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Urinary Uric Acid And Creatinine Ratio As A Marker of Perinatal Asphyxia

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Abstract
Background: *Perinatal asphyxia is a common neonatal problem and contributes significantly to neonatal morbidity and mortality. Only a third of deliveries in India are institutional. In the absence of perinatal records it is difficult to diagnose perinatal asphyxia retrospectively. There is a need to identify neonates with asphyxia who will be risk for hypoxic ischemic encephalopathy and multi-organ dysfunction.*
Objective: *To evaluate prospectively the value of urinary uric acid to creatinine (UA/UCR) ratio in early spot urine sample in diagnosing perinatal asphyxia.*
Method: *A study was conducted on 110 neonates comprising 55 cases and 55 controls born in Rajendra Institute of Medical Sciences. Spot urine sample collected within first day of life. A cut-off urinary uric acid to creatinine (UA/UCR) ratio value of >1.14 was taken as the cut-off level.*
Result: *The urinary UA/UCR ratios were found to be higher in asphyxiated infants (2.58±1.09) when compared with those in the controls (0.86±0.17; p<0.001).The cut-off (UA/UCR) value of >1.14 has 84% sensitivity with a specificity of 94% and has a positive predictive value of 93.33%with negative predictive value of 85.45%with an accuracy of 89%.*
Conclusion: *The urinary uric acid/creatinine ratio was found to be a good, early, simple and reliable screening test for the early diagnosis and assessment of perinatal asphyxia.*
Keywords : *Perinatal asphyxia,urinary uric acid to creatinine ratio*

I. Background

Perinatal asphyxia is a common neonatal problem and contributes significantly to neonatal morbidity and mortality. Globally, hypoxia of the newborn (birth asphyxia) or the fetus ("fresh stillbirth") is estimated to account for 23% of the 4 million neonatal deaths and 26% of the 3.2 million stillbirths each year [1]. An estimated 1 million children who survive birth asphyxia live with chronic neurodevelopmental morbidities, including cerebral palsy, mental retardation, and learning disabilities. Every hour, 104 children die as a result of asphyxia [1].

In India, between 250,000 to 350,000 infants die each year due to birth asphyxia, mostly within the first three days of life [2]. Data from National Neonatal Perinatal database (NNPD) suggests that perinatal asphyxia contributes to almost 20% of neonatal deaths in India [2].

Although asphyxia is associated with multiple organ injuries, especially with adverse neurological outcomes, management still focuses on supportive care. So, if the adverse effects of hypoxia on the newborn are considered, there is a need to identify infants who will be at high risk for hypoxic ischemic encephalopathy and early neonatal death as a consequence of perinatal hypoxia. A variety of markers have been examined to identify perinatal hypoxia including electronic fetal heart monitoring, low Apgar scores, cord pH, electroencephalograms (EEG), computed tomography (CT) and magnetic resonance imaging (MRI) scans and Doppler flow studies. The current problem, then becomes our inability to precisely distinguish the false positive affected from the true positive asphyxiated or compromised fetus. Several studies have been conducted to evaluate better markers that help distinguish an asphyxiated from non-asphyxiated neonates.

Perinatal asphyxia may result in adverse effects on all major body systems. Many of these complications are potentially fatal. In a term infant with perinatal asphyxia renal, neurologic, cardiac and lung dysfunction occurs in 50%, 28%, 25% and 23% cases respectively[3]. The extent of multi-organ dysfunction (MOD) determines the early outcome of an asphyxiated neonate with either the neonate succumbing as a consequence of organ damage or recovering completely. HIE refers to the central nervous system (CNS) dysfunction associated with perinatal asphyxia. Hypoxic ischemic encephalopathy (HIE) is the foremost concern in asphyxiated neonate because contrary to other system derangements this has the potential to cause serious long term neuromotor sequel among survivors.

Despite the increasing understanding of the mechanisms leading to and resulting from neonatal asphyxia, early determination of brain damage following hypoxic-ischemic events still remains the hardest problems in neonatal care.[4,5,6]

Neonatal hypoxia is one of the leading causes of neonatal mortality in developing countries. Birth asphyxia is an important cause of static development and neurological handicap both in term and pre term infants.[7]

Though there are more and more studies for understanding mechanisms leading to birth asphyxia, studies for early determination of tissue damages due to birth asphyxia are still lacking. This study is to evaluate the utility of urinary uric acid to creatinine ratio (UA/Cr ratio) as marker for early, easy and cost effective detection of perinatal asphyxia.

II. Materials And Methods

2.1: Source of Data

The study was a prospective study conducted on asphyxiated and healthy term neonates recruited from Neonatal Intensive Care Unit (NICU) and Post natal wards of Rajendra Institute of Medical Sciences, Ranchi from December 2014 to December 2015. Cases and Controls comprised of asphyxiated and healthy neonates, respectively. The urine samples from the 55 neonates comprising the cases and 55 neonates comprising the controls constituted the material for the study.

2.2: Method of Collection of Data

The study included two groups:

2.2.1 The case group: It included 55 neonates fulfilling the following criteria:

Inclusion criteria:

1. Gestational age ≥ 37 weeks.
2. Appropriate for gestational age.
3. APGAR score <7 at 1 minute after birth.
4. Need for positive pressure ventilation for >1 minute or first cry delayed >5 minutes.

Exclusion criteria:

1. Congenital malformations.
2. Maternal drug addiction.
3. Neonates born to mothers who would have received magnesium sulphate within 4 hours prior to delivery or opiods (pharmacological depression).
4. Hemolytic disease of the newborn.
5. Neonates born to mothers consuming alcohol
6. Neonates born to mothers who are smokers
7. Neonates born to mothers on anti epileptics.

2.2.2 *The control group: It included 55 term apparently healthy neonates appropriate for gestational age without signs of peinatal asphyxia as evidenced by normal fetal heart rate patterns, clear liquor and one minute Apgar score ≥7.*

All neonates included in the study had the following done:

1. Detailed maternal history, birth events, Apgar score, sex of the baby and weight of the baby were recorded on the precoded Performa. Gestational age was assessed by New Ballard scoring system.
2. Thorough clinical and neurological examination was done for all the neonates included in the study. The asphyxiated neonates (case group) were monitored for seizures, hypotonia and HIE in the immediate neonatal period in the NICU. Grading system used to grade the severity of HIE was SARNAT and SARNAT staging 1976.[8]The cases were also observed for other systemic effects of asphyxia.
3. Urine sample were collected from the neonates and sent for: The spot urine samples were collected within 6-24 hours of life. The procedure was carried out using sterile urine collection bags, after which urine samples were frozen at - 20°C until analyses could be carried out. Uric acid and creatinine in single urine sample were determined by auto analyzer.

III. Result

In our study, the mean urinary uric acid to creatinine ratio in cases was 2.58±1.09, whereas it was 0.86±0.17 in control group.

Table 1: Comparison of UUA/Cr ratio in the Two Groups Studied

UUA/Cr	Cases	Controls
Min-Max	0.78-4.94	0.42-1.14
Mean ± SD	2.58±1.09	0.86±0.17
Inference	UUA/Cr ration is significantly higher in study group compared to control with t=11.052; P<0.001**	

UUA/Cr ratio is significantly higher in study group compared to Control with t=11.052; P<0.001.

IV. Discussion

The present study revealed significant increase in UA/Cr ratio in early spot urine samples from asphyxiated full term newborns and also proved positive correlation between the urinary UA/Cr ratio. In a study by Pallab Basu et al (2008)[9] it was found that urinary UA/Cr ratio was significantly higher in cases than controls (3.1± 1.3 vs 0.96 ± 0.54; p < 0.001) which is similar to our study.Another study by BADER et al (1995)[10] also showed UA/Cr was higher in the asphyxiated group when compared to controls (2,06 + 1.12, vs.0.64 + 0.48; P < 0.001) which is similar to our study The results of the present study were in concordance with those of Reem Mahmoud and Dina El Abd (2010)[11] who reported Urinary UA/Cr ratios were higher in asphyxiated infants (2.9 ±0.73) when compared with the controls (0.72±0.35, P<0001).

Table 2: Comparative Study of Baseline Characteristics of Cases And Controls With Similar Studies.

Characteristics	Pallab Basu et al[9]		BADER et al[10]		Reem Mahmoud Dina El Abd[11]		Present study	
	Cases (n =31)	Control(n =31)	Cases (n =18)	Control (n =50)	Cases (n=40)	Control (n=20)	Cases (n=55)	Control (n=55)
Urinary uric acid and creatinine ratio	3.1±1.3	0.96±0.54	2.06±1.12	0.64±0.48	2.9±0.73	0.72±0.35	2.58±1.09	0.86±0.17

V. Conclusion

Perinatal asphyxia is a common neonatal problem and contributes significantly to neonatal morbidity and mortality. The signs of asphyxial injury are nonspecific and overlap with other illnesses. In the absence of perinatal records, it is difficult to retrospectively diagnose perinatal asphyxia. Infants with asphyxia have higher urinary uric acid to creatinine ratio. It might be used as an indicator for assessment of severity of birth asphyxia and post asphyxia renal injuries in neonates. So urinary uric acid to creatinine ratio can be used as an additional non-invasive, early, easy and cost effective biochemical marker of perinatal asphyxia which biochemically supports the clinical diagnosis.

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