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Original Research Article

Correlation of Clinical Diagnosis of Perinatal Asphyxia and Severity of HIE with Spot Urinary Uric Acid to Creatinine Ratio

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ABSTRACT

Retrospective diagnosis of perinatal asphyxia is an important challenge in country like India where nearly two-thirds of the child births are unsupervised and neonates with perinatal asphyxia are brought to hospital without any reliable perinatal history. The overlapping of signs and symptoms of perinatal asphyxia with various other conditions make the diagnosis more difficult. Mostly diagnosis is by clinical assessment and severity is assessed by SARNAT an SARNAT staging. This study was carried out in Dr. BSA Hospital and Medical College in 2016 using simple biochemical test UUA/Cr for assessing severity of HIE. This is a simple and readily available test in most of the hospitals. We found this test as a very useful biochemical marker for diagnosis of perinatal asphyxia and staging severity of HIE. There was a significant correlation between ratio of UUA/Cr to severity of HIE.

Keywords: HIE- hypoxic ischemic encephalopathy, AGA- appropriate for gestational age, FT- full term, UUA/Cr-Urinary Urinary Uric Acid to Creatinine ratio, APGAR score, NST-Non-reactive stress test, TMSAF-thick meconium stained amniotic fluid, LSCS-lower segment caesarian section, SNART and SNART staging of HIE

INTRODUCTION

In India perinatal asphyxia is a very important cause of neonatal morbidity and mortality. Every year 2,50,000 to 3,50,000 infants die secondary to perinatal asphyxia mostly in the first three days of life. [(1)] Data from National Neonatal Perinatal Database (NNPD) suggest that perinatal asphyxia is contributing to almost 20% of neonatal deaths in India. [(2)] Perinatal asphyxia is generally a clinical diagnosis based on recording of APGAR score at 1, 5 and 10 minutes of birth. Two-thirds of the deliveries in India take place outside the medical institutions and are unsupervised but contribute significantly to the total number of cases of perinatal asphyxia and HIE. In the absence of perinatal records it is very difficult to make a retrospective diagnosis of perinatal asphyxia and HIE due to overlapping signs and symptoms like hypotonia, lethargy, refusal to feed and seizures which may be due to various other causes. [(3)] This study was carried out to assess the diagnostic as well as supportive value of biochemical test like Urinary uric acid/Creatinine ratio (UUA/Cr) for diagnosis of perinatal asphyxia and grading the severity of HIE. UUA/Cr is a simple biochemical test and readily available making it a test of choice over other complicated investigations like EEG, cranial ultrasonography, cranial tomography, specific enzyme analysis which may be available in only selected tertiary care centers. Hypoxanthine is a catabolic product

of ADP, AMP accumulated during hypoxemia & anaerobic glycolysis. Following reperfusion of the hypoxic tissue, Hypoxanthine is oxidized to xanthine and uric acid. [4,5] It is UUA/Cr ratio which is being measured in the present study.

MATERIALS & METHODS

This is a Prospective Case Control study comparing sixty neonates with perinatal asphyxia to sixty normal neonates. It was carried out in Dr. BSA Medical College and Hospital in the year January 2016- November 2016. One spot urinary sample within 6-24 hours of birth of cases and controls was the study material. The study was carried out after approval of Ethical Committee of the hospital

Inclusion Criteria

i. Term neonates ≥37 weeks, AGA delivered per vagina or through LSCS who suffered asphyxia during perinatal period were included as cases. Perinatal asphyxia was diagnosed by presence of at least three of these:- [7]
ii. APGAR <7 at one minute [8,9]
iii. Requiring more than one minute of positive pressure of ventilation
iv. Umbilical artery blood sample collected within 30 minutes of birth showing metabolic or mixed academia & PH < 7. [6,10]
v. Intrapartum signs of fetal distress, as indicated by non reassuring NST on continuous electronic fetal monitoring and /or by thick meconium staining of the amniotic fluid (TMSAF)

Exclusion Criteria

a. Where mother received magnesium sulphate ≤ 4 hours of delivery or received opioid analgesic
b. History of mother consuming alcohol, smoker, drug addict or taking any epileptic drugs
c. Neonates with congenital malformation

Controls

Included sixty term healthy neonates, AGA with APGAR score of ≥ 7 at one minute, clear liquor and without any sign of perinatal asphyxia.

Maternal history, gestational age by New Ballard scoring, APGAR score at one, five and ten minute, birth weight, sex and any other important intrapartum events were recorded. Asphyxiated babies were resuscitated as per standard protocol and further monitored and managed for any adverse effect of asphyxia. [7] SARNAT and SARNAT staging was used for grading severity of HIE into mild, moderate and severe. One urine sample was collected in a sterile clean container within 06-24 hours of birth. It was frozen at -20°C and analyzed. Spectrophotometric uricase method and Jaffe's alkaline picrate method were used for estimation of urinary uric acid and Creatinine respectively by auto-analyzer (Roche / Hitachi 917).

Statistical Analysis

Percentage number for categorical measurements and Mean ± SD, (Min- Max) for continuous measurements were used. Values were considered significant at 5% level of significance. Inter group analysis on continuous scale was compared by Student t test. Homogeneity of variance was tested by Leven 1 s test. Parameters on categorical scale in two or more groups were checked for significance by Chi- square / Fisher Exact test. Microsoft word and Excel for graphs and tables and SSPS version 15, SAS 9.2 were used for data analysis.

RESULT

TABLE-1: DEMOGRAPHIC PROFILE OF CASES AND CONTROLS

PARAMETER	CASES (n=60)	CONTROLS (n=60)	Significance
GENDER			P=0.315
MALE	36	30	
FEMALE	24	30	
GESTATIONAL AGE			P=0.277
TERM	41	60	
POST DATED	14	0	
POST TERM	5	0	
BIRTH WT (Mean ± SD)	2.86 ± 0.47	3.10 ± 0.42	P=0.13
MATERNAL HISTORY			P=0.057
PRIMI	35	32	
MULTI	25	28	

TABLE-2: APGAR SCORE OF CASES AND CONTROLS

TIME	CASES		CONTROL		P VALUE
	<7	>7	<7	>7	<0.001
1 Minute	60	0	0	60	
5 Minute	22	38	0	60	
10 Minute	12	48	0	60	

Following parameters were statistically significant in cases over controls: -

1. LSCS and instrumental deliveries (P<0.001)
2. Non-reassuring NST (P=0.004)
3. Thick meconium stained liquor (P<0.005)
4. Low APGAR at 1, 5 and 10 minutes (P<0.001)

The mean UUA/Cr value in cases was (2.62 ± 1.05) compared to control group (1.06 ± 0.41), statistically significant (P<0.001). Further the mean SD value of UUA/Cr in different stages of HIE was as below:

Stage of HIE	Number	Mean ± SD	Min- Max
HIE – No	17	1.46 ± 0.73	0.782 - 2.65
HIE – Stage 1	19	2.81 ± 0.47	1.70 - 3.67
HIE – Stage 2	18	3.10 ± 0.66	2.36 - 4.02
HIE – Stage 3	06	4.41 ± 0.38	3.73 - 4.97

P value <0.001

In this study, we found mean ± SD value of UUA/Cr ratio in cases 2.62 ± 1.05 (Min – Max 0.82-4.97) compared to controls 1.06 ±0.21 (Min – Max 0.61-1.30). It was observed that UUA /Cr value of more than 1.47 as cut off value had a sensitivity of 89%, specificity of 94%, positive predictive value of 93%, negative predictive value of 85% and accuracy in diagnosis of 94%. There was also a positive correlation in value of UUA / Cr to severity of HIE.

DISCUSSION

In India, approximately two-thirds of child births are unsupervised i.e. no perinatal history is available but these constitute a large proportion of total cases of perinatal asphyxia. Retrospective diagnosis of birth asphyxia is very difficult due to overlap of symptoms of perinatal asphyxia with various other conditions in the newborn. Umbilical cord ABG estimation may also help in diagnosis of asphyxia if carried out in half an hour of birth but most of the time neonates present much later than half an hour. This simple biochemical test (UUA/Cr) in addition to clinical assessment may be of great help in diagnosis of perinatal asphyxia. UUA/Cr value may also compliment in grading of HIE usually carried out by SARNAT and SARNAT staging [(16)] based on clinical examination which is subject to observational variations. We observed that the cut off value of UUA/Cr of more than 1.47 for diagnosis of perinatal asphyxia with a sensitivity of 89% and specificity of 94%, PPV of 93% and NPV of 85% with an accuracy of 94% was similar to studies by Bader et al [(11)] and Chen et al. [(12)] There was a positive correlation in severity of HIE with increasing value of UUA / Cr. A fatal outcome has been predicted by Banupriya et al [(13)] with a cut off value of UUA/Cr of 2.34. Two asphyxiated newborns who had fatal outcome in our study had UUA/Cr ratio of 4.72 and 4.97. However, the number is very small to make any conclusion about cut off value of UUA/Cr to predict fatal outcome. It was also observed that the severity of HIE was better comparable with APGAR score at 5 and 10 minutes compared to at one minute similar to studies by Salustiano et al, [(14)] Ehrenstein et al. [(15)]

CONCLUSION

This simple and easily available biochemical test i.e. UUA/Cr ratio can be used as an additional marker in early diagnosis of perinatal asphyxia. It may also be used to help in grading the severity of the HIE carried out clinically by SNART & SNART staging which may have observational variations.

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