

Original Research Article

# Utility of APGAR score, urinary uric acid and creatinine ratio with perinatal asphyxia

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## Abstract

**Background:** Perinatal asphyxia is a common cause of neonatal morbidity and mortality in the neonatal period and long term neurologic disabilities among survivors. The overall neonatal mortality rate in India is 28/1000 live births. This study was to evaluate the utility of urinary uric acid to creatinine ratio (UA/Cr ratio) as non-invasive, easy, cheap and at the same time early biochemical means of asphyxia diagnosis and also to find out whether APGAR score is still an important tool for birth asphyxia diagnosis and its severity calculation.

**Materials and methods:** The present observational study was conducted at Neonatal care unit of UPUMS, Saifai, Etawah with study population of 121 newborns >34 week suffering from birth asphyxia admitted during the period of February 2017 to December 2018. All the data was collected, compiled, analyzed and interpreted statistically. The statistical analysis was done using SPSS (Statistical Package for Social Sciences) Version 21.0 statistical Analysis Software. The values were represented in Number (%) and Mean  $\pm$  SD.

**Results:** Gestational age of majority of overall neonates (86.78%) as well of Group I (85.71%) and Group II (87.93%) was 36-38 weeks. Gestational age of only 1 (1.59%) neonate of Group I was 38-40 weeks, gestational age of rest of the neonates of both the groups (12.70% and 12.07%) was 34-36 weeks. Gestational age of neonates of Group I and Group II was comparable ( $p=0.623$ ). The comparison of the UA/Cr ratios of 3 stages was also statistically significant. The urinary uric acid and creatinine ratio was progressively increasing ( $2.37\pm 0.34$ ,  $3.08\pm 0.51$ ,  $3.83\pm 0.49$ ) with the severity of asphyxia mild, moderate and severe respectively

**Conclusion:** Urinary UA/Cr ratio is an accessible, non-invasive, painless and cost-effective additional framework with good predictive value for diagnosing perinatal asphyxia. There exists still a need to study these parameters in the context of therapeutic hypothermia and how the parameters change over the period of treatment.

## Key words

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Perinatal asphyxia, Gestational age, APGAR score, UA/Cr ratios.

## Introduction

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Perinatal asphyxia is a common cause of neonatal morbidity and mortality in the neonatal period and long term neurologic disabilities among survivors [1]. The overall neonatal mortality rate in India is 28/1000 live births [2]. The diagnosis and grading of asphyxia can be difficult especially if relevant information at the time of delivery is not available [3, 4]. 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. Hypoxia leads to increased excretion of uric acid caused by metabolic changes, reflecting the cellular hypoxia has been reported by number of studies [5, 6]. At present the most commonly used diagnostic and prognostic indicator to assess asphyxia in neonate is apgar score [7]. This study was to evaluate the utility of urinary uric acid to creatinine ratio (UA/Cr ratio) as non-invasive, easy, cheap and at the same time early biochemical means of asphyxia diagnosis and also to find out whether APGAR score is still an important tool for birth asphyxia diagnosis and its severity calculation [7, 8].

## Materials and methods

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The present observational study was conducted at Neonatal care unit of UPUMS, Saifai, Etawah with study population of 121 newborns >34 week suffering from birth asphyxia admitted during the period of February 2017 to December 2018.

### Inclusion criteria

**Case group:** Term or preterm newborn >34 week (new ballard score) born with “failure to initiate and sustain breathing at birth” OR Apgar score as an Apgar score of <7 at one minute of life [9].

**Control group:** All term and preterm healthy infants >34 weeks with Apgar score of  $\geq 8$  at 5 minutes of age either of normal vaginal delivery or cesarean section delivery born in UPUMS SAIFAI.

### Exclusion criteria

Congenital malformations, maternal drug addiction, hemolytic disease of the newborn, neonates born to mothers consuming alcohol, neonates born to mothers who are smokers, neonates born to mothers on anti-epileptics, mothers having renal anomalies or chronic kidney disease/Hypertension.

The newborn that fulfilled the inclusion criteria and admitted in the Department of Pediatrics (NICU) was enrolled for the study after written informed consent obtained from parents. A new Ballard score was used for gestational age, birth weight was taken by automatic electronic machine. Relevant perinatal history, history regarding chronic kidney disease, history of hypertension in mother was taken and clinical findings noted. For staging of HIE Levene staging was used. Neonatal sepsis was ruled out. The markers of heart rate, respiratory efforts, tone, reflex activity and color were used to establish Apgar score at 1 minute and 5<sup>th</sup> minute of age.

For sample collection of the study about 3-5 ml urine sample was collected under aseptic condition within 24 hours of life in sterile urobag. Infants' Urinary uric acid, Urinary creatinine was measured by Randox semi-auto analyzer.

All the data was collected, compiled, analyzed and interpreted statistically. The statistical analysis was done using SPSS (Statistical Package for Social Sciences) Version 21.0 statistical Analysis Software. The values were represented in Number (%) and Mean  $\pm$  SD.

## Results

The present study was conducted in the Neonatal Care Unit of UPUMS, Saifai (Etawah) to evaluate the value of urinary uric acid/ creatinine (UA/UCR) ratio in early spot urine sample as an early marker of perinatal asphyxia. All the neonates with gestational age >34 weeks suffering from birth asphyxia were asked to participate, of which 63 neonates fulfilling the inclusion criteria were included in the study as Group I and 58 healthy neonates were included as Group II. Distribution of subjects was as per **Table - 1**. According to **Table - 2**, gestational age of majority of overall neonates (86.78%) as well of Group I (85.71%) and Group II (87.93%) was 36-38 weeks. Gestational age of only 1 (1.59%) neonate of Group I was 38-40 weeks, gestational age of rest of the neonates of both the groups (12.70% and 12.07%) was 34-36 weeks.

Gestational age of neonates of Group I and Group II was comparable ( $p=0.623$ ). According to **Table - 3**, range of Apgar score at 1 min among neonates of Group I was 2-5 (median 4.00) while that of Group II was 7-8 (median 7.00). At 1 min Apgar score of neonates of Group II ( $7.12\pm 0.33$ ) was significantly higher as compared to Group I ( $3.95\pm 0.66$ ). According to **Table - 4**, Urinary Uric acid and Urinary creatinine levels of Group I neonates were found to be higher as compared to Group II but difference was statistically significant only for S. Uric acid ( $2.55\pm 0.81$  vs.  $1.22\pm 0.23$  mg/dl) but not for Urinary creatinine ( $0.81\pm 0.15$  vs.  $0.77\pm 0.11$  mg/dl). Urinary Uric acid-Creatinine ratio of neonates of Group I ( $3.10\pm 0.67$ ) was found to be significantly higher as compared to Group II ( $1.57\pm 0.24$ ).

**Table - 1:** Group-wise Distribution of Study Population.

Group	Description	No. of subjects	Percentage
Group I	Newborn >34 weeks diagnosed cases of birth asphyxia with Apgar score <7 at 1 min (Cases)	63	52.1
Group II	Term or preterm healthy infants >34 weeks with Apgar $\geq 8$ at 5 min (Controls)	58	47.9
		121	100.0

**Table - 2:** Distribution of Study Population according to Gestational Age.

Gestational Age (Weeks)	Group I (n=63)		Group II (n=58)		Total (N=121)		
	No.	%	No.	%	No.	%	
34-36	8	12.70	7	12.07	15	12.40	
36-38	54	85.71	51	87.93	105	86.78	
38-40	1	1.59	0	0.00	1	0.83	
	$\chi^2=0.947$ (df=2); $p=0.623$						

**Table - 3:** Between Group Comparison of Apgar Score at 1 minute (Mann Whitney U test).

Group	No. of subjects	Min.	Max.	Median	Mean	S.D.
Group I	63	2	5	4	3.95	0.66
Group II	58	7	8	7	7.12	0.33
Total	121	2	8	5	5.47	1.67

Z=10.049;  $p<0.001$  (Sig.)

**Table - 4:** Between group comparison of urinary uric acid, urinary creatinine and uric acid-creatinine ratio.

	Group I (n=63)		Group II (n=58)		Student 't' test	
	Mean	SD	Mean	SD	't'	'p'
U. Uric acid (mg/dl)	2.55	0.81	1.22	0.23	11.967	<0.001
U. Creatinine	0.81	0.15	0.77	0.11	1.578	0.117
Uric acid: Creatinine Ratio	3.10	0.67	1.57	0.24	16.393	<0.001

All the neonates of Group II (100.0%) and 90.48% of Group I were alive at discharge. Out of 63 neonates of Group I, 6 (9.52%) expired before discharge. Incidence of expiry among Group I (9.52%) was significantly higher as compared to Group II (0.00%) ( $p=0.016$ ). Out of 63 neonates suffering from asphyxia, 13 (20.63%) were graded as Mild on Levene Stage, 36 (57.14%) as Moderate and rest 14 (22.22%) as Severe grade.

A subsequent increase with increase in severity of asphyxia was observed in Urinary Uric acid ( $1.62\pm 0.34$ ,  $2.45\pm 0.49$  and  $3.65\pm 0.46$  mg/dl), Urinary creatinine ( $0.68\pm 0.11$ ,  $0.80\pm 0.12$  and  $0.96\pm 0.13$  mg/dl) and Uric acid-Creatinine ratio ( $2.37\pm 0.34$ ,  $3.08\pm 0.51$  and  $3.83\pm 0.49$ ). All the associations were found to be statistically significant. All the between grade differences were also found to be statistically significant. Urinary uric acid levels of neonates with body weight  $\leq 2$  kg ( $2.99\pm 1.16$  mg/dl) was found to be higher as compared to neonates with body weight 2.1-2.5 kg ( $2.03\pm 0.84$  mg/dl), 2.6-3 kg ( $1.75\pm 0.87$ ) and  $>3$  kg ( $1.81\pm 0.70$  mg/dl). Association of Urinary uric acid levels of neonates with different birth weight was found to be statistically significant. Between group differences were statistically significant only with  $\leq 2$  kg birth weight. Though Urinary creatinine levels of neonates with birth weight  $\leq 2$  kg was higher as compared to those with 2.1-2.5, 2.6-3.0 and  $>3.0$  kg ( $0.88\pm 0.20$  mg/dl vs.  $0.77\pm 0.15$ ,  $0.79\pm 0.11$  and  $0.80\pm 0.12$ ) but difference was not found to be statistically significant.

Uric acid-Creatinine ratio of neonates with birth weight  $\leq 2$  kg ( $3.38\pm 0.93$ ) was higher as

compared to 2.1-2.5 kg ( $2.60\pm 0.84$ ), 2.6-3.0 kg ( $2.17\pm 0.92$ ) and  $>3$  kg ( $2.26\pm 0.77$ ). Difference of Uric acid-Creatinine ratio among neonates with different birth weight was found to be statistically significant. Between group differences were found to be statistically significant only between  $\leq 2$  kg vs. 2.6-3.0 kg and  $\leq 2$  kg vs.  $>3$  kg.

Our study was conducted on 58 control and 63 asphyxiated neonates. The mean gestational age and length of asphyxiated group was comparable there was no significant difference. But in weight there was significant difference present between asphyxiated and control group. The mean urinary uric acid and urinary creatinine ratio was significantly higher in asphyxiated group than the control group. There is positive correlation present between Urinary uric acid and creatinine with apgar score at 1<sup>st</sup> min and 5<sup>th</sup> min. The comparison of the UA/Cr ratios of 3 stages was also statistically significant. The urinary uric acid and creatinine ratio was progressively increasing ( $2.37\pm 0.34$ ,  $3.08\pm 0.51$ ,  $3.83\pm 0.49$ ) with the severity of asphyxia mild, moderate and severe respectively.

## Discussion

Low Apgar score is commonly used to as indicator of asphyxia in infants, but it may often be not available and may be reduced in premature infants. Other investigations that support the diagnosis of asphyxia would be required to improve availability of therapy. pH values are quickly normalized after the onset of respiration, due to the elimination of carbon dioxide and cannot be relied upon in patients that are transported. Additionally, lactate and base deficit are closely interconnected. The current

study asserts that, urinary UA/Cr ratio in spot urine sample within 24 hours of life 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 as it reflects an increased ATP degradation. Urinary UA/Cr ratio is simple, non-invasive, painless and economical investigation for the diagnosis of perinatal asphyxia. 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) [8], it was found that urinary UA/Cr ratio was significantly higher in cases than controls ( $3.1 \pm 1.3$  vs  $0.96 \pm 0.54$ ;  $p < 0.001$ ) 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 ( $2.9 \pm 0.73$ ) when compared with the controls ( $0.72 \pm 0.35$ ,  $P < 0.001$ ). Similar study was done by Deepak Kumar, et al. (2015) [12] on 110 neonates comprising 55 cases and 55 controls. The urinary uric acid and urinary creatinine were found to be higher in asphyxiated neonates ( $2.58 \pm 1.09$ ) when compared with control ( $0.86 \pm 0.17$ ). In a study by Aparna Varma Bhongir, et al. (2011) [13] on 31 control and 18 asphyxiated neonates, the mean urinary uric acid and creatinine ratio ( $2.58 \pm 0.48$  vs  $1.89 \pm 0.59$ ) is significantly higher in asphyxiated group than in the control group. Study by Lokesh Choudhary, et al. (2017) [14] on 200 neonates comprising 100 case and 100 control. The mean urinary uric acid and creatinine ratio was higher in cases than controls ( $2.68 \pm 1.06$  vs  $0.79 \pm 0.36$ ). Study by K P Patel, et al. (2016) [15] on 80 neonates comprising 40 asphyxiated and 40 healthy neonates. The mean urinary uric acid was found higher in asphyxiated neonates in compare to control ( $2.75 \pm 0.18$  vs  $1.78 \pm 0.23$ ). In a study by Shahin Nariman, et al. [16] on 362 preterm

neonates with mean gestational age  $32.7(\pm 3.9)$  week, the mean urinary uric acid and creatinine ratio was significantly higher in asphyxiated group ( $3.30 \pm 1.95$  vs  $1.36 \pm 0.42$ ). In these studies result was similar to our study showing urinary uric acid and urinary creatinine ratio can be used as an early marker of perinatal asphyxia.

## Conclusion

Urinary UA/Cr ratio is an accessible, non-invasive, painless and cost-effective additional framework with good predictive value for diagnosing perinatal asphyxia. There exists still a need to study these parameters in the context of therapeutic hypothermia and how the parameters change over the period of treatment.

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