Study of Urinary Uric Acid and Creatinine Ratio as Marker of Perinatal Asphyxia in Late Preterm and Term Neonates

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Abstract

Introduction: Perinatal hypoxia is one of the leading causes of perinatal mortality in developing countries. Both the Apgar score and arterial blood pH predict neonatal mortality in asphyxia. Apgar score alone does not predict neurologic outcome as it is influenced by various factors. The Apgar score is subjective and is usually reduced in premature neonates, and in some cases, the Apgar score may not be available. Other investigations for pH, lactate, and base deficit estimations are invasive and need rapid estimations. Whereas the urinary UA/Cr ratio is a simple, noninvasive, and economical investigation for the diagnosis of perinatal asphyxia.

Methods: This is a hospital-based analytical cross-sectional study conducted in the AJ Institute of Medical Science (AJIMS) Neonatal Intensive Care Unit (NICU) from July 2022 to April 2024. The study included 56 neonates, equally divided into two groups: 28 asphyxiated and 28 non-asphyxiated infants. Urine samples were collected from all participants within 6-24 hours after birth, and the UA/Cr ratio was measured and compared between the two groups. Additionally, cord blood pH and Apgar scores were recorded for all neonates. For the asphyxiated group, HIE grading was performed to assess the severity of the condition.

Inclusion criteria

Cases - All late preterm (gestational age between 34 weeks and 0 days, and 36 weeks and 6 days) and term neonates (≥37 weeks) with an Apgar score of 6 or less at five minutes of life and who need resuscitation with more than 1 minute of positive pressure ventilation before stable spontaneous respiration.

Controls - All late preterm and term neonates with APGAR score of 7 or higher at 5 minutes with no signs of asphyxia will be recruited as controls. Controls will be selected immediately after each case.

Exclusion criteria

Babies with major congenital malformations.

Neonates who are on diuretics before the collection of a urine sample.

Result: Our study showed a significantly higher mean urinary UA/Cr ratio in asphyxiated neonates compared to controls (2.8 ± 0.7 vs 1.6 ± 0.4, $p<0.001$). Urinary UA/Cr ratio cut off value of 2.24 provided the best balance of sensitivity (85.71%) and specificity (100%) for identifying HIE, with an AUC of 0.952. Our study found a strong negative correlation between urine UA/Cr ratio and cord blood pH ($r = -0.72$, $p<0.001$). We noted a strong positive correlation between the urinary UA/Cr ratio and LDH levels ($r=0.76$, $p<0.001$).

Conclusion: The study demonstrates that the urinary UA/Cr ratio is a highly sensitive and specific marker for perinatal asphyxia. With a cut-off value of 2.24, the UA/Cr ratio showed excellent diagnostic accuracy. This performance is comparable to or better than established markers like cord blood pH and Apgar scores. The study concludes that the urinary UA/Cr ratio is a sensitive and specific marker for perinatal asphyxia .Its non-invasive nature makes it particularly suitable for neonatal care.

Keywords: Apgar score, Cord blood pH, Hypoxic ischemic encephalopathy, Perinatal asphyxia, Serum LDH, Urinary uric acid /creatinine ratio.

Introduction

One of the most important phases in the life of an individual is the neonatal period. In terms of growth and development, it is very important because there is significant growth and development during the neonatal phase (1). Neonatal mortality rate (NMR) is considered one of the important indicators that reflects the quality of the health care delivery system and the development of country. (2, 3).

The NICU is the most effective place to reduce a country's newborn mortality. Respiratory disease is one of the common reasons for admission to NICU. The estimated incidence of neonates with respiratory failure requiring mechanical ventilation is approximately 18 per 1000 live births. (4)

One of the most important problems that is seen during the neonatal phase is neonatal sepsis and respiratory distress syndromes. These are the two most common causes of neonatal intensive care unit admissions during the neonatal period. (5-7)

Hypoxic respiratory failure is one of the prime causes that contribute to an increase in the risk of morbidity and mortality. Hypoxic respiratory failure is also known to be associated with a very bad neurological outcome. (4, 8) Respiratory diseases are associated with an increased risk of mortality, morbidity, and worse neurological outcomes. Hence, monitoring neonates using oxygen indicators is essential. (6-8)

Perinatal hypoxia is one of the leading causes of perinatal mortality in developing countries. Both the Apgar score and arterial blood pH predict neonatal mortality in asphyxia. (1,2)

The occurrence of perinatal asphyxia is in the range of 1% to 1.5% of total live births in the Western Hemisphere. Gestational age and birth weight are the two important 1 Introduction determinants associated with asphyxia, and it accounts for 23% of all neonatal deaths and 8% of childhood deaths. (3-5)

Apgar score alone does not predict neurologic outcome as it is influenced by various factors. Apgar score is subjective and is usually reduced in premature neonates, and in some cases, Apgar score may not be available.

Other investigations like pH, lactate, and base deficit estimations are invasive and need rapid estimations.

(9,10)Estimation of IL -6, glial fibrillary acidic protein, neuron-specific enolase requires modernized equipment and is expensive (9,10), whereas urinary uric acid/creatinine ratio is a simple, noninvasive, and economic investigation for diagnosis of perinatal asphyxia (11-15).

In perinatal asphyxia, due to hypoxia, there is failure of oxidative phosphorylation and ATP production. Due to lack of ATP and increased cellular destruction results in accumulation of ADP, which will then be catabolised to hypoxanthine, inosines and adenosine. Continuous tissue hypoxia and consequent reperfusion injury will result in hypoxanthine being oxidized to xanthine and uric acid in the presence of xanthine oxidase. This will increase uric acid production and cause it to enter blood from damaged tissue. Uric acid will then get excreted in urine, where it can be easily detected. (6)

Recent data has shown that urinary uric acid and creatinine ratio can also serve as an important marker to identify the degree of severity of birth asphyxia and hence guide management and the prognosis. (6-21)

Aims and Objectives

To assess the urinary uric acid/creatinine ratio as a marker for perinatal asphyxia compared with cord blood ABG analysis and Apgar score.

Methods and Materials

Study design: Analytical cross-sectional study.

Study duration: July 2022 To June 2023

Source of data: All late preterm and term neonates in the delivery room or in the Neonatal Intensive Care Unit (NICU) at AJ Institute of Medical Sciences, Mangalore, between July 2022 and June 2023. The hospital has a Level III NICU care facility with HFO and other advanced modes of ventilation, therapeutic hypothermia,

etc. Institutional ethics committee approval was obtained.

Sample size: 56

Inclusion criteria

Cases: All late preterm (gestational age between 34 weeks and 0 days, and 36 weeks and 6 days) and term neonates (≥37 weeks) with an Apgar score of 6 or less at five minutes of life and who need resuscitation with more than 1 minute of positive pressure ventilation before stable spontaneous respiration.

Controls: All late preterm and term neonates with APGAR score of 7 or higher at 5 minutes with no signs of asphyxia will be recruited as controls. Controls will be selected immediately after each case.

Exclusion criteria

- Babies with major congenital malformations.
- Neonates who are on diuretics before the collection of a urine sample.

Description of the process:

Data Collection Procedure:

- Institutional ethics committee approval obtained
- Informed consent obtained from the parents of neonates who fulfil the inclusion criteria.
- A detailed history obtained from the parents including antenatal, natal, postnatal history and family history.
- Vital signs, general examination and systemic examination recorded.
- Clinico-etiological diagnosis was made after detailed history and clinical examination
- Detailed maternal history, assessment of intrauterine fetal well being by continuous electronic fetal monitoring, meconium staining of amniotic fluid, mode of delivery, Apgar score, sex of the baby and

weight of the baby was recorded on the precoded proforma.

- Gestational age was assessed by New Ballard scoring system.

- Arterial blood gas analysis (ABG) in umbilical arterial blood in all neonates in case and control group collected.

- Urine samples collected in the first 24 hours of life by attachment of urine collection bags. Urine uric acid and creatinine in the sample is estimated.

- Uric acid concentration determined with auto analyser by spectrophotometric uricase method. Creatinine concentration will be estimated in the same instrument by Jeffes test

- Investigations to support the diagnosis of HIE such as serum LDH, CK-MB, blood urea nitrogen, serum creatinine, liver enzymes carried out in cases whenever required and also to rule out other causes of hypotonia, seizures, lethargy other than HIE with relevant investigations like blood glucose ,serum magnesium ,serum calcium , serum electrolytes, blood culture and sensitivity was done.

Statistical analysis

- Descriptive statistics was used to describe the baseline data.

- Continous variable was analysed by using Independent t-test. Pearson correlation coefficient will be used to test the strength of association between arterial blood pH and other variables. Receiver Operating Characteristic (ROC) plots will be used to determine the cut-off values of various parameters.

- P value <0.05 considered statistically significant.

Result

Groups	Male		Female		Total	P Value (Chi-square test)
	n	%	N	%	N	
GROUP 1	17	60.7%	11	39.29%	28	0.783 Not Significant
GROUP 2	18	64.29%	10	35.71%	28	
Total	35	62.5%	21	37.5%	56	

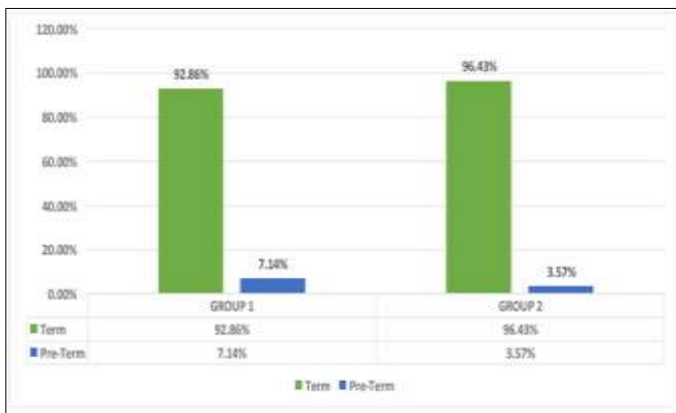Table 1: Gender wise distribution of Participants
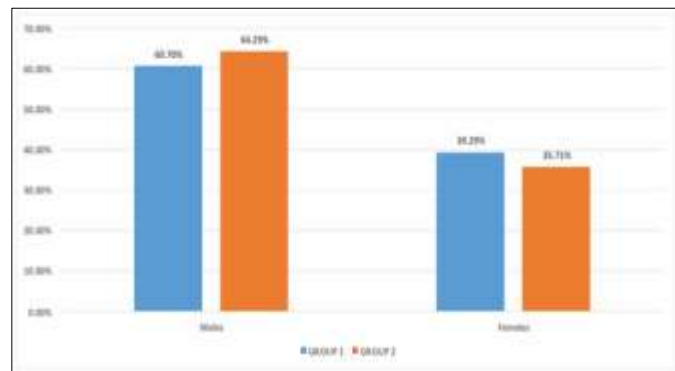
Graph 1: Gender wise distribution of Participants

This table presents the gender distribution of participants in two groups. Group 1 consists of 17 males (60.7%) and 11 females (39.3%), while Group 2 has 18 males (64.3%) and 10 females (35.7%). The overall total is 35 males (62.5%) and 21 females (37.5%), making 56 participants in total. The chi-square test yields a p-value of 0.783, indicating no significant difference in gender distribution between the groups.

Groups	GROUP 1		GROUP 2		Total	P Value (Fisher Exact test)
	N	%	N	%	n	
Term	26	92.86%	27	96.43%	53	0.553 Not Significant
Pre-Term	2	7.14%	1	3.57%	3	
Total	28	100%	28	100%	56	

Table 2: Term wise distribution of participants among group

Graph 2: Term wise distribution of participants among group

This table shows the term-wise distribution of participants. In Group 1, 26 are term neonates (92.86%) and 2 are pre-term (7.14%). Group 2 has 27 term neonates (96.43%) and 1 pre-term (3.57%). The total across both groups is 53 term (94.64%) and 3 pre-term (5.36%) neonates. The Fisher Exact test gives a p-value of 0.553, indicating no significant difference in term distribution between the groups.

| MH	Primi gravida		Multigravida		Total	P Value (Fisher Exact test)
	n	%	N	%	n	
GROUP 1	18	64.3%	10	35.7%	28	0.584 Not Significant
GROUP 2	16	57.1%	12	42.9%	28	
Total	34	100%	22	100%	56	

Table 3: Maternal history vs Groups
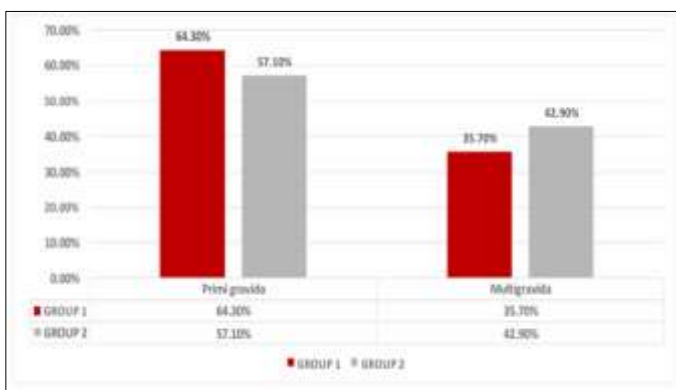
Graph 3: Maternal history vs Groups

This table explores the maternal history of the participants. Group 1 has 18 primigravida (64.3%) and

10 multigravida (35.7%). In Group 2, 16 are primigravida (57.1%) and 12 are multigravida (42.9%). Overall, there are 34 primigravida (60.7%) and 22 multigravida (39.3%). The Fisher Exact test results in a p-value of 0.584, showing no significant difference in maternal history between the groups.

| MOD	GROUP 1		GROUP 2		Total	P Value (Fisher Exact test)
	n	%	N	%	n	
Normal	12	42.86%	8	28.57%	20	0.358 Not Significant
Cessarean section	16	57.14%	20	71.13%	36	
Total	28	100%	28	100%	56	

Table 4: Mode of Delivery vs Groups
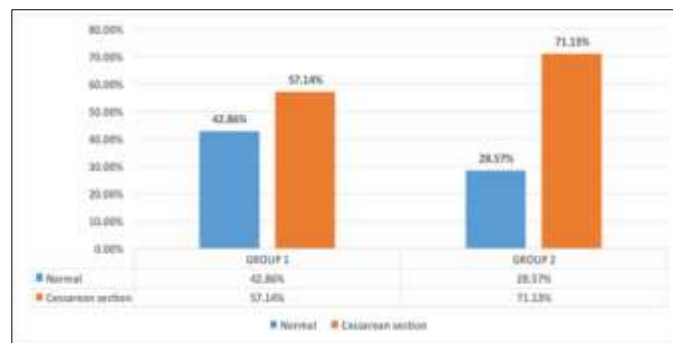
Graph 4: Table 4: Mode of Delivery vs Groups Group 1 has 12 normal deliveries (42.86%) and 16 cesarean sections (57.14%). Group 2 has 8 normal deliveries (28.57%) and 20 cesarean sections (71.13%). In total, there are 20 normal deliveries (35.71%) and 36 cesarean sections (64.29%). The Fisher Exact test yields a p-value of 0.358, indicating no significant difference in delivery mode between the groups.

| Foetal Distress	GROUP 1		GROUP 2		Total	P Value (Fisher Exact test)
	n	%	N	%	n	
NST-Reactive	23	82.14%	25	89.29%	48	0.445 Not Significant
NST-Nonreactive	5	17.86%	3	10.71%	8	
Total	28	100%	28	100%	56	

Table 5: Fetal distress Vs Groups
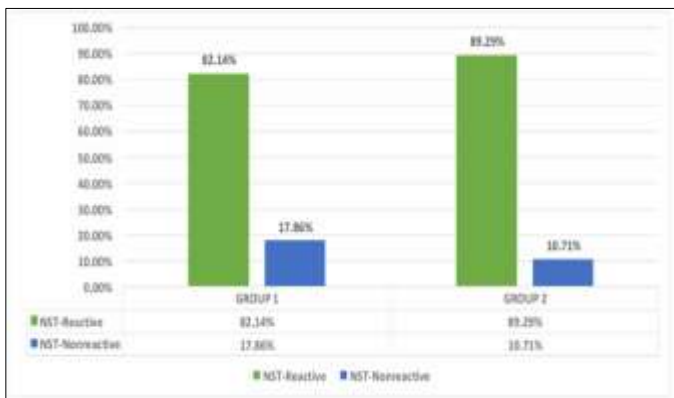
Graph 5: Fetal distress Vs Groups In Group 1, 23 neonates (82.14%) had reactive NST and 5 (17.86%) had non-reactive NST. Group 2 had 25 reactive NST (89.29%) and 3 non-reactive NST (10.71%). Overall, 48 neonates (85.71%) had reactive NST and 8 (14.29%) had non-reactive NST. The Fisher Exact test results in a p-value of 0.445, showing no significant difference in fetal distress between the groups.

HIE	GROUP 1		GROUP 2		Total	P Value (Fisher Exact test)
	N	%	n	%	n	
1	7	25%	0	0%	7	
2	10	35.7%	0	0%	10	
3	11	39.2%	0	0%	11	<0.001 Significant
No-HIE	0	0%	28	100%	28	
Total	28	100%	28	100%	56	

Table 6: Hypoxic Ischemic Encephalopathy Vs Groups
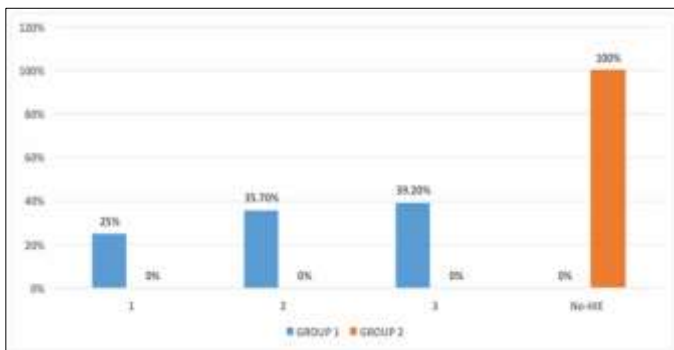
Graph 6: Hypoxic Ischemic Encephalopathy Vs Groups Group 1 has 7 cases of HIE grade 1 (25%), 10 of grade 2 (35.7%), and 11 of grade 3 (39.2%). Group 2 has no HIE cases, only 28 neonates (100%) with no HIE. The Fisher

Exact test results in a p-value of <0.001 ,indicating significant difference in HIE distribution between two groups .

	N	Mean-Birth Weight	Std. Deviation	P value (Student-t test)
GROUP 1	28	2.83	0.48	0.395 Not significant
GROUP 2	28	2.94	0.45	

Table 7: Mean Birth weight among two Groups
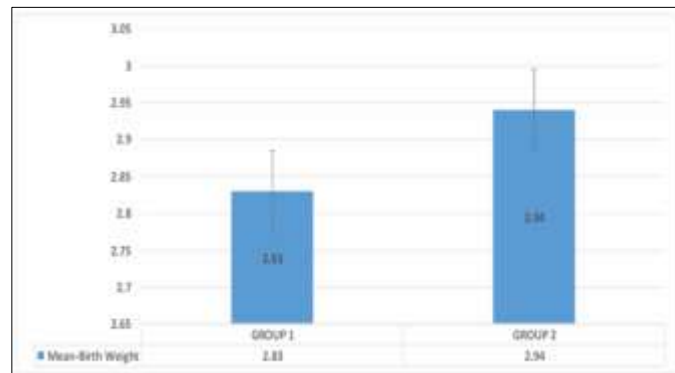
Graph 7: Mean Birth weight among two Groups This table compares the mean birth weight between the groups. Group 1 has a mean birth weight of 2.83 kg (SD = 0.48), and Group 2 has a mean of 2.94 kg (SD = 0.45). The Student's t-test yields a p-value of 0.395, showing no significant difference in mean birth weight between the groups.

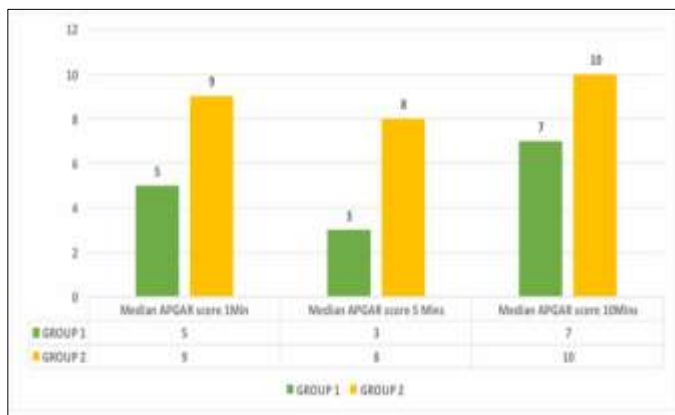|	N	Mean APGAR score	Median APGAR score	SD	P value (Mann-Whitney-U test)
GROUP 1	28	3.46	3	0.84	<.001 significant
GROUP 2	28	7.54	8	0.79	

Table 8: Median APGAR Score at 1 mins among two Groups

	N	Mean APGAR score	Median APGAR score	SD	P value (Mann-Whitney-U test)
GROUP 1	28	4.96	5	0.92	<.001 significant
GROUP 2	28	8.64	9	0.68	

Table 9: Median APGAR Score at 5 mins among two Groups

	N	Mean APGAR score	Median APGAR score	SD	P value (Mann-Whitney-U test)
GROUP 1	28	6.75	7	0.8	<.001 significant
GROUP 2	28	9.61	10	0.63	

Table 10: Median APGAR Score at 10 mins among two Groups


Graph 8: Median APGAR Score at 1 mins, 5 mins and 10 mins among two Groups

At 1 minute: Group 1 has a mean APGAR score of 3.46 (median = 3, SD = 0.84), while Group 2 has a mean of 7.54 (median = 8, SD = 0.79). The Mann-Whitney U test yields a p-value of <0.001, indicating a significant difference in APGAR scores at 0 minutes between the groups. At 5 minutes: Group 1 has a mean score of 4.96 (median = 5, SD = 0.92), and Group 2 has a mean of 8.64 (median = 9, SD = 0.68). The Mann-Whitney U test results in a p value of <0.001, showing a significant difference in APGAR scores at 5 minutes between the groups. At 10 minute: Group 1 has a mean score of 6.75 (median = 7, SD = 0.8), while Group 2 has a mean of 9.61 (median = 10, SD = 0.63). The Mann-Whitney U test gives a p-value of <0.001, indicating a significant difference in APGAR scores at 10 minutes between the group.

	N	Mean- ABG	Std. Deviation	P value (Student-t test)
GROUP 1	28	6.9	0.08	<.001 significant
GROUP 2	28	7.2	0.15	

Table 11: Mean ABG among two groups
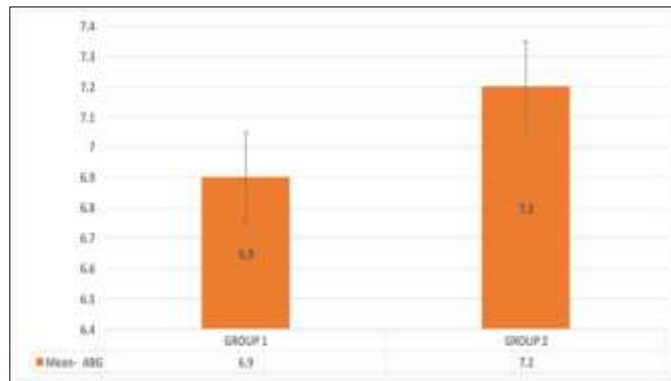
Graph 9: Mean ABG among two groups

Group 1 has a mean ABG of 6.9 (SD = 0.08), and Group 2 has a mean of 7.2 (SD = 0.15). The Student's t-test yields a p-value of <0.001, showing a significant difference in ABG levels between the groups.

| ABG	GROUP 1		GROUP 2		Total	P Value (Fisher Exac test)
	n	%	n	%	n	
<6.85	9	32.10%	0	0%	9	
6.85-7	17	60.7%	2	7.14%	19	
7-7.15	2	7.14%	5	17.8%	7	<0.001 Significant
7.15-7.3	0	0%	12	42.86%	12	
>7.3	0	0%	9	32.14%	9	
Total	28	100%	28	100%	56	

Table 12: ABG vs Groups
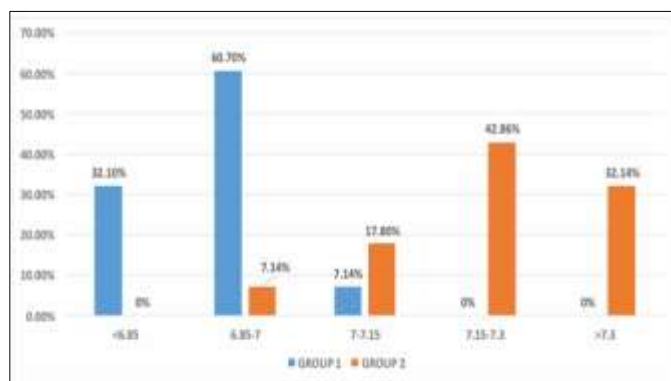
Graph 10: ABG vs Groups

This table details the distribution of ABG values among the groups. In Group 1, 9 neonates (32.10%) have ABG < 6.85, 17 (60.7%) have ABG between 6.85-7, 2(7.14%) have ABG between 7-7.15, and none have ABG > 7.3. In Group 2, none have ABG < 6.85, 2 (7.14%) have ABG between 6.85-7, 5 (17.8%) have ABG between 7-7.15, 12 (42.86%) have ABG between 7.15-7.3, and 9 (32.14%) have ABG > 7.3. The Fisher Exact test results in a p-value of <0.001, indicating a significant difference in ABG distribution between the groups.

Cut points	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Youden's index	AUC
7	88.57%	90.48%	93.94%	82.61%	0.79	0.963
7.01	85.71%	95.24%	96.77%	80%	0.81	0.963
7.02	82.86%	95.24%	96.67%	76.92%	0.781	0.963
7.03	82.86%	100%	100%	77.78%	0.829	0.963
7.05	80%	100%	100%	75%	0.8	0.963

Table 13: Different cut off values for ABG among HIE patients
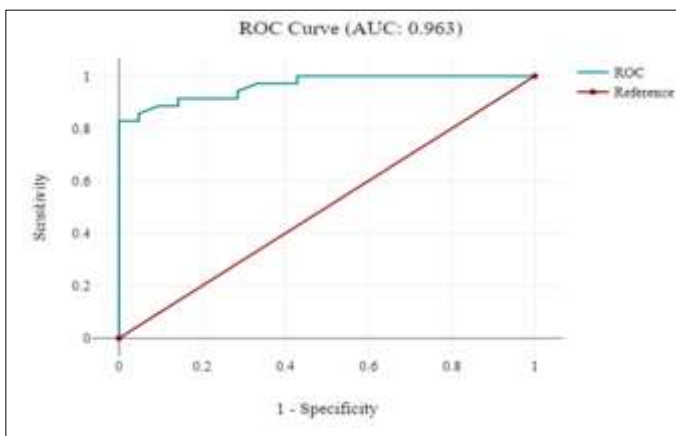
Graph 11: Different cut off values for ABG among HIE patients

This table presents various cut-off values for ABG and their corresponding sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), Youden's index, and Area Under the Curve (AUC) for identifying HIE patients. The cut-off value of 7.03

shows the highest Youden's index (0.829), indicating the best balance between sensitivity and specificity:

- Sensitivity: 82.86%
- Specificity: 100%
- PPV: 100%
- NPV: 77.7%
- AUC: 0.963

This suggests that an ABG value of 7.03 could be a good threshold for identifying neonates with HIE, with high accuracy (AUC 0.963).

	N	Mean-UUA/CR	Std. Deviation	P value (Student-t test)
GROUP 1	28	2.8	0.7	<.001 significant
GROUP 2	28	1.6	0.4	

Table 14: Mean UUA/CR ratio among two groups
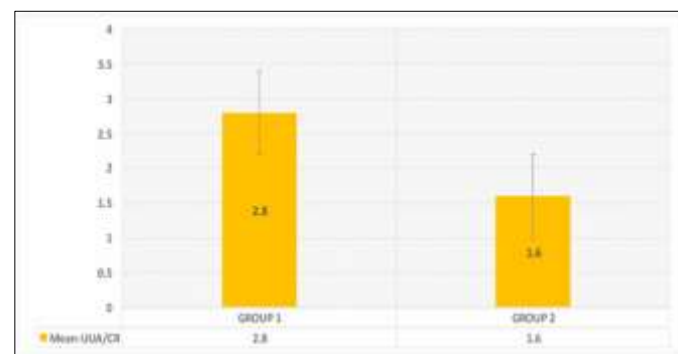
Graph 12: Mean UUA/CR ratio among two groups

This table compares the mean urinary uric acid/creatinine (UUA/CR) ratio. Group 1 has a mean UUA/CR of 2.8 (SD = 0.7), while Group 2 has a mean of 1.6 (SD = 0.4). The Student's t-test gives a p-value of <0.001, indicating a significant difference in UUA/CR ratios between the groups.

| UUA/CR Group	GROUP 1		GROUP 2		Total	P Value (Fisher Exact test)
	N	%	n	%	n	
<2.1	4	14.3%	25	89.2%	29	<0.001 Significant
>/=2.1	24	85.7%	3	10.8%	27	
Total	28	100%	28	100%	56	

Table 15: UUA/CR Vs Groups
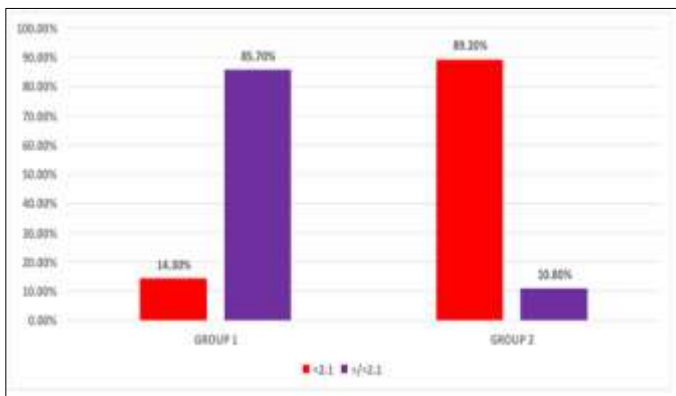
Graph 13: UUA/CR Vs Groups

This table shows the distribution of UUA/CR ratios among the groups. In Group 1, 4 neonates (14.3%) have UUA/CR < 2.1, and 24 (85.7%) have UUA/CR ≥ 2.1. In Group 2, 25 neonates (89.2%) have UUA/CR < 2.1, and 3 (10.8%) have UUA/CR ≥ 2.1. The Fisher Exact test results in a p-value of <0.001, indicating a significant difference in UUA/CR ratios between the groups.

Cut point	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Youden's index	AUC
2.2	85.71%	96.43%	96%	87.10%	0.821	0.952
2.24	85.71%	100%	100%	87.50%	0.857	0.952
2.27	82.14%	100%	100%	84.85%	0.821	0.952

Table 16: Different cut off values for UUA/CR among HIE patients
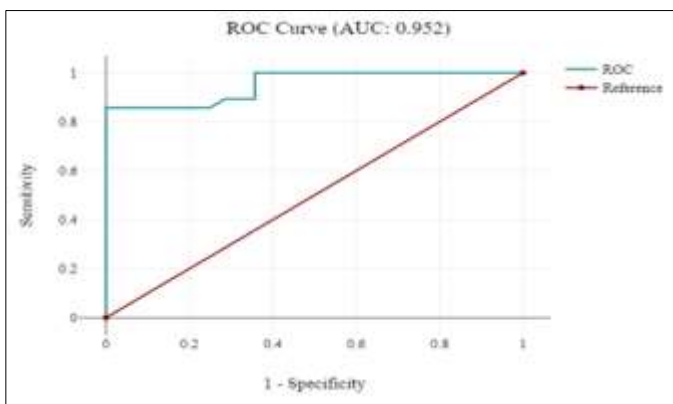
Graph 14: Different cut off values for UUA/CR among HIE patients

This table presents various cut-off values for the UUA/CR ratio and their corresponding sensitivity, specificity, PPV, NPV, Youden's index, and AUC for identifying HIE patients. The cut-off value of 2.24 shows the highest Youden's index (0.857), indicating the best balance between sensitivity and specificity: • Sensitivity: 85.71% • Specificity: 100% • PPV: 100% • NPV: 87.5% • AUC: 0.952 .This suggests that a UUA/CR ratio of 2.24 could be a good threshold for identifying neonates with HIE, with good accuracy (AUC 0.952).

|	N	Mean-Birth Weight	Std. Deviation	P value (Student-t test)
GROUP 1	28	859.8	417.05	<.001 significant
GROUP 2	28	165.03	129.95	

Table 17: Mean LDH among two groups
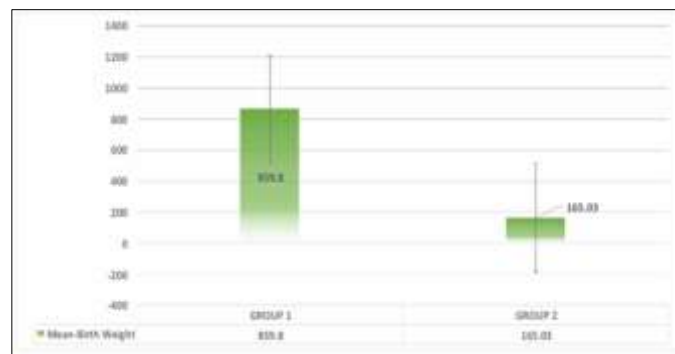
Graph 15: Mean LDH among two groups

This table compares the mean lactate dehydrogenase (LDH) levels. Group 1 has a mean LDH of 859.8 U/L (SD = 417.05), and Group 2 has a mean of 165.03 U/L (SD = 129.95). The Student's t-test yields a p-value of <0.001, indicating a significant difference in LDH levels between the groups.

Cut point	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Youden's index	AUC
423	89.29%	96.43%	96.15%	90%	0.857	0.983
450	89.29%	100%	100%	90.32%	0.893	0.983
468	85.71%	100%	100%	87.50%	0.857	0.983

Table 18: Different cut off values for LDH among HIE patients
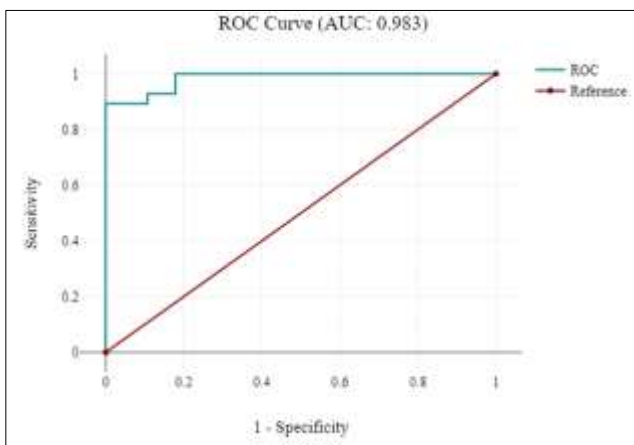
Graph 16: Different cut off values for LDH among HIE patients

This table presents various cut-off values for LDH and their corresponding sensitivity, specificity, PPV, NPV, Youden's index, and AUC for identifying HIE patients. The cut-off value of 450 shows the highest Youden's index (0.893), indicating the best balance between sensitivity and specificity:

- Sensitivity: 89.29%
- Specificity: 100%
- PPV: 100%
- NPV: 90.32%
- AUC: 0.983

This suggests that an LDH level of 450 could be a good threshold for identifying neonates with HIE, with high accuracy (AUC 0.983).

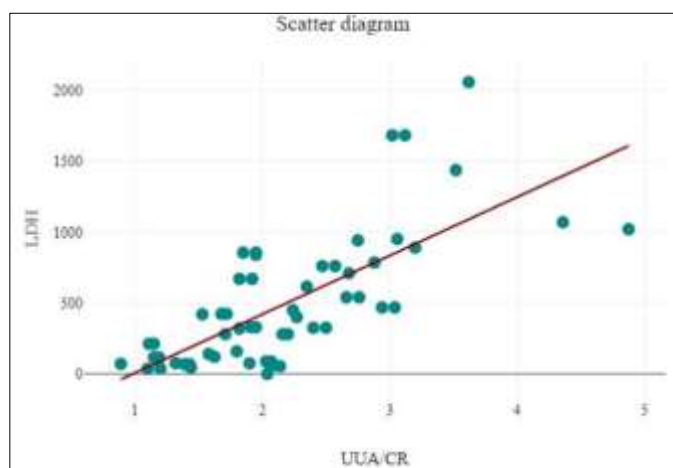|	r	p
ABG and UUA/CR	-0.72	<.001

Table 19: Correlation between ABG and UUA/CR ratio
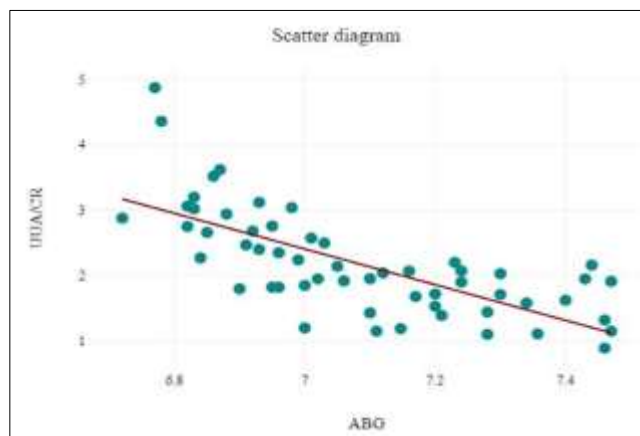
Graph 17: Correlation between ABG and UUA/CR ratio

This table presents the correlation between ABG and UUA/CR ratio. Correlation coefficient (r): -0.72 , p-value: <0.001 The strong negative correlation (-0.72) indicates that as ABG decreases (becomes more acidotic), the UUA/CR ratio increases. This relationship is statistically significant (p<0.001) and supports the use of the UUA/CR ratio as a marker for perinatal asphyxia.

	r	p
UUA/CR and LDH	0.76	<.001

Table 20: Correlation between ABG and LDH

Graph 18: Correlation between ABG and LDH

This table presents the correlation between ABG and LDH. Correlation coefficient (r): 0.76, p-value: <0.001 .The strong positive correlation (0.76) indicates that as ABG decreases (becomes more acidotic), LDH levels

increase. This relationship is statistically significant (p<0.001) and supports the use of LDH as another marker for perinatal asphyxia.

Discussion

This study aimed to evaluate the utility of the urinary uric acid/creatinine (UA/Cr) ratio as a marker for perinatal asphyxia in late preterm and term neonates, comparing it with established markers like cord blood ABG analysis and Apgar scores. Our study included 56 neonates, equally divided between the asphyxiated (Group 1) and non-asphyxiated (Group 2) groups. The groups were well-matched in terms of gender distribution, gestational age, maternal history, and mode of delivery, with no statistically significant differences observed. This demographic similarity enhances the reliability of our comparisons between the two groups.

Our results demonstrated significantly lower median Apgar scores of 3, 5, and 7 at 1, 5, and 10 minutes respectively, in the asphyxiated group compared to the control group; it was 8-10 among them (p<0.001 for all time points).Our study indicated significantly lower cord blood pH in the asphyxiated group compared to controls (mean 6.9 vs. 7.2, p<0.001). A key finding of our study was the significantly higher mean UA/Cr ratio in asphyxiated neonates compared to controls (2.8±0.7 vs 1.6±0.4, p<0.001). Our ROC analysis revealed that a UA/Cr ratio cut-off value of 2.24 provided the best balance of sensitivity (85.71%) and specificity (100%) for identifying HIE, with an AUC of 0.952. Our study found a strong negative correlation between UA/Cr ratio and cord blood pH (r=-0.72, p<0.001). In addition, we noted a strong positive correlation between the UA/Cr ratio and LDH levels (r=0.76, p<0.001), a relationship that has not been widely discussed in other research. This discovery implies that the UA/Cr ratio may indicate the extent of cellular damage in cases of asphyxia akin to LDH and warrants further exploration.

Limitations

Although our study offers valuable insights, it does have some limitations. While the sample size is sufficient for our primary objectives, a larger sample size would be beneficial for more comprehensive subgroup analyses. Additionally, we did not evaluate long-term outcomes, which could further confirm the prognostic value of the UA/Cr ratio. In the future, studies should consider conducting larger, multi-center trials to establish more conclusive cut-off values for clinical use. They should also incorporate longitudinal follow-up to correlate UA/Cr ratios with long-term neurodevelopmental outcomes. Furthermore, it would be beneficial to investigate the relationship between the UA/Cr ratio and other biochemical markers of asphyxia. Lastly, exploring the potential use of the UA/Cr ratio in guiding therapeutic interventions for perinatal asphyxia would be valuable.

Conclusion

The study demonstrates that the urinary UA/Cr ratio is a highly sensitive and specific marker for perinatal asphyxia. With a cut-off value of 2.24, the UA/Cr ratio showed excellent diagnostic accuracy .This performance is comparable to or better than established markers like cord blood pH and Apgar scores. The UA/Cr ratio showed a strong negative correlation with cord blood pH, reinforcing its validity as a marker of perinatal asphyxia.

As a urinary biomarker, the UA/Cr ratio offers a non-invasive method for assessing perinatal asphyxia, which is particularly advantageous in neonatal care, where minimizing invasive procedures is crucial. The study also evaluated lactate dehydrogenase (LDH) levels,

finding a strong positive correlation between UA/Cr ratio and LDH (r=0.76, p<0.001). This supports the use of the UA/Cr ratio as part of a panel of biomarkers for a more comprehensive assessment of perinatal asphyxia.

The cut-off value of 2.24 found in this study should be validated in larger, diverse cohorts.. Given its non-invasive nature and potentially lower cost compared to blood gas analysis, the use of the UA/Cr ratio should be particularly explored and promoted in resource-limited settings where sophisticated neonatal care may be less accessible.

Over all, this study provides strong evidence for the utility of urinary UA/Cr ratio as a valuable biomarker for perinatal asphyxia. Its high diagnostic accuracy, correlation with established markers, ability to reflect HIE severity, and non-invasive nature make it a promising tool for improving the diagnosis and management of perinatal asphyxia. Implementation of these recommendations could significantly enhance neonatal care practices and potentially improve outcomes for affected neonates.

Acknowledgement

References

1. Committee on Fetus and Newborn, Barfield WD, Papile LA, Baley JE, Benitz W, Cummings J, Carlo WA, et al . Levels of neonatal care. Pediatrics. 2012 Sep 1;130(3):587-97 .

2. Lawn JE, Kinney MV, Black RE, Pitt C, Cousens S, Kerber K, et al.. Neonate survival: a multi-country analysis of a decade of change. Health policy and planning. 2012 Jul 1;27(suppl_3):iii6-28

3. Oestergaard MZ, Inoue M, Yoshida S, Mahanani WR, Gore FM, Cousens S, et al. United Nations Inter-Agency Group for Child Mortality Estimation and the Child Health Epidemiology Reference Group. Neonatal mortality levels for 193 countries in 2009 with trends since 1990: a systematic analysis of progress, projections, and priorities. PLoS medicine. 2011 Aug 30;8(8):e1001080 .

4. Torres-Castro C, Valle-Leal J, Martínez-Limón AJ, Lastra-Jiménez Z, Delgado Bojórquez LC . Pulmonary complications associated with mechanical ventilation in neonates. Boletín Médico Del Hospital Infantil de México (English Edition) . 2016 Sep 1;73(5):318-24 .

5. Angus DC, Linde-Zwirble WT, Clermont G, Griffin MF, Clark RH. Epidemiology of neonatal respiratory failure in the United States: projections from California and New York. American journal of respiratory and critical care medicine. 2001 Oct 1;164(7):1154-60 .

6. Sivanandan S, Agarwal R, Sethi A . Respiratory distress in term neonates in low resource settings. InSeminars in Fetal and Neonatal Medicine 2017 Aug 1 (Vol . 22, No . 4, pp . 260-266). WB Saunders.

7. Gallacher DJ, Hart K, Kotecha S . Common respiratory conditions of the newborn. Breathe. 2016 Mar 1;12(1):30-42 .

8. Jensen EA, DeMauro SB, Kornhauser M, Aghai ZH, Greenspan JS, Dysart KC . Effects of multiple ventilation courses and duration of mechanical ventilation on respiratory outcomes in extremely low-birth-weight infants. JAMA pediatrics. 2015 Nov 1;169(11):1011-7 .

9. Naithani M, Simalti AK. Biochemical Markers in Perinatal Asphyxia. Journal of Nepal Paediatric Society. 2011 May 1;31(2).

10. Blennow M, Sävman K, Ilves P, Thoresen M, Rosengren L. Brain-specific proteins in the cerebrospinal fluid of severely asphyxiated newborn infants. Acta paediatrica. 2001 Oct;90(10):1171-5.

11. Kumar M, Jain N, Thora S, Kiran T. Urinary Uric Acid/Creatinine Ratio as an Additional Early Marker for Perinatal Asphyxia. (Journal of medical science and clinical research) July 2017. Vol 5 Issue 07 Page 25137-25140.

12. Siddharth PL, Prasad PL. Urinary uric acid or urinary creatinine ratio as a non invasive marker for perinatal asphyxia. International Journal of Contemporary Pediatrics. 2020 Jun;7(6):1378.

13. Erdag GC, Vitrinel A. Can urinary uric acid/creatinine ratio be used as an additional marker for neonatal asphyxia Int Pediatr. 2004;19(4):217-9.

14. Gulati K, Vishnoi SK, Choudhary S, Jora R. Urinary Uric Acid and Creatinine Ratio as a Marker of Perinatal Asphyxia. Iranian Journal of Neonatology. 2022 Jan 1;13(1).

15. Krishnana EP, Sekar SP, Ponnusamy V. Study of urinary uric acid and creatinine ratio as a marker of neonatal asphyxia for babies born in a tertiary care hospital. Int J Res Med Sci. 2017 Dec;5(12):5418-23.

16. Rai, Preeti Lata & Prasad, Prem. Urinary Uric Acid or Urinary Creatinine ratio as a non invasive marker for Perinatal asphyxia. International Journal of Contemporary Pediatrics. June 2020 Vol 7 no.6

17. Raivio KO. Neonatal hyperuricemia. J Pediatr. 1976 Apr;88(4 Pt 1):625-30.

18. Chanpura VR, Kacha MG. A study of urinary uric acid to creatinine ratio as a biochemical marker of perinatal asphyxia. International Journal of Contemporary Pediatrics. 2022 Jun;9(6):584.

19. Makhoul IR, Soudack M, Smolkin T, Sujov P, Epelman M, Eisenstein I, Magen D, Zelikovic I. Neonatal transient renal failure with renal medullary hyperechogenicity: clinical and laboratory features. Pediatr Nephrol. 2005 Jul;20(7):904-9. doi: 10.1007/s00467-005-1868-y. Epub 2005 May 7. PMID: 15880271.

20. Simmonds HA, Webster DR, Wilson J, Lingham S. An X-linked syndrome characterized by hyperuricemia, deafness, abnormalities. Lancet. 1982 Jul 10;2(8289):68-70.

21. Patel KP, Makadia MG, Patel VI, Nilayangode HN, Nimbalkar SM. Urinary uric acid/creatinine ratio-a marker for perinatal asphyxia. Journal of Clinical and Diagnostic Research: JCDR. 2017 Jan;11(1):SC08.