



NOVEL NON-INVASIVE DIAGNOSTIC PROCEDURE FOR BIRTH ASPHYXIA RELATED RENAL INJURY IN TERM NEWBORNS

Pediatrics

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ABSTRACT

Introduction- Perinatal asphyxia is a condition defined as hypoxemia, hypercapnea and acidosis in neonate.

Aims & objectives- To evaluate the utility of urinary uric acid levels within 48 hours of birth as means of identifying kidney injury in term asphyxiated neonates.

Material and methods-

Study design- Prospective observational cohort study

Settings- Tertiary level hospital in central India

Duration- July 2017 to June 2018.

Participants- Due to financial constraints 100 neonates were enrolled.

Statistical analysis was performed by IBM SPSS version 22 and Microsoft Excel. Test of significance by Mann-Whitney U test.

Results- The mean rank of urine uric acid level (24.13 vs. 15.46) was significantly higher in term asphyxiated as per urine output ($p=0.031$).

Conclusions- Urine uric acid value of 22.3 micromole/24 hr has a sensitivity (66.7 %), specificity (91.4%) for detecting kidney injury in asphyxiated term newborns.

KEYWORDS

Urine uric acid, birth asphyxia, neonatal kidney injury.

INTRODUCTION

Perinatal asphyxia is a condition where impaired gas exchange leads to hypoxemia, hypercapnea, and acidosis in fetus or neonate. The incidence of perinatal asphyxia is 2 to 10 per 1000 term newborns (1-5.6 % of all live birth) 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%), morbidity and chief cause of stillbirth (45.1%). [1] Birth asphyxia can involve any organ i.e. 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 2 molecules of Adenosine Triphosphate 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 (AMP) and Adenosine Diphosphate (ADP), which will then get catabolised 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 presence of xanthine oxidase. Increased excretion of uric acid caused by metabolic changes, reflecting the cellular hypoxia has been reported by number of studies [5, 6]. Urine uric acid/ creatinine ratio have been found to be raised in asphyxia in many studies but no study was relating urine uric acid with kidney injury.

Asphyxia mainly damages proximal convoluted tubule of kidney and due to which uric acid is not reabsorbed and neither secreted. Hence in this study, we tried to assess the value of urine uric acid in the identification of kidney injury in term asphyxiated patients in first 2 days of life.

MATERIAL AND METHODS-

Study design- Prospective observational cohort study

Settings- Neonatal Intensive Care Unit in tertiary level hospital in central India

Duration- July 2017 to June 2018.

Inclusion criteria-

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

1. Persistence of apgar score less than 3 at 5 minutes.

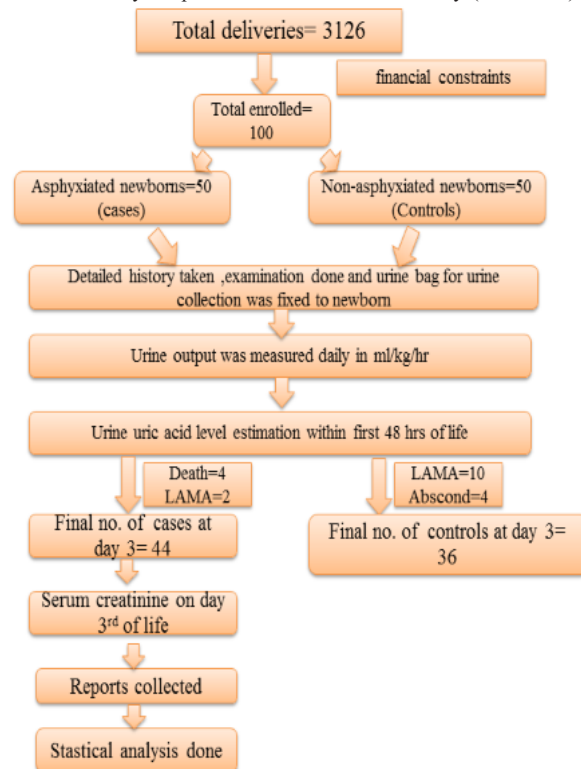
And/or

2. Newborns requiring resuscitation with positive pressure ventilation for >1 minute before achieving stable spontaneous respiration.

Exclusion criteria-

1. Newborns with any congenital urological anomaly.
2. Family h/o 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)



Flow chart Sample size of Newborns

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

Kidney injury-Abrupt decrease in glomerular filtration with or without underlying structural abnormalities often presents with Reduction in urine output (<1 ml/kg/hr for 6 hrs) 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 test. A p value of <0.05 was considered significant.

RESULTS-

Out of 100 neonates enrolled in study 20 neonates couldn't complete study and hence 36 normal and 44 asphyxiated neonates completed the study. Out 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.

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 (24.13 vs. 15.46) was significantly higher in term asphyxiated as per urine output (p=0.031) (table-1).

Table 1- Showing comparison between urine uric acid levels and term asphyxiated neonates as per urine output

Urine Output (ml/kg/hr)	No. of neonates (Asphyxiated)	Urine Uric Acid (micromol/24 hrs) mean Rank
Urine Output ≥1 ml/kg/hr	26(76.5%)	15.46
Urine Output <1 ml/kg/hr	8(23.5%)	24.13

- observed p value 0.031, significant

But 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).

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%), PPV (67%) in term asphyxiated newborns as per urine output (table-2).

Table 2- Comparison of sensitivity and specificity of urine uric acid test

Comparison group (Term newborns)	Urine uric acid (micromol/24 hrs)	Sensitivity	Specificity	PPV
Asphyxiated vs non-Asphyxiated newborns	16.10	61.4 %	72.2 %	73%
Among asphyxiated newborns as per urine output	22.3	66.7 %	91.4%	67%

DISCUSSION-

Perinatal asphyxia is a condition that can lead to alteration in normal functioning of various body organs but the most commonly affected organ is kidney. There are a no. of studies available that focused on urine UA/Cr ratio while considering asphyxiated and non-asphyxiated neonates.

In 2008, Pallab Basu [7] conducted a case control hospital based study over 12 months time on 31 asphyxiated and 31 normal newborn 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.

In 2017, Kinjal Prahalad bhai Patel [8] conducted a case control study at a teaching hospital in Central Gujarat. 40 healthy newborns and 40 asphyxiated newborns were collected, 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 the p value of 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 .

There was significant correlation between high urine uric acid values and term asphyxiated neonates as per urine output (Observed p value= 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 value=0.08).

Urine uric acid value =16.10 micromole/24 hr has a sensitivity(61.4 %), specificity(72.2%) for detecting asphyxia in term newborns. Similarly urine uric acid value =22.3 micromole/24 hr has a sensitivity (66.7 %), specificity(91.4%) for detecting kidney injury in term asphyxiated newborns.

This study shows that urine uric acid levels were high in asphyxiated term neonates as compared to non-asphyxiated term neonates. Urine uric acid levels were high in term asphyxiated neonates as per urine output but non-significant as per serum creatinine.

CONCLUSION-

In our study, urine uric acid was high in asphyxiated term neonates as compared to non-asphyxiated term neonates. Urine uric acid was high in term asphyxiated neonates as per urine output but non-significant as per serum creatinine.

Limitations-

We couldn't find 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 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, rise in serum creatinine levels are not seen even when 25% kidney's have been damaged.
5. Baseline serum creatinine was not taken.
6. We didn't monitor serial rise in serum creatinine levels instead we did only one 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 term newborns.

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