Open Access

Original Article

Association of Umbilical Cord Lactate Levels and Capillary Ph with Hypoxic-Ischemic Encephalopathy in Neonates Born with Intrapartum Asphyxia

Syed Awais Ul Hassan Shah, Ehsan Qadir, Zeeshan Ahmed, Farah Shahid*, Samina Shams Alam

Pak Emirates Military Hospital/National University of Medical Sciences (NUMS) Rawalpindi Pakistan, *Shifa College of Medicine, Islamabad Pakistan

ABSTRACT

Objective: To estimate the association of umbilical cord lactate levels and pH with Hypoxic-Ischemic Encephalopathy in neonates born with intrapartum asphyxia.

Study Design: Comparative cross-sectional study.

Place and Duration of study: Pediatrics Department, Pak Emirates Military Hospital, Rawalpindi Pakistan, from February 2021 to April 2022.

Methodology: The study was conducted on neonates born with suspicion of intrapartum asphyxia at our hospital. Umbilical cord lactate levels and capillary pH were performed within the first 30 minutes of birth. Then, neonates were admitted to the neonatal intensive care unit and followed up for three days to look for the presence and severity of Hypoxic-Ischemic Encephalopathy (HIE). Association was ascertained between raised lactate levels and negative base deficit with Hypoxic-Ischemic Encephalopathy.

***Results*:** A total of 1000 neonates were included in the final analysis. From 1000 neonates with intrapartum asphyxia, 790(79%) did not develop any grade of hypoxic-ischemic encephalopathy within the first three days of birth, while 210(21%) developed either Grade-I, II or III encephalopathies. Raised serum lactate and base deficit were significantly associated with the presence and severity of hypoxic-ischemic encephalopathy in neonates born with intrapartum asphyxia (p-value<0.001).

Conclusion: Both umbilical artery lactate levels and capillary pH performed within the first 30 minutes of birth were associated with the presence and severity of Hypoxic-Ischemic Encephalopathy in neonates included in our study. These results favour lactate levels as a predictor of Hypoxic-Ischemic Encephalopathy.

Keywords: Base deficit, Hypoxic-ischemic encephalopathy, Neonates.

How to Cite This Article: *Shah SAUH, Qadir E, Ahmed Z, Shahid F, Alam SS. Association of Umbilical Cord Lactate Levels and Capillary Ph with Hypoxic-Ischemic Encephalopathy in Neonates Born with Intrapartum Asphyxia. Pak Armed Forces Med J 2023; 73(2): 498-501. DOI: https://doi.org/10.51253/pafmj.v73i2.8491*

INTRODUCTION

Intrapartum asphyxia is a common finding in neonates born at various world centres, including Pakistan.[1] This condition gives rise to multiple physiological and biochemical responses in the body and may lead to serious consequences if not managed adequately in time. Hypoxic ischemic encephalopathy is one of the most serious consequences seen in neonates who suffer from intrapartum asphyxia at the time of birth.[2,3]

Various biochemical and clinical markers have been used to predict poor outcomes, including hypoxic-ischemic encephalopathy in neonates.[4,5] A previous study revealed that the highest recorded lactate level in the first hour of life and serial measurements of Lactate afterwards were important predictors of moderate to severe hypoxic-ischemic encephalopathy in neonates born with birth asphyxia.[6] Another study highlighted that around 1/5th of the newborns had high umbilical cord lactate levels. They were associated with various feto-maternal factors and predicted poor short-term neonatal outcome.[7] Lactate is an easy and cost-effective marker which can be incorporated into clinical practice to predict poor outcomes, especially hypoxic-ischemic encephalopathy in neonates born with birth asphyxia due to any cause.[8,9]

The early neonatal period is very important regarding the overall well-being of the baby. Any event during pregnancy or at the time of birth may adversely affect the health of a neonate, and the treating team needs to be aware of that, especially in the case of high-risk neonates. A local study published by Syed *et al*. in 2020 concluded that umbilical cord pH could predict poor outcomes in neonates and prolonged neonatal intensive care unit admission.[10] Some work has been published regarding the role of pH. However, limited local data has been available regarding the role of lactate levels in this regard. Therefore, we planned this study to look for an association of umbilical cord lactate levels and pH with Hypoxic-Ischemic Encephalopathy in neonates born with intrapartum asphyxia.

Correspondence: Dr Syed Awais Ul Hassan Shah, Department of Neonatology, Pak Emirates Military Hospital, Rawalpindi, Pakistan

Received: 05 Apr 2022; revision received: 02 Jul 2022; accepted: 04 Jul 2022

METHODOLOGY

The comparative cross-sectional study was conducted at the Nursing Intensive Care Unit of the Pak Emirates Military Hospital Rawalpindi from February 2021 to April 2022, after ethical approval from the Ethical Review Board Committee (IREB letter no, A/28/EC/424/2022 dated 31st March 2022). The sample size was calculated by WHO sample size calculator using the population proportion of hypoxic-ischemic encephalopathy in patients born with birth asphyxia as 1.4%.[11] Non-probability consecutive sampling technique was used to gather the sample.

Inclusion Criteria: All singleton births with markers of the severe hypoxic event during labour (fetal heart rate<100 or >160 beats/min, meconium staining, Low APGAR score, respiratory failure) were included in the study.

Exclusion Criteria: Neonates with etiologies other than birth asphyxia, congenital malformations, metabolic disorders, viral infections, bacterial infections and meningitis, septic shock, major organ failure or fetal injury during birth were excluded from the study. Those who could not be followed up or refused nursing intensive care admission in our hospital were also excluded.

Written informed consent from the parents or guardians of the potential participants or their caregivers, neonates who had suspected birth asphyxia and were fulfilling the above-mentioned inclusion and exclusion criteria were included in the study. Umbilical cord blood lactate levels and capillary gases were performed within 30 minutes of the birth of a baby. Neonates were kept in NICU and followed up for 72 hours for hypoxic-ischemic encephalopathy by a consultant neonatologist. Presence and severity of hypoxic-ischemic encephalopathy were determined by a consultant neonatologist based on clinical, laboratory and radiological findings.[12] Base deficit was considered significant if <12mmol/litre.[13] Umbilical cord lactate levels were considered significant if were >5mmol/litre.[14] All information from a patient was compiled in a structured proforma designed for this study.

Statistics Package for Social Sciences version 24.0 (SPSS-24.0) was used for the analysis. The characteristics of neonates participating in the study and the outcome variables were described with the help of descriptive statistics. In addition, Pearson chi-square analysis was done to evaluate the association of various parameters with the presence and severity of hypoxic-ischemic encephalopathy in our study participants. The *p*-values less than or equal to 0.05 were considered significant.

RESULTS

Twenty thousand births took place in the study period at our hospital. A total of 1000 neonates were included in the final analysis. Of them, 610(61%) were male, while 390(39%) were females. Table-I summarizes the general characteristics of study participants. The mean age of the neonates recruited in the study was 2.13±2.23 days.

Table-I: Characteristics of Neonates included in the Study (n=1000)

Study Parameters	n(%)
Age(years)	
Mean ± SD	2.13±2.23 days
Range (min-max)	1-3 days
Gender	
Male	610(61%)
Female	390(39%)
Raised Lactate Levels	
No	729(72.9%)
Yes	271(27.1%)
Significant Base Deficit	
No	677(67.7%)
Yes	323(32.3%)
Grades of Encephalopathy	
No	790(79%)
Stage I	167(16.7%)
Stage II	27(2.7%)
Stage III	16(1.6%)

From 1000 neonates with intra-partum asphyxia, 790(79%) did not develop any grade of hypoxic-ischemic encephalopathy within the first three days of birth, while 210(21%) developed either Grade I, II or III encephalopathies. In addition, 729(72.9%) did not have raised lactate levels, while 271(27.1%) had raised lactate levels. Of 1000 neonates, 677(67.7%) had no base deficit, while 323(32.3%) had a significant base deficit. Table-II shows the results of the statistical analysis. It was revealed that low birth weight (*p*-value-0.001), raised serum Lactate (*p*-value <0.001), and base deficit (*p*-value<0.001) were signifi-cantly associated with the presence and severity of hepatic ischemic encepha-lopathy in neonates who were born with intrapartum asphyxia.

DISCUSSION

Raised umbilical cord lactate levels and significant base deficit were associated with the presence and severity of hypoxic encephalopathy. As most of our pregnancies are unbooked and chances of intra or early post-partum complications in both mother and neonate are common, we need to identify practical and

Table-II: Association of Various Factors with presence and Severity of Hypoxic Ischemic Encephalopathy (n=1000)

Parameters	No encephalopathy	Stage-I	Stage-II	Stage-III	*p*-value
Lactate levels					
Within range	698(88.3%)	26(15.6%)	04(14.8%)	01(6.25%)	<0.001
Raised	92(11.7%)	141(84.4%)	23(85.2%)	15(93.75%)	
Base deficit					
Not significant	653(82.6%)	19(11.4%)	04(14.8%)	01(6.25%)	<0.001
Significant	137(17.4%)	148(88.6%)	23(85.2%)	15(93.75%)	
Premature Rupture of Membranes					
No	575(72.7%)	130(77.8%)	19(70.4%)	14(87.5%)	0.278
Yes	215(27.3%)	37(22.2%)	08(29.6%)	02(12.5%)	
Birth Weight					
Normal	625(79.1%)	111(66.4%)	16(59.2%)	14(87.5%)	0.001
Low birth weight	165(20.9%)	56(33.6%)	11(40.8%)	02(12.5%)	

cost-effective methods to pick high-risk cases for close monitoring. Umbilical cord pH levels have traditionally been used as predictors of encephalopathy in children suspected of birth asphyxia; in a country like ours, they are not performed even at secondary care level hospitals. We, therefore, conducted this study intending to look for an association of umbilical cord lactate levels and pH with Hypoxic-Ischemic Encephalopathy in neonates born with intrapartum asphyxia.

Van Anh *et al.* studied the role of umbilical cord blood lactate as an early predictor of hypoxic-ischemic encephalopathy in newborns with perinatal asphyxia. They concluded that raised umbilical cord lactate levels are associated with increased chances of hypoxic-ischemic encephalopathy and can be used to predict this serious complication in babies born with intrapartum asphyxia.[15] Umbilical artery lactate levels as a predictor of poor neonatal outcomes were studied by Allanson *et al.* They revealed that umbilical Lactate had good sensitivity and specificity for predicting neonatal neurological outcomes, including hypoxic-ischemic encephalopathy.[16] Our study concluded that both capillary pH and lactate levels performed within the first 30 minutes of birth were associated with the presence and severity of Hypoxic-Ischemic Encephalopathy in neonates included in our study. These results favour lactate levels as a predictor of Hypoxic-Ischemic Encephalopathy. Mooney *et al.* examined the use of an algorithm including measures of pH, Lactate, and base deficit to predict the occurrence of HIE in a prospective cohort of infants with perinatal asphyxia.[17] They revealed that all these parameters with other relevant clinical information make a useful model to predict presence and severity of HIE. The severity of perinatal asphyxia and early prognostic tools in neonates with hypoxic-ischemic encephalopathy was performed by Wales *et al.* in 2020.[18] It was concluded that various laboratory and electrophysiological testing and imaging techniques could be used for the said purpose. Therefore, we did not study electrophysiological and imaging techniques. However, two laboratory parameters, capillary pH and umbilical cord lactate levels, were associated with the presence and severity of HIE in neonates born with intrapartum asphyxia.

LIMITATIONS OF STUDY

This data was from one intensive nursing care unit and could not be generalized. Multiple confounding factors can impact base deficit and lactate levels; therefore, we cannot predict that high lactate levels and Significant base deficit were raised due to asphyxia and would lead to hypoxic-ischemic encephalopathy.

CONCLUSION

Both capillary pH and umbilical artery lactate levels performed within the first 30 minutes of birth were associated with the presence and severity of Hypoxic-Ischemic Encephalopathy in neonates included in our study. These results favour lactate levels as a predictor of Hypoxic-Ischemic Encephalopathy.

Conflict of Interest: None.

Authors' Contribution

SAUHS: Study design, data analysis, drafting the manuscript, critical review, approval of the final version to be published.

EQ: Conception, interpretation of data, drafting the manuscript, approval of the final version to be published.

ZA: Data acquisition, interpretation of data, approval of the final version to be published.

FS: & SSA: Conception, interpretation of data, drafting the manu-script, approval of the final version to be published.

REFERENCES

1. Al-Wassia H, Saber M. Admission of term infants to the neonatal intensive care unit in a Saudi tertiary teaching hospital: cumulative incidence and risk factors. Ann Saudi Med 2017; 37(6): 420-424. doi: 10.5144/0256-4947.2017.420.
2. Quddusi AI, Razzaq A, Hussain S, Hussain A. Pattern of neonatal admission at the Children's Hospital and the Institute of Child Health, Multan. J Ayub Med Coll Abb 2012; 24(2): 108-110.

3. Fisher AL, Sangkhae V, Presicce P, Chougnet CA, Jobe AH, Kallapur SG, et al. Fetal and amniotic fluid iron homeostasis in healthy and complicated murine, macaque, and human pregnancy. JCI Insight 2020; 5(4): e135321. doi: 10.1172 /jci.insight.135321.
4. Nadeem G, Rehman A, Bashir H. Risk Factors Associated With Birth Asphyxia in Term Newborns at a Tertiary Care Hospital of Multan, Pakistan. Cureus 2021; 13(10): e18759. doi:10.7759/ cureus.18759
5. Uleanya ND, Aniwada EC, Ekwochi U, Uleanya ND. Short-term outcome and predictors of survival among birth asphyxiated babies at a tertiary academic hospital in Enugu, South East, Nigeria. Afr Health Sci 2019; 19(1): 1554-1562. doi:10.4314/ ahs.v19i1.29.
6. Zhang S, Li B, Zhang X, Zhu C, Wang X. Birth Asphyxia Is Associated With Increased Risk of Cerebral Palsy: A Meta-Analysis. Front Neurol 2020;11:704. doi:10.3389/fneur.2020. 00704.
7. Shah S, Tracy M, Smyth J. Postnatal lactate as an early predictor of short-term outcome after intrapartum asphyxia. J Perinatol 2004 ; 24(1): 16-20. doi: 10.1038/sj.jp.7211023.
8. Ogik V, Muyingo M, Musooko M, Nankunda J. Umbilical artery lactate levels and associated maternal and newborn characteristics at Mulago National Referral Hospital: a cross-sectional observational study. BMJ Open 2021;11(8):e043827. doi:10.1136 /bmjopen-2020-043827.
9. Tu YF, Wu PM, Yu WH, Li CI, Wu CL, Kang L, et al. Lactate Predicts Neurological Outcomes after Perinatal Asphyxia in Post-Hypothermia Era: A Prospective Cohort Study. Life (Basel) 2021 ; 11(11): 1193. doi: 10.3390/life11111193.
10. Syed W, Liaqat N, Qazi Q, Yasmeen S. Relationship between immediate postpartum umbilical cord pH, fetal distress and neonatal outcome. Pak J Med Sci 2020 ; 36(7): 1529-1532. doi: 10.12669/pjms.36.7.2536.
11. Palsdottir K, Dagbjartsson A, Thorkelsson T, Hardardottir H. [Birth asphyxia and hypoxic ischemic encephalopathy, incidence and obstetric risk factors]. Laeknabladid 2007; 93(9): 595-601.
12. Wang Z, Zhang P, Zhou W, Xia S, Zhou W, Zhou X, et al. Neonatal hypoxic-ischemic encephalopathy diagnosis and treatment: a National Survey in China. BMC Pediatr 2021; 21(1): 261. doi: 10.1186/s12887-021-02737-6.
13. Martí Gamboa S, Pascual Mancho J, Rodrigo Rodríguez M, Ruiz Sada J, Castán Mateo S. pH, base deficit or lactate. Which is better for predicting neonatal morbidity? J Matern Fetal Neonatal Med 2017; 30(19): 2367-2371. doi: 10.1080/14767058.2016. 00000124 8936.
14. Tuuli MG, Stout MJ, Macones GA, Cahill AG. Umbilical Cord Venous Lactate for Predicting Arte-rial Lactic Acidemia and Neonatal Morbidity at Term. Obstet Gynecol 2016; 127(4): 674-680. doi:10.1 097/AOG.0000000000001339
15. Van Anh TN, Hao TK, Chi NTD, Son NH. Predictions of Hypoxic-Ischemic Encephalopathy by Umbilical Cord Blood Lactate in Newborns with Birth Asphyxia. Open Access Maced J Med Sci 2019 ; 7(21): 3564-3567. doi: 10.3889/oamjms.2019.581.
16. Allanson ER, Waqar T, White C, Tunçalp Ö, Dickinson JE. Umbilical lactate as a measure of acidosis and predictor of neonatal risk: a systematic review. BJOG 2017; 124(4): 584-594. doi: 10.1111 /1471-0528.14306.
17. Mooney C, O'Boyle D, Finder M, Hallberg B, Walsh BH, Henshall DC, et al. Predictive modelling of hypoxic ischaemic encephalopathy risk following perinatal asphyxia. Heliyon 2021; 7(7): e07411. doi:10.1016/j.heliyon.2021.e07411
18. Walas W, Wilińska M, Bekiesińska-Figatowska M, Halaba Z, Śmigiel R. Methods for assessing the severity of perinatal asphyxia and early prognostic tools in neonates with hypoxic-ischemic encepha-lopathy treated with therapeutic hypothermia. Adv Clin Exp Med 2020 ; 29(8): 1011-1016. doi: 10.17219 /acem/124437.

.....