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ORIGINAL RESEARCH

PREDICTORS OF HYPOXIC-ISCHEMIC ENCEPHALOPATHY SEVERITY IN ASPHYXIATED NEONATES: A PROSPECTIVE COHORT STUDY

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ABSTRACT

Background: Perinatal asphyxia remains a significant cause of morbidity and mortality among neonates, often leading to hypoxic-ischemic encephalopathy (HIE) and myocardial injury. Understanding the predictors and markers of these conditions is crucial for improving clinical management and outcomes.

Methods: A prospective cohort study enrolled 50 asphyxiated neonates at Tirunelveli Medical College Hospital, assessing demographic factors, clinical parameters, and Troponin I levels. Data were analyzed using Chi-square test to determine associations and significance.

Results: Demographic factors including gravida ($\chi^2(2) = 0.499$, $p = 0.499$), gestational age ($\chi^2 = 0.961$, $p = 0.961$), mode of delivery ($\chi^2 = 0.507$, $p = 0.507$), sex ($\chi^2 = 0.982$, $p = 0.982$), and birth weight ($\chi^2 = 0.499$, $p = 0.499$) showed no significant association with HIE severity. However, seizures ($p = 0.001$), ventilator requirement ($p = 0.006$), and shock ($p = 0.001$) were strongly associated with elevated Troponin I levels, indicative of myocardial injury.

Conclusion: Clinical parameters such as seizures, ventilator requirement, and shock are critical indicators of myocardial injury in asphyxiated neonates. Early recognition and management of these factors may improve outcomes and guide therapeutic interventions in neonatal intensive care settings.

Keywords: Perinatal asphyxia, hypoxic-ischemic encephalopathy, myocardial injury, neonatal intensive care, Troponin I, clinical predictors

INTRODUCTION

Perinatal asphyxia, a critical condition characterized by inadequate oxygenation and blood flow to vital organs, remains a significant cause of neonatal morbidity and mortality worldwide[1]. It occurs when there is a deprivation of oxygen and nutrients during the perinatal period, leading to potential damage to multiple organ systems, including the brain, heart, and lungs[2]. The consequences of perinatal asphyxia can be severe, often resulting in long-term neurological deficits or even death if not promptly managed.

Neonates experiencing perinatal asphyxia often present with a spectrum of clinical manifestations, ranging from mild respiratory distress to severe hypoxic ischemic

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encephalopathy (HIE), a condition characterized by neurological dysfunction due to oxygen deprivation during birth[3]. The severity of HIE is commonly assessed using the Sarnat and Sarnat staging criteria, which categorize infants based on clinical features such as consciousness level, tone, and reflex responses[4].

Among the various organs affected by perinatal asphyxia, the heart plays a crucial role. The heart's response to hypoxia involves complex physiological changes aimed at maintaining cardiac function under stress. One of the biomarkers that has garnered significant attention in assessing cardiac injury in neonates with perinatal asphyxia is cardiac Troponin I (cTnI). Cardiac Troponin I is a sensitive and specific biomarker released into the bloodstream following myocardial injury. Elevated levels of cTnI indicate myocardial damage, which can occur due to ischemia during episodes of perinatal asphyxia[5].

The early detection of myocardial injury in asphyxiated neonates is crucial for timely intervention and improved clinical outcomes[5]. By studying the role of cTnI as an early predictor of ischemic myocardial injury in these neonates, clinicians can potentially identify those at higher risk of adverse cardiac events early in their clinical course. This proactive approach allows for targeted interventions such as optimizing oxygen delivery, maintaining adequate hemodynamic stability, and initiating neuroprotective strategies to mitigate further damage[6].

Furthermore, correlating cTnI levels with the severity of HIE according to Sarnat staging provides valuable insights into the interplay between cardiac dysfunction and neurological outcomes in perinatal asphyxia[7]. Understanding this correlation enhances our ability to prognosticate and tailor management strategies based on individual patient risk profiles.

This study aims to contribute to the existing body of knowledge by elucidating the relationship between cTnI levels and neonatal outcomes in the context of perinatal asphyxia. By addressing these objectives, we seek to provide clinicians with a reliable tool for early risk stratification and intervention, ultimately improving the overall care and prognosis of neonates affected by this challenging condition.

The integration of cTnI assessment into the clinical management of asphyxiated neonates represents a promising avenue for enhancing diagnostic accuracy, prognostic capability, and therapeutic efficacy in this vulnerable patient population. Through rigorous investigation and analysis, this study seeks to advance our understanding of cardiac involvement in perinatal asphyxia and its implications for neonatal health outcomes.

MATERIALS & METHOD

Study Setting: This prospective cohort study was conducted over a period of one year, from March 2017 to February 2018, at the Special Newborn Care Unit (SNCU) of Tirunelveli Medical College Hospital, a tertiary care center in Tirunelveli, India.

Study Participants: The study included term asphyxiated neonates meeting the following inclusion criteria: gestational age greater than 37 weeks as determined by the New Ballard's Score, birth weight exceeding 2.5 kg, and an APGAR score of less than 7 at the first minute of life, consistent with the WHO Perinatal Neonatal Database. Neonates with congenital heart disease, congenital anomalies, sepsis, multiple gestations, respiratory distress syndrome, intrauterine growth restriction (IUGR), or born to mothers with preeclampsia were excluded.

Sample Size and Sampling Technique: Fifty term asphyxiated neonates admitted to the SNCU were enrolled in the study. Consecutive sampling was employed, where eligible neonates meeting the inclusion criteria and whose parents provided written informed consent were enrolled.

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Study Methodology: Upon enrollment, detailed clinical data including birth order, gestational age, sex, birth weight, and clinical features such as presence of seizures within 24 hours, shock, duration of inotropic support, and ventilator support were recorded using a prestructured proforma.

Study Tools: Laboratory assessments included measuring cardiac Troponin I levels using quantitative chemiluminescence assay on serum samples obtained within 6 hours of life. Other parameters monitored included complete blood count (CBC), renal function tests (RFT), electrocardiogram (ECG), echocardiogram (ECHO), and cranial ultrasound (USG).

Statistical Analysis: Data were entered into Microsoft Excel and analyzed using SPSS software version 25.0. Descriptive statistics were used to summarize demographic and clinical characteristics of the study population. The relationship between Troponin I levels and baseline parameters (gravida, gestational age, birth weight, sex, mode of delivery), severity of HIE, presence of shock, and outcomes of HIE were assessed using Chi-square test.

Ethical Issues: This study was approved by the ethical committee of Tirunelveli Medical College Hospital. Informed written consent was obtained from the parents or legal guardians of all participating neonates prior to enrollment. Confidentiality of patient data was strictly maintained throughout the study period.

RESULTS

This study investigated the associations between various demographic and clinical factors with the severity of Hypoxic Ischemic Encephalopathy (HIE) and Troponin I level in 50 asphyxiated neonates. Demographic factors including gravida, gestational age, mode of delivery, sex, and birth weight were analyzed for their correlation with HIE severity (Table 1). Primiparous and multiparous mothers showed no significant difference in the distribution of neonates across HIE stages ($\chi^2 = 0.499$, $p = 0.499$). Similarly, gestational age (>38 weeks vs. <38 weeks) did not significantly influence HIE severity distribution ($\chi^2 = 0.961$, $p = 0.961$). Mode of delivery (normal vs. LSCS) also showed no significant association with HIE severity ($\chi^2 = 0.507$, $p = 0.507$). Moreover, there was no significant difference in HIE severity based on sex (male vs. female) ($\chi^2 = 0.982$, $p = 0.982$). Birth weight (>3 kg vs. <3 kg) did not significantly affect HIE severity distribution ($\chi^2 = 0.499$, $p = 0.499$).

Table 1: Association between Demographic Factors and HIE Severity in Asphyxiated Neonates (n=50)

Variable	HIE I	HIE II	HIE III	Total (%)	P value
Gravida					
Primipara (n=32)	11	9	12	32 (36%)	0.499
Multipara (n=18)	9	3	6	18 (64%)	
Gestational Age					
>38 Weeks (n=29)	12	7	10	29 (58%)	0.961
<38 Weeks (n=21)	8	5	8	21 (42%)	
Mode of Delivery					
Normal Delivery (n=25)	8	7	10	25 (50%)	0.507
LSCS (n=25)	12	5	8	25 (50%)	
Sex					

ISSN: 0975-3583, 0976-2833 VOL15, ISSUE 7, 2024

Male (n=28)	11	7	10	28 (44%)	0.982
Female (n=22)	9	5	8	22 (56%)	
Birth Weight					
>3 kg (n=34)	12	8	14	34 (68%)	0.499
<3 kg (n=16)	8	4	4	16 (32%)	
Seizures					
Yes	0	10	16	26 (52%)	0.001
No	20	2	2	24 (48%)	

Note: HIE - Hypoxic Ischemic Encephalopathy; LSCS - Lower Segment Cesarean Section.

Troponin I levels were examined in relation to demographic factors (Table 2). Although there was a trend towards higher Troponin I levels in primiparous mothers compared to multiparous mothers (17 vs. 7, $p = 0.077$), this difference did not reach statistical significance. Gestational age (>38 weeks vs. <38 weeks) and mode of delivery (normal vs. LSCS) did not show significant differences in Troponin I levels ($p = 0.165$ and $p = 0.257$, respectively). Similarly, there were no significant differences in Troponin I levels based on sex (male vs. female) ($p = 0.981$) or birth weight (>3 kg vs. <3 kg) ($p = 0.087$).

Table 2: Association between birth history and Troponin I Levels in Asphyxiated Neonates (n=50)

Variable		**Troponin I Elevated**	**Troponin I Normal**	**P Value**
Gravida	Primipara	17	12	0.077
	Multipara	7	14	
Gestational Age	>38 Weeks	12	18	0.165
	<38 Weeks	12	8	
Mode of Delivery	Normal Delivery	14	11	0.257
	LSCS	10	15	
Sex	Male	13	12	0.981
	Female	11	14	
Birth Weight	>3 kg	22	19	0.087
	<3 kg	2	7	

Clinical factors were also evaluated for their association with Troponin I levels (Table 3). Neonates who experienced seizures showed a significantly higher proportion of elevated Troponin I levels compared to those without seizures (79% vs. 21%, $p = 0.002$). Similarly, neonates requiring ventilator support exhibited higher Troponin I level compared to those who did not require ventilation (75% vs. 25%, $p = 0.006$). Additionally, neonates who presented with shock had significantly higher Troponin I level compared to those without shock (91% vs. 9%, $p = 0.001$).

These findings suggest that while demographic factors such as gravida, gestational age, mode of delivery, sex, and birth weight may not independently influence HIE severity or Troponin I levels, clinical factors such as seizures, ventilator requirement, and shock are strongly associated

ISSN: 0975-3583, 0976-2833 VOL15, ISSUE 7, 2024

with elevated Troponin I levels in asphyxiated neonates. These results underscore the importance of clinical monitoring and timely intervention in managing neonates at risk of myocardial injury and adverse neurodevelopmental outcomes associated with HIE.

Table 3: Association between Clinical Factors and Troponin I Levels in Asphyxiated Neonates (n=50)

Clinical Factor	Troponin I Elevated (%)	Troponin I Normal (%)	P Value
Seizures			
Present	19 (79)	7 (26)	0.002
Absent	5 (21)	19 (74)	
Ventilator Requirement			
Yes	18 (75)	7 (26)	0.006
No	6 (25)	19 (74)	
Shock			
Present	22 (91)	5 (19)	0.001
Absent	2 (9)	21 (81)	

DISCUSSION

This study aimed to explore the relationships between demographic factors, clinical parameters, and Troponin I level in asphyxiated neonates, focusing on their implications for Hypoxic Ischemic Encephalopathy (HIE) severity and myocardial injury. The findings provide insights into potential predictors and markers of adverse outcomes in neonates exposed to perinatal asphyxia.

Demographic factors such as gravida, gestational age, mode of delivery, sex, and birth weight were examined for their association with HIE severity. Interestingly, no significant associations were found between these factors and the severity of HIE in our cohort. This suggests that traditional indicators such as maternal parity, gestational age, or mode of delivery may not independently predict the degree of neurological impairment in neonates following perinatal asphyxia. These findings are consistent with previous studies that have also failed to establish clear correlations between these demographic variables and HIE severity[8].

The lack of significant associations could be attributed to several factors. Firstly, the relatively small sample size in our study may have limited statistical power to detect subtle effects. Additionally, the multifactorial nature of HIE, influenced by complex interactions between maternal, fetal, and obstetric variables, may obscure direct causal relationships[9]. Future research with larger cohorts and more detailed longitudinal data could provide further clarity on the roles of these demographic factors in HIE pathogenesis.

Troponin I, a sensitive biomarker of myocardial injury, was evaluated in relation to both demographic and clinical factors in our study. Our results revealed significant associations between clinical indicators such as seizures, ventilator requirement, shock, and elevated Troponin I levels. Neonates who experienced seizures, required ventilatory support, or presented with shock showed markedly higher Troponin I levels, indicating myocardial stress and potential injury[10].

The observed association between seizures and elevated Troponin I levels highlights the interplay between neurological and cardiac pathology in asphyxiated neonates. Seizures are a

ISSN: 0975-3583, 0976-2833 VOL15, ISSUE 7, 2024

common manifestation of HIE and can lead to systemic hypoxia and ischemia, contributing to myocardial dysfunction. Similarly, the need for ventilatory support and the presence of shock reflect the severity of systemic compromise and may exacerbate cardiac injury through mechanisms such as reduced oxygen delivery and increased myocardial workload[11].

The clinical implications of elevated Troponin I levels extend beyond acute myocardial injury. They may serve as a prognostic marker for adverse outcomes in neonates with HIE, including long-term neurological sequelae and mortality. Early detection and monitoring of Troponin I levels could aid in risk stratification and guide therapeutic interventions aimed at mitigating myocardial damage and improving overall outcomes[12].

Effective management of neonates with perinatal asphyxia requires a multidisciplinary approach that addresses both neurological and cardiac sequelae. Prompt recognition of clinical indicators such as seizures, shock, and ventilatory compromise is crucial for timely intervention and minimizing secondary injury[13]. Our findings highlight the importance of intensive monitoring and early intervention strategies aimed at optimizing cardiovascular function and reducing myocardial stress in these vulnerable neonates.

Pharmacological interventions targeting myocardial protection and neuroprotection hold promise in mitigating the adverse effects of perinatal asphyxia. Therapies such as hypothermia, which has been shown to improve neurological outcomes in neonates with moderate to severe HIE, may also confer cardioprotective benefits by reducing metabolic demands and preserving myocardial function[14]. Future research should explore the dual therapeutic potential of interventions that target both neurological and cardiovascular pathways in neonatal hypoxic-ischemic injury.

Despite its contributions, our study is not without limitations. The retrospective nature and relatively small sample size may limit the generalizability of our findings to broader neonatal populations. Additionally, the observational design precludes causal inference, and confounding variables not accounted for in our analysis may influence the observed associations. Future studies with larger, prospective cohorts and comprehensive longitudinal data are warranted to validate our findings and elucidate the mechanistic links between clinical parameters, Troponin I levels, and long-term outcomes in asphyxiated neonates.

Further exploration of novel biomarkers and advanced imaging modalities may also enhance our understanding of cardiac and neurological injury in neonates with perinatal asphyxia. Biomarkers indicative of oxidative stress, inflammation, and metabolic dysfunction could provide additional insights into the pathophysiological mechanisms underlying myocardial and neurological injury. Integrating multimodal approaches in clinical research may facilitate personalized risk stratification and tailored therapeutic strategies in neonatal intensive care settings.

CONCLUSION

This study contributes valuable insights into the complex interplay between demographic factors, clinical parameters, and myocardial injury markers in neonates exposed to perinatal asphyxia. While demographic factors alone may not predict HIE severity, clinical indicators such as seizures, ventilator requirement, and shock are strongly associated with elevated Troponin I levels, highlighting their potential as prognostic markers and targets for therapeutic intervention.

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ISSN: 0975-3583, 0976-2833 VOL15, ISSUE 7, 2024

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