Journal of Current and Advance Medical Research
January 2021, Vol. 8, No. 1, pp. 12-16
http://www.banglajol.info/index.php/JCAMR
ISSN (Print) 2313-447X
ISSN (Online) 2413-323X
NLM Catalog ID 101673828
DOI: https://doi.org/ 10.3329/jcamr.v8i1.52475

ORIGINAL ARTICLE

Risk Factors and Primary Diseases Responsible for Acute Kidney Injury among Neonates

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[**Received on:** 1 November 2020; **Accepted on:** 20 December 2020; **Published on:** 1 January 2021]

Abstract

Background: There are several risk factors and diseases related with the acute kidney injury among neonates. **Objective:** The purpose of the present study was to find out the risk factors and primary disease responsible for acute kidney injury among neonates. **Methodology:** This cross-sectional study was conducted in the Department of Paediatric Nephrology at Bangabandhu Sheikh Mujib University, Dhaka, Bangladesh from May 2018 to July 2019 for a period of one year. Patients with the age group of less than 1 months who were at risk of AKI, and admitted in the inpatient department of Pediatrics and allied at Bangabandhu Sheikh Mujib University, Dhaka, Bangladesh in both sexes were selected as study population. To detect AKI, serum creatinine was measured at 0 h (baseline), 48 h and 5th day respectively. **Result:** A total number of 52 patients who fulfilled the inclusion criteria were enrolled in this study. Among them 10 cases were in neonatal age group. The mean age was 10.8±5.4 days with female predominance. The risk factors of AKI in neonate was only pre-renal; mostly due to hypovolemia which was 3(60.0%) cases followed by sepsis and asphyxia which were 1(20.0%) case in each. The most patients had sepsis which was 4(40.0%) cases followed by congenital heart disease which was 2(20.0%) cases. **Conclusion:** In conclusion hypovolemia, sepsis and asphyxia are the most common risk factors of acute kidney injury among the neonates. [*Journal of Current and Advance Medical Research, January 2021;8(1):12-16*]

Keywords: Risk factors; primary diseases; acute kidney injury; neonates

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Cite this article as: Luna SA, Akter S, Jesmin T, Haque SS, Uddin GM, Roy RR. Risk Factors and Primary Diseases Responsible for Acute Kidney Injury among Neonates. J Curr Adv Med Res 2021;8(1):12-16
Funding: This study has been performed without any funding from outside else.
Conflict of Interest: There was no conflict of interest to any of the authors.
Contributions to authors: Luna SA, Akter S, Jesmin T: literature collection, data collection, analysis; Haque SS, Uddin GM, Roy RR: involved in manuscript writing & revision of the manuscript;

Introduction

Acute kidney injury (AKI) can be defined as the abrupt onset loss of renal function, leading to decrease in glomerular filtration rate (GFR), and impaired control of fluid, electrolytes and acid-base balance[1]. It is a major health problem with pooled incidence of 33.7% and pooled AKI-associated mortality is 13.8% in pediatric age group globally[2]. AKI in the newborn is also a common problem in the neonatal intensive care unit (NICU) with an incidence ranging from 6% to 24.0% cases[3]. It is an independent risk factor for chronic kidney disease (CKD) within 1 to 3 years after an episode of AKI up to 46.8% cases[4]. In developing countries this data is lacking[5].

AKI in the developed world predominantly occurs in hospital settings and is associated with multiple risk factors like sepsis, hypotension, surgery, nephrotoxic agents, the illness in developing countries is chiefly community acquired like acute gastroenteritis, malaria, snake bite, or poisoning[6]. The risk factors and etiology of neonatal AKI are often multifactorial, mostly pre renal including hypovolemia secondary to dehydration, increased insensible loss due to use of phototherapy, radiant warmer and hypotension which accounts for ~85% of neonatal AKI; hypoxemia due to respiratory distress syndrome and severe birth asphyxia another leading causes[7].

It is difficult to depend upon urine output to diagnose AKI as it may be normal, decreased or increased in case of AKI related to nephrotoxic drugs[8]. In this study rising of serum creatinine from baseline has been used according to KDIGO definition to diagnose AKI. Though serum creatinine is a conventional marker to diagnose AKI, it has many drawbacks. It can be influenced by age, gender, diet, muscle mass, dehydration, inflammatory illness, hepatic disease, maternal creatinine[9] and delay between occurrence of significant renal damage and the increase in serum creatinine level up to 3 days after an insult[10]. The purpose of the present study was to find out the risk factors and primary disease responsible for acute kidney injury among neonates.

Methodology

This cross-sectional study was conducted in the Department of Paediatric Nephrology with the collaboration of Paediatric Gastroenterology, Paediatric Neurology, Paediatric Neonatology and Microbiology and Immunology at Bangabandhu Sheikh Mujib University, Dhaka, Bangladesh from May 2018 to July 2019 for a period of one year. Patients with the age group of less than 1 months, who were at risk of AKI, and admitted in the inpatient department of Pediatrics and allied at Bangabandhu Sheikh Mujib University, Dhaka, Bangladesh during this study period in both sexes were selected as study population. Patients with nephrotic syndrome at risk of AKI due to hypovolemia or shock, sepsis, use of nephrotoxic drugs for at least 5 days or patients other than nephrotic syndrome with hypovolemia, use of nephrotoxic drugs for at least 5 days and patients with obstructive uropathy and congenital heart disease needed to use radiocontrast agent were included in this study. Patient already diagnosed as AKI, preterm or patients with hypothyroidism and malignancy were excluded from this study. Patients were selected by purposive sampling technique. Neonate with day of life (DOL) up to 3 days were excluded from this study as maternal creatinine reflects up to 3rd DOL. AKI was defined by any of the two: increase SCr $\geq$ 0.3 mg/dl within a 48 h period or increase SCr $\geq$ 1.5 times or $\geq$ 50% from baseline within 7 days period. In case of using cyclosporine and NSAID risk was considered when patient had associated fever / diarrhea / inadequate fluid intake / use of other nephrotoxic drug and pre renal causes was considered as volume correction, drug dose reduction of CsA and withdrawal of NSAID resulted kidney function became normal. Anthropometry was assessed by measuring height, weight and body mass index (kg/m²). Data was collected with appropriate questionnaire containing proper history, clinical examination and findings of laboratory reports of enrolled patients who fulfilled the inclusion criteria after taking informed written consent. All the cases were numbered chronologically. The data were collected and edited manually. The entered data were checked, verified and analyzed by appropriate computer software. Statistical analysis was performed by using SPSS for windows version 22. The data were presented in tubular or diagrammatical form. All qualitative data were expressed as frequency and percentages. All quantitative data were expressed as mean ± SD. An analysis plan was developed keeping in view with the objectives of the study. Unpaired t-test and paired t-test were done whenever required. For all statistical test $p < 0.05$ was considered statistically significant. Prior to the commencement of this study, the thesis protocol was placed and approved by the Institutional Review Board of BSMMU, Dhaka. For recruitment of study population permission was taken from Pediatrics and allied department. Every ethical issue was discussed with the patient's parents regarding the study. Parents were clearly informed about the nature and purpose of the study, procedures

followed, risk associated with it and benefits from the study in easily understandable local language.

Result

A total number of 52 patients who fulfilled the inclusion criteria were enrolled in this study. Among them 10 cases were in neonatal age group. The mean age was 10.8 ± 5.4 days with female predominance. The mean age in AKI group was 10.8 ± 5.4 days. Mostly were female. There was no significant difference between AKI and non-AKI group. There was no difference in baseline serum creatinine and cystatin C values between two groups (Table 1).

Table 1: Demographic and Lab Parameters of the Study Subjects

Parameters	AKI	Non-AKI	P value
Age (days)	10.8±5.4	9.9±6.6	0.804
Gender			
• Male	2 (40.0%)	3 (60.0%)	1.000
• Female	3 (60.0%)	2 (40.0%)	
*Creatinine	0.62±0.17	0.61±0.06	0.923
**Cystatin C	1.71±0.42	1.56±0.19	0.501

Unpaired t-test was done; *Baseline in mg/dl; ** Baseline in mg/L

The risk factors of AKI in neonate was only pre-renal; mostly due to hypovolemia which was 3(60.0%) cases followed by sepsis and asphyxia which were 1(20.0%) case in each. There was no renal or post-renal risk factors found among the study population (Table 2).

Table 2: Risk Factors in Study Subjects with AKI in Neonatal Age Group

Risk factors	Frequency	Percent
Pre-renal	**5**	**100.0**
• Hypovolemia	3	60.0
• Sepsis	1	20.0
• Asphyxia	1	20.0
Renal	**0**	**0.0**
Post renal	**0**	**0.0**

The most patients had sepsis which was 4(40.0%) cases followed by congenital heart disease which was 2(20.0%) cases; one presented with heart failure and another one had cyanotic congenital heart disease.

One patient had volvulus neonatorum undergone surgery. One had duodenal atresia and 1 had infantile hypertrophic pyloric stenosis. Only 10% had perinatal asphyxia (Figure I).

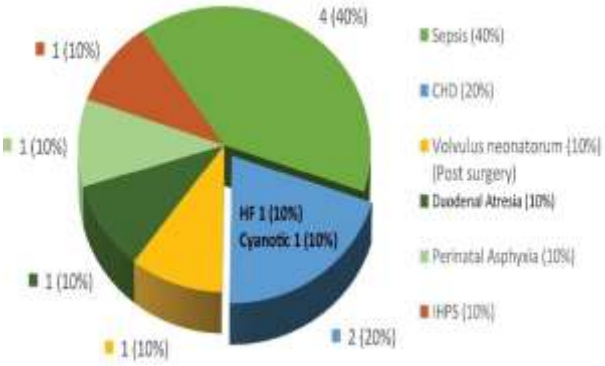

Figure I: Distribution of Primary Diseases in Neonatal Age Group (n=10)

No parameter had significant effect on serum cystatin C at 0 and 48 hours. In 0 hour the gender, height, BMI were related with negatively. However, after 48 hours the negative relation was found in gender, height, BMI, hypovolemia, sepsis and drugs. All these were not statistically significant (p>0.05) (Table 3).

Table 3: Multiple Linear Regression Analysis to Explore the Association of Age, Sex, Anthropometrical Variables and Risk Factors with Serum Cystatin C at 0 h and 48 h in study subjects (n=52)

Variables	0 hour		48 hours	
	OR	P value	OR	P value
Age	0.524	0.269	0.364	0.473
Sex	-0.023	0.903	-0.093	0.648
Weight	1.496	0.270	1.089	0.454
Height	-1.743	0.184	-1.218	0.384
BMI	-0.397	0.547	-0.191	0.788
Hypovolemia	0.045	0.892	-0.372	0.302
Sepsis	0.003	0.989	-0.026	0.915
Drugs	0.025	0.947	-0.282	0.491
Contrast agent	-0.578	0.116	-0.535	0.175

Discussion

In neonatal age group the mean age was 10.8±5.4 days and female were more (60.0%). Almost similar finding was found by Momtaz et al[11] where the average age was 7.4±6.2 days, mostly were female in full term neonate with AKI.

Among renal causes nephrotoxic drug was the most important cause of AKI in this study. Afroz et al[12] found among renal causes 12.5% was drug induced. This showed no similarity with the finding of current study possibly due to different methodology. Aminoglycoside suggested to cause AKI mainly due to incurring tubular damage. Mantan et al[13], however, reported much higher incidence (46.0%) and most of them for amikacin. The present study has also showed similar finding.

The current study revealed that hypovolemia (60.0%) was a prominent pre renal risk factor of AKI in neonate due to dehydration following persistent vomiting, heart failure and surgical intervention. The other risk factors were sepsis and asphyxia. Momtaz et al[11] found that sepsis was the most (77.5%) common cause of neonatal AKI followed by hypovolemia (46.9%) and asphyxia (4.0%). In this study asphyxiated newborn developed cardiogenic shock due to hypoxia.

Ghobrial et al[3] found 78.12% asphyxiated neonate developed pre renal AKI, among them 88.0% were in HIE stage II and developed AKI within 72 to 96 h after birth. Though this is not consistent with present study, the risk factor was also pre renal in current study due to poor renal perfusion and developed AKI within 96 to 120 h. Sepsis was present in 20% cases in this study. This difference of incidence is possibly due to small sample size.

Ozdemir et al[14] found with use of nonionic low osmolar contrast agent in cardiac catheterization 34.7% children with congenital heart disease developed CIN in spite of maintaining proper hydration. No associated risk factors were effective in that study. This incidence is almost similar to present study. Here CIN developed in 30% patient who used radiocontrast agent. But dose of contrast agent was slightly higher (4.1 ml/kg) in previous study. Our patients developed CI-AKI with low dose (3 ml/kg). Possible explanation is that not maintaining proper hydration in present study subjects. Despite the fact that there are no comprehensive studies done on CIN in large paediatric groups.

In this study explored that no parameters like age, sex, height, weight, BMI and risk factors of AKI had significant effect on cystatin C. Bokenkamp et al[15] found serum cystatin C reflects renal function independent of age, gender, height and body mass composition. This finding is similar to the finding of present study. Schwartz et al[16] found that the production apparently independent of inflammatory conditions, muscle mass, sex, age (after 1 month). Another study[13] has been reported that older age, male gender, greater weight, greater height and higher C- reactive protein levels were independently associated with higher serum cystatin C levels. Martensson et al[17] found inflammatory response induced by sepsis had no impact on the levels on cystatin C in plasma. The present study showed similar finding.

Conclusion

In conclusion hypovolemia is the most common risk factors of acute kidney injury among the neonates. Furthermore, sepsis is found among the study population. Asphyxia is also reported among the neonates. In this study no renal or post-renal risk factors are found in the study population. Among primary diseases the most patients is sepsis followed by congenital heart disease, heart failure and cyanotic congenital heart disease. In addition volvulus neonatorum undergone surgery, duodenal atresia and infantile hypertrophic pyloric stenosis are also found among the neonates. Therefore, the risk factors among the neonated should be excluded very carefully.

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