International Journal of Contemporary Pediatrics
Sood A et al. Int J Contemp Pediatr. 2022 Jul;9(7):653-657
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: https://dx.doi.org/10.18203/2349-3291.ijcp20221608

Original Research Article

Evaluation of renal function among term neonates with perinatal asphyxia

Arvind Sood[1], Arunima Bhardwaj[1]*, Surinder Singh[1], Jagjjit Singh Chahal[2]

[1]Department of Pediatrics, [2]Department of Biochemistry, Indira Gandhi Medical College, Shimla, Himachal Pradesh, India

Received: 09 January 2022
Revised: 23 May 2022
Accepted: 25 May 2022

***Correspondence:**
Dr. Arunima Bhardwaj,
E-mail: arunimaaaa244@gmail.com

ABSTRACT

Background: Perinatal asphyxia is a significant cause of morbidity and mortality amongst neonates in developing countries. The incidence of perinatal asphyxia in developed countries is 2 per 1000 live births, but the rate is 10 times higher in developing countries due to inadequate access to neonatal and maternal care. Among neonates with HIE, it is difficult to predict which newborn will develop renal dysfunction so there is urgent need for publication about relations of severity of HIE and renal dysfunction
Methods: This prospective case control study was conducted on 50 term neonates as cases and 50 term neonates in control group. Neonates in case groups were diagnosed according to WHO definition of HIE and age and sex matching of babies were done. Serum creatinine was measured one baseline and another after 48 hours of life.
Results: The study shows mean maternal age 25.24±4.65 in the cases and 27.44±4.17 in control group, gravida of 1.64±0.89, 1.60±0.78 in case and control group, APGAR score at 1 minute & 5minutes 3.40±1.34, 5.62±1.55 in cases and 7.0±0.0, 9.0±0.0 in control group which is statistically significant ($p<0.001$). Among cases 78% had moderate birth asphyxia and 22% had severe perinatal asphyxia. Among cases 62% (31/50) babies developed AKI and among cases with AKI 20 (62.5%) developed prerenal AKI and 37.5% (12/31) developed intrinsic AKI.
Conclusions: The detection renal dysfunction at an early stage can help in early intervention and prevention of irreversible renal damage and thus, will improve overall survival of these asphyxiated neonates. Serum creatinine levels correlates with severity of HIE.

Keywords: AKI, Fractional excretion of sodium, RFI, Hhypoxic ischemic encephalopathy

INTRODUCTION

Perinatal asphyxia is a common cause of neonatal morbidity and mortality. Its incidence is about 1-10% per 1000 live births.[1] The world health organizations has defined birth asphyxia as "failure to initiate and sustain breathing at birth" and based on APGAR score as an Apgar score of <7 at one minute of life.[2] Asphyxia can cause multiorgan dysfunction due to redistribution of cardiac output. Perfusion to more vital organs like heart brain and adrenals is maintained at the expense of kidneys, gut and skin. As a consequence, kidney is one of the frequently injured organs due to perinatal asphyxia.[3] kidneys are very sensitive organ to oxygen deprivation, renal insult may occur within 24 hours of a hypoxic ischemic episode which if prolonged, may even cause irreversible cortical necrosis.[4] The presence of perinatal asphyxia and its severity appears to correlate with the increasing incidence of AKI.[4,5] Asphyxia is an important cause of AKI and transient kidney impairment with

adverse effects, especially in initial five days of birth.[3] Acute kidney Injury has replaced the term acute renal failure by most critical care and nephrology societies to highlight the importance of detecting this process at the time of injury rather than to wait until complete failure has occurred. Early recognition of renal injury is important for maintenance of fluid and electrolyte homeostasis[4].

Current diagnostic approach of AKI is based on an acute decrease of GFR, as reflected by an acute rise in serum creatinine (SCr) levels and/or decline in urine output over a given time interval.[6-8] Due to paucity of such studies especially from this part of country, we intended to do this study.

Aim of the study

Aim of the current study was evaluation of renal function among term neonates with HIE and its correlation with degree of HIE.

METHODS

The present study of evaluation of renal function among term neonates with HIE and its correlation with degree of HIE was carried out in the neo-natal unit of tertiary care institution at Indira Gandhi medical college Shimla from September 2019 to September 2020. Cases were enrolled after obtaining informed consent from parents of all study participants in their own language.

Study design

Current study was a prospective case control study.

Inclusion criteria

Inclusion criteria for current study were; babies born at term with perinatal asphyxia as evidenced via any one of the following**:** APGAR score <7 at 1 min of life, fetal bradycardia (HR<100 beats/min) clinical evidence of hypoxic ischemic encephalopathy using Sarnat and Sarnat staging of HIE. Babies who needed positive pressure ventilation for more than 1 minute at birth or need of mechanical ventilation at birth.

Exclusion criteria

Exclusion criteria for current study were; preterm (POG<37 weeks), post term (POG >42 weeks**)**, babies whose mother had significant illness like eclampsia, diabetes mellitus or who have received drugs like aminoglycosides, ACE inhibitors or indomethacin and mother with renal impairment, babies with significant illness like sepsis, Rh incompatibility, babies with congenital renal malformation and those who died within 3 day Gestational age, birth weight, relevant perinatal history and examination findings were recorded in predesigned Performa. Term appropriate for gestational age (AGA) newborns delivered during the study period matched for hours after birth and sex with 1 min Apgar score more than 7 were enrolled as controls from the postnatal ward of the same hospital. Gestation age assessment was based on the accurate recollection of date of the last menstrual period of mother, when doubt existed; assessment of newborn using Expanded New Ballard score was used.

On the basis of APGAR score at 1 min the asphyxiated neonates were further grouped in to moderate (score 4-6) and severe asphyxia (score 3 or less). Neurological examination was done using Sarnat and Sarnat scoring. All the neonates were managed as per standard NICU protocol. Two millilitres of venous samples was collected at birth and after 48 hours and before 72 hours of life for estimation of electrolytes, blood urea (modified Berthelot strategy) and serum creatinine. Creatinine was estimated on Roche fully automated chemistry analyzer in the department of Biochemistry. For estimation of serum electrolytes ion selective electrode principle was used.

Urine output was monitored by applying plastic collection bag or by catheterization if required. Care was taken to prevent contamination of urine with stool. The blood and urine sample thus were sent for estimation of sodium, potassium, urea, creatinine. Also, urinary osmolality was done after 24 hours and before 48 hours of life. All urinary samples were evaluated for proteinuria, urine specific gravity between 24 to 48 hours of life. RFI and FeNa were calculated in all cases and controls between 24 to 48 hours of life. AKI is defined as an abrupt (within 7 days) reduction in kidney function currently defined as an absolute increase in serum creatinine of more than or equal to 0.3 mg/dl, a percentage increase in serum creatinine of more than or equal to 50% (1.5-fold from baseline) or a reduction in urine output (documented oliguria of <0.5 ml/kg per hour over 24 hours). Modified KDIGO classification was used to categorize AKI. Asphyxiated neonates who fulfilled above criteria were diagnosed to have AKI and were given a fluid challenge of 20 ml/kg with normal saline and monitored for urine output. If urine output fails to ensue despite fluid challenge, intravenous loop diuretics (frusemide) were administered. If despite these interventions, urine output still <1 ml/kg/hr, neonates were diagnosed to have intrinsic AKI.

Data entry and statistical analysis

The collected data were transformed into variables, coded and entered in Microsoft Excel. Data were analyzed and statistically evaluated using Epi-info version 7.2.3.1. Quantitative data was expressed in mean ± standard deviation or median with interquartile range and depends on normality distribution difference between two comparable groups were tested by student's t-test (unpaired) or Mann Whitney 'U' test while for more than two groups ANNOVA test or Kruskal Wallis H test followed by posthoc test was used. Qualitative data were

expressed in percentage. Statistical difference between the proportions was tested by chi square test or Fisher's exact test. Spearman correlation coefficient was used to see the correlation between two quantitative variables. 'P' value less than 0.05 was considered statistically significant. Sample size was calculated using Epi-info version 7.2.3.1 by taking confidence interval (two sided) 95% and power of 80% and assumption of expected mean difference of AKI values of 26.95. The sample size comes out to be 47 to each group.

RESULTS

There were 50 cases of perinatal asphyxia and 50 matched controls. There was no significant difference between studied groups as regarding gestational age, weight, sex, maternal age and parity. There was statistically significant difference among Apgar score at 1 and 5 minutes between cases and controls as shown in (Table 1).

Table 1: Baseline characteristics in asphyxiated and non-asphyxiated babies.

Variables	Cases (N=50)	Controls (N=50)	P value
	Mean±SD	Mean±SD	
Maternal age (years)	25.24±4.65 (18-36)	27.44±4.17 (20-37)	0.01
Gravida	1.64±0.89 (1-4)	1.60±0.78 (1-5)	0.86
APGAR score at 1 minute	3.40±1.34 (1-6)	7.0±0.0 (7-7)	<0.001
APGAR score at 5 minutes	5.62±1.55 (2-9)	9.0±0.0 (9-9)	<0.001
Length of baby	49.68±1.52 (47.5-52)	49.78±1.56 (47-53)	0.75
Birth weight (kgs)	2.93±0.34 (2.5-3.7)	2.92±0.31 (2.5-3.5)	0.81
Gestational age (weeks)	39.16±1.02	38.77±0.98	0.07

Table 2: Mode of delivery in asphyxiated and non-asphyxiated babies.

Mode of delivery	Cases (N=50)		Controls (N=50)	
	N	%	N	%
Normal vaginal delivery	23	46.0	36	72.0
Assisted vaginal delivery	6	12.0	4	8.0
Emergency LSCS	21	42.0	8	16.0
Elective LSCS	0	0.0	2	4.0

Table 3: Renal function tests in asphyxiated and non-asphyxiated babies.

Variables	Cases (N=50)	Controls (N=50)	Intergroup P value
	Mean±SD	Mean±SD	
Creatinine clearance (ml/min/1.73m^2)	17.51±4.62 (8.3-28.6)	24.32±6.01 (12-39)	<0.001
Urine output (ml/kg/hr)	1.17±0.69 (0.2-3.5)	1.59±0.22 (1.24-2.1)	<0.001
Urine creatinine (mg/dl)	17.35±6.02 (8-33)	15.58±1.95 (10-28)	<0.001
Urine pH	5.09±0.18 (4.9-6)	6.05±0.38 (5-7)	<0.001
Urine specific gravity	1.017±0.007 (1.01-1.03)	1.021±0.007 (1.01-1.05)	0.01
Urine K^+ (m mol/l)	16.25±3.03 (10-25)	17.50±3.56 (11-26)	0.06
Urine Na^+ (m mol/l)	47.6.±14.2 (16-88)	18.78±2.51(13-23)	<0.001
FeNa (%)	2.12±0.89 (1-4.1)	1.25±0.42 (0.58-2.70)	<0.001
RFI	3.1±1.53(1.1-8)	1.73±0.58 (0.8-3.6)	<0.001
Urine osmolality	426.92±107.84 (249-610)	602.72±40.35 (520-680)	<0.001

Assisted vaginal delivery and emergency cesarean section were more common among cases (12%, 42%) as compared to controls (8%, 16%). Among cases 78% had moderate birth asphyxia and 22% had severe perinatal asphyxia.

Most common mode of resuscitation among cases was bag and mask ventilation (61%). Among cases five babies (10%) had no HIE while eleven babies (22%) developed HIE-stage I, 24 babies (48%) developed HIE-stage II and 10 babies (20%) developed HIE-stage III. There was statistically significant difference among different stages of HIE in serum creatinine, blood urea, urine sodium, creatinine clearance and renal indices like FeNa and RFI were also among cases 62% (31/50) babies developed AKI and among cases with AKI 20 (62.5%) developed prerenal AKI and 37.5% (12/31) developed intrinsic AKI.

Urine parameters like creatinine clearance, urine output, urinary creatinine, Ph, urinary sodium, fractional

excretion of sodium, renal failure index and osmolality all showed statistically significant difference between cases and controls except urine potassium and urine specific gravity as shown in (Table 3). In this study as HIE stage progressed from stage-I to stage-III there was increase in values of blood urea, serum creatinine, urinary sodium, FeNa, RFI, along with fall in creatinine clearance and this difference was statistically significant ($p<0.001$).

Table 4: Distribution of renal parameters among different stages of HIE.

HIE staging	Stage 1 (N=11)	Stage 2 (N=24)	Stage 3 (N=10)	P value
Creatinine clearance	20.90±2.81	16.90±3.10	12.09±3.15	<0.001
Serum Creatinine	1.1±0.131	1.469±0.24	2.01±0.32	<0.001
Blood urea	46±4.6	75.1±8.34	92.8±12.3	<0.001
Urine Na^+	50.27±13.04	70.92±27.24	107.1±23.02	<0.001
FeNa	2.12±0.77%	3.77±2.33%	8.86±2.20%	<0.001
RFI	3.81±2.30	6.48±3.59	14.38±5.03	<0.001

Table 5: Comparison of current study findings with earlier published reports.

Studies	Year	AKI (%)	Oliguric AKI (%)	Non oliguric AK (%)
Aggarwal et al[4]	2005	68	42	58
Gupta et al[9]	2005	47.1	22	78
Seema Rai etal[10]	2016	43	41.86	58.14
Chaudhary et al[11]	2020	58.6	39.03	60.97
Present study	2021	62	25	75

DISCUSSION

Perinatal asphyxia is a very common problem in neonatal intensive care units and is an important cause of neonatal mortality and morbidity.[1] As kidneys are very sensitive organs to oxygen deprivation, renal insufficiency can take place within 24 hours of a hypoxic ischemic insult which if prolonged may lead to irreversible cortical injury.[4] Kidneys are most commonly involved in ischemia.[3]And, insight drawn from previous studies puts AKI between 50-72%.[5,6,8] Kidneys are most commonly involved in ischemia.[3] And, insight drawn from previous studies puts AKI between 50-72%.[5,6,8]

Limitations

Limitations of current study were; maternal creatinine values were not considered. CVP monitoring, NIBP, EEG, and imaging studies were not done. Long term follow up of babies with AKI was not done to look for any residual renal damage on follow up.

CONCLUSION

Perinatal asphyxia remains to be one of the very important cause of neonatal renal failure. Most common form of AKI among neonates with birth asphyxia is prerenal and it responds to fluid resuscitation with 100% recovery. In birth asphyxia even non-oliguric babies may also have AKI, hence monitoring of urine output along with serum and urinary parameters are crucial for early detection of AKI. AKI in birth asphyxia has very robust positive correlation with HIE staging.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. National Neonatal-Perinatal Database. Available at: https://www.newbornwhocc.org/pdf/nnpd_report_2002-03.PDF. Accessed on 23 November 2021.
2. Odd D, Heep A, Luyt K, Draycott T. Hypoxic-ischemic brain injury: Planned delivery before intrapartum events. J Neonat Perinat Med. 2017; 10(4):347-53.
3. Carter BS, McNabb F, Merenstein GB. Prospective validation of a scoring system for predicting neonatal morbidity after acute perinatal asphyxia. J Pediatr. 1998;132(4):619-23.
4. Agarwal R, Deorari A, Paul V. AIIMS protocol in neonatology. 2nd ed. United States of America: Elsevier; 2019;419.
5. Eichenwald E, Hansen A. Cloherty and Stark's Manual of Neonatal Care. 7th ed. USA: Lippincott Williams & Wilkins; 2010.
6. Brezis M, Rosen S. Hypoxia of the renal medulla its implications for disease. N Engl J Med. 1995; 332(10):647-55.
7. Barry B, Brenner M. Harrisons principles of internal medicine. in: Harrisons principles of internal medicine. 16th ed. 2005;1644-6.
8. Aggarwal A, Kumar P, Chowdhary G, Majumdar S, Narang A. Evaluation of renal functions in asphyxiated newborns. J Trop Pediatr. 2005;51(5): 295-9.

9. Gupta BD, Sharma P, Bagla J, Parakh M, Soni JP. Renal failure in asphyxiated neonates. Indian Pediatr. 2005;42(9):928-34.
10. Rai S, Singh N. Renal Status in Birth Asphyxia. J Trop Pediatr. 2016;3(5):3.
11. Chaudhary R, Tiwari AK, Usmani F. Study of incidence of acute kidney injury in asphyxiated neonates with hypoxic ischemic encephalopathy. Int J Contemp Pediatr. 2020;7(11):2205-9.

Cite this article as: Sood A, Bhardwaj A, Singh S, Chahal JS. Evaluation of renal function among term neonates with perinatal asphyxia. Int J Contemp Pediatr 2022;9:653-7.