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Original Research Article

A Study of Correlation Between Apgar Score and Urinary Uric Acid to Creatinine Ratio in Perinatal Asphyxia

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ABSTRACT

Background: Perinatal asphyxia refers to an impairment of the normal oxygenation during birth and the ensuing adverse effects on the neonate. Low Apgar score is commonly used to as an indicator of asphyxia, but it may not be available in all newborns, especially in extramural babies. Also, Apgar score alone does not predict neurologic outcome as it is influenced by various factors. So, the present study was conducted to find correlation between Apgar score and urinary uric acid to creatinine ratio in babies with perinatal asphyxia.

Methodology: The present study was an observational case control study conducted in tertiary care hospital in southern part of Gujarat state. We recruited 56 babies with moderate to severe asphyxia and compared them with 56 babies without asphyxia. Uric acid (UA) to creatinine (Cr) ratio was calculated on spot urine samples within 24 hours of birth and a Receiver Operator Curve (ROC) was plotted.

Results: Mean UA/Cr ratio among cases was 2.58±1.15 as compared to control group where the ratio was 0.71±0.21 ($p < 0.00001$). Using the ROC curves, cut off of UA/Cr of 1.24 was found to have a sensitivity of 94.6% and specificity of 98.2%. Area under the curve was 98.8%. A significant negative linear correlation was found between urinary UA/Cr ratio and the Apgar score ($r = -0.7188$, $p < 0.001$) among cases.

Conclusions: Urinary uric acid to creatinine ratio is a useful marker to diagnose perinatal asphyxia when Apgar scores are unavailable and also to judge the severity of asphyxia.

Keywords: Apgar Score, Perinatal Asphyxia, Urinary Uric Acid to Creatinine Ratio

INTRODUCTION

Perinatal asphyxia is one of the leading causes of neonatal morbidity and morbidity in developing countries.[1,2] In babies with perinatal asphyxia, there is impaired cerebral blood flow and gas exchange. In developing countries, many deliveries are not attended by personnel trained in resuscitation. In such cases, accurate diagnosis and grading of asphyxia is challenging.[3,4] Perinatal asphyxia impairs cerebral oxidative metabolism and leads to anaerobic glycolysis. So, 2 molecules of ATP are produced instead of 38 molecules produced during aerobic glycolysis.[5,6] Prolonged hypoxia further leads to failure of oxidative phosphorylation causing accumulation of AMP and ADP. These are further catabolized to adenosine, inosine and hypoxanthine. When there is reperfusion injury, hypoxanthine is oxidized to xanthine and uric acid in presence of xanthine oxidase. This increased uric acid is then excreted in urine, which can be detected by spot analysis.[7]

India contributes close to 25% of global burden of neonatal mortality.[8] Apgar score is most commonly used parameter

to assess the severity of birth asphyxia.[9] However, in extramural deliveries, it isn't available many times. Measurement of other metabolites like xanthine, hypoxanthine, etc. in serum is costly.[10,11] So this study was undertaken to assess the correlation between urinary uric acid to creatinine ratio and Apgar score.

METHODOLOGY

The present study was conducted in the Department of Paediatrics of a tertiary care hospital in South Gujarat. Ethics clearance was obtained from institutional ethics committee before starting the study. Data collection was done between January 2017 to September 2017.

A total of 112 babies were included in study. 56 babies more than 35 weeks of gestation, with Apgar score of 7 or more were included as controls. 56 newborns more than 35 weeks of gestation with Apgar score of 6 or less at 5 minutes after birth were selected as cases. Selection of cases was done by non-random sampling. In the absence of regional estimates, we took level of significance at 90%, alpha error of 5% and estimated incidence of asphyxia was 5.2% in our unit. Babies with congenital malformations, suspected metabolic disease and those born to mothers having hypertension, diabetes mellitus, toxemia of pregnancy, and receiving general anesthesia were excluded. The spot urinary samples within 24 hours of birth were collected in sterilized disposable urine bag and analyzed in hospital laboratory for UA/Cr ratio. Urinary uric acid was estimated by auto analyzer by spectrophotometric uricase method. Urinary creatinine was also estimated in same instrument by using Jaffe's alkaline picrate method. The results obtained were compared with the Apgar score of the patient in order to determine the utility of ratio in determining severity of disease.

For statistical analysis, the data was entered in MS-Excel database. Descriptive analyses for inter-group comparison were done using unpaired t-test and chi-square test. Receiver operating characteristic (ROC) plots were used to determine the cut-off values of UA/Cr. A p value of < 0.05 was considered significant. Bivariate distribution analysis was used to determine the correlations {two-tailed Karl Pearson's coefficient of correlation (indicated as "r") was used to identify the correlation between numerical variables}. Confidence intervals at 95% confidence limit of the parameters were also determined.

RESULTS

The demographic details of cases and controls are shown in Table-1. Mean birth weight among cases was 2.67±0.68 Kg and among the controls was 2.82±0.65 Kg. Mean gestational age of cases was 36.96±2.97 weeks and among the controls was 37.67±2.89 weeks. Both groups were comparable.

Table-1: Demographic details of cases and controls

	Cases	Controls
Number	56	56
Female/ Male (n)	20/36	23/33
Birth Weight (Kg)	2.67±0.68	2.82±0.65
Gestational Age (Weeks)	36.96±2.97	37.67±2.89
Vaginal delivery [n (%)]	41 (73.21%)	44 (78.5 %)
LSCS [n (%)]	15 (26.7%)	12 (21.42 %)
Inborn / Out born (n)	47/9	44/12

Among the cases, 27 (48.21%) had moderate birth asphyxia and 29 (51.78%) had severe birth asphyxia. Of the 56 cases, 19 were having Hypoxic-ischemic encephalopathy (HIE) stage 1, 19 had HIE stage 2 and 18 had HIE stage 3, using the Sarnat and Sarnat scoring system. Mean Apgar score at 5 minutes of birth was 3.44±1.30 among the cases as compared to the control group where the mean score was 8.17±0.43. This difference was statistically significant. ($p < 0.00001$). Mean UA/Cr ratio among cases was 2.58±1.15 as compared to control group where the ratio was 0.71±0.21. This difference was statistically significant ($p < 0.00001$). Among the 19 patients with HIE stage 1, the mean UA/Cr was 1.54±0.33 as compared to 0.71±0.21 among the controls ($p < 0.001$). Among the 19 patients with HIE stage 2 the mean UA/Cr was 2.36±0.47. Among the 18 patients with HIE stage 3, the mean UA/Cr was 3.94±0.87 (Figure-1). Table-2 shows that patients with HIE Stage 3 had higher ratio of UA/Cr and also mortality was higher (69%) as compared to patients with HIE Stage 2 (15.7%) and HIE Stage 1 (10.5%). Using the ROC curves, cut off of UA/Cr of 1.24 was found to have a sensitivity of 94.6% and specificity of 98.2%. Area under the curve (AUC) was 98.8%. (Figure-2).

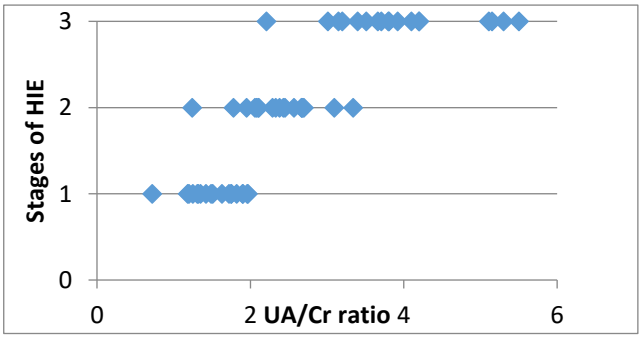

Figure-1: Distribution of UA/Cr among stages of HIE

Table-2: Urinary Uric Acid to Creatinine ratio in relation to HIE

	HIE Stage 1	HIE Stage 2	HIE Stage 3
Number	19 (34 %)	19 (34 %)	18 (32 %)
UA/Cr	1.54 ± 0.33	2.36 ± 0.47	3.94 ± 0.87
Mortality	2 (10.5 %)	3 (15.7 %)	11 (69 %)
Discharged	17 (89.5 %)	16 (84.3 %)	7 (31 %)

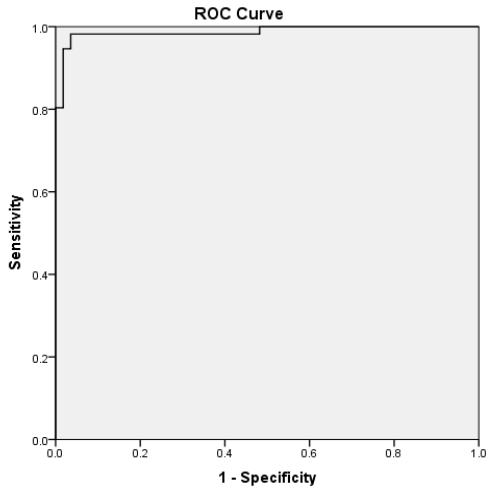

Figure-2: ROC curve for UA/Cr

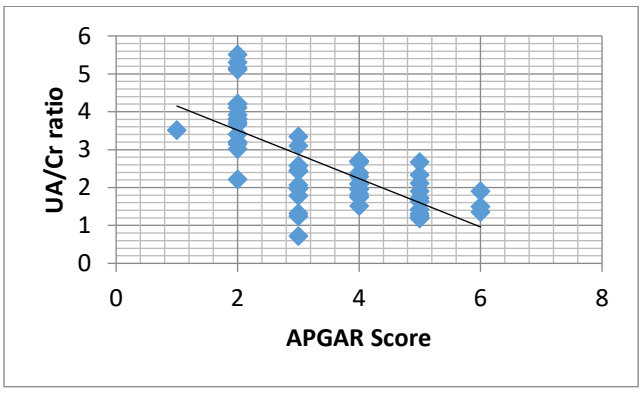

Figure-3: Correlation between UA/Cr and Apgar score

Karl Pearson coefficient was used to find correlation between UA/Cr and Apgar score (Figure-3).
A significant negative linear correlation was found between urinary UA/Cr ratio and the Apgar score ($r = -0.7188$, $p < 0.001$) among cases. No significant correlation was found between urinary UA/Cr ratio and the Apgar score among controls ($r = 0.0027$, $p < 0.107$).

DISCUSSION

The present study was conducted to determine whether urinary uric acid to creatinine ratio can be used as a cheap, non-invasive and quick method to determine the severity of birth asphyxia and whether this ratio can be used to predict the prognosis in neonates with perinatal asphyxia. Low Apgar score is mostly commonly used for diagnosis of asphyxia in infants, but it may often be not available if delivery is not attended by trained personnel. Other investigations that support the diagnosis of asphyxia would be required in such case. This study shows that urinary UA/Cr ratio > 1.24 in spot urine sample within 24 hours of life had 94.6% sensitivity, 98.2% specificity with AUC of 98.8% ($p < 0.0001$) is a better marker for perinatal asphyxia. Increased urinary UA/Cr ratio can thus be considered a useful investigation for impaired oxygen delivery in the newborn.

In the present study, the mean UA/Cr ratio was 2.58±1.15 among the cases and 0.71±0.21 among the controls. This difference was statistically significant. Similar results were obtained by Pallab Basu et al.[12] i.e., 3.1±1.3 vs 0.96±0.54 ($p < 0.001$) and also by K Sathya Praveen Reddy et al[13] i.e., 2.65 ± 053 ($p < 0.001$). Bader et al found increased UA/Cr ratios in the urinary samples of 18 term newborns asphyxiated in the first 24 hours of life. They concluded that these ratios showed significant correlation with the asphyxia scores.[14] Kumar et al. conducted a study 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/Cr) ratio value of >1.14 was taken as the cut-off level. The urinary UA/Cr ratios were found to be higher in asphyxiated infants (2.58±1.09) when compared with those in the controls (0.86 ± 0.17) which also is in favor of our study. Our results are also supported by Chen et al. who suggested that urinary ratio of UA to creatinine was significantly higher in both full term and preterm infants with perinatal asphyxia than in those without perinatal asphyxia.[15]

In our study, the value of urinary uric acid to Creatinine among cases with HIE stage 3 (3.94±0.87) were higher than those in cases with HIE stage 2 (2.36±0.47) and stage 1 (1.54±0.33). These differences were statistically significant. Our results were in concordance with results obtained by Erdag et al. in a similar study.[16] Thus, we can conclude that these ratios can be used to predict the severity of HIE i.e., the higher the ratio, the higher will be the stage of HIE. Our study shows that mortality was significantly higher in those patients with higher UA/Cr. Shahin Nariman et al had also concluded that the Urinary uric Acid /Creatinine ratio increases with the severity of disease and is associated with

longer duration of stay and adverse outcome. Thus, it can be said that the increasing value of this ratio can be a useful guide to determine the outcome in these patients. In our study using the ROC curves, cut off of UA/Cr of 1.24 was found to have a sensitivity of 94.6% and specificity of 98.2%. Area under the curve was 98.8%. In similar study conducted by K Patel et al, cut off value found using ROC plots was 2.3. Sensitivity and specificity at this point was 100%. AUC was 100 %.[17] In the present study there was significant negative linear correlation between Apgar score and UA/Cr ratio ($r = -0.7188$, $p < 0.001$). In a similar study conducted by Basu et al, a significant negative linear correlation was found between urinary UA/Cr ratio and the Apgar score ($r = -0.857$, $p < 0.001$) among cases.[12] Similar findings were also observed in study by Krishnan AR et al., with $r = -0.52$, $p = 0.001$.[18]

LIMITATIONS OF THE STUDY

It is a single center study with a small sample size, so result cannot be generalized on whole population. Many of birth asphyxia patients do not pass urine within 24 hours of life. In our study, we did not correlate urinary UA/Cr with other biochemical markers. We have not included the use of cord blood pH in determining severity of birth asphyxia.

CONCLUSIONS

Urinary UA/Cr ratio is an accessible, non-invasive, painless and cost-effective investigation with good predictive value for diagnosing perinatal asphyxia. Further multicentric studies and systematic reviews are needed to study its utility in this aspect.

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