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Evaluation of renal function among term neonates with perinatal asphyxia

[1]Dr. Nasima Banu, [2]Dr. Vijay Kumar Sukhani, [3]Dr. Ramya, [4]Dr. Sushma V

[1,2]Associate Professor, [3]Assistant Professor, Department of Pediatrics, RIMS, Raichur, Karnataka, India

[4]Resident, Department of Pediatrics, RIMS, Raichur, Karnataka, India

Corresponding author:Dr. Nasima Banu

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Abstract

Introduction: Perinatal asphyxia is relatively a significant etiology of morbidity and mortality among the neonates in various developing countries like India. Therefore the incidence of developing perinatal asphyxia in developed countries is observed to be 2 per 1000 live births but this rate is 10 times higher in many of the developing countries since there is inadequate access to the neonatal and maternal care. Hence the present study has been conducted to evaluate the renal function among the term neonates reported with perinatal asphyxia.

Materials and Methodology: Throughout the study, veracity is well-maintained at any cost and the study participants are free to withdraw from the study at any time during the study progress. All the study participants were informed about the study procedure and a written informed consent is obtained from their parents/guardians. It will be taken in accordance with the principles of declaration of Helsinki as revised in 2013. This study has been intended to be carried out in Neonatal Intensive care unit (NICU, RIMS, Raichur) and this study has been adopted as a prospective case control study. The collected data were transformed into variables, coded and entered in Microsoft Excel. Quantitative data was expressed in mean ± standard deviation or median with interquartile range and depends on normality distribution difference between two comparable groups.

Results: Out of 102 newborns were observed to be suffering from perinatal asphyxia, 73 (72%) were males and 29 (28%) were female neonates. A total of 33 (32%) newborns had reported with severe birth asphyxia (Apgar score 0-3 at 1 minute of life) and 69 (68%) had moderate birth asphyxia (APGAR score 4-6 at minute of life). When observed on the day-1, average serum urea and creatinine were seem to be 20.09±14.54 mg/dL and 0.88±0.51 mg/dL and the urine output was found to be 1.27±0.43 mL/kg/hr.

Conclusion: The renal impairment in perinatal asphyxia could be effectively used as an early predictor or disease severity and are quite helpful in the early management and routine vigorous monitoring of the neonates.

Keywords: renal function, glomerular filtration rate, renal dysfunction, serum urea, serum creatinine

Introduction

Perinatal asphyxia could be defined as the condition majorly resulting from lack of oxygen (hypoxia) or lack of perfusion (ischemia) to fetus or newborn which has the potential to cause multiple organ dysfunction of sufficient magnitude and duration.[1] The burden of asphyxia at birth among neonates is relatively so high that every hour 104 children generally die due to the condition and the condition is very alarming in many developing countries like India which reported between 250,000 to 350,000 infant deaths annually that happen mostly within the first

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three days of life.[2] According to the world health organizations, birth asphyxia has been defined as "failure to initiate and sustain breathing at birth" and based on APGAR score as an APGAR score of less than 7 at one minute of life.[3] Asphyxia can result in multi-organ dysfunction due to redistribution of cardiac output. Perfusion to more vital organs like heart, brain and adrenals is normally maintained at the expense of kidneys, gut and skin. As a consequence of birth asphyxia, kidney is one of the most frequently injured organs due to perinatal asphyxia.[4] The reported incidence of renal injury among asphyxiated babies has been reported between 50–72% in various published studies.[5] Early recognition of renal injury plays a crucial role for the maintenance of fluid and electrolyte homeostasis.

Acute renal failure has been seemed to be occurring in 61% of infants observed with severe asphyxia and this condition is mostly non-oliguric. Various renal functions like glomerular filtration rate (GFR) and fractional sodium excretion (FENa) were observed to be impaired significantly and reported upto 60% among the asphyxiated babies particularly among those with clinical presentation was expected to be severe in grading.[6] Hence the present study has been conducted to evaluate the renal function among the term neonates reported with perinatal asphyxia.

Materials and methodology

The study has been started after seeking prior approval from the institutional ethical committee as per the norms followed from the institute. Throughout the study, veracity is well-maintained at any cost and the study participants are free to withdraw from the study at any time during the study progress. All the study participants were informed about the study procedure and a written informed consent is obtained from their parents/guardians. It will be taken in accordance with the principles of declaration of Helsinki as revised in 2013. This study has been intended to be carried out in Neonatal Intensive care unit (NICU, RIMS, Raichur) and this study has been adopted as a prospective case control study.

The various inclusion criteria that has been followed in this study include, those neonates with APGAR score of less than 7 at 1 minute of life, Fetal bradycardia (HR<100 beats/min), Babies in need of positive pressure ventilation for more than 1 minute at birth or in need of mechanical ventilation at birth. Certain exclusion criteria been followed that include preterm (POG <37 weeks), post-term (POG > 42 weeks), those babies whose mother had significant illnesses like eclampsia, diabetes mellitus or under certain medications like aminoglycosides, ACE inhibitors or indomethacin, babies with observed illnesses like sepsis, Rh incompatability, babies with congenital malformations and those who died within 3 days of gestational age.

Neonates of either sex were admitted with proven perinatal asphyxia, will be screened. These children will be included through purposive sampling. Relevant perinatal history and examination findings will be 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 will be enrolled as controls from the postnatal ward of the same hospital. Gestation age assessment will be 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 will be used. On the basis of APGAR score at 1 min the asphyxiated neonates will be further grouped in to moderate (score 4-6) and severe asphyxia (score 3 or less). Two milliliters of venous samples will be 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 will be estimated on Roche fully automated chemistry analyzer. For estimation of serum electrolytes ion selective electrode principle will be used. Urine output will be monitored by applying plastic collection bag or by catheterization if required. Care will be taken to prevent contamination of urine with stool. The blood and urine sample thus will be sent for estimation of sodium, potassium, urea, creatinine. Also,

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urinary osmolality will be done after 24 hours and before 48 hours of life. All urinary samples will be evaluated for proteinuria, urine specific gravity between 24 to 48 hours of life. RFI and FENa will be calculated in all cases and controls between 24 to 48 hours of life.

The collected data were transformed into variables, coded and entered in Microsoft Excel. 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. 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.

Results

Out of 102 newborns were observed to be suffering from perinatal asphyxia, 73 (72%) were males and 29 (28%) were female neonates. A total of 33 (32%) newborns had reported with severe birth asphyxia (Apgar score 0-3 at 1 minute of life) and 69 (68%) had moderate birth asphyxia (APGAR score 4-6 at minute of life). When observed on the day-1, average serum urea and creatinine were seem to be 20.09±14.54 mg/dL and 0.88±0.51 mg/dL and the urine output was found to be 1.27±0.43 mL/kg/hr. Out of 102 asphyxiated newborns, 41 (40.7%) had observed with normal renal function (Group - A) and the remaining 61 (59.3%) had observed with abnormal renal function (Group - B) When observed on the day – 3, mean serum urea was around 24.44±14.13 mg/dL and mean serum creatinine was 0.92±0.54 mg/dL with the measured urine output was 1.28±0.39 mL/kg/hr. In group – B, mean serum urea and creatinine was estimated relatively higher and urine output is relatively lower when compared to Group – A.

When evaluated on the day – 10, mean serum urea, creatinine and urine output were quantified at 10.31±2.15 mg/dL, 0.34±0.21 mg/dL and 1.42±0.22 mL/kg/hr. In this point of time, 98 (96.6%) newborns had reported with normal renal functions while the remaining 4 (3.4%) ahd abnormal renal functions. When comparing the Group – A and Group – B, results were statistically significant between serum urea, creatinine and urine output on day – 10.

Table – 1: Mean serum urea, creatinine and urine output between group A (Normal RFT and Urine output) and group B (Abnormal RFT and Urine output) on post-natal day 1, 3 and 10

RFT	Days	Group – A (n=41)	Group – B (n=61)	Total (n=102)	P - value
Serum urea (mg/dL)	**Day – 1**	6.61±2.24	29.33±11.92	20.09±14.54	<0.001
	Day – 3	10.29±1.68	33.79±10.41	24.44±14.13	<0.001
	Day - 10	10.04±1.22	17.85±6.65	10.31±2.15	<0.001
Serum creatinine (mg/dL)	**Day – 1**	0.35±0.09	1.23±0.31	0.88±0.51	<0.001
	Day – 3	0.38±0.11	1.29±0.36	0.92±0.54	<0.001
	Day – 10	0.31±0.10	1.19±0.15	0.34±0.21	<0.001
Urine output (mL/kg/hr)	**Day – 1**	1.38±0.19	1.17±0.51	1.27±0.43	0.006
	Day – 3	1.39±0.23	1.19±0.46	1.28±0.39	0.003
	Day - 10	1.44±0.22	1.19±0.19	1.42±0.22	0.024

Discussion

Perinatal asphyxia has been known to produce multiple organ dysfunctions. In the present study, various biochemical parameters are majorly suggestive of renal dysfunctions, urine output and hemodynamic condition of the asphyxiated neonates were profoundly monitored

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and are found to have significant differences. It is very crucial to understand that acute kidney injury can also be resulted in neonates who are in non-oliguric. In this study, 82% of the neonates were observed with abnormal renal function tests which were non-oliguric which was comparable to the results obtained in a study conducted by *Gupta* BD et al where non-oliguric renal failure was observed to be around 78%.[7] Few earlier studies by *Aggarwal* A et al reported with 56% of the asphyxiated neonates observed with abnormal renal functions which was almost identical to the results obtained from this present study.[8] Other studies by *Mohan* PV and *Pai* MP had observed with 72% of the neonates were reportedly suffering from asphyxia wither oliguric or non-oliguric renal failure.[9]

Renal functions assessed by *Jayaswal* A et al in 40 neonates of different HIE stages on day 3 and 5 of age showed significant difference.[10] Similar to our finding in their study as the HIE stage increased biochemical derangement increased. In a study by *Medani* SA et al found AKI in 54.1% of neonates diagnosed as HIE. Contemporary to other studies most of them belonged to stage II (63%) of HIE, instead of stage III. This can be due to the variation in age group according to days of life in their study and higher mortality in stage III.[11] Similar to most of the studies *Reddy* S et al had also found ARF in 100% of stage III, 81.2% of stage II and least 7.1% of neonates suffering from stage I.[12]

The major strength of the study were observed to be adequate sample size, permissible error for sample size calculation and well defined age levels were used to denote the renal dysfunction for efficient enrolling study. In this study, it has been noted that neonates with normal maternal serum urea and serum creatinine (before delivery) to remove maternal effects of renal function test. All the asphyxiated neonates had been screened for acute renal failure at the earliest so thay they can be effectively treated at the pre-renal failure stage only without letting them to progress to intrinsic renal failure since there has been high mortality.

Conclusion

Renal dysfunction is relatively a common findings in all the neonates affected with perinatal asphyxia. Renal derangement indirectly increases with the severity of the condition. Therefore the renal impairment in perinatal asphyxia could be effectively used as an early predictor or disease severity and are quite helpful in the early management and routine vigorous monitoring of the neonates.

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