higher will be the possibility of developing AKI.[20] The present study is first of its kind in our local population of Sargodha and has found that acute renal failure is a frequent complication in asphyxiated neonates and is related to the severity of birth asphyxia on Sarnat grading. It is therefore advocated that in future practice, asphyxiated neonates should

be monitored for renal function particularly those with more severe asphyxia so that timely identification and management can improve the outcome in such cases. [21-24]

Conclusion:

Acute renal failure was observed in a substantial proportion of asphyxia neonates and was related to severity of birth asphyxia which warrants routine monitoring of asphyxia neonates to timely identify and manage this complication in future practice to improve the outcome.

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Authors' contribution	
Muhaz Khatib ur Rehman	Drafting of the manuscript and preparation of the initial version of the work.
Hina Batool Siddiqui	Data analysis and contribution to interpretation of analytical outcomes.
Quratul Ain	Statistical analysis and verification of statistical methods and results.
Nadia Bashir.	Interpretation of data and contribution to scientific discussion of findings
Abeer Asif	Data collection and organization of research data.
Saba Mushtaq	Critical analysis of the manuscript and intellectual review to improve scientific quality.
Rimsha Iqbal	Data collection and assistance in compiling research data.