# Effects of Neonatal Septicemia on Renal Function

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Original Research Article

**ABSTRACT**

An observational hospital based prospective study was conducted on 70 neonates with sepsis admitted in the Neonatology unit, Department of Paediatrics, MLB Medical College, Jhansi from Aug. 2016 to Sep. 2017 to evaluate the incidence of renal involvement in cases of neonates with septicemia and other contributing factors complicating acute kidney injury in them**.** Sepsis was diagnosed on the basis of either a positive sepsis screen [Immature: Total neutrophil ratio(I:T) > 0.2, micro –Erythrocyte Sedimentation Rate (ESR) > age in days +2 mm or >15 mm, C-Reactive Protein(CRP)> 1mg/dl, Total Leukocyte Count(TLC)<5000/ $mm^3$ ; 2 or more positive)] or a positive blood culture in symptomatic neonates. Acute kidney injury (AKI) was diagnosed if the serum creatinine was >1.5mg/dL with or without oliguria and with or without blood urea nitrogen (BUN) >20mg/dl on two separate occasions at least 24 hours apart. Oliguria was diagnosed when urine output was less than 1ml/Kg/hr.

Out of the 70 neonates with sepsis, AKI was found in 23% (n=16) cases and majority of cases i.e. 75% (n=12) were nonoliguric, only 25% (n=4) were oliguric**.** The association of Shock,Prolonged Rupture of Membranes(PROM) and Foul Smelling Liquor (FSL) was also significant in neonates with AKI(68.75%vs 29.63%,p<0.05,60%vs 40%, p<0.05, 100%, p<0.05 respectively). Perinatal asphyxia did not significantly increase the occurrence of AKI in septic neonates**.** The mortality was higher in neonates with oliguric AKI (75%) as compared to non oliguric AKI (41.66%). AKI occurred in 23% neonates with sepsis. It was observed that AKI secondary to neonatal sepsis was predominantly nonoliguric. Factors like shock, prolonged rupture of Membranes (PROM), foul smelling liquor (FSL) and culture positivity were significant risk factors for development of AKI in sepsis.

**KEY WORDS:** acute kidney injury(AKI), acute renal failure, neonatal sepsis.

## INTRODUCTION:

Sepsis remains a leading cause of morbidity and mortality among neonates in the intensive care facilities[1]. It is responsible for about 30-50% of the total neonatal deaths in the developing countries[2]. Kidney is one of the most important organs to be affected in multiple organ dysfunction syndrome (MODS) due to sepsis. Acute renal failure (ARF) is characterized by sudden impairment in kidney function that results in the retention of nitrogenous waste products[3]. 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 administration and urological anomalies with asphyxia and sepsis being the most common[4].

The kidneys of neonates are particularly susceptible to hypo-perfusion because of the physiologic characteristics of the neonatal kidneys, including high renal vascular resistance, high plasma renin activity, low glomerular filtration, decreased intra-cortical perfusion rate and decreased re-absorption of sodium in the proximal tubules[5]. Prerenal azotemia is the most common type of AKI encountered in the neonates (85%)[6].

Newborns who have had ARF are predisposed to the development of chronic renal failure in the future. Therefore, this study was undertaken with the aim to evaluate the incidence of renal involvement in cases of neonates with septicemia and other contributing factors complicating acute kidney injury in them.

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## MATERIALS AND METHODS:

The present study was observational prospective study conducted on 70 neonates with

sepsis admitted in the Neonatology unit, Department of Pediatrics, MLB Medical College, Jhansi from Aug. 2016 to Sep. 2017 after seeking due approval from the Institutional Ethics Committee.

All babies admitted to the Neonatal Intensive Care Unit (NICU) suspected of neonatal sepsis, both early onset (EOS) or late-onset (LOS), were assessed for the presence of acute kidney injury. The cases were divided into following two groups and compared: (a) Babies having neonatal sepsis and complicated by AKI (Group I); (b) those with neonatal sepsis without AKI (Group II).

Sepsis was diagnosed on basis of either a positive sepsis screen and/or a positive blood culture in symptomatic neonates. It was considered positive if ≥2 of the 4 criteria were present, which included CRP >1.0 mg/dl , Micro ESR > age in days + 2mm or > 15mm fall in 1st hour , Leucopenia : TLC <5000/cmm with low absolute neutrophil count (< 1800cells/ cmm) and Immature: total neutrophil ratio >0.2 [7]. AKI was diagnosed if serum creatinine was >1.5mg/dL adjusted for gestational and postnatal age with or without oligouria and with or without blood urea nitrogen (BUN) >20mg/dl on two separate occasions at least 24 hours apart. Oliguria was diagnosed when urine output was <1ml/Kg/hr [8,9,10] . It was assured that the neonates were well hydrated and received adequate fluids.

All neonates with clinical features of sepsis like refusal to feed, lethargy, sclerema, increased abdominal girth by 2 cm, seizure, increased respiratory rate >60/min, chest retraction, grunting, central cyanosis, hypothermia (axillary temperature <36°C), hyperthermia (axillary temperature >37.5°C), bradycardia- heart rate <100/min and tachycardia- heart rate >160/min were included in the study.

The exclusion criteria comprised of: a) infants who were already on antibiotics, b) neonates with congenital anomalies or urogenital malformation; and c) neonates whose parents or guardians did not agree to be a part of study.

After selection of cases, detailed antenatal, natal and postnatal history was taken, clinical examination and investigation were recorded in the performa. All selected cases had a full clinical evaluation including assessment of gestational age, birth weight, gender, age of onset of sepsis, history of PROM and foul smelling liquor, etc. The gestational age was assessed using the Modified Ballard Score [11].

Urine quantification was done either by bag collection or urethral catheterization. The collected urine sample was sent for routine microscopy. Blood culture was sent immediately to Department of Microbiology after admission of a suspected case before the start of antibiotics. Blood urea nitrogen was done using Modified Urease-Berthlot Method. Serum creatinine was done using chemical analyser by modified Jaffe's method.

The data was analysed statistically using Chi Square test p-value of <0.05 was considered as significant.

## RESULTS:

Among the 70 cases, 16 (23%) developed AKI and were categorized as group I and the remaining 54 (77%) neonates without AKI served under group II. Among these neonates, 30 were male and 40 were female with a male to female ratio of 1:1.3. In group I, male: female ratio was 1:1 while in group II, male: female ratio was 1:1.4. Out of total 16 septic neonates with AKI, only 6 i.e. (37.5%) weighed < 2500gm and 10 (62.5%) weighed ≥2500gm.

Total 13 neonates belonged to gestational age group 34-36 weeks, out of which 3 neonates developed AKI (23.08%). A total of 57 neonates belonged to >36 weeks of gestational age group, out of which 13 cases developed AKI (22.8%) (Table 1). Refusal to feed was present in 85.70%, lethargy 80%, hyperthermia 71.4% , hypothermia 28.57% ,apnea (67.14%) and abdominal distension (57.14%). Excessive cry, vomiting and convulsions were present in 50%, 15.71% and 21.42% newborns respectively. Sclerema and buldging fontanelle were present in 13 cases each while umbilical sepsis was present in 10 cases (Table 2)

Twelve cases (75%) had non oliguric renal failure while 4 cases (25%) had oliguric renal failure. Out of total 16 cases of AKI in septicemic group, 8 newborns died i.e. (50%). Out of 4 neonates who belonged to oligouric type of renal failure, 3 of them i.e. (75%) died, while in non oligouric renal failure, 5 out of 12 i.e. 41.66% expired. 68.75% septic neonates had shock in AKI and 29.63% septic neonates had shock in the group without AKI.Hence,shock was significantly associated with AKI($p<0.05$) ( Table 3 A). 71.4% septic neonates with a positive blood culture developed AKI as compared to only 10.7% septic neonates with a negative blood culture. Hence, blood culture positivity was a significant predictor of AKI in neonatal sepsis ($p<0.05$) (Table 3 B).

Coagulase negative staphylococci was predominant organism and was isolated in all septic neonates with AKI (100%). Among all the 4 neonates

**Table 1:** Distribution of neonates based on demographic variables.

| Variables | Group I (n=16) Septic neonates with AKI | | Group II (n=54) Septic neonates without AKI | |
|---|---|---|---|---|
| | No. | % | No. | % |
| No. of Cases | 16 | 23 | 54 | 77 |
| Gestational Age(weeks) | | | | |
| 34-36 weeks | 3 | 23.07 | 10 | 76.93 |
| >36 weeks | 13 | 22.80 | 44 | 77.20 |
| Birth Weight(in kgs) | | | | |
| <2.5 kg | 6 | 37.50 | 10 | 18.50 |
| ≥2.5 kg | 10 | 62.50 | 44 | 81.50 |
| Males | 8 | 50 | 22 | 40.70 |
| Females | 8 | 50 | 32 | 59.25 |
| Male:Female ratio | 1:1 | | 1:1.4 | |

who had foul smelling liquor had 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 18.1% of them developed AKI. Hence, foul smelling liquor was found to be a significant risk factor for AKI in sepsis ($p<0.05$) (Table 3 C).

Neonates who had PROM >24 hours as risk factor for sepsis, 60% of them developed AKI as compared to only 16.6% in the absence of PROM as a risk factor. Hence, PROM of >24 hours was a significant risk factor for AKI in sepsis ($p<0.05$) (Table 3D) AKI was present in only 16% of septic neonates with perinatal asphyxia and in 23.4% of neonates without perinatal asphyxia. Hence, perinatal asphyxia was not found to be significant risk factor for AKI in sepsis ($p>0.05$) (Table 3C).

## DISCUSSION:

In this study, it was found that out of 70 septic neonates who were enrolled, 16 (23%) had AKI. This is comparable to that of study conducted by Mathur et al , Gaurav Jagrawal et al and Durga D et al[12,15,16], where the incidence of AKI in septic neonates was found to be 26%, 31.77% and 24% respectively.

In this study, out of total 16 septic neonates with AKI, only 6 neonates i.e. (37.5%) weighed < 2500gm. 10 (62.5%) out of total 16 septic neonates with AKI weighed ≥ 2500gm. This result is similar to the study conducted by Durga et al[16], who also found that out of 11 septic neonates who weighed <2.5kg, only 36.4% had AKI. Gaurav Jagarwal et al[15] found that 31.25% neonates with weight <2.5kg developed AKI. This was in contrast to the findings of Mohammad H Salah, SK Pradhan et al, Ahesanali M Holda[13,6,14], where they found a higher incidence of AKI in septic neonates who weighed <2.5 kg and considered it as an important risk factor for the development of AKI.

It was observed that incidence of AKI was almost equal in both the preterm and term neonates with sepsis. Total 13 neonates belonged to gestational

**Table 2:** Clinical profile of septicemia of newborn: It admission.

| Signs and Symptoms | No. of cases (n=70) | % |
|---|---|---|
| **Symptoms** | | |
| Refusal to feed | 60 | 85.70 |
| Lethargy | 56 | 80.00 |
| **Temperature change** | | |
| Hypothermia | 20 | 28.57 |
| Hyperthermia | 50 | 71.42 |
| Abdominal distension | 40 | 57.15 |
| Excessive cry | 35 | 50.00 |
| Vomiting | 11 | 15.71 |
| Convulsions | 15 | 21.42 |
| **Sign** | | |
| Apnea | 47 | 67.14 |
| Sclerema | 13 | 18.57 |
| Umbilical sepsis | 10 | 14.28 |
| Bulging fontanelle | 13 | 18.57 |

**Table 3**: A) Association of Shock and AKI; B)Distribution of neonates based on blood culture; C) Distribution of neonates based on foul smelling liquor as a risk factor for AKI in sepsis; D) Distribution of neonates based on prolonged rupture of membranes as a risk factor for AKI in sepsis; and, E) Distribution of neonates based on perinatal asphyxia.

| | | Neonates with AKI Group I (n=16) | | Neonates without AKI Group II (n=54) | | Total | p-value |
|---|---|---|---|---|---|---|---|
| | | No | % | No | % | | p<0.05 |
| A) Shock | Present | 11 | 68.15 | 16 | 29.63 | 27 | (p=0.0047) |
| | Absent | 5 | 31.25 | 18 | 70.37 | 43 | Significant |
| | Total | 16 | | 54 | | 14 (100%) | |
| B) Blood culture | Positive | 10 | 71.4 | 4 | 28.6 | 56 (100%) | p<0.05 |
| | Negative | 6 | 10.7 | 50 | 89.3 | 70 (100%) | (p=0.0001) |
| | Total | 16 | | 54 | | 70(100) | |
| C) Foul smelling liquor | Present | 4 | 100 | 0 | 0 | 4(100%) | |
| | Absent | 12 | 18.1 | 54 | 81.9 | 66(100%) | p<0.05 |
| | Total | 16 | 23.0 | 54 | 77.0 | 70(100) | (p=0.00152) |
| D) PROM (>24hours) | Present | 6 | 60.0 | 4 | 40.0 | 60(100%) | |
| | Absent | 10 | 16.6 | 50 | 83.4 | 10(100%) | p<0.05 |
| | Total | 16 | 23.0 | 54 | 77.0 | 70(100) | (p=0.00893) |
| E) Perinatal asphyxia | Present | 15 | 23.0 | 49 | 76.56 | 64 (100%) | p<0.05 |
| | Absent | 1 | 16.0 | 5 | 83.0 | 6(100%) | (p=0.8962) |
| | Total | 16 | 23.0 | 54 | 77.0 | 70(100) | |

age group 34-36 weeks, out of which 3 neonates developed AKI (23.08%). A total of 57 neonates belonged to > 36 weeks of gestational age group, out of which 13 cases developed AKI (22.8%). These findings were similar to the study conducted by Mathur et al , Gaurav Jagrawal et al and Durga et al who found mean gestation of neonates with ARF similar to those without ARF[12,15,16].

However, in the study conducted by Mohammad H et al and S K Pradhan et al majority of the septic neonates who developed AKI were preterm (44.3%,43.3% respectively)[13,6]. This was probably due to the fact that their study included a higher number of preterm neonates. In our study, it was observed that ARF secondary to neonatal sepsis was predominantly non oliguric. The incidence of oliguria in neonatal sepsis was only 25%. This study contradicts the general perception that ARF in neonates is commonly oliguric. Our study supports Mathur et al , who revealed the incidence of oliguric ARF in neonatal sepsis to be 15%[12]. Ahesanali M Hold et al and Gaurav Jagrawal et al also found ARF in sepsis to be predominantly non oliguric, while oliguric ARF accounted for 13.5% and 20.58% respectively [13,15].

Among various risk factors for sepsis, it is found that prolonged rupture of membranes (>24 hrs), and foul smelling liquor during labour were significant risk factors for development of AKI in sepsis (p<0.05). It is also observed that perinatal asphyxia did not significantly increase the occurrence of AKI in septic neonates (p>0.05). These findings were similar to that of the results obtained by Mohd H et al, Gaurav Jagrawal et al and Durga et al[13,15,16]. However, SK Pradhan et al differ in their study and found it to be a significant risk factor[6].

Culture positive sepsis was higher for the group with AKI. It was noted that 71.4% neonates with a positive blood culture developed AKI as compared to only 10.7% with negative blood culture. Blood culture positivity was significantly associated with AKI in sepsis (p<0.05). Correlation between the pathogenic organism with AKI could not be established because from almost all blood culture positive septic neonates with AKI, growth of coagulase negative staphylococci was isolated and could not be compared with other pathogens as the number of other pathogenic organism was meagre. This finding is in concordance to the study conducted by Durga D et al, where 80% of the neonates with a

positive blood culture developed AKI as compared to only 20% with negative blood culture[16]. On the other hand, Mathur et al, SK Pradhan et al and Gaurav Jagrawal et al found culture positivity did not significantly differ between septic neonates with AKI and without AKI [6,12,15].

We also found in this study that 68.75% neonates had shock in AKI and 29.63% neonates had shock in without AKI group. Mathur et al and Gaurav Jagrawal et al similarly found shock to be significantly associated with AKI[12,15]. Recent study by Gaurav Jagrawal et al is also similar to our study. They reported 70.59% neonates had shock in AKI and 24.66% neonates had shock in without AKI group[15]. Durga D et al, also found that the need for inotropic support for shock was a significant parameter of morbidity associated with AKI in sepsis [16].

In present study, the mortality rate in oliguric cases was 75% while in non oliguric was 41.66%. This is similar to findings of few authors who reported mortality in oliguric ARF to be significantly higher (Brion LP, et al , Chevalier RL, et al )[17,18].

## CONCLUSION :

The present study reveals that AKI is a very common entity among septic neonates and associated with high mortality. AKI complicating neonatal sepsis is predominantly non-oliguric. Coexisting shock, presence of prolonged rupture of membranes(>24 hours),foul smelling liquor and culture positive sepsis are important risk factors contributing significantly towards AKI in sepsis. Perinatal asphyxia did not significantly increase the incidence of AKI in septic neonates. Thus, it can be inferred that early recognition of risk factors for developing AKI may reduce the risk of its occurrence.

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