www.jmscr.igmpublication.org
Impact Factor 5.84
Index Copernicus Value: 83.27
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: https://dx.doi.org/10.18535/jmscr/v5i7.136

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Original Article

Urinary Uric Acid/Creatinine Ratio as an Additional Early Marker for Perinatal Asphyxia

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Abstract
Background: *Perinatal asphyxia is one of the leading causes of perinatal morbidity and mortality. Feasible and early biochemical marker to diagnose and predict neurologic outcome is a great need of time as Apgar score alone is influenced by various factors. This study was conducted to validate the utility of urinary uric acid to creatinine ratio (UA/Cr ratio) in asphyxia diagnosis.*
Aim: *To validate the urinary uric acid/creatinine ratio as an additional marker for perinatal asphyxia.*
Materials and Methods: *The present case control study was conducted at a tertiary care superspeciality Hospital associated with medical college. Data of 50 healthy newborns and 79 asphyxiated newborns were collected. (UA/Cr) ratio was measured from the spot urine sample collected within 24 hours of birth. Statistical analysis was performed by student t-test and Receiver Operating Characteristic (ROC) plots.*
Results: *In our study the mean value of urine UA / Cr ratio among the cases was 2.632 and among controls was 0.866 (p <0.0001) and UA /Cr as an individual variable were statistically significant. ROC curve analysis done proved that a score of 1.92 or more delineates babies into asphyxiated newborns. A score of 1.9 has a sensitivity of 94.8% and specificity of 94% and area under the ROC curve is 0.995.*
Conclusions: *diagnosis of perinatal asphyxia should be supported by other investigations so that early decision can be taken about the level of care and prognosticate the baby. Interleukins, enzymes and imaging techniques require experienced personnel well equipped laboratories and are expensive. Non-invasive urinary UA/Cr ratio may be an answer to these issues as it easy, time and cost effective.*

Introduction

Perinatal asphyxia is an insult of central nervous system along with other organ system of fetus or the newborn due to lack of oxygen (hypoxia) and/or a lack of perfusion (ischemia)[(2)].

The incidence of perinatal asphyxia is about 1-1.5% of live births and is inversely related to the gestational age and birth weight.[(2)] Perinatal asphyxia may result in fetal demise, neonatal death or multi-organ dysfunction.[(3,4)] Follow-up studies indicate 25% or more of infants who survive perinatal asphyxia, subsequently demonstrate spectrum of sequelae ranging from subtle developmental disabilities such as learning disabilities, attention deficit problems to more obvious problems such as cerebral palsy, mental

retardation, and seizure disorder, visual and auditory problems.[3,5]

The diagnosis and evaluation of perinatal asphyxia is problematic and objective means of assessing the severity are lacking.[6] There are no specific criteria to identify the neonate with asphyxia who are at a greater risk for encephalopathy and therefore most likely to be benefitted from newer intervention.[7] On follow-up there are no standard guidelines to determine which babies suffered an asphyxia insult during birth.

In the modern era various biochemical markers are used to establish the diagnosis of perinatal asphyxia and validate the prognosis. Neuron specific enolase, IL-6, glial fibrillary acidic protein, urinary lactate/ creatinine ratio are various markers used to determine the neuro-developmental outcome. [8, 9, 10, 11] Estimation of interleukin and enzyme require modernized equipments, expert manpower, and are expensive.

Uric acid and creatinine are metabolites, excreted in the urine, the estimation of which is both time and cost effective. Various studies done in the recent past have proved the utility of uric acid/ creatinine ratio as a marker of neonatal asphyxia. [1,12,13,14] Hence, this study was undertaken with the objective to validate the urinary uric acid/ creatinine ratio as a marker of neonatal asphyxia .

Materials and Methods

The study was carried out for period of 11 months at level 3 NICU of M.Y Hospital and associated CNBC a tertiary care superspeciality Hospital associated with medical college, which acts as a referral centre for a large number of primary and secondary levels hospitals, conducting more than 12000 deliveries in a year, and catering to a large population of neonates both inborn as well as outborn. 129 neonates admitted in the NICU within 24 hours of birth whether inborn or outborn were recruited in study. Seventy nine term babies with evidence of intrapartum fetal distress, five minute APGAR less than 6 and who need resuscitation for more than one minute were taken as case. Fifty term babies without sign of birth asphyxia and had APGAR score more than 7 admitted for other reasons were enrolled as control. The sample size was based the fact that about 15-19% of all NICU admissions are because of birth asphyxia. Babies with congenital malformation, suspected metabolic disease, prematurity, with serum creatinine more then 2 and who fail to pass urine were excluded from study, Urine sample was collected in a sterile container within the first 24 hours of life and were processed immediately.

Uric acid level in urine was measured by auto analyzer by uricase / peroxidase method and creatinine was measured by same instrument by alkaline picrate method. The ratio of uric acid and creatinine in both cases and controls were obtained and compared using student t test.

ROC curve analysis was used to determine cut off value of parameters to diagnose true disease. In the above test p-value less than 0.05 were taken to be statistically significant. The data was analyzed using Medcalc software.

Results

During the study period 1754 babies were admitted in our NICU, among which 587 were term babies. Out of 1754 babies there were 267 asphyxiated neonates contributing to 15% of admissions. Out of 102 neonates 79 babies fulfilled the inclusion criteria, and included in the study (fig 1). 50 term neonates admitted to the NICU due to other problems were selected as control. Base line demographic profile of case and control were comparable (fig/table 2). HIE among the asphyxiated neonates were staged according to Sarnat and Sarnat staging 12 hourly intervals for the first 3 days to see the progression in HIE staging. 44(55.69%) of cases belonged to stage I, 30(37.97%) cases to stage II, and5 (6.32%) to stage III (fig/table-3).Urinary uric acid and creatinine were estimated in both cases and controls and compared. The mean urine UA among the cases was 82.04, 82.61, and 130 respectively and p value was 0.682 which was

statistically insignificant (fig/table-3). 32.79, 31.44, and 30.2 were the mean urine creatinine values in stages I, II, and III respectively and p value was 0.352 and was not statistically significant (fig/table-3). The mean urine UA/ Cr among the cases in stage I, II, and III was 2.478, 2.553, and 4.464 respectively and p value was <0.05 (fig/table-3). In our study the mean value of urine UA / Cr ratio among the cases was 2.632 and among controls was 0.866 p value was <0.0001 and UA /Cr as an individual variable were statistically significant(fig/table-3).18 babies had urine UA/Cr ratio of < 1.92 while 61 babies had a ratio of more than 1.92. ROC curve analysis done proved that a score of 1.92 or more delineates babies into asphyxiated newborns. A score of 1.9 has a sensitivity of 94.8% and specificity of 94% and area under the ROC curve is 0.995 (table/fig-4). Therefore a value of urine UA/Cr >1.9 identifies neonates as asphyxiated babies and ratio of < 1.9 into normal counterparts.

Discussion

The diagnosis of perinatal asphyxia is always associated with uncertainty and standard guidelines to assess the severity are lacking.[6] Despite the increasing understanding of the mechanisms leading to and resulting from perinatal asphyxia early determination of brain damage following hypoxic ischemic events still remains one of the hardest problems in neonatal care.[1] Their clinical manifestation, their individual potentials to respond to the asphyxia insult to recover vary among the newborns. Prediction of perinatal asphyxia and their severity is essential for the physicians to plan treatment, prognosticate outcome and counsel parents.

Of late new biochemical parameters are being evaluated with the hope of using them for the definition and diagnosis of perinatal asphyxia.[8,9,10,11] Currently emphasis is being placed on noninvasive, time and cost effective investigatory modalities. Interleukins, enzymes and imaging techniques require experienced personnel well equipped laboratories and are expensive. Estimation of urine uric acid and creatinine which are byproduct of anaerobic metabolism requires simple kits and are cost effective.

In this study we have used one such parameters to diagnose and prognosticate, birth asphyxia and related complications.

All babies were evaluated for urine UA / Cr ratio. In our study the mean value of urine UA / Cr ratio among the cases was 2.632 and among controls was 0.866. The p value was <0.0001 and UA /Cr as an individual variable were statistically significant. 18 babies had urine UA/Cr ratio of < 1.92 while 61 babies had a ratio of more than 1.92. Statistical analysis done proved that a score of 1.92 or more delineates babies into asphyxiated newborns. A score of 1.9 has a sensitivity of 94.8% and specificity of 94% and area under the ROC curve is 0.995. Therefore a value of urine UA/Cr >1.9 identifies neonates as asphyxiated babies and ratio of < 1.9 into normal counterparts. The results were similar to the other studies. In the study done by ClierErdag the mean urine UA/Cr ratio among the asphyxiated neonates was 2.29 +/- 1.14 while among the controls it was .81 +/-0.59. (1) The studies done by Bader and Akisu also proved that the ratio was higher in the asphyxiated group when compared with the controls (2.11 Vs 0.64). [6, 12] These positive results may help the clinicians to identify the etiology of convulsions without history of asphyxia.

Limitation

Limitations of our study are small sample size, single centre study and methodological in nature.

This is single centre study with relatively small sample size, a Multicentre studies with more sample size along with more detail on asphyxiated neonates such as duration of labor, duration of resuscitation, time to first breath, etc will allow us to utilize more variables in multivariate analysis and further improve upon the predictive value of this marker.

Conclusion

1) Urinary UA/ Cr > 1.9 also suggests that the babies have suffered from perinatal asphyxia.

Reference

1. Erdag GC, Vitrinel A, "Can urinary uric acid/ creatinine ratio be used as an additional marker for neonatal asphyxia." International Pediatrics 2004; vol 19(4): 217-219.
2. Aurora S, Snyder EY, Perinatal asphyxia. In: John P Cloherty et al, Manual of neonatal care, Lippincott Williams and Wilkins, 5th ed. 2004, Chap 27: 536-555.
3. Stoll BJ, Kleigman RM, Nervous system Disorders. In: Behrman RE, Kleigman RM, Jenson HB. In: Nelson's Textbook of Pediatrics, Saunders,17th ed 2004,Chap 88:561-9.
4. Perinatal Morbidity report of the health care commuter expert panel on perinatal morbidity, National health and medical research Council. Australian government public service 1998.
5. Shaywitz BA. Perinatal Asphyxia. In: MacMillan JA et al, Oski's Pediatrics Principles and Practice: Lippincott Williams and Wilkins, 3rd ed 1999, Chap 34: 235-237
6. Bader D, Gozal D, Weigner-Abend M, Berger A, Lanir A. Neonatal urinary uric acid/ creatinine ratio as an additional marker of perinatal asphyxia; Eur J Pediatr. 1999 Sep; 154 (9): 747-9.
7. Perlman JM. Markers of asphyxia and neonatal brain injury; NEJM 1999 Jul; 341 (5); 361-5.
8. Thornberg E, Thiringer K, Hagberg H, Kjellmer I. Neuron specific enolase in asphyxiated newborns: association with encephalopathy and cerebral function monitor trace. Arch Dis Child Fetal Neonatal, ed 1995 Jan; 72(1): F39-42.
9. Martín-Ancel A, García-Alix A, Pascual-Salcedo D, Cabañas F, Valcarce M, and Quero J. Interleukin-6 in the Cerebrospinal Fluid After Perinatal Asphyxia Is Related to Early and Late Neurological Manifestations. Pediatrics, Novemeber 1997; 100(5): 789-794.
10. Blennow M, Hagberg H, Rosengren L. Glial fibrillary acidic protein in the cerebrospinal fluid: a possible indicator of prognosis in full term asphyxiated newborn infants?. Pediatr Res, March 1995; 37 (3): 260-4.
11. Huang CC, Wang ST, Chaochang Y, Lin KP, Pei- Linwu. Measurement of the urinary lactate: creatinine ratio for the early identification of newborn infants at risk for HIE. NEJM July 1999; 341 (5): 328-335.
12. Akisu M, Kulturusay N. Value of the urinary uric acid to creatinine ratio in term infants with perinatal asphyxia. Acta Pediatr Jpn Feb 1998; 40(1): 78-81.
13. Chen HJ, Tsai KS. Urinary uric acid to creatinine ratio as an additional marker of perinatal asphyxia. J Formos Med Assoc Oct 2000; 99(10): 771-4.
14. Tekgul H, Yalaz M, Kutukculer N, Ozbek S, Kose T, Akisu M et al. Value of biochemical markers for outcome in term infants with asphyxia. Pediatr Neurol Nov 2004; 31(5): 326-332.