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Efficacy of Umbilical Cord Lactate Level in Predicting the Hypoxic Ischemic Encephalopathy (HIE) in Neonates After Perinatal Asphyxia

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ABSTRACT

Objective: To compare the umbilical artery lactate level in different grades of Hypoxic Ischemic Encephalopathy in neonates with perinatal asphyxia.

Study Design: Cross-sectional study.

Place and Duration of Study: Pak Emirates Military Hospital, Rawalpindi Pakistan, from Dec 2021 to Feb 2022.

Methodology: A group of 70 neonates with gestational age of 36 weeks (252 days) and above, who were reported to have any late deceleration, meconium staining of liquor, low 5 minute APGAR score and need for neonatal resuscitation for more than 1 minute, were selected and their umbilical artery lactate levels were measured. Neonates were classified into two groups by using Sarnet and Sarnet classification with Group-A having neonates with No or Mild Hypoxic Ischemic Encephalopathy and Group-B with Moderate to Severe Hypoxic Ischemic Encephalopathy.

Results: A total of 70 patients were enrolled in the study with median gestational age of 267 days and mean weight of 2.70±0.60 kg. A total of 45 neonates were found to have No or mild Hypoxic Ischemic Encephalopathy (Group-A) with mean lactate level of 3.64±1.49 mmol/L and 25 diagnosed with moderate to severe Hypoxic Ischemic Encephalopathy (Group-B) had mean lactate level of 9.40±2.26 mmol/L. Mean lactate levels were significantly raised for Moderate to Severe Hypoxic Ischemic Encephalopathy ($p \leq 0.005$).

Conclusions: The umbilical artery lactate level can be used as a predictor of moderate-to-severe Hypoxic Ischemic Encephalopathy in neonates suffering from perinatal asphyxia.

Keywords: Hypoxic Ischemic Encephalopathy, Lactate Level, Perinatal Asphyxia, Umbilical Artery.

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INTRODUCTION

Hypoxic ischemic encephalopathy (HIE) is one of the most alarming complications encountered in neonates suffering from perinatal asphyxia, with a frequency of around 2 to 3 per 1000 live birth in developed countries and more in developing countries, and accounting for 6% to 9% of all neonatal deaths.[1,2] It can be variable in presentation, ranging from complete recovery in mild cases to severe neurologic disability in the form of epilepsy, cerebral palsy or even death in the most severe cases.[3,4] For early detection of HIE, several biomarkers are considered to have promising results which are interpreted in context of history, physical examination, radiologic and laboratory findings.[5] Early diagnosis and categorization of HIE, is of paramount importance because of a brief therapeutic window, where applying a novel therapy, termed Total Body Cooling, can prevent further damage in moderate to severe disease.[6] Moreover, level of intensive care given to suffering neonates can be decided and parents are counseled as per the likely outcome with avoidance of potential side effects of neuroprotective medications can be another benefit.[7] Lactic acid is an invariable product in the event of hypoxia resulting from poor tissue perfusion, hence, serum lactate level may provide evidence for asphyxia. Thus, we planned this study, to find out correlation of the umbilical artery lactate level with the HIE grade and hence early prediction of HIE.[8,9] Birth asphyxia is diagnosed when several specific criteria are met, such as, the presence of severe acidosis, indicated by a pH level below 7.00 in an umbilical artery blood sample taken at birth, along with a persistently low APGAR score of 0-3 for 5 minutes or longer. Additionally, the infant must display neurologic manifestations following the asphyxia insult, such as seizures, coma, or hypotonia, and there must be evidence of multi-organ involvement.[10]

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METHODOLOGY

This cross-sectional study was carried out at Pak Emirates Military Hospital (PEMH), Rawalpindi Pakistan, after getting approval of Ethics Review Board (ERC Number 1396/22) for the study period, over 3 months, from December 2021 to February 2022. The minimum sample size calculated for the study was 70 where the reported average prevalence for HIE was 6% with a 95% confidence level and 5% margin of error as reported by Workineh *et al*.[11] Nonprobability consecutive sampling technique was used and a total of 70 participants were enrolled.

Inclusion Criteria: Full term neonates of either gender, aged 36 weeks or above, with late deceleration and meconium staining of liquor, APGAR score less than 7 at 5 minutes and in need of neonatal resuscitation for more than 1 minute.

Exclusion Criteria: Neonates with chromosomal disorders, congenital anomaly, cardiac defects, other causes of impairment of oxygenation e.g. respiratory causes, neuromuscular disorder and metabolic disorders.

Blood from umbilical artery was collected in heparinized bottles and sent within 30 min of collection for lactate level. The neonates were categorized into either Group-A (with No or Mild HIE) or Group-B (with Moderate or Severe HIE). Lactate measurements were recorded and correlated with the clinical status of baby. New born were assessed and categorized by using Sarnet and Sarnet classification for HIE.[12] Data was collected and analyzed by using IBM Statistical Package for Social Sciences (version 23.0). The mean along with standard deviation was reported for quantitative data. Mean values of lactate level were compared using the student t-test and *p*-value of ≤0.05 was adopted as significant.

RESULTS

A total of 70 patients were enrolled in the study out of which 31(44.40%) were males and 39(55.60%) were females, with a median gestational age of 267 days and mean weight of 2.70±0.60 kg. We found 25 neonates to have Moderate or Severe HIE with gender wise distribution shown in Figure. The 5-min APGAR score for None to Mild HIE, was 8.00±0.75 and for Moderate to Severe HIE, it was 5.20±1.60 with significant *p*-value of 0.037. A total of 45 neonates were found to have No or Mild HIE with mean lactate level of 3.64+1.49 mmol/L and 25 patients diagnosed with Moderate to Severe HIE had mean lactate level of 9.40±2.26 mmol/L ($p< 0.001$), as shown in Table.

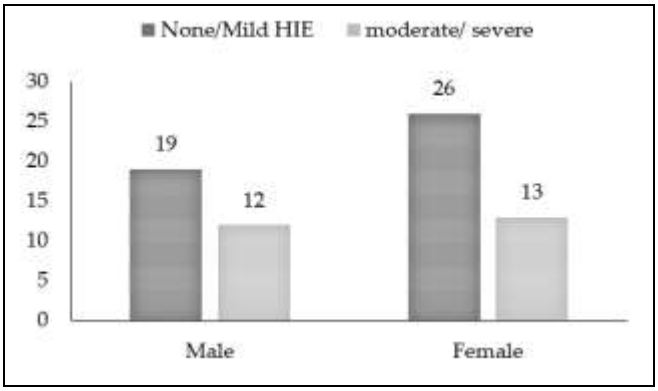

Figure: Gender Wise Distribution of Neonates (n=70)

Table: Relationship of Mean Lactate Level With Grades of HIE (n=70)

Variable	Group A (n=45)	Group B (n=25)	*p*-value (≤0.05)
5-min APGAR Mean±SD	8.70±0.70	5.28±1.62	0.037
Lactate level(mmol/l) Mean±SD	3.64±1.49	9.40±2.26	0.001

DISCUSSION

Perinatal hypoxia is a serious emergency resulting from disruption of oxygen supply for tissue energy leading to anaerobic metabolism, where, if the process is not checked, the maintenance of the energy balance is disturbed, creating anaerobic metabolic products, such as lactate and hydrogen ions, thus, a high plasma lactate can be present in various conditions, like hypoxia, cardiac disease, infection, or convulsions, whereas primary lactic acidosis can be caused by some inborn errors of metabolisms like pyruvate metabolism and respiratory chain defects due to which lactate is superior to pH for predicting neonatal morbidity especially perinatal asphyxia.[13] Lactate production precedes low pH and persists longer, making lactate level a more discriminating predictor of neonatal morbidity, especially in the context of perinatal asphyxia leading to HIE.[14] Westgren et al. inferred that efficacy of umbilical arterial lactate level and acid base analysis in predicting 5-minute APGAR score <4 is similar[2] and a large study found umbilical arterial lactate to be as authenticated as base deficit in predicting 5-min APGAR <4 or 7.[15] A number of other studies found umbilical arterial lactate to be superior to pH or even base excess for predicting adverse neonatal outcomes.[16-18] Our results showed that umbilical arterial lactate is a more discriminating measure of neonatal morbidity at term than pH and lactate was more sensitive and specific than pH with the

additional advantage of simplicity of measurement. Future studies should focus on the comparative predictive ability of lactate and pH for long-term outcomes in newborn with birth asphyxia.

LIMITATION OF STUDY

This study had several important limitations. The relatively small sample size and single-center design may limit the generalizability of the findings. The short study duration of just three months might not provide a comprehensive representation of cases throughout the year. The cross-sectional design only provides a snapshot at one point in time, without follow-up data to assess the long-term correlation between lactate levels and clinical outcomes. Additionally, due to lack of resources, other potential confounding factors such as maternal conditions, mode of delivery, or specific resuscitation interventions were not considered in the analysis.

CONCLUSION

High umbilical artery lactate values correlate with low pH and Base deficit and are a reliable tool for assessing the severity of fetal asphyxia. Increasing lactate concentration after birth is better predictor of severe HIE.

Conflict of Interest: None.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

MBA & IA: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

BA & SH: Conception, data analysis, drafting the manuscript, approval of the final version to be published.

MTN & ST: Data acquisition, critical review, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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