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Usefulness Of Urinary Uric Acid/Creatinine Ratio In Predicting Perinatal Asphyxia

Raja Senathi Radha MD[1], Karthic Kumar Kathavarayan MD[2], Jakanattane Venkatakrishnan MD[3]

[1]Assistant Professor, Department of Paediatrics, Government Sivagangai Medical College, Tamil Nadu, India
[2]Assistant Surgeon, Government Headquarters Hospital and DNB PG Teaching Institute, Cuddalore, Tamil Nadu, India
[3]Assistant Professor, Department of Paediatrics, Aarupadai Veedu Medical College and Hospital, Puducherry, India

***Corresponding Author:**
Dr. Jakanattane. V
Assistant Professor, Department of Paediatrics,
Aarupadai Veedu Medical College and Hospital, Puducherry

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Abstract

Introduction

Perinatal Asphyxia is the most common cause of morbidity and mortality in developing countries. The diagnosis of perinatal asphyxia based on apgar score in low resource settings may be difficult because most of the times relevant information regarding delivery is unavailable. Therefore, an alternative method is needed for diagnosis and grading which will be cost-effective.

Aim

To assess the urinary uric acid/creatinine ratio in relation to Apgar score to predict perinatal asphyxia in our clinical setting.

Methodology

This was a case control study conducted at a Tertiary Care Teaching Hospital in Southern Tamil Nadu. Data was collected for 80 healthy newborns and 80 asphyxiated newborns. Spot urine sample was collected within 24 hours of delivery and urinary uric acid, creatinine were measured. Statistical analysis was performed by Independent t-test, spearman correlation and Receiver Operating Characteristic (ROC).

Results

The mean urinary uric acid/creatinine ratio in cases [1.60± 0.77] were significantly higher compared to the controls [0.85±0.12](p value <0.0001). The correlation between Apgar score at five minutes and Urinary uric acid/ creatinine ratio was negative and significant(Spearman's rho= -0.552), p value<0.0001. Receiver operating characteristic plots showed the urinary uric acid/creatinine ratio with criterion ≥0.93 had predicted perinatal asphyxia with Sensitivity 90%, Specificity 80% and AUC 0.95 (p value<0.0001).

Conclusion

Urinary uric acid/creatinine ratio within 24 hours of life is safe, easily accessible, non-invasive, harmless and cost-effective marker with good predictive value for identifying perinatal asphyxia in a low resource setting.

Keywords: APGAR Score, Asphyxia prediction, Urinary uric acid/creatinine ratio

INTRODUCTION

Perinatal Asphyxia is the most common cause of morbidity and mortality in developing countries [1]. It is characterised by an impaired gas exchange thereby causing hypoxemia, hypercapnia and acidosis in neonate [2]. In developing countries, low resource settings may lead to difficulty in diagnosing and

grading asphyxia as most of the times relevant information regarding delivery is not available [3]. Although good number of studies are available stating the mechanisms that lead to birth asphyxia [4], studies on early markers of tissue damage due to birth asphyxia are insufficient. At present, the most commonly used assessment method in a low resource setting for diagnosis of birth asphyxia in neonate is apgar score [5]. Many factors like prematurity, fetal malformations, maternal medications affect apgar score and hence it is not useful in predicting the neurological outcome [6]. Apart from apgar score, other investigations such as Blood Gas Analysis, measuring the levels of xanthine, hypoxanthine, neuron specific enolase, inflammatory cytokines (Tumor Necrosis Factor-α, Interleukin-1-β, Interleukin-8) are available, but these are costly and not suitable for low resource settings [7, 8]. Therefore, an alternative method is needed for diagnosis and grading which will be cost effective. Measurement of urinary uric acid and creatinine could be a better alternative as reported by few studies. Hence this study was conducted to assess the urinary uric acid/creatinine ratio in relation to Apgar score to predict perinatal asphyxia in our clinical setting.

MATERIALS AND METHOD

The study was conducted in Department of Paediatrics and Neonatology of a Tertiary Care Teaching Institute of Southern Tamil Nadu, India after the approval of Institutional Ethical Committee. The study was a Prospective Case Control Study, done from July 2014-June 2015. After getting parental consent, we included 160 neonates in the study (80 cases and 80 controls). 80 neonates with ≥34 weeks of gestation admitted to Neonatal Intensive Care Unit (NICU) with an apgar score of ≤6 at 5 minutes were included in case group. 80 neonates with ≥34 weeks of gestation with an apgar score of ≥7 at 5 minutes with no signs of asphyxia were included in control group. Neonates with major congenital malformations, metabolic diseases, and anuria were excluded from our study. Other exclusion criteria being neonates born to mother with hypertension, diabetes mellitus, receiving general anaesthesia or other drugs that may cause depression in newborns and history of febrile illness in mother within2 weeks before delivery. A proforma was used to record details such as gestational age, birth weight, perinatal history and relevant clinical findings.

Spot urine sample was collected within 24 hours of delivery. Collection of urinary sample was done via urinary bag pasted around the genital region with aseptic precautions. The spot urine sample collected was analysed in the hospital laboratory for uric acid and creatinine using spectrophotometric uricase method and modified kinetic jaffe's method respectively.

Statistical analysis was performed using Microsoft excel 2013 and SPSS 16. p-value of less than 0.05 was considered statistically significant. Receiver operating characteristics (ROC) plots were used to determine the cut-off values of various parameters.

RESULTS

Our study included 42 males and 38 females in asphyxiated group, while 39 males and 41 females were included in control group. The difference in sex distribution occurred mainly because the babies were matched for gestational age rather than sex. The mean gestational age in asphyxia group and control group were 37.38±1.95 weeks and 37.61±2.08 weeks respectively. The mean birth weight in asphyxiated newborns and normal newborns were 2.68±0.43 kg and 2.75±0.39 kg respectively as shown in table 1.

The mean Apgar score at 1 minute in cases and controls were 3.61±0.77 and 6.76±0.55 respectively. The mean Apgar score at 5 minute in cases and controls were 5.65±0.81 and 8.45±0.50 respectively (p value <0.05) as shown in table 2.

The mean urinary uric acid and urinary uric acid/creatinine ratio in cases [27.08±11.95, 1.60± 0.77] were significantly higher when compared to the controls [17.25±4.62, 0.85±0.12] (p value <0.0001) as shown in table 3.

Receiver operating characteristic (ROC) plots showed the urinary uric acid/creatinine ratio with criterion ≥0.93 had predicted perinatal asphyxia with Sensitivity 90%, Specificity 80% and AUC (Area Under Curve) 0.95 (p value<0.0001) as shown in fig 1. The correlation between Apgar score at five minutes and Urinary uric acid/ creatinine ratio was negative and significant (Spearman's rho= -0.552), p value<0.0001.

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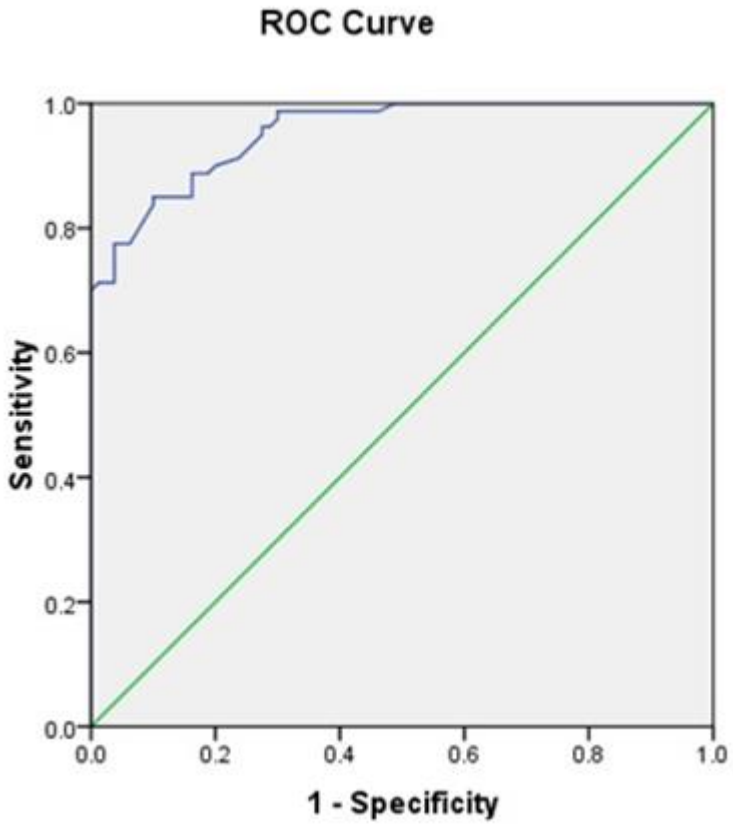
Figure 1: Diagnostic Cut-off of Urinary Uric Acid/ Creatinine Ratio Using Roc Curve (derived from statistical analysis of our study using software and not taken from external source)



The urinary uric acid creatinine ratio of the Hypoxic Ischaemic Encephalopathy (HIE) stage 1 babies were significantly lower than that of Stage 2 ($p<0.0001$) and Stage 3 ($p<0.0001$) children. The ratio of the HIE stage 2 babies were significantly lower than that of HIE Stage 3 babies ($p<0.0001$) as shown in table 4. The correlation between HIE stage and Urinary uric acid/ creatinine ratio was positive and significant (Spearman's rho=0.866), p value<0.0001.

DISCUSSION

Our study included a total of 160 cases (80 cases and 80 controls). We included preterm babies equal to 34 weeks or greater, since babies with lesser gestational age have an elevated body uric acid levels which would be reflected in the urine and also because of the immaturity of the kidneys, the excretion would be more.

The mean urinary uric acid to creatinine ratio between cases and controls was 1.60+0.77 vs 0.85+0.12 respectively. This was comparable with other studies done by Chen et al [9] which showed the mean urinary uric acid to creatinine ratio between cases and controls to be 1.53+0.71 vs 0.73+0.45 respectively. Similar observation was made in a study by Bader et al [10].

In our study, the difference in ratio between various HIE staging were HIE1 vs HIE2 vs HIE3 - 1.1950+0.20860 vs 2.438+0.367 vs 3.315+0.40423 which was statistically significant. This was comparable with the study done by Varma et al [11] where it was 1.23+0.52 vs 2.01+0.42 vs 4.24+0.79 and statistically significant. The results were also comparable with the study done Akisu et al [12]. The correlation between apgar score at 5 minutes and urinary uric acid creatinine ratio was negative and significant ($r= -0.552$, $p<0.0001$) and this was in comparison with the study done by Basu et al who also found negative correlation with statistical significance ($r = -0.857$, $p<0.001$).

Perinatal asphyxia is known for its potential to cause permanent damage to the newborn. The most commonly used indicator for asphyxia is low apgar score, but many times it is unavailable in low resource setting and also it may be reduced in case of

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prematurity [6]. Advancements in the investigations supporting the diagnosis of asphyxia have concerns like availability and cost to perform in a low resource setting. From our study, urinary uric acid/creatinine ratio >0.93 in spot urine within 24 hours of life had sensitivity 90%, specificity 80% with AUC 0.95 ($p<0.0001$) is a better marker of perinatal asphyxia in a low resource setting. Increased urinary uric acid/creatinine ratio may reflect impaired oxygen delivery in the neonate as it indicates an increased Adenosine Tri Phosphate (ATP) degradation [13].

CONCLUSION

Urinary uric acid to creatinine ratio within 24 hours of life is safe, easily accessible, non-invasive, harmless and cost-effective marker with good predictive value for identifying perinatal asphyxia in a low resource setting.

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TABLES

Parameters	Control	cases
Sex Males Females	 39(48.75%) 41(51.25%)	 42(52.5%) 38(47.5%)
Gestational age	37.61±2.08	37.38±1.95
Birth weight	2.75±0.39	2.68±0.43

Table 1: Profile Of The Study Participants

Apgar score	Controls	Cases
At 1 minute	6.76±0.56	3.61±0.77
At 5 minutes	8.45±0.50	5.65±0.81

Table 2: Comparison of Apgar scores between cases and controls

Parameters	Controls	Cases	pvalue
Urinary Uric acid	17.25±4.62	27.08±11.95	<0.0001
Urinary Creatinine	20.26±4.74	17.56±4.78	<0.0001
Urinary Uric acid/ creatinine ratio	0.85±0.11	1.60±0.77	<0.0001

Table 3: Comparison of Biochemical Parameters between Cases and Controls

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HIE	N=160 (cases+controls)	Urinary Uric acid/Creatinine Ratio Mean±SD
No HIE	96	0.87±0.11
HIE stage 1	37	1.19±0.21
HIE stage 2	17	2.44±0.38
HIE stage 3	10	3.32±0.40

Table 4: Comparison of Urinary uric acid/Creatinine ratio across HIE stages

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