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Original Research Article

Clinical profile and outcome of acute kidney injury in neonatal sepsis in a tertiary care centre

Divya Durga*, Sudha Rudrappa

Department of Pediatrics, Mysore Medical College and Research Institute, Mysore, Karnataka, India

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***Correspondence:**
Dr. Divya Durga,
E-mail: dr.divyadurga@gmail.com

ABSTRACT

Background: Septicemia remains a leading cause of morbidity and mortality among neonates with AKI complicating as many as 3.4 to 24% of them. The actual incidence of renal failure in all sepsis cases is not documented. There are several studies in the literature on renal failure in neonates which were based on older definitions using blood urea and urine output as parameters. The major limitation of the older studies was that they did not use the current acute kidney injury network (AKIN) definition. In the present study, we have attempted to investigate AKI in neonatal sepsis using the AKIN definition based on serum creatinine (Table1). We also attempted to determine the predictors of AKI in neonatal sepsis.
Methods: The present study was an explorative study conducted in the neonatal unit of Cheluvamba hospital attached to Mysore Medical College and Research Institute in which a total of 50 neonates with clinical/ culture positive sepsis were enrolled during the period of June 2014 to June 2015.
Results: These neonates were investigated for the presence of AKI based on serum creatinine values of three consecutive days and were divided into two groups. Group 1 consisted of septic neonates with AKI and group 2 consisted of septic neonates without AKI. Both the groups were followed up till discharge or death. The risk factors associated with sepsis were compared in both the groups and predictors of morbidity and mortality associated with AKI in sepsis were also determined.
Conclusions: Incidence and mortality associated with AKI in sepsis was found to be 24% and 75% respectively. Factors like PROM, foul smelling liquor, > 3 unclean vaginal examinations during labour were significant risk factors for development of AKI in sepsis. Culture positivity, associated meningitis, DIC, shock and need for assisted ventilation were poor prognostic indicators and were significantly associated with mortality.

Keywords: AKIN, Neonatal sepsis

INTRODUCTION

Neonatal sepsis is one of the major global health problems. Thirty eight percent of all childhood deaths occur in neonates[1]. Ninety nine percent of these neonatal deaths occur in low-income and middle-income countries.[1] In developing countries like India, sepsis contributes to 37% of all neonatal deaths.[2] As per the National Neonatal Perinatal Database (NNPD) 2002 - 2003, the incidence of neonatal sepsis is 30 per 1000 live births3. Sepsis affects many important organs of the body leading to multiple organ dysfunction syndrome (MODS) of which kidney is one of the most important organs to be affected.

Acute renal failure (ARF) is characterized by sudden (within 48 hours) impairment in kidney function that results in the retention of nitrogenous waste products, e.g.

urea and alters the regulation of ECF volume, electrolytes and acid base homeostasis.[3] It affects 8-24% of critically ill neonates and mortality rate ranges between 10 to 61%.[4] The common conditions contributing to kidney injury in neonates according to various studies are perinatal asphyxia, neonatal sepsis, respiratory distress syndrome, dehydration, heart failure, nephrotoxic drug medication and urological anomalies with asphyxia and sepsis being the most common.[4]

While sepsis has been said to be one of the important predisposing causes of renal injury, the actual incidence of renal failure in all sepsis cases is not documented. This is because one usually suspects renal injury when the neonate develops oliguria. However, up to 1/ 3rd of the cases of acute renal injury in neonates present with normal urine output.[8,9]

Most of the studies on renal failure in neonates use one of the several old definitions.[10,12,13] More recent studies on renal injury using the AKIN definition are scarce in the entire pediatric age group. It is to bridge this gap in our current knowledge on this subject that this study was planned. With sepsis being so common in our country and with AKI occurring in nearly one-fourth of septic neonates and causing mortality in nearly one-fifth of those affected, AKI in septic neonates was a very relevant subject of study. We also attempted to determine the predictors of AKI in septic neonates and also to ascertain if there was any difference between small for gestational age and appropriate for gestational age neonates in this context.

METHODS

A sample size of 50 neonates admitted to the NICU of Cheluvamba hospital attached to MMC and RI, showing symptoms/ signs of clinical sepsis or culture positive sepsis.

Purposive sampling technique and explorative study was conducted.

Inclusion criteria

Neonates admitted to the NICU of Cheluvamba hospital and had symptoms/ signs of sepsis.

Group-I

This group included all neonates with culture positive sepsis or clinical sepsis as per the CDC definition and had evidence of acute kidney injury.

Group-II

This group included all neonates with culture positive sepsis or clinical sepsis as per the CDC definition and did not have evidence of acute kidney injury.

Exclusion criteria

- Neonates with single kidney, dysplastic kidney, hydronephrosis or cystic kidneys
- All neonates initially suspected to have sepsis but later found to have a negative blood culture and/ or not having features of clinical sepsis as per CDC definition.

Our study was a hospital based explorative study conducted at our NICU over a period of one year from June 2014 to June 2015. The incidence of sepsis in our hospital is around 30 per 1000 live births. All neonates who were born in this hospital and presented with symptoms and signs of sepsis or neonates who were born to mothers with potential risk factors for sepsis were enrolled in the study. However, those with antenatal diagnosis of renal malformation/ anomalies were excluded from the study.

Blood culture, sepsis screen (CRP, TLC, ANC and IT ratio) and serum creatinine (first three consecutive days of illness) were sent for all the neonates who were included in our study. Blood culture was done in the Department of Microbiology at our hospital. CSF examination was also done for all neonates with symptomatic sepsis. Sepsis screen was considered positive if 2 or more of the following parameters were positive (Table 3).

On the basis of serum creatinine values of three consecutive days, all the neonates with suspected sepsis were evaluated for acute kidney injury. The presence of Acute Kidney Injury was classified based on the definition given by the Acute Kidney Injury Network (Table 1). The two groups were treated as per nursery protocols and were followed till discharge or death.

Descriptive statistics, contingency table analysis, independent sample ‘t’test were used for statistical analysis and ‘p’ value < 0.05 was considered to be statistically significant using SPSS software (version 16.0).

CDC (centre of disease control) definition for neonatal sepsis.

Culture positive sepsis (blood culture positive)

This must meet any one of the following criteria

True pathogen detected - baby has a recognized pathogen cultured from 1 or more blood cultures and organism cultured from blood is not related to an infection at another site and clinician institutes appropriate treatment for septicaemia.

Common skin contaminant detected - common skin contaminant is cultured from 2 (or more) blood samples

drawn on separate occasions and organism cultured from blood is not related to an infection at another site.

Baby has at least one of the signs or symptoms enlisted in Table 2.

Physician institutes appropriate treatment for septicemia

Clinical sepsis (blood culture negative)

Baby has all of the following:

Existence of predisposing risk factors - maternal fever within 7 days before delivery or foul smelling liquor or prolonged rupture of membranes (>18 hours.)

Or radiological evidence of pneumonia or culture for peritoneal/ pericardial/ pleural fluid comes positive or positive septic screen (as per existing protocols at individual sites).

- Any one of the clinical sign/ symptoms as enlisted above in Table 2.
- Blood culture not done or no organism has been detected in blood
- Physician institutes appropriate treatment for sepsis

If septic screen has been done twice in the last 24 hours of point of clinical suspicion, the result of second one should be taken in account.

Positive septic screen consists of two of the four parameters, namely;

- Total leucocyte count (<5000/mm^3 or absolute neutrophil count <1800/mm^3)
- Band to total polymorph ratio of > 0.2
- C-reactive protein >1mg/dl.

Table 2 Signs and Symptoms of sepsis in a newborn.

RESULTS

Various risk factors of sepsis like gestation, birth weight, antenatal events (fever, UTI, obstetric complications like pregnancy induced hypertension, gestational diabetes etc.), prolonged labour, prolonged rupture of membranes, number of vaginal examinations, foul smelling liquor, meconium stained liquor, perinatal asphyxia, use of nephrotoxic drugs etc. were assessed and analysed for their contribution in the development of AKI. Morbidity in these neonates was analysed in terms of duration of hospital stay, time taken for the initiation of feeds, presence of shock, need for inotropes and assisted ventilation, presence of MODS and DIC. Outcome of AKI in sepsis was assessed in terms of discharge with normal renal parameters, deranged renal parameters or death.

The results obtained were analyzed and illustrated in tables.

Table 1: AKIN definition.

Stages	Serum creatinine	Urine output
Stage I	Increase by >0.3 mg% or 1.5-1.99 times from the baseline value.	<0.5 ml/kg/hr in 6 hours
Stage II	2- 2.99 times of the baseline value	<0.5 ml/kg/hr in 12 hours
Stage III	3 times the baseline value or creatinine value >4 mg% or rapid rise by >0.5 mg% /day	<0.3 ml/kg/hr in 24 hours or Anuria for 12 hours

Table 2: Signs and symptoms of sepsis in newborn.

Presenting symptoms (PSM)	
1. Feeding difficulty	7. Breathing difficulty
2. Convulsions	8. Vomiting
3. Movement only when stimulated	9. Diarrhoea
4. Fever	10. Umbilical discharge
5. Cold to touch	11. Ear discharge
6. Apnea	
Presenting signs (PSG)	
1. Temperature > 38^0C	8. Severe chest indrawing
2. Heart rate >180/min	9. Lethargy/ drowsiness
3. CRT >3 sec	10. Cyanosis
4. Temperature < 37^0C	11. Bulging fontanel
5. Heart rate <100/min	12. Abdominal distension
6. Grunting	13. Umbilical sepsis
7. Respiratory rate >60/min	14. Multiple (>10) skin pustules

Table 3: Sepsis screen.

Test	Value indicative of abnormal test
TLC	<5000/cu.mm
I/t ratio	>0.20
ANC	<1800/cu.mm
CRP	>10mg/l

A total of 50 neonates with evidence of clinical/ culture positive sepsis as per the CDC definition were enrolled into the study. Among the 50 cases 12 (24%) of them developed AKI and were categorized as group 1 (cases) and the remaining 38 (76%) neonates without AKI served as controls under group 2. Among the 50 neonates with sepsis, 22 were males and 28 were females with a male to female ratio (M:F) of 1:1.3. Hence, gender was not a significant risk factor for AKI in sepsis (p>0.05) (Table 4).

As per the distribution, group 1 had 8 (66.6%) AGA neonates and 4 (33.4%) were SGA. In group 2 33 (86.8%) were AGA neonates and 5 (13.2%) were SGA.

There was no significant difference in the incidence of AKI in sepsis in AGA and SGA neonates of both the groups (p>0.05). Majority of the neonates i.e 6/12 (50%) in group 1 and 25/38 (65.7% in group 2 weighed between 2.5 - 3 kgs. 4 (33.3%) neonates in group 1 and 7 (18.5%) neonates in group 2 weighed less than 2.5 kgs. 2 (16.7%) neonates in group 1 and 6 (15.8%) neonates in group 2 weighed above 3 kgs. Birth weight was not found to be a significant factor contributing to AKI in sepsis (p>0.05).

Table 4: Distribution of neonates based on demographic variables.

Demographic variables	Group 1 (n = 12)		Group 2 (n = 38)	
	No.	%	No.	%
No. of cases	12	24	38	76
Gestational age (weeks)				
34 - 36 weeks	2	16.6	7	19
≥ 37 weeks	10	83.4	31	81
Birth weight (in kgs) (mean ± SD)	2.74±0.48		2.72±0.36	
<2.5 kg	4	33.3	7	18.5
2.5 - 3 kgs	6	50	25	65.7
> 3 kgs	2	16.7	6	15.8
Males	6	50	16	15.8
Females	6	50	22	42.1
Male:Female ratio	1:1		1:1.3	
Blood urea (mean±SD)	156.83±56.4		27.9±3.0	
Serum creatinine (mean±SD)	3.55±1.98		0.64±0.07	

Maternal parameter

Among the 12 neonates in group 1, 33.3% of them were born to mothers aged less than 20 years. In group 2 13.15% of neonates were born to mothers aged more than 20 years.

Hence, maternal age was not significant in contributing to AKI in sepsis (p>0.05).

It was found that in group 1 majority of neonates (75%) were born to primiparous mothers. Similarly, in group 2 majority neonates (42.1%) were born to primiparous mothers. Hence, maternal parity was not significant in contributing to AKI in sepsis (p>0.05).

Table 5: Distribution of neonates based on prolonged rupture of membranes as a risk factor for AKI in sepsis.

PROM (> 24 hrs)	Group 1	Group 2	Total	p Value
Present	5 (62.5%)	3 (37.5%)	42 (100%)	0.005
Absent	7 (16.7%)	35 (83.3%)	8 (100%)	
Total	**12 (24%)**	**38 (76%)**	**50 (100%)**	

All the neonates in group 1 were born to mothers with singleton pregnancy. In group 2, 3 (7%) neonates were born to mothers with multiple pregnancy. Hence, multiple pregnancy was not a significant factor in contributing to the incidence of AKI in sepsis (p>0.05).

Among the 42 neonates who had PROM of >24 hours as risk factor for sepsis, 62.2% of them developed AKI as compared to only 16.7% in the absence of PROM as a risk factor This was statistically significant (p -0.005). Hence, PROM of >24 hours was a significant risk factor for AKI in sepsis (p<0.05) (Table 5).

Table 6: Distribution of neonates based on foul smelling liquor as a risk factor for AKI in sepsis.

Foul smelling liquor	Group 1	Group 2	Total	p Value
Present	3 (100%)	0 (0%)	3 (100%)	0.001
Absent	9 (19.1%)	38 (80.9%)	47 (100%)	
Total	**12 (24%)**	**38 (76%)**	**50 (100%)**	

Among all neonates who had foul smelling liquor as a risk factor for sepsis, all of them developed AKI (100%) whereas in neonates who did not have foul smelling liquor as a risk factor, only 19.1% developed AKI. This was statistically significant (p - 0.001). Hence, foul

smelling liquor was found to be a significant risk factor for AKI in sepsis (p<0.05) (Table 6).

In both the groups, none of the antenatal events were found to significantly affect the incidence of AKI in sepsis (p>0.05) (Table 7).

Table 7: Distribution of neonates based on antenatal events.

Antenatal events	Group 1	Group 2	p Value
Normal	9	32	0.705
Fever	2	3	
Gestational diabetes mellitus (GDM)	0	1	
Urinary tract infection (UTI)	1	1	
Pregnancy induced hypertension (PIH)	0	1	
Total	**12**	**38**	

Prolonged labour as risk factor for sepsis was present in 42% of neonates in group 1 and in 57.1% of neonates in group 2. Prolonged labour was not a significant risk factor for the development of AKI in sepsis (p>0.05).

Only 20.8% of neonates had AKI when less than 3 vaginal examinations were done during labour. This was statistically significant (p - 0.01). Hence, >3 unclean vaginal examinations during labour was a significant risk factor for AKI in sepsis (p<0.05) (Figure 1). It was found that with the presence of meconium stained liquor as risk factor for sepsis, 33.3% neonates had AKI and 66.7% did not develop AKI. Hence, meconium stained liquor was not a significant risk factor for AKI in sepsis (p>0.05).

AKI was present in 20% of neonates with perinatal asphyxia and in 24.4% of neonates without perinatal asphyxia. Hence, perinatal asphyxia was not found to be significant risk factor for AKI in sepsis (p>0.05) (Table 8). It was found that with the usage of nephrotoxic drugs like aminoglycosides, indomethacin etc. 42.9% had AKI and 57.1% did not develop AKI. Hence, usage of nephrotoxic drugs was not a significant risk factor for development of AKI in sepsis (p>0.05).

It was found that blood culture positivity was a significant (p -0.000) predictor of AKI in sepsis as 80% neonates with a positive blood culture developed AKI compared to only 10% with negative blood culture. Hence, blood culture positivity was a significant predictor of AKI in neonatal sepsis (p<0.05) (Table 9).

It was found that meningitis was a significant predictor of AKI in sepsis as 80% of neonates with CSF analysis suggestive of meningitis had AKI in comparison to only 17.8% neonates with a normal CSF analysis. This was statistically significant (p - 0.002). Hence, CSF analysis suggesting meningitis was a significant risk factor for the development of AKI in sepsis (p<0.05) (Table 9). Parameters of morbidity and mortality associated with AKI in sepsis.

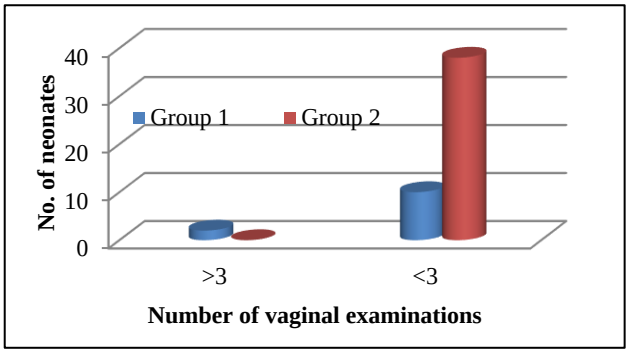

Figure 1: Distribution of neonates based on number of unclean vaginal examinations as risk factor for AKI in sepsis.

Table 8: Distribution of neonates based on perinatal asphyxia as a risk factor for AKI in sepsis.

Perinatal asphyxia	Group 1	Group 2	Total	p Value
Absent	11 (24.4%)	34 (75.6%)	45 (100%)	0.825
Present	1 (20.0%)	4 (80%)	5 (100%)	
Total	**12 (24%)**	**38 (76%)**	**50 (100%)**	

Table 9: Distribution of neonates based on blood culture and CSF analysis.

Blood culture	Group 1	Group 2	Total	p Value
Positive	8 (80%)	2 (20%)	10 (100%)	0.000
Negative	4 (10%)	36 (90%)	40 (100%)	
Total	**12 (24%)**	**38 (76%)**	**50 (100%)**	
CSF analysis				0.002
Normal	8 (17.8%)	37 (82.2%)	45 (100%)	
Suggestive of meningitis	4 (80%)	1 (20%)	5 (100%)	
Total	**12 (24%)**	**38 (76%)**	**50 (100%)**	

Table 10: Distribution of neonates based on duration of hospital stay and time taken to initiate feeds as a parameter of morbidity related to AKI in sepsis.

Hospital stay	Group 1	Group 2	Total	p Value
<5 days	0 (0%)	7 (100%)	7 (100%)	0.000
5-10 days	5 (14.3%)	30 (85.7%)	35 (100%)	
>10 days	7 (87.5%)	1 (12.5%)	8 (100%)	
Total	12 (24.0%)	38 (76%)	50 (100%)	
Day of starting feeds				
No feed	1 (100%)	0 (0%)	1 (100%)	0.000
1-4 days	4 (9.4%)	38 (90.6%)	42 (100%)	
5-10 days	7 (100%)	0 (0%)	7 (100%)	
Total	**12 (24%)**	**38 (76%)**	**50 (100%)**	

The morbidity associated with AKI in sepsis was assessed in terms of

- Duration of hospital stay
- Time required to start feeds
- Requirement of assisted ventilation
- Requirement of inotropic support for shock
- DIC.

The fatality associated with AKI in sepsis was assessed based on

- Number of septic neonates with AKI needing assisted ventilation, inotropic support, DIC, who survived
- Outcome of AKI in sepsis in terms of survival with preserved renal functions, deranged renal functions and death.

Hospital stay - All neonates who stayed in the hospital for less than 5 days belonged to group 2. This was statistically significant (p -0.000) (Table 10).

Time for initial feeds - We needed an average of 5 - 10 days to initiate feeds in majority of neonates (7/11) in group 1. This was due to several risk factors like shock, DIC, assisted ventilation etc. However, in group 2 we could initiate feeds in all neonates within the first 4 days of life. Hence, time taken for the initiation of feeds was a significant parameter to assess the morbidity associated with AKI in sepsis (p<0.05) (Table 10).

Table 11: Outcome of septic neonates (with AKI) who needed assisted ventilation as a parameter to predict fatality.

Assisted ventilation	Discharged with normal renal function	Discharged with deranged renal function	Death	Total	p Value
Not needed	7 (87.5%)	0 (0%)	1 (12.5%)	8 (100%)	0.05
Needed	1 (25%)	1 (25%)	2 (50%)	4 (100%)	
Total	**8 (66.7%)**	**1 (8.3%)**	**3 (25%)**	**12 (100%)**	

Table 12: Outcome of septic neonates (with AKI) who needed inotropic support as a parameter to predict fatality.

Inotropic support for shock	Discharged with normal renal function	Discharged with deranged renal function	Death	Total	p Value
Not needed	3 (100%)	0 (0%)	0 (0%)	3 (100%)	0.368
Needed	5 (55.6%)	1 (11.1%)	3 (33.3%)	9 (100%)	
Total	**8 (66.7%)**	**1 (8.3%)**	**3 (25%)**	**12 (100%)**	

Need for assisted ventilation - Of the 50 neonates included in our study, 4 neonates needed assisted ventilation and all of them belonged to group 1. This was statistically significant (p - 0.000). Hence, need for assisted ventilation was a significant parameter for morbidity in AKI (p 0.05).

Outcome

Of the 4 septic neonates who had AKI and needed assisted ventilation, 50% died and 25% had deranged renal functions at discharge. Among those who did not need assisted ventilation, 87.5% were discharged with

normal renal functions and mortality was only 12.5%. This was statistically significant (p - 0.05). Hence, the requirement of assisted ventilation was a significant predictor of fatality associated with AKI in sepsis (p<0.05) (Table 11).

Inotrops - Of the 50 septic neonates, 9 of them needed inotropic support for shock and all of them belonged to group 1. Among those who did not need inotropic support, majority (92.7%) of them were from group 2. This was statistically significant (p - 0.000). Hence, need for inotropic support for shock was a significant parameter of morbidity associated with AKI in sepsis (<0.05).

Outcome

Though shock was one of the significant factor of morbidity for AKI in sepsis, it was found that out of the 9 neonates in group 1 who needed inotropic support, 5 (55.6%) of them were discharged with normal renal functions and 3 (33.3%) of them died. Hence, due to the improved management of shock in the tertiary care centres, shock did not prove to be a significant predictor of mortality in our study (p>0.05) (Table12).

DIC - It was found that all the 3 septic neonates who developed DIC belonged to group 1, whereas majority (80.9%) of neonates who did not have DIC belonged to group 2. This was statistically significant (p - 0.001). Hence, presence of DIC was a significant predictor of morbidity for AKI in sepsis (p<0.05).

Outcome

In group 1, 66.7% of neonates died in the presence of DIC in comparison to only 11.1% of neonates who died in the absence of DIC. This was statistically significant (p - 0.013). Hence, DIC was a significant predictor of fatality for AKI in sepsis (p<0.05) (Table 13).

Table 13: Outcome of septic neonates (with AKI) with DIC as a parameter to predict fatality.

DIC	Discharged with normal renal function	Discharged with deranged renal function	Death	Total	p Value
Absent	8 (88.9%)	0 (0%)	1 (11.1%)	8 (100%)	0.013
Present	0 (0%)	1 (33.3%)	2 (66.7%)	4 (100%)	
Total	**8 (66.7%)**	**1 (8.3%)**	**3 (25%)**	**12 (100%)**	

Table 14: Comparison of septic neonates with and without AKI.

Parameters	Group1 n, (%)	Group2 n, (%)	Survival (%)	Expiry (%)	p Value (S/NS)
M:F ratio	1:1	1:1.3	92%	8%	0.631
Preterm (<37 weeks)	2 (16.7%)	7 (19%)	100%	0	0.89
Term (>37 weeks)	10 (83.3%)	31 (81%)	90%	10%	0.89
SGA	4 (33.4%)	5 (13.2%)	100%	0%	0.113
Mean birth weight (in kgs)	2.74±0.48	2.72±0.36	92%	8%	0.52
PROM (>24 hours)	5 (62.5%)	3 (37.5%)	75%	25%	0.005
Foul smelling liquor	3 (100%)	0 (0%)	33.3%	66.7%	0.001
Prolonged Labour	3 (42.9%)	4 (57.1%)	85.7%	14.3%	0.208
>3 unclean vaginal examinations	2 (100%)	0 (0%)	50%	50%	0.01
Meconium stained liquor	2 (33.3%)	4 (66.7%)	83.3%	16.7%	0.56
Perinatal asphyxia	1 (20%)	4 (80%)	80%	20%	0.825
Nephrotoxic drugs	3 (42.9%)	4 (57.1%)	71.4%	28.6%	0.20
Blood culture positivity	8 (80%)	2 (20%)	70%	30%	0.000
Meningitis	4 (80%)	1 (20%)	80%	20%	0.002
Duration of hospital stay	7 (87.5%)	1 (12.5%)	75%	25%	0.000
Day of starting feeds	7 (100%)	0 (0%)	57.1%	42.9%	0.000
Assisted ventilation	4 (100%)	0 (0%)	50%	50%	0.000
Shock	9 (100%)	0 (0%)	66.7%	33.3%	0.000
DIC	3 (100%)	0 (0%)	33.3%	66.7%	0.000
Mortality	3 (75%)	1 (25%)	92%	8%	0.007

Table 15: Poor prognostic factors associated with AKI in sepsis.

Poor prognostic parameters	p Value
PROM	0.005
Foul smelling liquor	0.01
>3 Vaginal examinations in labour	0.01
Blood culture positivity	0.000
Meningitis	0.002
Assisted ventilation	0.000
Shock	0.000
DIC	0.000

There was 75% mortality of neonates in group 1 as compared to 25% mortality in group 2. Only 66.7% of neonates in group 1 recovered as compared to 97.4% of neonates who recovered in group 2. This was statistically significant (p - 0.007).

Hence, presence of AKI was a significant contributor in the mortality in neonatal sepsis (p<0.05).

Distribution of neonates based on outcome and comparison of septic neonates with and without AKI is shown in the and table respectively (Table 14).

DISCUSSION

In the present study, the risk factors and outcome of septic neonates with AKI was compared to that of septic neonates without AKI. We have used the current definition of AKI (i.e AKIN definition) to investigate the presence of kidney injury in septic neonates.

In this study it was found that, of 50 septic neonates who were enrolled 12 (24%) had AKI. This f is comparable that of study conducted by Mathur et al where 26% of septic neonates were found to have AKI.[6] In the study conducted by Jayashree et al, Mohammad H et al, and SK Pradhan et al. the incidence of AKI in septic neonates was found to be 20%, 31.6% and 27.2% respectively.[10,17,24,25]

In this study, we had 11 septic neonates weighing less than 2.5 kgs and 36.4% of them had AKI. We did not find LBW to significantly affect the occurrence of AKI in septic neonates (p - 0.52). This was in contrast to the findings of Mathur et al, and SK Pradhan et al, where they found a higher incidence of AKI in septic neonates who weighed less than 2.5 kgs. We found a lower incidence of AKI in LBW septic neonates as compared to other studies as our sample size was probably less and LBW neonates constituted only a minority of them.[6,24]

This study included 9 preterm neonates (18%) with a mean gestational age of 35±2 weeks of which 22.2% had AKI. We also included 9 SGA septic neonates of which 44.4% had AKI. We did not find gestational age to significantly affect the incidence of AKI in septic neonates (p - 0.89). We also found that the incidence of AKI did not significantly differ between AGA and SGA babies (p - 0.113). These findings were similar to the study conducted by Mathur et al. However, in the study conducted by Mohammad H et al, majority of the septic neonates who developed AKI were preterm (44.3%).[25] This was probably due to the fact that their study included a higher number of preterm neonates. In the study conducted by SK Pradhan et al, the incidence of AKI was higher in septic neonates who were born preterm (43.3%). However, they did not find any difference in the incidence of AKI between SGA and AGA neonates and these results were similar to our study.[24]

Among the various risk factors for sepsis, we found that prolonged rupture of membranes (> 24 hours), foul smelling liquor and > 3 unclean vaginal examinations during labour were significant risk factors for development of AKI in sepsis (p - 0.005, 0.001 and 0.01 respectively).

On the other hand, we also found that the other risk factors for sepsis like perinatal asphyxia, prolonged duration of labour and meconium stained liquor did not significantly increase the occurrence of AKI in septic neonates (p - 0.825, 0.208 and 0.56 respectively). These findings were similar to that of the results obtained by Mathur et al., and Mohammad H et al.[6,25] They too found that perinatal asphyxia did not significantly affect the occurrence of AKI in septic neonates. This was probably related to the improved fluid management in such neonates. However, in the study conducted by SK Pradhan et al., perinatal asphyxia was present in 78% of septic neonates with AKI and hence perinatal asphyxia was found to be a significant risk factor (p - 0.043) to predict the occurrence of AKI in septic neonates in their study.[24]

In this study all the 4 septic neonates who needed assisted ventilation belonged to group 1. Only 16.4% of neonates (8/46) who did not need assisted ventilation belonged to group 1. We also found that among the 4 septic neonates who needed mechanical ventilation, 50% of them died

and 25% of them had deranged renal functions at discharge. Among the neonates who did not need assisted ventilation 87.5% of them were discharged with normal renal functions. Hence, we found that the requirement for assisted ventilation was a significant parameter to predict morbidity and fatality associated with AKI in sepsis ($p < 0.05$). This was in contrast to the findings of Mohammad H et al, who did not find any significant difference in the incidence of AKI in septic neonates who were mechanically ventilated. Their result was probably related to the sick neonates being ventilated electively and early in the course of the disease which resulted in lesser incidence of AKI.[25]

In the present study, all the 9 neonates who needed inotropic support for shock belonged to group 1. Most of the neonates (38/41 - 92.7%) who did not need inotropic support belonged to group 2. Hence, we found that the need for inotropic support was a significant parameter to predict the occurrence of AKI in septic neonates (p - 0.000).

All the 3 septic neonates with DIC belonged to group 1. Of these 3 neonates, 2 (66.7%) of them died and the remaining one (33.3%) had deranged renal function at discharge. Hence, we found that DIC was a significant factor to predict morbidity and fatality associated with AKI in sepsis. These results were similar to the results obtained by Mohammad H et al. ($p <0.05$), Mathur et al ($p < 0.05$), and SK Pradhan et al ($p <0.05$). They all found that the need for inotropic support for shock and the presence of DIC were significant parameters to predict the occurrence of AKI in sepsis.[6,24]

In this study, of the 4 septic neonates who died, 3 (75%) of them belonged to group 1 and this was statistically significant (p - 0.007). This finding was similar to the results obtained by Mathur et al., SK Pradhan et al, Jayashree et al, and Mohammad H et al, where they found the mortality rates in septic neonates with AKI to be 72.2%, 70.2%, 54.5% and 50% respectively. These consistent findings reiterate the fact that when sepsis is complicated with AKI there is significant increase in the mortality of such neonates.[6,10,24,25]

In the present study, we found that prolonged rupture of membranes (> 24 hours), presence of foul smelling liquor, more than 3 unclean vaginal examinations during labour, blood culture positivity, presence of shock and meningitis were poor prognostic indicators with a significant statistical association for the development of AKI in sepsis. Factors like DIC and need for assisted ventilation were found to be significant factors to predict fatality associated with AKI in sepsis.

CONCLUSION

AKI occurred in 24% of neonates with sepsis. Presence of prolonged rupture of membranes (> 24 hours), foul smelling liquor and > 3 unclean vaginal examinations during labour were important risk factors contributing significantly towards AKI in sepsis ($p = 0.005$, 0.01 and 0.01 respectively).

Factors like birth weight, gestational age, and male gender did not significantly affect the incidence of AKI in both groups. Maternal risk factors like multiple pregnancy, parity, maternal age, antenatal events like fever, UTI, presence of obstetric complications like PIH, GDM etc. did not contribute towards development of AKI in sepsis. Perinatal asphyxia, prolonged labour, presence of meconium stained amniotic fluid and use of nephrotoxic drugs did not significantly increase the incidence of AKI in septic neonates.

Culture positive sepsis and associated meningitits were higher for the group with AKI and was significantly associated with AKI in sepsis and served as poor prognostic indicators ($p<0.01$ and $p = 0.007$ respectively). DIC, shock and need for mechanical ventilation were higher in group 1 ($p <0.001$ each). DIC and need for assisted ventilation were significantly associated with mortality in AKI ($p <0.001$).

Longer duration of hospital stay and increased time taken for initiation of feeds in septic neonates with AKI served as a significant parameter of morbidity associated with AKI. The mortality was three times higher in neonates with AKI (75%, $p = 0.007$).

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