



Urinary Uric Acid/Creatinine Ratio - A Marker for Birth Asphyxia

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ABSTRACT

Background: Perinatal hypoxia is one of the leading causes of perinatal mortality in developing countries. Despite the important advances in perinatal care in the past decades, Birth asphyxia remains a stubborn condition leading to significant mortality and morbidity. The present study was conducted to Assess the Urinary Uric Acid /Creatinine Ratio as a Marker For Birth Asphyxia In Comparison With Cord Blood ABG Analysis And Apgar Score Monitoring.

Material and methods: 68 term newborns among all the study group were divided into 2 groups of 34 birth asphyxia and 34 normal babies of whom umbilical cord arterial blood Ph, urinary uric acid and urinary creatinine levels and their ratio was compared.

Results: The mean gestational age among the Normal term newborns and term newborns with Birth Asphyxia was almost similar in both the groups. we assessed the modes of delivery among the term newborns with birth asphyxia and the normal term newborns. We observed that majority of the study subjects were delivered by normal delivery. Mean birth weight(kg) of cases(asphyxiated newborns) and controls(normal newborns) were compared and we did not find any statistically significant association. we assessed the APGAR SCORE among the term newborns with birth asphyxia and term normal newborns at 1 and 5 mins of life.

Mean APGAR at 1 minute and 5 minutes of cases was significantly lower than that of controls. Mean Cord Arterial Blood pH, pO₂ of cases (asphyxiated group) was significantly lower than controls and pCO₂ is observed to be higher than in controls(normal newborns). Mean Urinary uric acid and Mean Urinary Creatinine of cases (asphyxiated group) was higher than in controls(normal newborns).

In the present study In Asphyxiated and control group, mean urinary UA/Cr ratio was higher in asphyxiated group compared to controls(normal newborns) (2.65+/-0.53 VS 1.57+/-0.25). This is significant. The umbilical cord blood pH had significant positive correlation with 1st minute Apgar

score, 5th minute Apgar, while urinary UA/Cr ratio had significant negative correlation with cord blood pH ($r = -0.63$, $p = 0.002$). Urinary UA/Cr ratio with criterion of >2.3 had 88.24% sensitivity, 94.12% specificity with AUC of 0.971 ($p < 0.001$) had a better predictive value.

Conclusion: Urinary UA/Cr ratio is an accessible, non-invasive, painless, cost-effective supportive framework with good predictive value for use as an additional marker for birth 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.

Keywords: *Discourteous Behaviour, High School Students, Duhok City*

INTRODUCTION

Perinatal hypoxia is one of the leading causes of perinatal mortality in developing countries. Despite the important advances in perinatal care in the past decades, Birth asphyxia remains a stubborn condition leading to significant mortality and morbidity. Birth asphyxia has an incidence of 1 to 6 per 1,000 live full-term births, and represents the third most common cause of neonatal death (23%) after preterm birth (28%) and sepsis (26%). [1] If the hypoxemia is severe enough, the tissues and vital organs (muscle, liver, heart, and ultimately the brain) will develop an oxygen debt. Anaerobic glycolysis and lactic acidosis will result. [2] Asphyxia is an impairment of gas exchange that results not only in the deficit of oxygen in blood but also an excess of carbon dioxide causing acidosis. The acidosis further leads to hypotension and ischemia culminating in hypoxic-ischemic injury. The brain is especially vulnerable to damage by hypoxia and ischemia because it has one of the highest oxygen requirements and one of the highest base line blood flow of all the organs in a term neonate. [3,4] Early indicators of tissue damages due to birth asphyxia are lacking and not widely studied. Prolonged hypoxia, produces failure of oxidative phosphorylation and ATP production. Decreased ATP and increased cellular destruction will be causing an increase of Adenosine Monophosphate (AMP) and Adenosine Diphosphate (ADP), which will then get broken down to its constituents of adenosine, inosine and hypoxanthine. Continuous tissue hypoxia and resulting reperfusion injury will lead to hypoxanthine being oxidized to xanthine and uric acid in the presence of xanthine oxidase. This will increase the uric acid production and cause it to enter blood from damaged tissues. This uric acid will then get excreted in urine where it can be easily detected. [5,6]

MATERIALS AND METHODS

The study was carried out in the Department of Paediatrics Krishna Hospital, KIMS, KARAD. All deliveries are attended by residents trained in neonatal resuscitation. Sixty eight term neonates were recruited for the study. Thirty four term babies with 37 weeks of gestations with apgar score ≥ 7 at 5 min with no signs of asphyxia were recruited as controls and Thirty four term babies with >37 weeks of gestations admitted to NICU with apgar score of 6 or less at 5 minutes of birth were recruited as cases. Babies with congenital malformations, suspected metabolic disease on treatment with diuretics, suffering from anuria and those born to mothers having hypertension, diabetes mellitus, toxemia of pregnancy, receiving general anaesthesia, phenobarbitone and other drugs likely to cause depression in babies. The spot urinary samples within 6-24 hours of birth were collected by staff nurse 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 estimated in same above instrument by using Jaffe's alkaline picrate method. ABG values from ABG GEM Premier were taken. Analysis has been performed using the commercially available statistical Software SPSS (Statistical Packages for Social Sciences) 25.0 Software, and Excel 2021. The p-value of less than 0.05 has been considered statistically significant. Pearson correlation coefficient has been used to test the strength of association

between arterial blood pH and other variables. Receiver Operating Characteristic (ROC) plots have been used to determine the cutoff values of various parameters and their significance.

OBSERVATIONS AND RESULTS

There were 32 females and 36 males in both groups. The mean gestational age and birth weight of asphyxiated group (38.65±1.21 weeks, 2.98±0.29 kg) were significantly lower than the control group (38.75±1.25 weeks, 3.09±0.03 kg) respectively (p<0.05).

Urinary UA/Cr ratio showed negative correlation with arterial blood pH (r= -0.18, p=0.2713), which was not significant.

Mean of various parameters like Apgar 5th min, arterial blood pH, Partial Pressure of Oxygen

(pO₂) (mm Hg) values (6.08, 7.01, 36.41) respectively were significantly lower in asphyxiated group than control group-values (8.97, 7.37, 60.17) respectively (p<0.0001). Mean of various parameters like Partial Pressure of Carbondioxide (PCO₂) (mm Hg), urinary uric acid (mg/dl), and urinary uric acid/ creatinine ratio values (47.97, 36.93, 2.65) respectively were significantly higher in asphyxiated group than control group-values (40.43, 19.88, 1.57) respectively (p<0.0001).

TABLE 1: Comparison of baseline characteristics of asphyxiated group and controls

Baseline Characteristics	Cases (N=34)		Controls (N=34)		Unpaired t-value	p-value
	Mean	SD	Mean	SD		
Gestational Age	38.85	1.21	38.75	1.25	0.36	0.72
Birth Weight	2.98	0.29	3.09	0.3	1.47	0.15
APGAR at 1 min.	3.85	0.82	7.17	0.45	20.6	<0.0001*
APGAR at 5 min.	6.08	0.7	8.97	0.17	22.94	<0.0001*

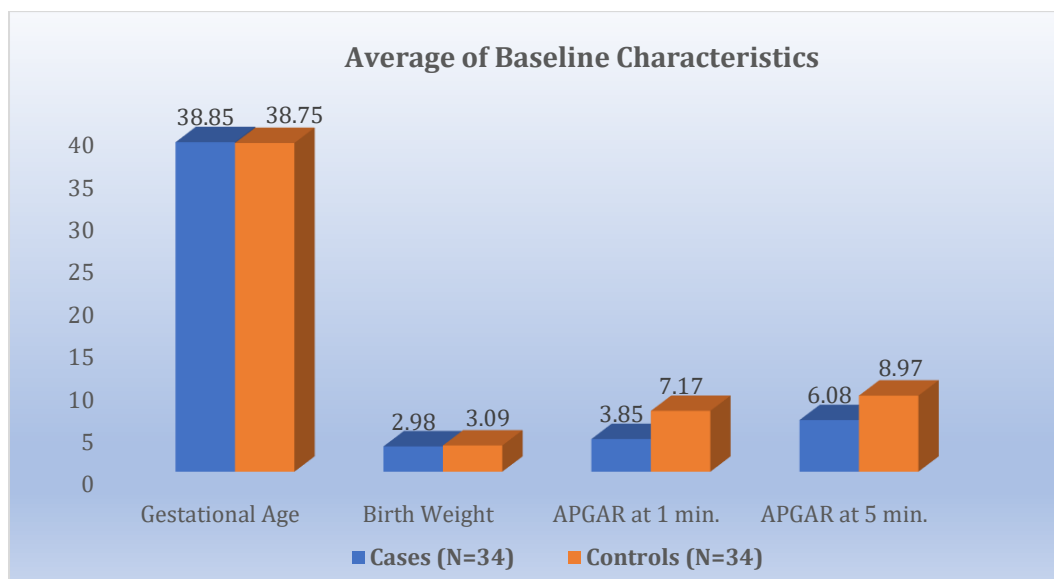


FIGURE 1: Comparison of Mean of baseline characteristics of asphyxiated group and controls.

TABLE 2: Comparison of Cord Arterial Blood pH of asphyxiated group and controls.

Cord Arterial Blood pH	Cases (N=34)	Controls (N=34)	Unpaired t-value	p-value
Mean	7.01	7.37	12.44	<0.0001*
SD	0.17	0.03		

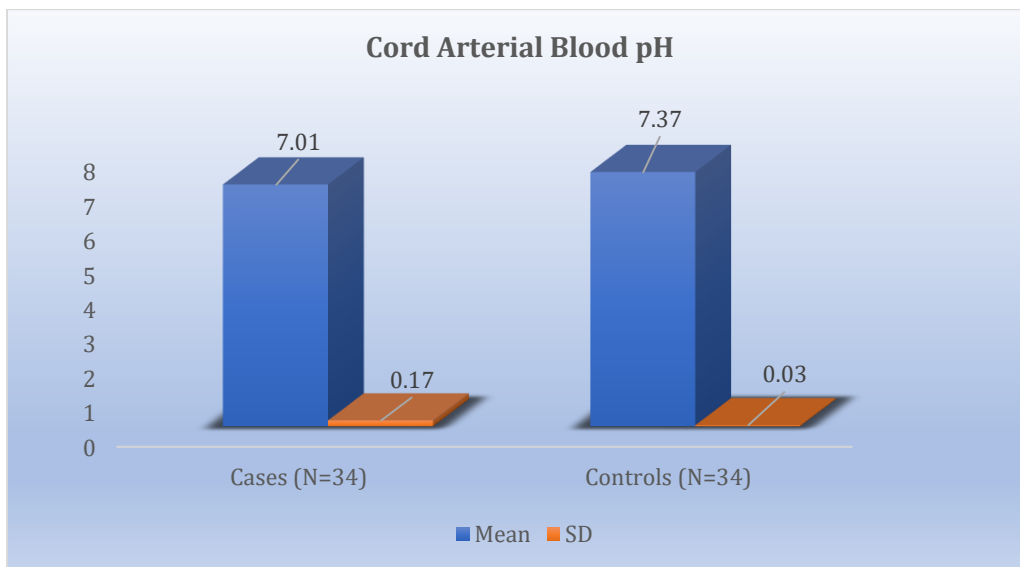


FIGURE 2: Comparison of Cord Arterial Blood pH of asphyxiated group and controls.

Mean Cord Arterial Blood pH of asphyxiated group and controls are 7.01 and 7.37 respectively.

TABLE 3: Comparison of pO₂ of asphyxiated group and controls.

pO ₂	Cases (N=34)	Controls (N=34)	Unpaired t-value	p-value
Mean	36.41	60.17	37.79	<0.0001*
SD	2.38	2.79		

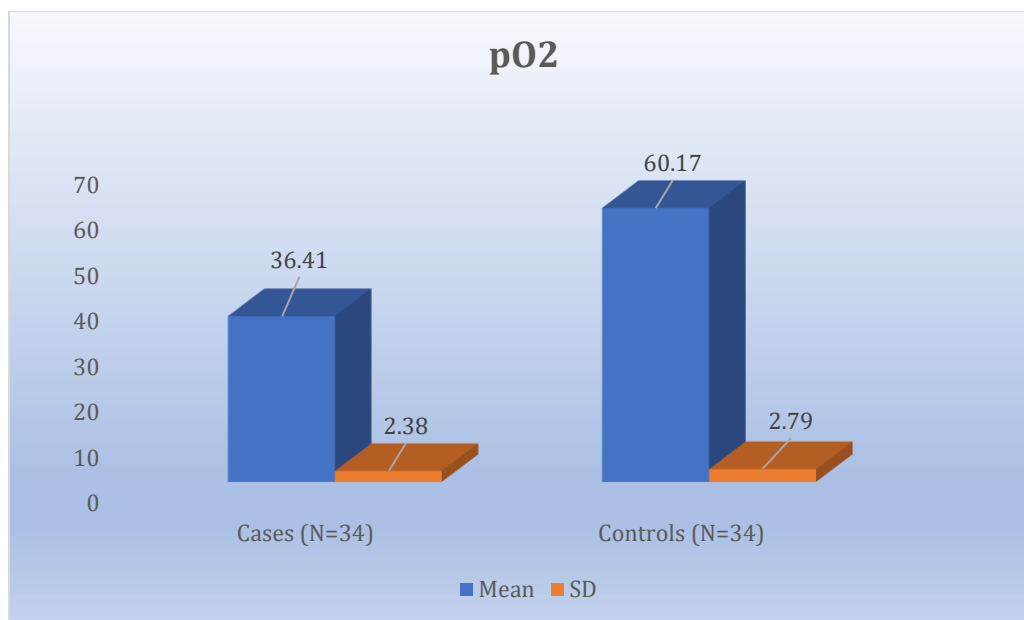


FIGURE 3: Comparison of Cord Arterial Blood pH of asphyxiated group and controls.

Mean pO₂ of asphyxiated and control groups are 36.41 and 60.17 respectively.

TABLE 4: Comparison of pCO₂ of asphyxiated group and controls.

pCO ₂	Cases (N=34)	Controls (N=34)	Unpaired t-value	p-value
Mean	47.97	40.43	7.12	<0.0001*
SD	3.44	3.88		

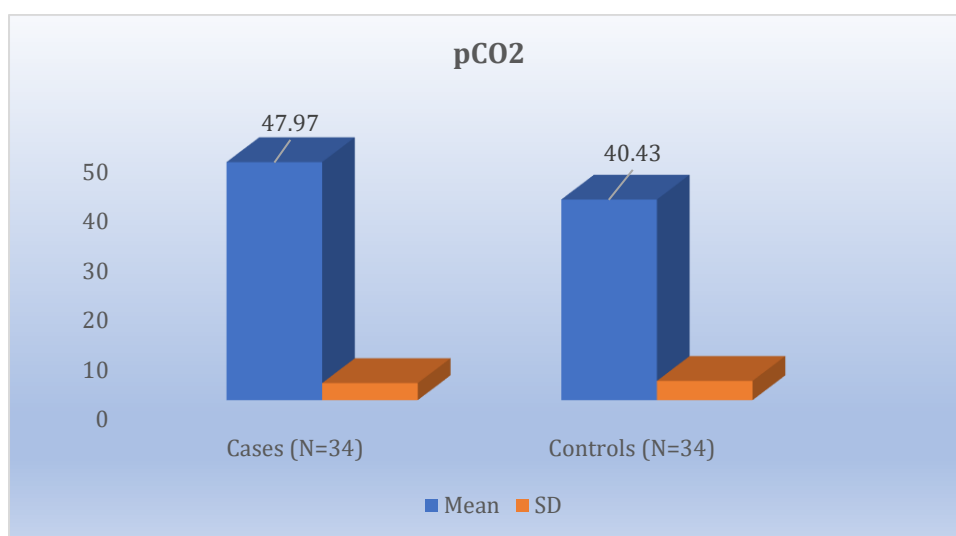


FIGURE 4: Comparison of pCO₂ of asphyxiated group and controls.

Mean pCO₂ values of asphyxiated group is 47.97mmHg and control group was 40.43mmHg.

TABLE 5: Comparison of urinary uric acid of asphyxiated group and controls.

Urinary uric acid (mg/dl)	Cases (N=34)	Controls (N=34)	Unpaired t-value	p-value
Mean	36.93	19.88	13.39	<0.0001*
SD	7.09	2.19		

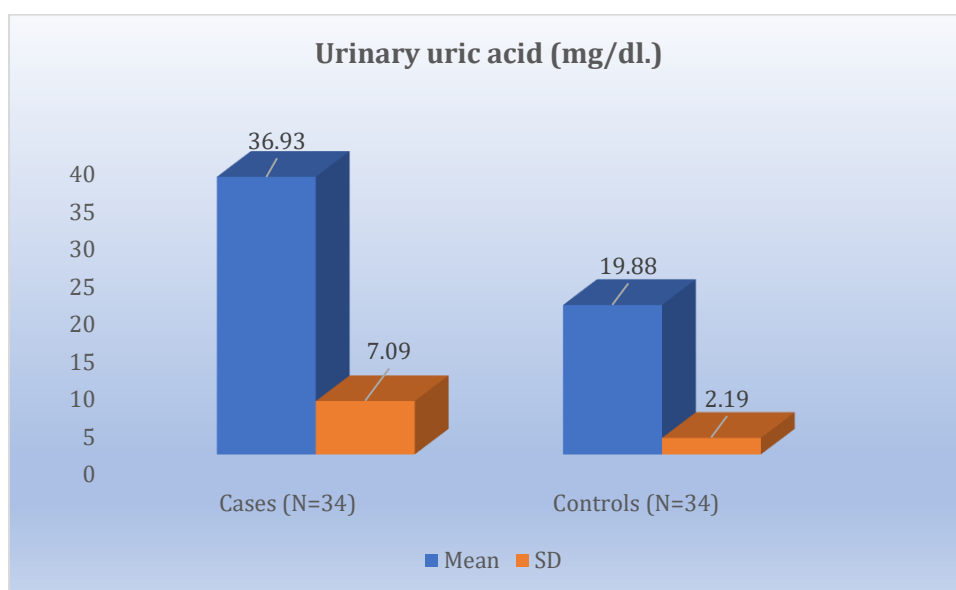


FIGURE 5: Comparison of urinary uric acid of asphyxiated group and controls.

Mean Urinary uric acid value of asphyxiated group is 36.93mg/dl and control group was 19.88mg/dl.

TABLE 6: Comparison of urinary creatinine of asphyxiated group and controls.

Urinary Creatinine (mg/dl)	Cases (N=34)	Controls (N=34)	Unpaired t-value	p-value
Mean	14.12	12.83	2.83	0.006*
SD	2.11	1.6		

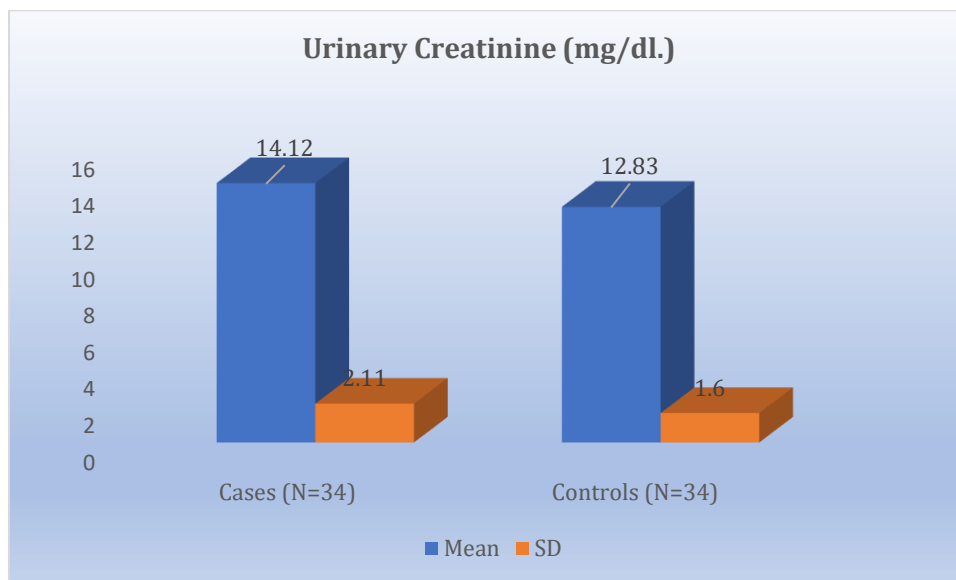


FIGURE 6: Comparison of urinary creatinine of asphyxiated group and controls.

Mean urinary creatinine value of asphyxiated group is 14.12mg/dl and of control group is 12.83mg/dl

TABLE 7: Comparison of Urine Uric acid/ Ur Creatinine Ratio of asphyxiated group and controls.

Urine Uric acid/ Ur Creatinine Ratio	Cases (N=34)	Controls (N=34)	Unpaired t-value	p-value
Mean	2.65	1.57	10.69	<0.0001*
SD	0.53	0.25		

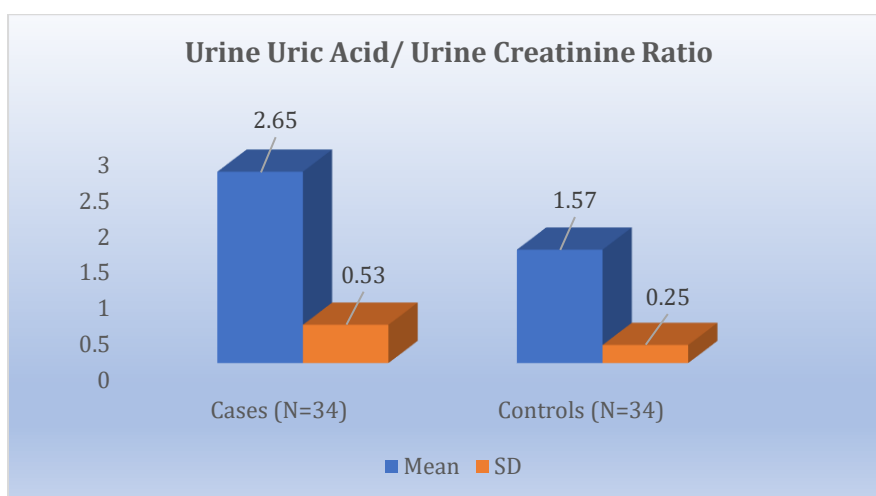


FIGURE 7: Comparison of urine uric acid/ ur creatinine ratio of asphyxiated group and controls.

Mean urinary uric acid/ creatinine ratio of asphyxiated group is 2.65 and of control group is 1.57.

TABLE 8: ROC curve analysis of study parameters predictive values of biochemical parameters for perinatal asphyxia such as arterial blood pH, pO₂, pCO₂, and UA/Cr ratio, Apgar at 1st min and Apgar at 5th min.

Study Parameters	Cut off value	Sensitivity	Specificity	AUC	P-value	95% confidence interval of AUC
pH	7.2	100	100	1	<0.0001	0.96, 1.000
pO ₂	42	86.42	96	0.92	<0.0001	0.869, 0.986
pCO ₂	44	81.56	90	0.918	<0.0001	0.897, 0.993
Urinary Uric Acid/Creatinine ratio	2.3	100	100	1	<0.0001	0.95, 1.000
Apgar at 1st min.	8	100	100	1	<0.0001	0.97, 1.0
Apgar at 5th min.	6	100	100	1	<0.0001	0.945, 1.000

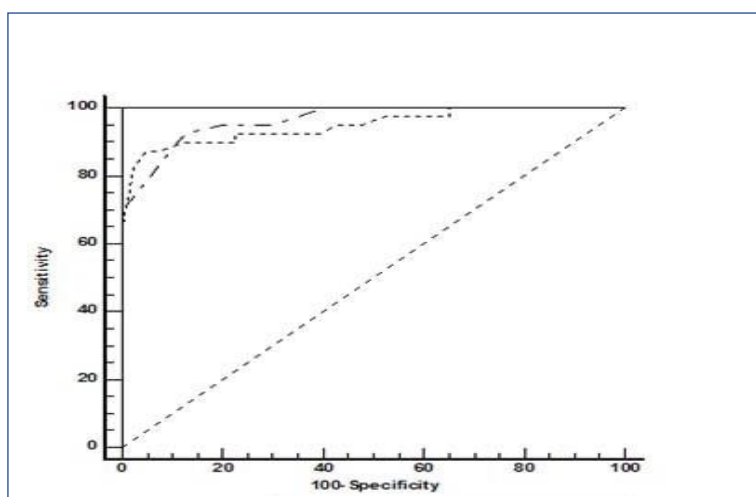


FIGURE 8: ROC curve analysis of study parameters in this study.

DISCUSSION

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

Urinary UA/Cr ratio is simple, non-invasive and economical investigation for the diagnosis of perinatal asphyxia. Combined use of arterial blood pH, apgar scores and UA/Cr ratio can help in early decision making about the level of care the new born requires. There have been very few

studies from developing countries that have focused on this parameter. Basu et al., showed that the urinary UA/Cr ratios were significantly higher in cases than controls (3.1 ± 1.3 vs 0.96 ± 0.54 ; $p < 0.001$) and among asphyxia patients [8], a significant negative linear correlation was found between the UA/Cr ratio and the apgar score ($r = -0.857$, $p < 0.001$). Current study is in consonance with many other studies that have looked at low apgar score and urinary UA/Cr ratio [4,7,12,18,20].

Bader D et al ,reported that the UA/Cr was higher in the asphyxiated group when compared to controls($2.06 + 1.12$, vs. $0.64 + 0.48$; $p < 0.001$), these are similar type findings with our results.

According to Bhongir, et al, mean urinary UA/Cr ratio was (2.58 ± 0.48 vs 1.89 ± 0.59).The urinary

UA/Cr ratio had significant negative correlation with cord blood pH, and umbilical cord blood pH had significant positive correlation with 5th minute Apgar ($r=0.44$, $p=0.002$). Urinary UA/Cr ratio with cutoff of >2.43 had 80% sensitivity, 87.5% specificity with AUC of 0.84 ($p=0.003$).

According to Chen HJ et al, Urinary UA/Cr ratio was higher in asphyxiated term and premature infants with and without perinatal asphyxia than term healthy infants ($p<0.05$). When the urinary ratio of UA to Cr was greater than 0.95, perinatal asphyxia was identified with a sensitivity of 80% and a specificity of 71% in term infants. Their study included premature infants also. [7,8,9,10]

In the present study In Asphyxiated and control group, mean urinary UA/Cr ratio was (2.65 \pm 0.53 VS 1.57 \pm 0.25). This is significant. The umbilical cord blood pH had significant positive correlation with 1st minute Apgar score, 5th minute Apgar, while urinary UA/Cr ratio had significant negative correlation with cord blood pH ($r=-0.63$, $p=0.002$). Urinary UA/Cr ratio with criterion of >2.3 had 88.24% sensitivity, 94.12% specificity with AUC of 0.971 ($p<0.001$) had a better predictive value.

CONCLUSION

Urinary UA/Cr ratio is an accessible, non-invasive, cost-effective supportive framework with good predictive value for use as an additional marker for birth asphyxia.

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