

ORIGINAL ARTICLE

CLINICAL PROFILE AND OUTCOME OF ACUTE KIDNEY INJURY IN PATIENTS WITH NEONATAL SEPSIS

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Background: Acute kidney injury (AKI) in patients with neonatal sepsis is associated with worse outcomes. This study was conducted with an aim of developing an insight into the magnitude of this problem in our region. **Methods:** This descriptive cross-sectional study was conducted at Neonatology Unit of Ayub Teaching Hospital from 1st Jul 2019 to 31st Dec 2019. All neonates diagnosed as cases of neonatal sepsis and having acute kidney injury were included in the study. Patient characteristics were recorded on a structured proforma and analysed using SPSS-20. **Results:** A total of 115 neonates were included in the study. Among the study population, 75 (65.2%) were male and 40 (34.8%) were female. A total of 77 (67%) patients were diagnosed as having early onset neonatal sepsis and 38 (33%) patients presented with late onset neonatal sepsis. History of delayed cry at birth was present in 57 (49.6%) patients. A total of 83 (72.2%) patients were discharged, 22 (19.1%) patients expired, 4 (3.5%) patients were referred and 6 (5.2%) patients left against medical advice. There was a statistically significant difference in outcome in relation to history of delayed cry ($p=0.002$) and involvement of other organ systems in addition to AKI ($p=0.002$). **Conclusion:** Acute kidney injury is quite prevalent in neonates with sepsis. Asphyxiated newborns with sepsis and AKI are more prone to adverse outcomes.

Keywords: acute kidney injury, neonatal sepsis, mortality

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INTRODUCTION

Acute kidney injury (AKI) implies failure of the renal system to get rid of the nitrogenous waste products and maintain fluid and electrolyte balance.¹ New-borns in general and preterm babies in particular have a predilection for developing acute kidney injury owing to the immaturity of the renal mechanisms in this age group.² Studies from the different regions of the world have reported an incidence of 8–24% AKI in neonatal population with the variation being based on the type of study population. AKI in neonates has recently been a focus of interest owing to the improvement in survival rates of critically ill neonates due to advanced management protocols. AKI in neonatal age group is postulated to be associated with development of chronic kidney disease later in life.³ Both term and preterm sick admitted neonates, without pre-existing renal disease, quite frequently suffer from acute kidney injury.⁴

Pre renal acute kidney injury is the commonest form of renal injury in neonates. It occurs either due to poor perfusion or ischemic injury to the kidneys. There are a multitude of underlying aetiologies but most studies document birth asphyxia and sepsis to be the most common. The physiological qualities of the new-born renal system including high vascular resistance, high rennin activity, decreased glomerular filtration and low intra cortical perfusion rates predispose them to acute tubular necrosis.⁵

There are a myriad of features based on the severity of renal damage with the treatment options ranging from simple medical management to renal replacement therapy, peritoneal dialysis and hemodialysis.⁶ Studies from different regions of the world have documented sepsis as the leading cause of acute kidney injury in neonatal population. Acute kidney injury secondary to septicaemia has also been considered a major determinant of poor neonatal outcome.^{7,8}

Neonatal sepsis implies the clinical and systemic manifestations arising from bacterial, viral or fungal invasion of the body. Sepsis is considered to be a significant cause of morbidity and mortality in neonatal population. The disease manifestations are manifold ranging from mild presentations to severe systemic and multi-organ involvement. The exact incidence vary in different regions of the world^{9,10}, and is estimated to be 1 to 50 per 1,000 live births.¹¹ Recent estimates from a meta analysis documented 2,202 cases of neonatal sepsis per 100,000 live births with a mortality of 11–19%. Globally, these figures predict an estimated incidence of 3 million cases of sepsis in neonates.¹²

Worldwide neonatal sepsis is estimated to be responsible for 3% to 30% cases of paediatric mortality per year. Neonatal sepsis is categorized as early onset neonatal sepsis (EONS) and late onset neonatal sepsis (LONS) based on the disease

manifestations in neonates from birth to seven days of life and from second week of life to 28 days of life, respectively.¹¹

Sepsis is a major cause of neonatal deaths in our region and acute kidney injury in these patients further worsens the prognosis. There is paucity of data on frequency, clinical profile and outcomes of AKI in septic neonates in our region. The present study is aimed at developing an insight into the magnitude of this problem.

PATIENTS AND METHODS

This was a descriptive cross-sectional study conducted at Neonatology Unit of Ayub Teaching Hospital from 1st July 2019 to 31st Dec 2019. Approval of the hospital ethical committee was obtained. A total of 1,028 neonates were admitted in Neonatology Unit with sepsis during this time period. Out of these, 115 patients fulfilled the criteria of acute kidney injury and were included in the study. Patients with deranged renal profile secondary to congenital anomalies of the urinary tract were excluded from the study. Acute kidney injury was defined as serum creatinine levels >1.5 mg/dL and/or urine output less than 0.5 ml/Kg/hr. Sepsis was defined either on the basis of clinical criteria (based on EMA Sepsis scoring)¹³ and/or microbiological isolation of organisms on cultures.

Patient characteristics like age, gender, weight, gestational age, duration of hospital stay, mode of delivery, place of delivery, type of sepsis, and outcome were recorded on a structured proforma. Serum values of urea, creatinine, sodium and potassium were also recorded. Data was entered and analysed using SPSS-20. Descriptive statistics were used to calculate mean and standard deviation for age, weight, duration of hospital stay serum urea, creatinine and serum electrolytes. Categorical variables like gender, type of sepsis, gestational age, history of delayed cry at birth, mode of delivery, place of delivery and outcome were described as frequencies and percentages. Significance testing in case of categorical variables was done using Chi-square test, and $p < 0.05$ was considered significant.

RESULTS

Out of a total of 1,028 neonates, 115 (11.1%) with sepsis were included in the study. Mean age of the patients was 6.49 ± 6.855 days, and mean weight was 2.52 ± 0.652 Kg. Mean duration of hospital stay was 7.54 ± 4.105 days (Table-1).

Of the total patients with acute kidney injury, 75 (65.2%) were male and 40 (34.8%) were female. A total 77 (67%) patients were diagnosed as having early onset neonatal sepsis and 38 (33%) patients presented with late onset neonatal sepsis. Mode of delivery was vaginal delivery in 94 (81.7%) patients and caesarean

section in 21 (18.3%). A total of 95 (82.6%) babies were born at full term while 20 (17.4%) were preterm. History of delayed cry at birth was present in 57 (49.6%) patients. A total of 61 (53%) patients presented with involvement of other organ systems in addition to acute kidney injury (Table-2).

Eighty-three (72.2%) patients recovered and sent home on treatment, 22 (19.1%) patients expired, 4 (3.5%) patients were referred to hospitals with facilities for dialysis and intensive care, and 6 (5.2%) patients left against medical advice. Patients were further categorized as survivors 87 (75.7%), and non-survivors 28 (24.3%) on the basis of outcome (presuming those who left against medical advice as non-survivors) (Table-2).

There was no statistically significant difference in outcome in relation to gender ($p=0.706$), type of sepsis ($p=0.458$), gestation ($p=0.730$) and mode of delivery ($p=0.678$). The difference was statistically significant when outcome was assessed in relation to history of delayed cry ($p=0.002$) and involvement of other organ systems in addition to AKI ($p=0.002$) (Table-3).

Table-1: Patient characteristics (n=115)

Patient characteristics	Mean±SD
Age (days)	6.49±6.855
Weight (Kg)	2.527±0.652
Duration of hospital stay (days)	7.54±4.105
Serum urea (mg/dL)	122.669±72.037
Serum creatinine (mg/dL)	2.128±0.966
Serum sodium (mEq/L)	137.973±12.788
Serum potassium(mEq/L)	5.081±1.128

Table-2: Demographic characteristics of participants (n=115)

Variables	No. of patients	Percentage
Gender		
Male	75	65.2
Female	40	34.8
Mode of delivery		
Vaginal delivery	94	81.7
C Section	21	18.3
Type of sepsis		
Early onset	77	67
Late onset	38	33
Gestational age		
Full term	95	82.6
Preterm	20	17.4
Delayed cry at birth		
Yes	57	49.6
No	58	50.4
Multi-organ failure		
Yes	61	53
No	54	47
Outcome		
Discharged on home treatment	83	72.2
Expired	22	19.1
Referred to other centres	4	3.5
Left against medical advice	6	5.2
Survival		
Survivors	87	75.7
Non-survivors	28	24.3

Table-3: Patient characteristics in relation to outcome

Variables	Survivors	Non-survivors	p
Gender			
Male	56	19	0.736
Female	31	9	
Mode of delivery			
Vaginal delivery	70	24	0.531
C Section	17	4	
Gestational age			
Full term	73	22	0.517
Preterm	14	6	
Type of sepsis			
Early onset	55	22	0.133
Late onset	32	6	
Delayed cry at birth			
Yes	36	21	0.002
No	51	7	
Multi-organ failure			
Yes	39	22	0.002
No	48	6	

DISCUSSION

Acute kidney injury was documented in 11.1% septic neonates in our study. The incidence of AKI was reported to be 4.24% in one study¹⁴ from India, while another study¹⁵ AKI was reported to be in 26% of the septic neonates. Studies from different regions of the world have reported different incidences of AKI that may be attributed to demographic differences. Furthermore the variability can also be explained keeping in view the different definitions used to define AKI in different studies.

Acute kidney injury in septic neonates was more common in males as compared to female neonates in our study. Similar results are reported in studies from Iran¹⁶, Pakistan¹⁷, and Western India¹⁴ where AKI was predominantly documented in male neonates. However, Momtaz *et al*⁸ have documented a female preponderance in their study. History of delayed cry at birth was documented in nearly half of the study population in our study. Shalaby MA *et al*¹⁸ have also reported birth asphyxia as a significant risk factor for AKI in sick neonates in a study from Saudi Arabia. Low apgar scores and asphyxia at birth are postulated to be significant risk factors of AKI in neonates irrespective of sepsis in a large number of studies^{14,19}.

The majority of our study population presented with acute kidney injury secondary to early onset sepsis. Nearly three quarter of the neonates included in our study were full term. Mwamanenge *et al*²⁰ in a study on critically ill neonates in Tanzania, have reported similar results with nearly 81% of neonates with AKI presenting in the first 7 days of life. Also this study documented AKI predominantly in full term neonates.²⁰ Another study from Iran⁸ showed that full term neonates were primarily affected by acute kidney injury. We found that majority of the patients who presented with AKI secondary to neonatal sepsis were born through

vaginal delivery. Lee CC *et al*²¹ also documented similar results in their study where caesarean section was presumed to be protective against neonatal AKI.

Nearly a quarter of patients enrolled in our study expired (presuming those who left against medical advice as non survivors). Ali *et al*¹⁷ reported a mortality of 14.9% in neonates with acute kidney injury in a study conducted in Multan. Mortazavi *et al*¹⁵ reported a mortality rate of 20.5%, while another study from Turkey²² reported a mortality of 23.8% in sick neonates with AKI. Our results are generally in agreement with these studies.

CONCLUSION

Acute kidney injury is quite prevalent in neonates with sepsis and is a significant cause of mortality and morbidity. Asphyxiated newborns with sepsis and AKI are more prone to adverse outcomes. Early diagnosis and meticulous management is required to improve outcomes in these patients.

LIMITATIONS OF THE STUDY

Due to an overburdened neonatology unit and paucity of resources in our setting we could not use the newer definition of acute kidney injury according to Kidney Disease Improving Global Outcomes criteria. Further studies are recommended for evaluating outcomes in patients with different stages of acute kidney injury.

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