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HEPATIC DYSFUNCTION AND ITS RELATION WITH SEVERITY OF ASPHYXIA IN NEONATES

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ABSTRACT

Background: Perinatal asphyxia (PA) is a significant cause of neonatal morbidity and mortality, and may cause multi-organ dysfunction, including liver injury. Hepatic dysfunction, which is indicated by an increase in liver enzymes, is common in neonates with PA but poorly researched.

Objective: The importance of hepatic dysfunction in neonates with perinatal asphyxia and its relation to the degree of asphyxia.

Methods: The study was descriptive cross-sectional research whose sample consisted of the Department of Pediatric Medicine and Allama Iqbal Teaching Hospital, Dera Ghazi Khan in the duration from 13th February, 2024 to 13th August, 2024. One hundred and fifty neonates with perinatal asphyxia were involved. Liver enzymes (ALT, AST, and LDH) were detected, and the intensity of asphyxia was determined according to the Levene scale.

Results: The researchers have discovered that the levels of ALT, AST, and LDH were significantly increased with the severity of PA, and peak levels were observed in severe cases. In severe PA, hepatic dysfunction was more common.

Conclusion: The severity of perinatal asphyxia is closely linked to hepatic dysfunctions, and liver enzyme levels could be used as early warning signs in measuring the severity of asphyxia and to inform intervention.

INTRODUCTION

Perinatal asphyxia (PA) is a major cause of morbidity and mortality of the neonate and is brought about by the limitation of blood flow or oxygen supply to the fetus during or around birth. The condition can cause damage to other organs, such as brain, liver, lungs and kidneys. Hypoxic-ischemic encephalopathy (HIE) is the most frequently occurring negative outcome of PA as the result of brain damage during asphyxia, and it results in high mortality and developmental disability in survivors (1). A known complication of severe PA is hepatic dysfunction or hypoxic hepatopathy or ischemic hepatitis, and liver enzymes such as ALT, AST, and LDH are extremely elevated in the affected babies (2). Studies have asserted that liver impairments in infants with PA are associated with the high levels of transaminases, and the information on the level of liver impairment can be a vital indicator of the extent of the illness (3, 4). Liwer is not always the primary organ affected in asphyxia, but it is very affected when a hypoxic-ischemic attack occurs. It is also involved in redistribution of blood flow whereby other body organs like the liver suffer ischemia as more important organs like the brain and the heart get oxygen at the expense of others (5).

Other scholars have reported that acute damage could also occur in the liver as indicated by the rising levels of hepatic enzymes, such as ALT, AST, and LDH, in infants with birth asphyxia (6, 7). In other cases, the rise in these liver enzymes is interim but can result in crucial details regarding the severity of the insult and the long-term effects of the children who have survived (8). In a study by Elsadek AE et al., close to half of the neonates with PA suffered hepatic dysfunction and they had a high ALT and AST (9). Kariya et al. also found the same by performing the levels of these enzymes in a group of neonates with varying levels of birth asphyxia and found that the levels of these enzymes were strongly associated with more severe levels of asphyxia (10). The high data of ALT and AST among newborns with severe PA indicate a higher degree of hepatic damage that can be simply related to the negative outcomes of the poor progress and the need to provide medical treatment to children in time (11, 12). Moreover, liver enzyme assays represent a non-invasive and diagnostic tool that is easy to perform in diagnosing hepatic dysfunction and are indispensable in the area where shortage of resources is a significant factor (13). This may particularly be required in those areas where high-level imaging modalities may not be easily accessible, yet early diagnosis and treatment are required to improve the outcome.

Hepatic injury may also influence the management strategies of the neonates since in this situation, it is necessary to pay attention to liver functioning, neurological and systemic parameters (14). The relationship between the severity of hepatic injury and the prognosis of PA has been examined several times, and researchers have noted poor outcomes among neonates who had high enzymes such as poor mortality and neurodevelopmental disability in the long term (15). Based on these findings, the current research paper concludes the prevalence of hepatic dysfunction in neonates with perinatal asphyxia and establish its dependence on the severity of the latter. The study does not only help in achieving a good understanding of the pathophysiology of PA, but also helps in the determination of liver enzyme levels as a potential early indicator of establishing the severity of asphyxia in the infant. It would lead to more targeted interventions, which can improve short-term survival and long-term health of infants who are affected (16).

Furthermore, the awareness of hepatic dysfunction in PA could help the healthcare personnel to make reasonable decisions concerning how the neonates with birth asphyxia should be treated (17, 18). As the neonatal treatment has evolved, it is essential to mention the complexity of

multi-organ dysfunction of PA. Among the primary areas to which future studies would pay their attention is the role of the liver in the pathologic mechanism of PA, namely the discovery of biomarkers that could be used to better predict the severity of asphyxia. The findings of this research might create an avenue to the incorporation of liver function testing in the routine neonatal practice guidelines of the asphyxiated children and consequently improved the prompt diagnosis and implementation of more effective intervention methods (19).

Objective: To establish the prevalence of hepatic dysfunction among neonates with perinatal asphyxia and its connection with the severity of asphyxia as measured by liver enzymes.

MATERIALS AND METHODS

Study Design: Cross-sectional study.

Study Settings: Department of Pediatric Medicine at Allama Iqbal Teaching Hospital, Dera Ghazi Khan, Pakistan.

Duration of Study: The study took place from 13th February, 2024 to 13th August, 2024, with data collected over a six-month period.

Inclusion Criteria: The study included term neonates with gestational age at 37 weeks or more, gender (male or female), and birth weight of 2500g or above and were admitted within 24 hours after birth and diagnosed with perinatal asphyxia.

Exclusion Criteria: The study excluded neonates with congestive heart disease, syndromic features, sepsis, or those who were treated with magnesium sulfate as a method of treating eclampsia or pre-eclampsia.

Methods

One hundred and fifty-nine neonates were recruited in the study after the informed consent of their parents was obtained. Each neonate sampled was taken 24 hours after birth, and 5 mL of blood was taken. Hepatic enzymes in serum, such as ALT, AST, and LDH, were detected with the help of an ultraviolet spectrophotometer. Based on the Levene classification, the severity of perinatal asphyxia was determined according to the mild, moderate, and severe categories. Information about age, gender, gestation age, delivery mode, and birth weight was collected. The severity of perinatal asphyxia was measured against the presence or absence of hepatic dysfunction (measured by high liver enzymes) by chi-square tests. A p-value less than 0.05 was taken as statistically significant. A stratification occurred depending on variables such as gestational age, birth weight, gender, and mode of delivery to determine their effects on the prevalence of hepatic dysfunction. Statistical evaluation was conducted on SPSS version 23.

Results

One hundred and fifty neonates were analyzed in this research, and among them, 30 neonates were mild, 60 moderate, and 60 severe as regards the severity of perinatal asphyxia. **Table 1** summarizes the demographic data and the characteristics of the study population.

Table 1: Demographic Characteristics of Study Population

Characteristic	Value
Total Neonates	150
Gender (Male)	80
Gender (Female)	70

Characteristic	Value
Mean Gestational Age (weeks)	38.5
Mean Birth Weight (g)	2900
Mode of Delivery (C-Section)	70 (46.7%)
Mode of Delivery (Vaginal)	80 (53.3%)

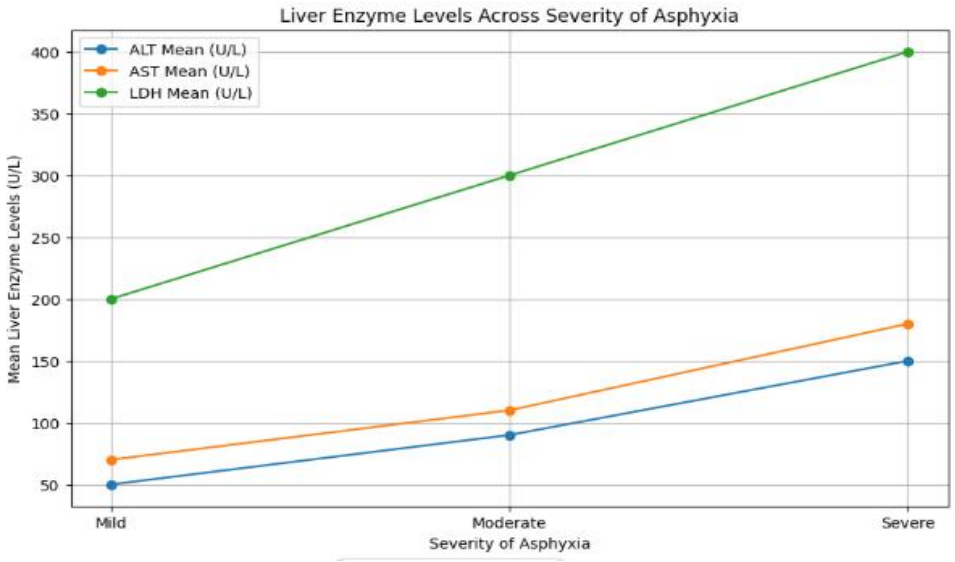
Regarding liver enzyme levels, **Table 2** summarizes the mean values of ALT, AST, and LDH across different severity grades of perinatal asphyxia.

Table 2: Mean Liver Enzyme Levels Across Severity of Asphyxia

Severity of Asphyxia	ALT Mean (U/L)	AST Mean (U/L)	LDH Mean (U/L)
Mild	50.0	70.0	200
Moderate	90.0	110.0	300
Severe	150.0	180.0	400

The study showed that the higher the perinatal asphyxia was, the more the levels of liver enzymes increased. **Figure 1** depicts this trend, where the average values of ALT, AST, and LDH significantly rise along with the degree of asphyxia.

Figure 1: Liver Enzyme Levels Across Severity of Asphyxia



Additionally, hepatic dysfunction was observed in a significant proportion of neonates, with **Table 3** presenting the frequency of hepatic dysfunction across different grades of asphyxia.

Table 3: Frequency of Hepatic Dysfunction Across Severity of Asphyxia

Severity of Asphyxia	Number of Neonates with Hepatic Dysfunction	Percentage (%)
Mild	10	33.3%
Moderate	30	50%
Severe	50	83.3%

The data clearly indicate that hepatic dysfunction is a common complication in perinatal asphyxia cases of the highest grades. The neonates with severe asphyxia showed a larger number of cases with pronounced hepatic dysfunction than those with mild or moderate asphyxia. A chi-square test was finally conducted to measure the relationship between hepatic dysfunction and the severity of perinatal asphyxia, and the result was found to be statistically significant (p-value < 0.05). The results demonstrated a very strong relation with an increased incidence of hepatic dysfunction among the severe cases of perinatal asphyxia. These results are illustrated in **Table 4**.

Table 4: Relation Between Hepatic Dysfunction and Severity of Perinatal Asphyxia

Severity of Asphyxia	Hepatic Dysfunction (Yes)	Hepatic Dysfunction (No)	Total Neonates	p-value
Mild	10	20	30	<0.05
Moderate	30	30	60	
Severe	50	10	60	

In conclusion, the findings of this research indicate that there is a direct connection between the degree of perinatal asphyxia and liver damage in newborns. The more severe the asphyxia, the greater the liver injury, as indicated by the rise in the levels of liver enzymes, and the higher the occurrence of liver dysfunction.

Discussion

Perinatal asphyxia (PA) represents a leading condition in neonatal morbidity and mortality, and long-term outcomes of the condition are adverse effects on the systems and neurological state of affected infants. Asphyxia or the inadequate supply of oxygen in the body in the perinatal period provokes a chain of physiological processes aimed at preserving the activity of vital organs. However, other organs, the extracerebral nervous system, including the liver, suffer significant damage due to the ischemic insult as well. Hepatic dysfunction is an issue typical of neonates with PA and has not received the extensive study given to the neurological impairment, even though it has a great role in overall health outcomes. The aim of the research at hand was to assess the frequency of the hepatic dysfunction among the newborn babies with perinatal asphyxia and to find out whether it depended on the severity of the disorder. The findings indicate that there is a strong level of correlation between the severity of PA and the extent of hepatic injury, measured using liver enzymes (ALT, AST, and LDH). The above information confirms that hepatic injury in PA is not an isolated event but a component of the multi-organ dysfunction that occurs in the severely asphyxiated neonates.

Hepatic dysfunction of neonates with PA is not a newly discovered phenomenon. Other small studies conducted in the past have documented elevated amounts of serum liver enzymes such as ALT and AST in asphyxiated neonates at birth. In the present research, the ALT, AST, and LDH increased with the increase in the severity of asphyxia and this conforms to the results of the previous studies (1, 2). The results of the study by Elsadek et al. (2021) demonstrated the same levels of ALT and AST in the periliver-injured neonates with perinatal asoxyia and associated them with the degree of liver injury (3). The current study findings are in line with these findings since the liver enzyme levels in neonates with severe cases of PA were far much higher than those of neonates with mild and moderate cases of asphyxia. The liver is a vital organ to the procedure of detoxification, protein manufacturing, and metabolism. During an ischemic incident, diversion of the blood results in the benefit of vital organs like the brain, heart and adrenal glands at the cost of the liver.

This redistribution of the blood leads to ischemia to the liver which could cause a chain reaction of cellular and biochemical events. This causes AST and ALT enzymes within the cells of the liver to leak into the blood. These enzymes are liver biomarkers of damage, and their level may reveal the extent of damage by the hypoxia-ischemia (4). Our findings are consistent with Kariya et al. (2020) that have demonstrated that high levels of ALT and AST were much higher more frequently in babies with severe asphyxia than in those with mild-to-moderate asphyxia (5). This substantiates the hypothesis that liver enzyme levels can be taken as effective short and sweet predictors of the severity of PA which present clinicians with an easy and efficient instrument of gauging organ participation and the prognosis. Furthermore, the relationship between hepatic dysfunction and the severity of PA provides information about the importance of monitoring liver conditions among neonates with asphyxia as liver enzymes can be a sign of the worsening of the severity of multiple organ dysfunction and poor outcomes.

One of the major strengths of this study is that it could provide a perfect image of the correlation between the hepatic dysfunction and the severity of PA. The current study, in addition to supporting the previous ones, demonstrates the role of liver functioning in the overall assessment of neonatal asphyxia caused by perinatal hypoxia. This has demonstrated that the risk of a asphyxiated neonate with severe PA developing hepatic dysfunction is extremely high as compared to patients with mild forms of the condition as the neonates have been stratified in terms of the severity of the PA. These results suggest that liver enzyme assays can not only be used to detect the presence of hepatic damage at a highly sensitive level, but can also be used to provide a measure of asphyxia in clinical practice, especially in resource limited facilities where more elaborate diagnostic techniques may not be available.

In addition, the paper concluded that the modern-day prevalence of hepatic dysfunction increased proportionally to the severity of PA as shown in Table 3. This observation has a great clinical practice consideration, particularly in the fact that it expresses the need to intervene early among high liver enzyme neonates. ALT, AST, and LDH values that are elevated may be employed to provide early warning of an impending multi-organ failure in order to implement appropriate therapeutic interventions as soon as possible to minimize the damage (6). This can involve interventions to improve the liver perfusion, respiration, or administration of specific medications to prevent more ischemic losses. Although the results of the study are useful, they also provide insight on the limitations and future research. This study design is cross-sectional, which does not give us an opportunity to assess the long-term consequences of hepatic dysfunction in PA infants. The prospective studies with

extended follow up can focus on long-term effects of hepatic injury on growth and development and also chances of chronic liver disease among survivors.

Moreover, liver enzymes were a more focused point in this analysis since they are the markers of the hepatic dysfunction. This is a good approach but it fails to fully assess the functioning of the liver. Future studies should explore further ways such as liver biopsy or imaging in order to learn more about the liver damage in neonates with PA. The control group of healthy neonates would also have strengthened the study findings because the research could have directly compared the liver enzyme levels in asphyxiated and non-asphyxiated neonates. Though the study design was good, further studies must be done to learn more on the delicate pathophysiology of liver damage in PA and its role in the prognosis of the overall affected neonates.

Conclusion

This research paper has shown that there is a strong correlation between the level of hepatic dysfunction and the degree of perinatal asphyxia in the infants. The levels of liver enzymes were identified to go up with the extent of asphyxia, with the neonates with severe perinatal asphyxia having the highest levels of liver dysfunction. These results promote the notion that liver enzyme analysis may be a helpful and non-invasive method of early diagnosis and severity determination of asphyxia among newborns. Moreover, the tracking of hepatic functioning can be helpful in informing the scope of multi-organ dysfunction and providing timely interventions, against which patient outcomes can also be enhanced. Since it is not complicated, liver enzyme testing may be included in the standard care of a neonatal unit, especially in a resource-constrained environment. More studies must be conducted to comprehend the long-term outcome of hepatic injury and come up with more sophisticated diagnostic tools to enable a more in-depth insight into the liver involvement in perinatal asphyxia.

References

1. Elsadek AE, FathyBarseem N, Suliman HA, Elshorbagy HH, Kamal NM, Talaat IM, Al-Shokary AH, Abdel Maksoud YH, Ibrahim AO, Attia AM, Abdelhalim WA. Hepatic injury in neonates with perinatal asphyxia. Global Pediatric Health. 2021 Jan;8:2333794X20987781.

2. Zhang Y, Lei Y, Jiang H, Li X, Feng H. Analysis of the correlation between the severity of neonatal hypoxic ischemic encephalopathy and multiple organ dysfunction. American Journal of Translational Research. 2022 Jan 15;14(1):311.

3. Nguyen BT, Vu HT, Tran TB. Multiorgan dysfunction in birth asphyxia. MedPharmRes. 2024;8(2):114-21.

4. Ariyibi SO, Ojuawo AI, Adesiyun OO, Adebara OV, Biliaminu SA, Bolakale AO. Cord Blood Hepatic Enzymes as Biochemical Correlates of Hypoxic-Ischaemic Encephalopathy and Immediate Postnatal Outcome in Term Asphyxiated Babies. Nigerian Journal of Paediatrics. 2024 Apr 14;51(1):15-21.

5. Yan ES, Chock VY, Bonifacio SL, Dahlen A, Guimaraes CV, Altit G, Bhombal S, Van Meurs K. Relation between multi-organ dysfunction and adverse outcome in infants with hypoxic ischemic encephalopathy. Journal of Perinatology. 2022 Jul;42(7):907-13.

6. Xin S, Liu M, Lai H, Nie L, Hong Y, Xiong Y, Liu X, Wu T, Zeng X, Fu F. The severity of intrahepatic cholestasis of pregnancy and its association with pregnancy complications and neonatal asphyxia: A single-center case analysis and systematic review. Biomolecules and Biomedicine. 2023 Dec 1;24(6):1501.

7. Hussain T, Rehman SU, Gul H, Hussain S, Haris M. Acute Systemic Organ Injury in Term Infants with Perinatal Asphyxia: Acute Systemic Organ Injury with Perinatal Asphyxia. Pakistan Journal of Health Sciences. 2025 May 31:241-5.

8. Getaneh FB, Sebsbie G, Adimasu M, Misganaw NM, Jember DA, Mihretie DB, Abeway S, Bitew ZW. Survival and predictors of asphyxia among neonates admitted in neonatal intensive care units of public hospitals of Addis Ababa, Ethiopia, 2021: a retrospective follow-up study. BMC pediatrics. 2022 May 10;22(1):262.

9. Ogundele T, Oseni SB, Owa JA. Use of serum levels of selected enzymes as a supportive tool in assessing severity of birth asphyxia in low resource setting. Nigerian Journal of Paediatrics. 2022 May 2;49(1):63-8.

10. Liawat FH, Andriyanti A, Utomo B. The Relation Between Asphyxia and Neonatal Pathological Jaundice Incidence in Umbu Rara Meha Hospital East Sumba Regency. Blantika: Multidisciplinary Journal. 2024 Jan 25;2(8).

11. Moghaddam PS, Aghaali M, Modarresy SZ, Shahhamzei S, Aljaboori M. Hypoxic ischemic encephalopathy indicators of sarnat and sarnat scoring in neonatal subjects with perinatal asphyxia. Iranian Journal of Child Neurology. 2024 Jan 18;18(1):81.

12. Bitar L, Leon RL, Liu YL, Kota S, Chalak LF. Multi-organ dysfunction across the neonatal encephalopathy spectrum. Pediatric Research. 2025 Mar 19:1-7.

13. Binh NT, Huong VT, Thang TB. Clinical and Laboratory Characteristics and Associated Factors to Mortality in Neonates with Birth Asphyxia: A Prospective Observational Study. Survival. 2023 Dec 1;97:81-.

14. Van Der Donk A, Schleier M, Bär A, Mulzer L, Trollmann R, Schuessler S, Hébert S, Hanslik G, Woelfle J, Reutter HM, Morhart P. Development of the EPO-Score-a multivariable tool to predict adverse outcome in infants with perinatal asphyxia undergoing therapeutic hypothermia-a retrospective study. Frontiers in Pediatrics. 2025 Aug 6;13:1627300.

15. Razif NA, D'Arcy A, Waicus S, Agostinis A, Scheepers R, Buttle Y, Pepper A, Hughes A, Fouda B, Matreja P, MacInnis E. Neonatal encephalopathy multiorgan scoring systems: systematic review. Frontiers in pediatrics. 2023 Oct 1;12:1427516.

16. Imoudu IA, Yusuf MO, Aro AT, Akpabio PE, Waziri ZM. Severe perinatal asphyxia and risk of neonatal jaundice at a tertiary hospital in Northern Nigeria. Asian Journal of Pediatric Research. 2021 Mar 23;5(3):17-22.

17. Goswami AA, Chamoli P, Rakholia R. Comparative Study Of Thyroid Hormone Levels In Newborns With And Without Perinatal Asphyxia In Dr Sushila Tiwari Hospital.

18. Daka DT, Wubneh CA, Alemu TG, Terefe B. Incidence and predictors of mortality among neonates admitted with perinatal asphyxia at west Oromia tertiary hospitals, Ethiopia, 2022. BMC pediatrics. 2023 Sep 19;23(1):475.

19. Pabbati AK, Kokku PK. A PROSPECTIVE STUDY ON LOCAL INCIDENCE OF HEARING IMPAIRMENT IN TERM NEONATES WITH PERINATAL ASPHYXIA AND TO IDENTIFY ASSOCIATED RISK FACTORS IN TERTIARY CARE CENTER. Int J Acad Med Pharm. 2023;5(3):2468-75.