DOI: https://doi.org/10.54393/pjhs.v6i5.3058

PAKISTAN JOURNAL OF HEALTH SCIENCES
(LAHORE)
https://thejas.com.pk/index.php/pjhs
ISSN (E): 2790-9352, (P): 2790-9344
Volume 6, Issue 05 (May 2025)

OPEN ACCESS

Original Article

Acute Systemic Organ Injury in Term Infants with Perinatal Asphyxia

Tariq Hussain[1], Sijad Ur Rehman[1*], Inayatullah1, Haji Gul[1], Saddam Hussain[1] and Muhammad Haris[1]

[1]Department of Pediatric Medicine, Gajju Khan Medical College, Swabi, Pakistan

ARTICLE INFO

Keywords:
Perinatal Asphyxia, Multiple Organ Injury, Neonatal Resuscitation, Renal Dysfunction

How to Cite:
Hussain, T., Rehman, S. U., Inayatullah, ., Gul, H., Hussain, S., & Haris, M. (2025). Acute Systemic Organ Injury in Term Infants with Perinatal Asphyxia: Acute Systemic Organ Injury with Perinatal Asphyxia. Pakistan Journal of Health Sciences, 6(5), 241-245. https://doi.org/10.54393/pjhs.v6i5.3058

***Corresponding Author:**
Sijad Ur Rehman
Department of Pediatric Medicine, Gajju Khan Medical College, Swabi, Pakistan
drsijad@yahoo.com

Received Date: 18th March, 2025
Revised Date: 16th May, 2025
Acceptance Date: 27th May, 2025
Published Date: 31st May, 2025

ABSTRACT

Perinatal asphyxia is a major contributor to neonatal morbidity and mortality. This leads to multiple organ dysfunction (MODS). **Objectives:** To assess the extent of acute organ system injury in term newborns with perinatal asphyxia, focusing on clinical and biochemical markers indicative of MOSD. **Methods:** This descriptive cross-sectional study involved 50 term newborns diagnosed with perinatal asphyxia. Clinical manifestations and biochemical markers, including renal and liver function tests, were analyzed to evaluate the extent of organ dysfunction. Fifty term newborns diagnosed with perinatal asphyxia were enrolled through non-probability convenience sampling. Clinical assessments included evaluations of the neurological, cardiovascular, respiratory, renal, and hepatic systems. Biochemical tests measured serum creatinine, serum ALT, and CKMB levels to assess kidney, liver, and myocardial function, respectively. Data were analyzed using descriptive statistics and Chi-square tests to examine the relationship between perinatal asphyxia and multi-organ injury, with a significance level of $p \leq 0.05$. **Results:** The severity of perinatal asphyxia was significantly correlated with the incidence of organ damage. Serum creatinine levels were elevated in 18 (36%) neonates, ALT levels were elevated in 20 (40%) neonates, and CKMB levels were elevated in 23 (46%) neonates. In some cases, early intervention was linked to improved neurological outcomes. **Conclusions:** This study emphasizes the critical need for early diagnosis and prompt intervention to prevent extensive organ damage in newborns with perinatal asphyxia. The severity of organ dysfunction is closely related to the degree of asphyxia, highlighting the importance of comprehensive monitoring and targeted treatment strategies. Further research is essential to develop better protective interventions for these infants.

INTRODUCTION

Perinatal asphyxia is defined as inadequate blood flow or gas exchange in the fetus or newborn during the perinatal period (before, during, and after delivery) [1, 2]. This critical event triggers a series of pathophysiological processes due to impaired oxygen and nutrient delivery, leading to systemic and neurological complications [3, 4]. These complications can vary in severity, depending on the duration and intensity of the asphyxia, and can cause lasting damage to multiple organ systems, including the brain, kidneys, liver, and heart [5-8]. Several studies have demonstrated the widespread effects of perinatal asphyxia on organ systems, but the extent of involvement varies. For instance, a study of 46 cases showed that all patients (100%) had central nervous system involvement, while 80% exhibited liver damage characterized by elevated ALT levels [9, 10]. Cardiac dysfunction, as evidenced by elevated cardiac enzymes, was present in 78% of cases, and renal injury, as indicated by elevated serum creatinine levels, was observed in 72% of cases [11]. Similarly, another study of 60 newborns found that 95% had involvement of at least one organ system, with cardiovascular dysfunction being the most common (95%), followed by renal injury (37%), liver dysfunction (22%), and central nervous system involvement (20%) [12]. A separate study of 56 newborns with perinatal asphyxia found that 22 of them had liver injury, as evidenced by elevated ALT levels [13]. Further research indicates that the mortality rate associated with perinatal asphyxia remains substantial. In a cohort of 267 neonates, 18% exhibited perinatal asphyxia, with a case fatality rate of 37.5% [14]. Additionally, a study

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on 152 asphyxiated neonates revealed that renal involvement occurred in 64%, respiratory dysfunction in 45%, cardiovascular impairment in 32%, and liver injury in 16% [15].

This study aims to provide a detailed analysis of acute systemic organ injuries in term neonates affected by perinatal asphyxia, aiming to identify potential risk factors that could guide improved clinical interventions and therapeutic strategies.

METHODS

This descriptive cross-sectional study was conducted from March 2023 to October 2023 at Bacha Khan Medical Complex, District Sawabi, Khyber Pakhtunkhwa. The study included 50 neonates diagnosed with perinatal asphyxia. Non-probability convenience sampling was used to select the participants. Ethical approval was obtained from the institutional ethical review board with approval No. 2509/PF/GKMC. Written informed consent was obtained from the parents or legal guardians of all participating neonates. Data were collected through a pre-designed questionnaire that included both clinical assessments and laboratory investigations. The inclusion criteria for the study were term neonates (gestational age between 37 and 42 weeks) diagnosed with perinatal asphyxia based on clinical criteria. These included abnormal fetal heart rate, Apgar scores less than 7 at 5 minutes post-delivery, and signs of organ dysfunction (e.g., altered consciousness, respiratory distress, and hypotonia). Exclusion criteria were preterm neonates, infants with congenital malformations or genetic disorders, and neonates with known systemic diseases unrelated to perinatal asphyxia. Clinical assessments were performed by trained pediatricians to evaluate organ system dysfunction, including the neurological, cardiovascular, respiratory, renal, and hepatic systems. Seizures within the first 24 hours were noted as indicators of neurological involvement. Serum CKMB, creatinine, and ALT levels were measured to assess myocardial injury, renal function, and liver function, respectively, while respiratory involvement was noted if resuscitation was required. All laboratory assays were validated according to manufacturer protocols and ISO 15189 standards, with regular quality control checks and control samples to ensure accuracy, sensitivity, and reproducibility.The sample size was calculated using the formula for estimating proportions in cross-sectional studies: n =Z2.*p*. (1-*p*)/E2.With a confidence level of 95% (Z=1.96Z = 1.96 Z=1.96), an estimated proportion of 0.5 (p=0.5p = 0.5 p=0.5), and a margin of error of 10% (E=0.1E = 0.1 E=0.1), the required sample size was 50 neonates.This ensures sufficient power for statistical analysis. Descriptive statistics were used to summarize the data, including frequencies and percentages for categorical variables (e.g., mode of delivery, seizure occurrence) and means and standard deviations for continuous variables (e.g., serum creatinine, ALT levels, CKMB levels). Chi-square tests were applied to determine the association between perinatal asphyxia and multi-organ injury. A p-value of ≤0.05 was considered statistically significant. Data analysis was performed using SPSS version 28.0.

RESULTS

A total of 50 neonates diagnosed with perinatal asphyxia were included in the study. The mean gestational age of the patients was 38.68 ± 1.096 weeks, with a minimum of 36 weeks and a maximum of 41 weeks, indicating a homogenous group of term pregnancies. The relatively low standard deviation suggests that the gestational ages were closely clustered around the mean. The mean serum alanine transaminase (ALT) level was 92.60 ± 113.522, with values ranging from 10 to 540. The significant variability in ALT levels among patients suggests differing degrees of liver function or hepatic damage. Serum creatinine levels had a mean of 1.0416 ± 0.74409, ranging from 0.30 to 4.80. This broad range indicates that the renal function of the neonates varied, with some showing significant renal impairment. The mean creatine kinase MB (CKMB) level was 197.64 ± 299.557, with values spanning from 12 to 1430, suggesting a wide range of myocardial stress or damage, and indicating that some neonates likely experienced severe cardiac issues (Table 1).

Table 1: Descriptive Statistics of Key Variables

Variables	Minimum	Maximum	Mean ± SD	Units
Gestational Age (Week)	36	41	38.68 ± 1.096	Weeks
APGAR Score at 5 Minutes	1	3	2.58 ± 0.575	-
Duration of Resuscitation	1	3	1.78 ± 0.708	Minutes
ALT Levels (U/L)	10	540	92.60 ± 113.522	U/L
Creatinine Levels	0.30	4.80	1.0416 ± 0.74409	Mg/dL
CKMB Levels	12	1430	197.64 ± 299.557	U/L

Regarding gestational age, the majority of the neonates (47, 94%) were between 37-40 weeks of gestation, confirming that most were full-term. Only 2 (4%) were born before 37 weeks, and 1 (2%) was born after 40 weeks. Delivery modes were predominantly normal vaginal deliveries (44, 88%), with 3 (6%) requiring C-sections and 3 (6%) assisted deliveries. At 1 minute post-delivery, 13 (26%) infants had an Apgar score of 1-3, requiring immediate medical intervention, while 37 (74%) had scores between 4-6. No neonates had an Apgar score between 7-10 at this stage. By 5 minutes post-delivery, 2 (4%) neonates had a score of 1-3, 17 (34%) scored between 4-6, and 31 (62%) had scores between 7-10. All 50 neonates required resuscitation. The duration of resuscitation varied, with 19 (38%) needing 1-3 minutes, 23 (46%) requiring 4-7 minutes, and 8 (16%) requiring 7-10 minutes. Seizures were reported

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in 47 (94%) of the patients within 24 hours of birth, while 3 (6%) did not experience seizures. For renal function, 32 (64%) patients had serum creatinine levels between 0.1-0.9, indicating normal renal function, while 18 (36%) exhibited elevated levels greater than 0.9, indicating potential renal impairment. In terms of liver function, 30 (60%) patients had ALT levels below 50, while 6 (12%) had levels between 51-100, and 14 (28%) exhibited ALT levels greater than 100, indicating varying degrees of liver dysfunction. Regarding myocardial injury, 27 (54%) patients had CKMB levels between 0-100, while 23 (46%) had levels greater than 100, indicating different degrees of myocardial stress or damage. The majority of neonates (47, 94%) had a favorable outcome and were discharged, while 3 (6%) expired (Table 2).

Table 2: Frequency Distribution of Key Clinical and Laboratory Variables

Variables	n (%)	Cumulative Percentage (%)
Gestational Age		
<37 Weeks	2 (4.0%)	4.0
37-40 Weeks	47 (94.0%)	98.0
>40 Weeks	1 (2.0%)	100.0
Mode of Delivery		
Normal Vaginal Delivery (NVD)	44 (88%)	88.0
C-Section	3 (6.0%)	94.0
Assisted delivery	3 (6.0%)	100.0
APGAR Score at 1 min		
1-3	13 (26.0%)	26.0
4-6	37 (74.0 %)	100.0
7-10	0 (0%)	0
APGAR Score at 5 min		
1-3	2 (4.0 %)	4.0
4-6	17 (34.0 %)	38.0
7-10	31 (62.0 %)	100.0
Duration of Resuscitation		
1-3 Minutes	19 (38.0 %)	38.0
4-7 Minutes	23 (46.0 %)	84.0
7-10 Minutes	8 (16.0%)	100.0
Seizure in the Last 24 Hours		
Yes	47 (94.0%)	94.0
No	3 (6.0%)	100.0
Serum Creatinine Levels		
0.1-0.9	32 (64.0%)	64.0
> 0.9	18 (36.0%)	100.0
ALT Levels		
<50	30 (60.0%)	60.0
51-100	6 (12.0%)	72.0
> 100	14 (28.0%)	100.0
CKMB Levels		
0-100	27 (54.0%)	54.0
>100	23 (46.0%)	100.0
Outcome of the Patient		
Discharged	47 (94.0%)	94.0
Expired	3 (6.0%)	6.0

Chi-square tests were conducted to assess associations between perinatal asphyxia and organ injuries. The results revealed no significant association between the duration of resuscitation and the occurrence of seizures (p=0.695) or between serum creatinine levels and the duration of resuscitation (p=0.512). However, a significant association was observed between liver function (ALT levels) and perinatal asphyxia (p = 0.0339), suggesting that perinatal asphyxia is related to an increased incidence of liver dysfunction. No significant association was found between CKMB levels (myocardial injury) and the duration of resuscitation (p=0.416) (Table 3).

Table 3: Crosstab Analysis of Duration of Resuscitation (in Minutes) Across Various Factors

Variables	Category	1-3 Minutes	4-6 Minutes	7-10 Minutes	Chi-Square (p-value)
Gestational Age	<37 Weeks	0	2	0	0.703
	37-40 Weeks	19	20	8	
	>40 Weeks	0	1	0	
Mode of Delivery	NVD	16	21	7	0.754
	C-Section	2	1	0	
	Assisted Delivery	1	1	1	
Seizure in Last 24 Hours	Yes	18	22	7	0.695
	No	1	1	1	
Serum Creatinine Levels	0.1-0.9	14	13	5	0.512
	>0.9	5	10	3	
ALT Levels	<50	8	16	6	0.0339
	51-100	4	2	0	
	>100	7	5	2	
CKMB Levels	0-100	8	14	5	0.416
	>100	11	9	3	

DOI: https://doi.org/10.54393/pjhs.v6i5.3058

Outcomes	Discharged	19	21	7	0.376
	Expired	1	2	1	

DISCUSSION

This study investigated 50 cases of perinatal asphyxia to explore the potential association with multi-organ injury. The mean gestational age of the cohort was 38.68 weeks. The resuscitation duration varied considerably, with 19 patients (38.0%) requiring 1-3 minutes, 23 patients (46.0%) needing 4-7 minutes, and 8 patients (16.0%) requiring 7-10 minutes. Seizures were observed in 47 patients (94.0%), while 3 patients (6.0%) did not experience seizures. Serum creatinine levels revealed that 32 patients (64.0%) had values between 0.1-0.9 mg/dL, and 18 patients (36.0%) had levels above 0.9 mg/dL. Regarding liver function, ALT levels were below 50 U/L in 30 patients (60.0%), between 51-100 U/L in 6 patients (12.0%), and exceeded 100 U/L in 14 patients (28.0%). CKMB levels showed that 27 patients (54.0%) had values between 0-100 U/L, and 23 patients (46.0%) had values greater than 100 U/L. In terms of clinical outcomes, 47 patients (94.0%) were discharged, and 3 patients (6.0%) expired. A statistically significant association was found between elevated ALT levels and perinatal asphyxia (p=0.0339), while no significant relationship was observed for seizures (p=0.695), serum creatinine (p=0.512), or CKMB levels (p=0.416) with the duration of resuscitation. The findings of this study are consistent with previous research on perinatal asphyxia and its effects on organ function. Atta *et al.*, examined the frequency of acute kidney injury (AKI) in newborns with congenital asphyxia and reported an AKI prevalence of 10.5% in their cohort of 105 newborns. This study showed that AKI was more common in infants weighing between 1.9 and 2.5 kg, and there was no difference in the prevalence of AKI based on maternal preeclampsia, gestational age, or mode of delivery. These results are consistent with the observation of renal dysfunction in our study, although the overall incidence of AKI in our study was low [16]. Similarly, Shrestha *et al.*, investigated the relationship between hypoxic ischemic encephalopathy (HIE) and renal dysfunction in infants with perinatal asphyxia. This study showed that 72% of patients had kidney problems, and 57% of oliguric cases had abnormal kidney function. The development of HIE was strongly associated with renal dysfunction, and mortality was higher in patients with severe HIE (stage III) compared with those with moderate HIE (stage II), consistent with study results on the impact of HIE on vascular dysfunction [17]. Moreover, Gedefaw *et al.*, in Ethiopia, the study also confirmed the association between perinatal asphyxia and AKI, identifying several risk factors, including cesarean delivery, low birth weight, third-stage HIE, and lack of prenatal care. Their results revealed a higher prevalence of AKI than reported in previous studies, indicating the need for targeted interventions to address risk factors in infants with perinatal asphyxia [18]. In terms of liver function, Tarcan *et al.*, examined liver enzymes in infants with perinatal asphyxia and compared them with healthy controls. Their study found that 48% of asphyxiated infants had poor liver function and elevated enzyme levels on the first day of life. The severity of liver insufficiency correlates with the degree of HIE, supporting the notion that liver enzyme assays may serve as early markers of organ dysfunction in infants with perinatal asphyxia. This finding complements our results, especially the significant association between ALT level and perinatal asphyxia [19]. A systematic review of cases of organ failure (OF) after perinatal asphyxia further confirms the results of our study. MOF, which affects the kidneys, liver, gastrointestinal tract, and, in severe cases, the heart, has a major impact on childhood morbidity and mortality. This study identified MOF as a common cause of perinatal asphyxia and highlighted the importance of holistic management strategies for organ disease management [20].

CONCLUSIONS

It was concluded that most clinical factors, such as gestational age, mode of delivery, seizure activity, and urinary markers, did not significantly influence resuscitation time. However, elevated ALT levels were strongly linked to prolonged resuscitation, underscoring the importance of monitoring liver function. These findings highlight the need for careful, individualized monitoring and suggest that liver function, especially ALT, can guide clinical decision-making in neonates with perinatal asphyxia.

Authors Contribution

Conceptualization: TH
Methodology: TH, SUR, HG, SH, MH
Formal analysis: TH, I
Writing review and editing: TH, I, HG

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

Source of Funding

The author received no financial support for the research, authorship and/or publication of this article.

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