

Spot Urine Uric Acid Level as Early Marker of Kidney Injury in Birth-asphyxiated Newborns

Darshan Kataria¹, Karan Joshi², Jyoti Singh³

¹Post Graduate, Department of Pediatrics, Shyam Shah Medical college and Gandhi Memorial Hospital, Rewa - 486001, Madhya Pradesh, India, ²Associate Professor, Department of Pediatrics, Shyam Shah Medical college and Gandhi Memorial Hospital, Rewa - 486001, Madhya Pradesh, India, ³Professor and Head, Department of Pediatrics, Shyam Shah Medical college and Gandhi Memorial Hospital, Rewa - 486001, Madhya Pradesh, India

Abstract

Introduction: Perinatal asphyxia is a condition defined as hypoxemia, hypercapnia, and acidosis in neonate. Cellular hypoxia leads to increased excretion of uric acid. This study was conducted to assess the feasibility of urine uric acid level for the identification of kidney injury in asphyxiated newborns in first 48 h of life.

Aims and objectives: The aims and objectives of this study were to evaluate the utility of urinary uric acid levels within 48 h of birth as non-invasive and early biochemical means of identifying kidney injury in birth asphyxiated neonates.

Material and methods: Study design - this was a prospective observational cohort study. Settings - this study was conducted at neonatal intensive care unit in tertiary level hospital in Central India. Duration - the study duration was from July 2017 to June 2018. Due to financial constraints, 100 neonates were enrolled and urine sample collected within 48 h of life was evaluated for urine uric acid level. On day 3rd of life, serum creatinine was done. Statistical analysis was performed by Mann-Whitney *U*-test.

Results: The mean rank of urine uric acid (32.76 vs. 20.29) was significantly higher in term newborns as per asphyxia ($P = 0.005$). The mean rank of urine uric acid (24.13 vs. 15.46) was significantly higher in term asphyxiated as per urine output ($P = 0.031$). However, the mean rank of urine uric acid (23.29 vs. 16.00) was not significant in term asphyxiated newborns as per serum creatinine ($P = 0.08$).

Conclusions: Urine uric acid = 16.10 $\mu\text{mole}/24\text{ h}$ has a sensitivity (61.4%) and specificity (72.2%) for detecting asphyxia in newborns. Similarly, urine uric acid = 22.3 $\mu\text{mole}/24\text{ h}$ has a sensitivity (66.7%) and specificity (91.4%) for detecting kidney injury in asphyxiated newborns.

Key words: Birth asphyxia, Neonatal kidney injury, Urine uric acid

INTRODUCTION

Perinatal asphyxia is a condition where impaired gas exchange leads to hypoxemia, hypercapnia, and acidosis in fetus or neonate. The incidence of perinatal asphyxia is 2–10/1000 term newborns (1–5.6% of all live births). In India, 0.5–1 million cases of birth asphyxia are seen per year and it comes out to be the main cause of mortality (28.8%) and morbidity and chief cause of

stillbirth (45.1%).^[1] Birth asphyxia can involve any organ, i.e., the kidney (50%), heart (25%), or brain (28%) and hence can lead to multisystem failure. As the severity of birth asphyxia increases, the chances of having kidney injury also increase. Brief hypoxia damages cerebral oxidative metabolism leading to an anaerobic glycolysis, yielding only two molecules of adenosine triphosphate (ATP) as compared to 32 molecules of ATP during aerobic conditions.^[2] Lack of ATP and increased cellular destruction will cause an accumulation of adenosine monophosphate and adenosine diphosphate, which will then get catabolized to its constituents of adenosine, inosine, and hypoxanthine.^[3,4] Continuous tissue hypoxia and consequent reperfusion injury will result in hypoxanthine being oxidized to xanthine and uric acid in the presence of xanthine oxidase. Increased excretion of uric acid caused by metabolic changes, reflecting

Access this article online



www.ijss-sn.com

Month of Submission : 12-2018
Month of Peer Review : 01-2019
Month of Acceptance : 01-2019
Month of Publishing : 02-2019

Corresponding Author: Dr. Karan Joshi, Associate Professor HIG-75C, Jaiprakash Narayan Nagar, Behind P.K. School, Rewa - 486001, Madhya Pradesh, India. Phone: +91-9425184975. E-mail: darshank300@gmail.com

the cellular hypoxia, has been reported by a number of studies.^[5,6] Urine uric acid: creatinine ratio has been found to be raised in asphyxia in many studies, but no study was relating to urine uric acid with kidney injury. Hence, in this study, we tried to assess the value of urine uric acid in the identification of kidney injury in asphyxiated patients in first 2 days of life.

MATERIALS AND METHODS

Study Design

This was a prospective observational cohort study.

Settings

This study was conducted at neonatal intensive care unit in tertiary level hospital in Central India.

Duration

The study duration was from July 2017 to June 2018.

Inclusion Criteria

Newborns of both sexes irrespective of gestational age or birth weight having:

1. Persistence of Apgar score <3 at 5 min and/or
2. Newborns requiring resuscitation with positive pressure ventilation (PPV) for >1 min before achieving stable spontaneous respiration were included in the study.

Exclusion Criteria

The following criteria were excluded from the study:

1. Newborns with any congenital urological anomaly.
2. Family history of genetic disorder (disease running in families).
3. Newborn who could not be included due to researcher financial constraints.

Initially, 250 newborns came as sample size, but, due to financial constraints, only 100 patients were enrolled in the study (Flow chart).

The urine sample was collected within first 48 h of life with all aseptic precautions and was assessed for uric acid by autoanalyzer using spectrophotometry uricase method. Serum creatinine was analyzed on the 3rd day of life by Jaffe's alkaline picrate method, respectively.

Kidney injury

An abrupt decrease in glomerular filtration with or without underlying structural abnormalities often presents with:

- Reduction in urine output (<1 ml/kg/h for 6 h) and/or
- Serum creatinine value of >1.5 mg/dl irrespective of gestational age and days of life.

Analysis was performed using the commercially available statistical software-IBM SPSS version 22 and Microsoft Excel. The statistical analysis between variables was done using Mann-Whitney U-test. $P < 0.05$ was considered to be statistically significant.

RESULTS

Of 100 neonates enrolled in study, 20 neonates could not complete the study, and hence, 36 normal and 44 asphyxiated neonates completed the study. Of 80 neonates, 55 (68.75%) neonates were male. As per gestational age, 23 (28.7%) neonates were pre-term, 2 (2.5%) were post-term, and 55 (68.8%) were term neonates [Table 1 and Chart 1].

The mean rank of urine uric acid (32.76 vs. 20.29) was significantly higher in term asphyxiated newborns than in term non-asphyxiated newborns ($P = 0.005$). The mean rank of urine uric acid (13.13 vs. 11.40) was not statistically significant in preterms as per asphyxia indicator ($P = 0.561$) [Table 2].

The mean rank of urine uric acid (24.13 vs. 15.46) was significantly higher in term asphyxiated as per urine output ($P = 0.031$) [Table 3]. However, the mean rank of urine uric acid (23.29 vs. 16.00) was not significant in term asphyxiated newborns as per serum creatinine ($P = 0.08$) [Table 4].

Urine uric acid has a sensitivity (61.4%), specificity (72.2%), and PPV (73%) in asphyxiated term newborns. Similarly, urine uric acid has a sensitivity (66.7%), specificity (91.4%), and PPV (67%) in term asphyxiated newborns as per urine output [Table 5].

DISCUSSION

Perinatal asphyxia is a condition that can lead to alteration in normal functioning of various body organs, but the

Table 1: Distribution of sample as per gestational age and birth asphyxia

| Asphyxia indicator | Total number of patients | Pre-term | Term | Post-term |
|--------------------|--------------------------|----------|------|-----------|
| Yes | 44 | 8 | 34 | 2 |
| No | 36 | 15 | 21 | 0 |

Table 2: Comparison of urine uric acid in term and preterm neonates as per asphyxia indicator

| Asphyxia Indicator | Number of newborns | | Urine uric acid ($\mu\text{mole}/24\text{ h}$) mean rank | |
|--------------------|--------------------|------|--|-------|
| | Preterm | Term | Preterm | Term |
| Yes | 8 | 34 | 13.13 | 32.76 |
| No | 15 | 21 | 11.40 | 20.29 |

P value in term=0.005, significant, P value in preterm=0.561, non-significant

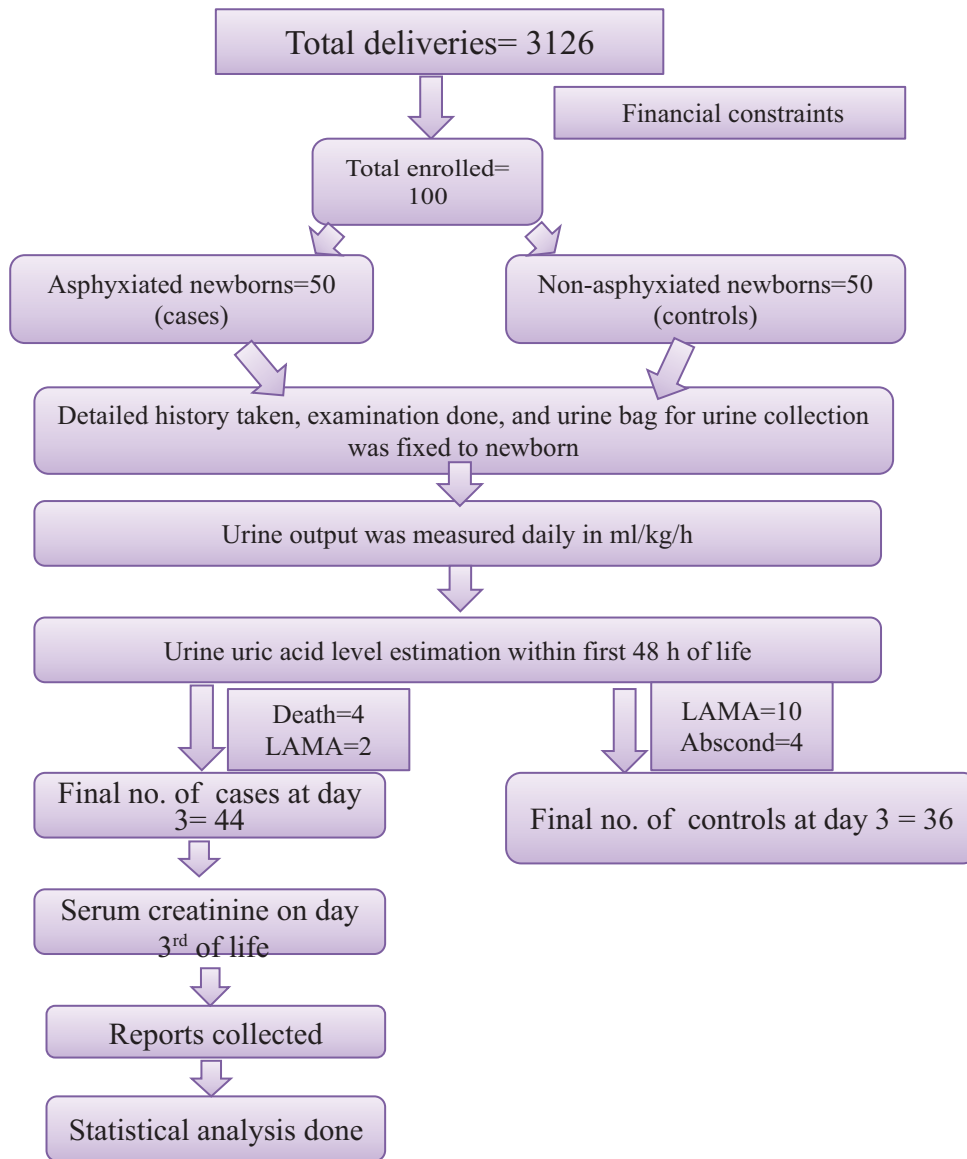


Chart 1: Flow chart sample of newborn

Table 3: Comparison between urine uric acid and term asphyxiated neonates as per urine output

| Urine Output (ml/kg/h) | Number of neonates (asphyxiated) | Urine uric acid (µmole/24 h) mean rank |
|-------------------------|----------------------------------|--|
| Urine output ≥1 ml/kg/h | 26 | 15.46 |
| Urine output <1 ml/kg/h | 8 | 24.13 |

Observed $P=0.031$, significant

Table 4: Comparison of urine uric acid in term asphyxiated neonates as per serum creatinine

| Serum creatinine level (mg%) | Number of neonates | Urine uric acid (µmole/24 h) mean rank |
|------------------------------|--------------------|--|
| Serum creatinine ≤1.5 | 27 | 16.00 |
| Serum creatinine >1.5 | 7 | 23.29 |

P value=0.08, non-significant

most commonly affected organ is the kidney. There are a number of studies available that focused on urine UA/Cr

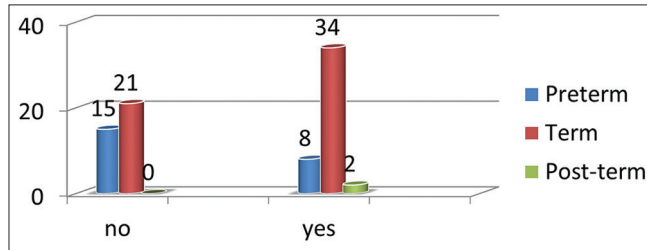
ratio while considering asphyxiated and non-asphyxiated neonates.

In 2008, Basu *et al.*^[7] conducted a case-control hospital-based study over 12 months' time on 31 asphyxiated and 31 normal newborns to see whether urinary uric acid and creatinine ratio can be used as a marker of perinatal asphyxia. It was found that the ratios were significantly higher in cases than controls (3.1 ± 1.3 vs. 0.96 ± 0.54 ; $P < 0.001$) and among asphyxia patients.

Table 5: Comparison of sensitivity and specificity of urine uric acid test

| Comparison group (term newborns) | Urine uric acid ($\mu\text{mole}/24\text{ h}$) | Sensitivity (%) | Specificity (%) | PPV (%) |
|--|--|-----------------|-----------------|---------|
| Asphyxiated versus non-asphyxiated newborns | 16.10 | 61.4 | 72.2 | 73 |
| Among asphyxiated newborns as per urine output | 22.3 | 66.7 | 91.4 | 67 |

PPV: Positive pressure ventilation

**Figure 1: Asphyxia indicator**

In 2017, Patel *et al.*^[8] conducted a case-control study at a teaching hospital in Central Gujarat. 40 healthy newborns and 40 asphyxiated newborns were collected, and the mean (UA/Cr ratio) (2.75 ± 0.18 vs. 1.78 ± 0.23) was significantly higher in asphyxiated group than in the control group ($P < 0.0001$).

In our study, we observed that $P = 0.005$ for comparing urine uric acid level between term asphyxiated and term non-asphyxiated neonates was less than the calculated P value at 95% confidence interval. Thus, we concluded that urine uric acid was higher in term asphyxiated as compared to term non-asphyxiated newborns.

We observed $P = 0.561$ (95% confidence interval) when comparison was made between urine uric acid in preterm asphyxiated and non-asphyxiated newborns.

There was a significant correlation between high urine uric acid values and term asphyxiated neonates as per urine output (observed $P = 0.031$), but non-significant correlation was seen between high urine uric acid values and term asphyxiated neonates as per serum creatinine values (observed $P = 0.08$).

Urine uric acid value = $16.10 \mu\text{mole}/24\text{ h}$ has a sensitivity (61.4 %) and specificity (72.2%) for detecting asphyxia in newborns. Similarly, urine uric acid value = $22.3 \mu\text{mole}/24\text{ h}$ has a sensitivity (66.7%) and specificity (91.4%) for detecting kidney injury in asphyxiated newborns.

CONCLUSIONS

In our study, urine uric acid was high in asphyxiated term neonates as compared to non-asphyxiated term

neonates. Urine uric acid was not statistically significant in preterm asphyxiated and preterm non-asphyxiated newborns. Urine uric acid was high in term asphyxiated neonates as per urine output but non-significant as per serum creatinine.

Limitations

We could not find a significant correlation between urine uric acid and serum creatinine in term asphyxiated newborns due to:

1. Sample size was small.
2. Time period boundation or shorter duration of the study.
3. It may be likely that the high serum creatinine in some newborn without kidney injury was due to high maternal levels.
4. Normally, a rise in serum creatinine levels is not seen even when 25% kidneys have been damaged.
5. Baseline serum creatinine was not taken.
6. We did not monitor serial rise in serum creatinine levels instead we did only 1 time evaluation.
7. Due to cost factor, urine uric acid estimation of only 80 neonates was possible.

Recommendations

Urine uric acid was higher in term asphyxiated newborns as per urine output. Thus, it is recommended that a larger study with more cohorts needed to validate urinary uric acid as non-invasive and early biochemical means of identifying kidney injury in asphyxiated newborns.

REFERENCES

1. Deorari A, Paul VK, Aggarwal R, Upadhyay A, Chawla D, Girish G. National Neonatal-Perinatal Database. New Delhi: All India Institute of Medical Sciences; 2005.
2. Rich PR. The molecular machinery of Keilin's respiratory chain. *Biochem Soc Trans* 2003;31:1095-105.
3. Manzke H, von Kreudenstein PS, Dörner K, Kruse K. Quantitative measurements of the urinary excretion of creatinine, uric acid, hypoxanthine and xanthine, uracil, cyclic AMP, and cyclic GMP in healthy newborn infants. *Eur J Pediatr* 1980;133:157-61.
4. Deorari A, Vinod KP, Aggarwal R, Aggarwal R, Upadhyay A, Chawla D, *et al.* National neonatal-perinatal database. *Natl Neonatol Forum NNPD Netw Nodal Centre : AIIMS, New Delhi, 2002-2003*;1-70.
5. Pietz J, Guttenberg N, Gluck L. Hypoxanthine: A marker for asphyxia. *Obstet Gynecol* 1988;72:762-6.
6. Lam HS, Ng PC. Biochemical markers of neonatal sepsis. *Pathology* 2008;40:141-8.

7. Basu P, Som S, Choudhuri N, Das H. Correlation between apgar score and urinary uric acid to creatinine ratio in perinatal asphyxia. *Indian J Clin Biochem* 2008;23:361-4.
8. Patel KP, Makadia MG, Patel VI, Nilayangode HN, Nimbalkar SM. Urinary uric acid/Creatinine ratio a marker for perinatal asphyxia. *J Clin Diagn Res* 2017;11:SC08-10.

How to cite this article: Darshan Kataria, Joshi K, Singh J. Spot Urine Uric Acid Level as Early Marker of Kidney Injury in Birth-Asphyxiated Newborns. *Int J Sci Stud* 2019;6(11):27-31.

Source of Support: Nil, **Conflict of Interest:** None declared.