Original Article

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Paediatrics Section

Evaluation of Renal Artery Resistive Index as a Predictor of Acute Kidney Injury in Perinatal Asphyxia: A Prospective Observational Study

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ABSTRACT

Introduction: Acute Kidney Injury (AKI) is a serious but challenging complication of perinatal asphyxia. Doppler flowmetric studies have demonstrated the potential for its prediction. Renal artery resistive index, a non-invasive modality and prompt intervention can help in early detection of AKI.

Aim: To evaluate the utility of renal artery resistive index as a predictor of acute kidney injury in perinatal asphyxia.

Materials and Methods: The present prospective observational study was conducted at Department of Paediatrics, VPIMS , Lucknow, Uttar Pradesh, India from December 2019 to February 2021. Sixty newborns with perinatal asphyxia were enrolled in the study. At enrollment, sex, gestational age at birth, mode of delivery, birth weight, and Apgar scores at 1 and 5-min were recorded. Renal artery Resistive Indices (RRI) were measured using color doppler at 2-24 hr and 48-72 hr intervals. Maternal Serum Creatinine (S.Cr) levels were assessed at enrollment. Neonatal S.Cr. levels were assessed at enrollment and every 24-hr interval till day 7. The chi-square test was used for proportions, whereas the independent samples t-test was used to compare the mean values. Comparative differences were considered significant at 'p' value <0.05.

Results: The majority of newborns were males 38 (63.3%), born at term 37 (61.7%), through caesarean delivery 40 (66.7%), and had a birth weight of >2500 g, 34 (56.7%). The incidence of AKI was found in 17 neonates (28.3%). No significant association between AKI and the demographic, baseline characteristics of the newborns was observed. RRI at 2-24 hr as well as 48-72 hr too did not significantly associated with AKI (p-value 0.460 and 0.423, respectively).

Conclusion: RRI failed to predict AKI in newborns with perinatal asphyxia. Additional studies with large sample sizes and incorporation of other non-invasive measures such as Near Infrared Spectroscopy (NIRS) may provide more insight into this relationship.

Keywords: Doppler flowmetry, Hypoxic ischaemia, Neonate, Renal insufficiency, Serum creatinine

INTRODUCTION

Perinatal asphyxia is defined by the World Health Organisation (WHO) as the failure to initiate and sustain breathing at birth [1]. It is a major contributor to neonatal mortality worldwide, accounting for 24% of all neonatal deaths [2-4]. Acute kidney injury (AKI) is more common in asphyxiated neonates and can adversely affect overall prognosis [5]. The prevalence of kidney involvement in birth asphyxia was approximately 56% [6]. Kidneys are very sensitive to hypoxia and renal insufficiency can occur within 24 hours of hypoxic insult, which, if prolonged, may lead to irreversible injury [7]. AKI is characterised by a sudden impairment of renal function that results in altered fluid, electrolyte, and acid-base balance [7]. Acute kidney injury (AKI) in birth asphyxia can further complicate the management of an asphyxiated newborn and result in severe morbidity and mortality [8].

Currently doppler ultrasound is rapidly gaining ground as a screening tool for critically ill patients. The use of cardiac, lung, cranium and abdominal ultrasound in sick and crashing neonates has become a standard policy. However, renal ultrasound, which can be easily incorporated into screening, is not commonly performed. Renal vasoconstriction is an early manifestation of acute kidney injury (AKI). Renal Doppler ultrasound can be used to measure the renal resistive index (RRI), a sonographic index that reflects alterations in the blood flow profile of the intrarenal arcuate or interlobar arteries. It reflects the relationship between the decline in speed, loss of flow ("flow velocity") between the peak of systole and end of diastole in (renal) blood vessels: RRI= (peak systolic velocity- end diastolic velocity)/(peak systolic velocity) [9]. Data on the predictive value of RRI for AKI development, independent of other risk factors, are controversial in literature [10,11].

Given the frequency of AKI in perinatal asphyxia, the present study aimed to evaluate the utility of renal artery resistive index as a predictor of acute kidney injury in perinatal asphyxia.

MATERIALS AND METHODS

The present prospective observational study was carried out at the Department of Paediatrics, Vivekananda polyclinic and institute of medical sciences, Lucknow, Uttar Pradesh, India over a period of 14 months from December 2019 to February 2021. Study was commenced after obtaining approval from the Institutional Ethics Committee (VPIMS/ME/IEC/CC/Nov.2019) and informed consent from the parents.

Inclusion criteria: A total of of 60 newborns (both term and preterm) diagnosed with perinatal asphyxia were included. For the purpose of study perinatal asphyxia was defined as Apgar score of 0-3 at 1-minute or cord pH of ≤7.1 or base deficit of >12 mmol/l [3].

Exclusion criteria: Neonates with major congenital malformations and chromosomal anomalies, renal and cranial malformations detected antenatally or postnatally and suspected sepsis were excluded from the study.

Sample size calculation: Sample size projections were based on a previous study [9], and the mean difference in end-diastolic velocity between perinatal asphyxia cases with AKI and controls was found to be 1.2 with an effect size of 0.882. Targeting similar differences in RRI in perinatal asphyxia patients with and without AKI, the sample size for the two groups was 22 in each group. The sample size was estimated using G Power version- 3.1.9.2 (Düsseldorf University, Germany). However, considering the prospective nature of the study, assuming the prevalence of AKI in the cohort to be 40%, a total sample size of 55 was obtained. After creating contingency provisions of 10% and rounding off, the targeted sample size was 60.

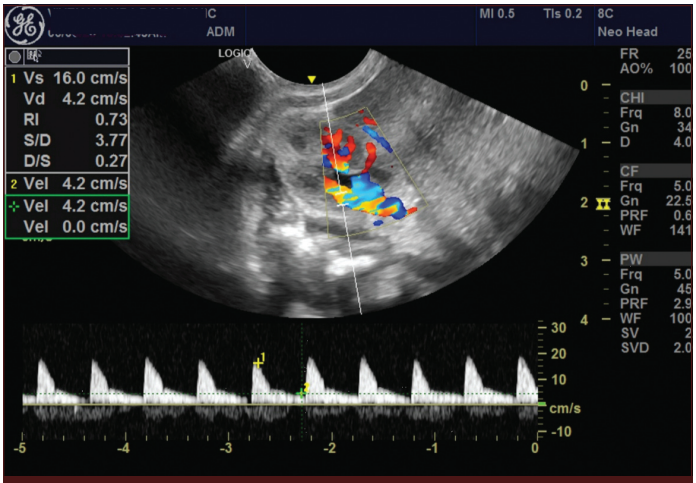
Study Procedure

At enrollment, details such as gender, gestational age at birth, mode of delivery, birth weight, and Apgar scores at 1 and 5-min were recorded. All newborns were followed-up till day 7 for the occurrence of AKI. AKI was defined as [12-14]:

1. Serum creatinine >1.5 mg/dL for at least 24-48 hours if the mother renal function is normal.
2. Serum creatinine rise >0.3 mg/dL over baseline.
3. Serum creatinine fails to fall below the maternal plasma creatinine within 5-7 days.

Doppler studies of the renal artery blood flow velocity were performed on days 1-3. The first renal artery doppler examination was conducted after the first 2 hours of life. Blood flow velocities were studied in two windows: 2-24 hours and 48-72 hours. GE Logic V2 with neonatal probe 8c was used for renal artery doppler ultrasonography. The renal artery was sampled 5-10 mm from the abdominal aorta in the sagittal plane at the lowest insonation angle (<15°). After a stable velocity recording of more than 10 consecutive beats, three consecutive waveforms with the highest possible velocities were recorded for the Peak Systolic Velocity (PSV) and End Diastolic Velocity (EDV) [Table/Fig-1]. The images were crosschecked by an expert Radiologist. The Resistive Index (RI) [15] was then calculated using the following formula:

RI= (PSV-EDV)/PSV.



[Table/Fig-1]: Measurement of RRI.

Both the left and right renal arteries were assessed. For the purpose of this study, average of two was considered as the representative value.

STATISTICAL ANALYSIS

Data were analysed using the IBM Statistical Package for Social Sciences (SPSS) software (version 25.0). Categorical data are shown as numbers and percentages ,continuous data are shown as mean±standard deviation. The chi-square test was used for proportions, whereas the independent samples t-test was used to compare the mean values. Comparative differences were considered significant at 'p' value <0.05.

RESULTS

The majority of newborns were males 38 (63.3%), born at term 37 (61.7%), through caesarean delivery 40 (66.7%), and had a birth weight of >2500 g 34 (56.7%). At 1-min, the maximum 26 (43.3%) had Apgar score 3-4 whereas at 5-min, the majority had Apgar score >7 48 (80%). Mean RRI at 2-24 and 48-72 hrs were 0.75±0.09 and 0.75±0.10 respectively. The incidence of AKI was 28.3% [Table/Fig-2].

S. no	Variables	Number of neonates	Percentage
1.	**Sex**		
	Male	38	63.3
	Female	22	36.7
2.	**Gestational age at birth**		
	<37 weeks	23	38.3
	≥37 weeks	37	61.7
3.	**Mode of delivery**		
	LSCS	40	66.7
	NVD	20	33.3
4.	**Birth weight**		
	≤1500 g	2	3.3
	1501-2000 g	6	10.0
	2001-2500 g	18	30.0
	>2500 g	34	56.7
5.	**Apgar score at 1-min**		
	3-4	26	43.3
	5-6	18	30.0
	≥7	16	26.7
6.	**APGAR score at 5-min**		
	3-4	4	6.7
	5-6	8	13.3
	≥7	48	80.0
7.	**Incidence of AKI**		
	Yes	17	28.3
	No	43	71.7
8.	**Mean renal artery RI±SD (2-24 hr)**	0.75±0.09	
9.	**Mean renal artery RI±SD (48-72 hr)**	0.75±0.10	

[Table/Fig-2]: Profile of Neonates enrolled in the study (n=60).

No significant association of AKI was observed with sex (p=0.363), gestational age at birth p=0.761), mode of delivery (p=0.685), birth weight (p=0.690), or Apgar score at 1 and 5-minutes intervals (p=0.690 and 0.070 respectively). At both 2-24 hr and 48-72 hr, the mean RRI was higher in the AKI group than the non-AKI group, however this difference was not statistically significant (p-value 0.460 and 0.423 respectively) [Table/Fig-3].

S. no.	Variables	Total number of neonates	With AKI	Without AKI	Statistical significance
1.	**Sex**				
	Male	38	12 (31.6%)	26 (68.4%)	χ^2=0.538; p=0.363
	Female	22	5 (22.7%)	17 (77.3%)	

2.	**Gestational age at birth**				
	<37 weeks	23	6 (26.1%)	17 (73.9%)	χ^2=0.093; p=0.761
	≥37 weeks	37	11 (29.7%)	26 (70.3%)	
3.	**Mode of delivery**				
	LSCS	40	12 (30.0%)	28 (70.0%)	χ^2=0.164; p=0.685
	NVD	20	5 (25.0%)	15 (75.0%)	
4.	**Birth weight**				
	≤1500 g	2	0	2 (100%)	χ^2=1.486; p=0.690
	1501-2000 g	6	2 (33.3%)	4 (66.7%)	
	2001-2500 g	18	4 (22.2%)	14 (77.8%)	
	>2500 g	34	11 (32.4%)	23 (67.6%)	
5.	**APGAR at 1-min**				
	3-4	26	10 (38.5%)	16 (61.5%)	χ^2=1.486; p=0.690
	5-6	18	5 (27.8%)	13 (72.2%)	
	≥7	16	2 (12.5%)	14 (87.5%)	
6.	**APGAR score at 5-min**				
	3-4	4	1 (25.0%)	3 (75.0%)	χ^2=5.315; p=0.070
	5-6	8	5 (62.5%)	3 (37.5%)	
	≥7	48	11 (22.9%)	37 (77.1%)	
7.	**Mean Renal artery RI±SD (2-24 hr)**		0.76±0.07	0.74±0.09	t=0.744; p=0.460
8.	**Mean Renal artery RI±SD (48-72 hr)**		0.77±0.08	0.75±0.11	t=0.806; p=0.423

[Table/Fig-3]: Association of AKI with profile of neonates.
Percentages have been calculated row-wise

DISCUSSION

In the present study, the incidence of AKI was 28.3%. In contrast to the present study, Ramaswamy VV et al., in their study reported AKI in 43.3% of their neonates [9]. The findings in the present study are in agreement with those of El Meneza S et al., who reported an incidence of 29.6% [16]. High variability in the incidence of AKI among asphyxiated neonates has been reported, ranging from 7 to 72% [17-19]. The relatively lower incidence of AKI in present study could be due to the strict exclusion criteria that ruled out neonates with various abnormalities, including renal, congenital, and probable sepsis.

In the present study, observed average RRI at 2-24 and 48-72 hrs interval as 0.75±0.09 and 0.75±0.10 respectively. Compared to present study, El Meneza et al., in their study reported the mean renal artery RI values at day 1 in 0.73±0.03 to 0.86±0.6 range and at day 3 in 0.71±0.03 to 0.78±0.07 range [16]. In the study by Ramaswamy VV et al., day 1 mean RI was 0.76±0.10 while on day 3 it was 0.79 [9]. In the present study, no significant association between the incidence of AKI and RRI at either follow-up intervals was found. Ramaswamy et al., in their study did not find a significant association between renal artery parameters and AKI on either day 1 or day 3 observations [9]. Similarly, El Meneza S et al., in their study found no predictive value for AKI prediction for day 1 value, although they did find that the mean RI of nephropathy cases was significantly higher than that of cases without nephropathy [16]. Both these studies included investigations with inclusion of a control group and found a significant difference in these parameters between cases and controls in general. While the predictive role of these parameters is more important for the prediction of AKI in perinatal asphyxia cases, the presence of a significant difference between perinatal asphyxia cases and healthy controls does not hold much value.

As such, the present study did not find a significant association between doppler flowmetric parameters of the renal artery and the prediction of AKI in neonates with perinatal asphyxia. Considering the fact that perinatal asphyxia poses a dynamically changing clinical and physiological profile of the patients, it is essential that the problem must be assessed taking into account additional factors than those studied in the present work. Further studies with larger sample sizes could help to understand this problem in a more pragmatic manner.

Limitation(s)

Being a single centre study, the results might not be representative of broader populations or applicable to other clinical settings. The present study focused on short term outcomes, long-term renal and neurodevelopmental outcomes in asphyxiated neonates were not assessed.

CONCLUSION(S)

The present study found no significant correlation between RRI and AKI in perinatal asphyxia. The results suggest that RRI may not be a reliable predictor of AKI in this population. The findings of the current study contribute to the ongoing researches of optimal non-invasive diagnostic approaches for AKI in neonates. Additional studies with large sample sizes and incorporation of other non-invasive measures such as Near Infrared Spectroscopy (NIRS) may provide more insight into this relationship.

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