Acute kidney injury in neonatal sepsis: prevalence, and outcome

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Abstract
Background: Acute kidney injury (AKI) is an acute and reversible increment in serum creatinine levels regardless of associated or not with a decrease in urine output. AKI is very common among septic neonates. The high mortality among septic neonates with AKI stresses the need for screening them for renal failure. Early recognition of risk factors for AKI may reduce the risk of its occurrence.
Objective: This study aimed to evaluate AKI's prevalence and outcome in neonates with neonatal sepsis in our hospital.
Patients and methods: This study was an observational cross-section study carried out on all neonates ≥ 28 weeks admitted to our hospital in 6 months duration. History, examinations, and urine output were assessed and followed up regularly. Laboratory investigations included CBC, CRP, ESR, urine analysis, Urea and Creatinine, and Blood culture.
Results: AKI presented in 67.2% of septic neonates based on oliguria while raised serum creatinine, shown in 4.5% of cases. Mean urine output was (1.26 ± 0.6) ml/kg/hr, 60 % of patients with AKI were males, 38% were preterm, 47% were LBW, and mortality was 51.1%.
Conclusion: more than two-third of neonates with sepsis had AKI. Gestational age and weight were less in cases with AKI, with more than half of them were full-term and ≥ 2.5 kg. Gender was not a significant risk factor for AKI in sepsis. Mortality was significantly higher in AKI, mainly in full-term and low birth weight. Dead neonates with AKI were less anemic, less leucopenic, and more thrombocytopenic than living.
Keywords: sepsis, kidney injury, oliguria**.**

Introduction

Acute kidney injury (AKI) is defined as an acute and reversible increase in serum creatinine (SCr) levels, regardless of associated or not with a reduction in urine output (oliguria/ anuria). AKI is a complex disorder with clinical manifestations ranging from mild injury to complete kidney failure, requiring renal replacement therapy, peritoneal, or hemodialysis **(Singbartl and Kellum, 2012; SiewandDeger, 2012)**. Some studies recognize that even small increments in SCr levels increase morbidity and mortality **(Zappitelli et al., 2009; Alkandari et al., 2011)**. Evaluating AKI in infants and neonates is a challenge as renal function, serum creatinine, and glomerular filtration rate varies by the growth of the baby **(Jetton and Askenazi, 2006)**. The current AKI diagnosis is troublesome and based on two main findings: changes in SCr and urine output **(Askenaziet al., 2006)**. It is revealed that AKI is a very common entity among septic neonates. As the latent period for the development of AKI in neonatal sepsis is short, together with the high mortality among septic neonates with AKI, it becomes mandatory to screen the septic neonates for renal failure. Early determination of risk factors for

developing AKI may reduce the risk of its occurrence **(Jagrawal et al., 2016)**.

This study aimed to evaluate AKI's prevalence and outcome in neonates with neonatal sepsis in our hospital.

Material and methods

This study was an observational cross-section study carried out on the neonatal intensive care unit (NICU) at our hospital from beginning of August 2017 to the end of January 2018.

Inclusion criteria

- All Neonates (Full-term and preterm ≥ 28 weeks) admitted to NICU at our hospital with proved neonatal sepsis, age from (1 – 28) days.

Exclusion criteria

- Post-operative neonates
- Cases with gross congenital anomalies of the kidney and urinary tract.
- Patients with birth asphyxia or a history of hypoxic-ischaemic encephalopathy
- Neonates with a maternal history of kidney failure.

Definitions

Neonatal sepsis diagnosis was made based on either a positive sepsis screen or a positive blood culture in symptomatic neonates. The screen was only positive if two or more of the following were present: CRP > 1 mg/dl, ESR > 15mm in the first hour, Total leucocyte count <5000/ mm or >15000/mm3. **Acute kidney injury**was defined as a rise in serum creatinine or a decrease in urine output. Increase in serum creatinine >1.5 mg/dl irrespective of the day of life **(Askenaziet al., 2006).Oliguria** defined as urine output < 1ml/Kg/hr**(Levy et al., 2003)**

Methods

All neonates were subjected to full history taking, clinical examinations emphasizing urethral, meatal abnormalities, palpable bladder and kidneys, urine output were assessed and then were followed up regularly. Laboratory investigations including complete blood count (CBC), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), urine analysis, urea and creatinine, and blood culture were done.

Methodology of the lab investigations
Sample collection

Blood sampling: 8 ml of peripheral blood; 1ml was taken in EDTA vacutainer for CBC, 2ml was taken in plain vacationer for ESR and CRP, and 5ml was taken in a conventional 2-bottle broth for blood culture.

Blood culture: The blood cultures were processed in a conventional 2-bottle broth blood culture system (BACTEC; Becton Dickinson, MD, United States of America). All of the isolates were identified using standard procedures as described by the National Committee for Clinical Laboratory Standards guidelines **(Qazi and Stoll, 2009)**.

Urine sampling

Urine analysis: Microscopic urinalysis was influenced by the preparation of the specimen (centrifuged &uncentrifuged). Urine microscopy was done to look for the presence of WBC or bacteria. When uncentrifuged urine is examined microscopically, pyuria is defined by ≥ 10 leukocytes per high power field and bacteriuria by the presence of any bacteria per 10 oil immersion field of Gram-stained smear **(Saadehand Mattoo, 2011)**or >5 leukocytes per high power field in a centrifuged sample **(Tsai et al., 2016).**

Statistical methodology

All the statistical analyses performed using SPSS version 22. Summary of measures

reported as mean ± standard deviation (SD) for quantitative variables such as age, weight, and urine output and percentages for categorical variables such as mode of delivery and type of organism.The differences in distribution evaluated using the chi-square test for categorical variables and T-test for quantitative variables. *P* Value ≤ 0.05 was considered statistically significant.

Results

Our study included 67 neonates with confirmed neonatal sepsis.

Growth in blood culture is presented in (23) 34.3% of cases. Isolated organisms were Staphylococcus, Klebsiella Pneumoniae, and Enterobacter cocci. Antibiotic Sensitivity showed that 22.4 % of cases were sensitive to Ciprofloxacin, 9% to Clindamycin and Rifampicin, 4.5% to Imipenem, and Erythromycin [Table.1].

Table 1. Isolated Organisms and Antibiotic Sensitivity of the Blood Culture

Variable		N = 67	
Growth: Yes		23 (34.3%)	
Organism			
● **Staphylococcus**		**11 (16.4%)**	
● **KlebsiellaPneumoniae**		**7 (10.4%)**	
● **Enterobacter cocci**		**5 (7.5%)**	
Antibiotic Sensitivity		**Antibiotic Sensitivity**	
● **Ciprofloxacin**	**15 (22.4%)**	● **Gentamycin**	**3 (4.5%)**
● **Clindamycin**	**6 (9.0%)**	● **Penicillin**	**3 (4.5%)**
● **Rifampicin**	**6 (9.0%)**	● **Cefotaxime**	**2 (3.0%)**
● **Imipenem**	**3 (4.5%)**	● **Tetracycline**	**1 (1.5%)**
● **Erythromycin**	**3 (4.5%)**	● **Chloramphenicol**	**1 (1.5%)c**

Diagnosis of Acute Kidney Injury presented in 45 (67.2%) of the studied septic neonates as oliguria presented in 67.2% of patients while high serum creatinine presented only in three (4.5%) of cases. The mean urine output was (1.26 ± 0.6) ml/kg/hr, and the mean total urine output was (77.16 ± 44.4) ml/day, [Table.2].

Table 2. Diagnosis of Acute Kidney Injury among the studied Patients

Variable	N = 67
Acute Kidney Injury	45 (67.2%)
Oliguria: Yes	45 (67.2%)
High serum creatinine	3 (4.5%)
Urine Output (ml/kg/hr)	
● **Mean ± SD**	1.26 ± 0.6
● **Median (Range)**	1 (0.5 – 3.5)
Total Urine Output (ml/day)	
● **Mean ± SD**	77.16 ± 44.4
● **Median (Range)**	65 (10 - 175)

Socio-demographic data of all studied cases showed in [Table.3], while socio-demographic data of cases with AKI showed that 60 % of cases were males. The mean gestational age was (35.98 ± 3.3) weeks with 38% were preterm, 80% of cases with AKI delivered by cesarean section (C.S). The cases' mean weight was (2.38 ± 0.8) kg, with 47% were LBW. In-hospital delivery was 71 %, blood culture was positive in 24.4% of patients, and mortality was 51.1% in patients with AKI.

Table 3.Socio-demographic characteristics of the studied cases

Variable	n = 67	Variable	n = 67
Age in days ● Mean ± SD ● Median (Range)	 5.02 ± 0.7 3 (1 - 29)	**Sex** ● Female ● Male	 26 (38.8%) 41 (61.2%)
Gestational age/weeks ● Mean ± SD ● Median (Range)	 36.16 ± 3.1 37 (27 - 40)	**Gestational age Category** ● < 37 weeks ● ≥ 37 weeks	 26 (38.3%) 41 (61.7%)
Birth Weight in Kg ● Mean ± SD ● Median (Range)	 2.52 ± 0.9 2.5 (1 - 4)	**Birth Weight Category** ● < 1 kg ● 1 – 1.5 kg ● 1.5 – 2.5 kg ● ≥ 2.5 kg	 2 (3%) 8 (11.9%) 19 (28.4%) 38 (56.7%)
Mode of Delivery ● CS ● VD	 54 (80.6%) 13 (19.4%)	**Hospital Stay/days** ● Mean ± SD ● Median (Range)	 2.84 ± 0.2 2 (1 - 11)
In/Out- hospital delivery In-hospital delivery Out-hospital delivery	 49 (73.1%) 18 (26.9%)		

Preeclampsia was the most frequently encountered maternal obstetric disorders among studied cases, followed by PROM then Gestational DM, while in cases with AKI, PROM was the first, followed by preeclampsia, [Table.4].

Table 4. Maternal obstetric disorder and clinical presentation of studied cases

Variable	n = 67	Variable	n = 67
Preeclampsia	9 (13.4%)	**Body Temperature** Hypothermia	 54 (80.6%)
PROM	7 (10.4%)	**Hypoactivity**	21 (31.3%)
Gestational Diabetes	3 (4.5%)	**Skin Manifestations** Delayed capillary refill time Skin Mottling	57 (85.1%) 47 (70.1%)
Anti-partum Haemorrhage	2 (3%)	**RR:** Tachypnoea Bradypnea	4 (6%) 1 (1.5%)
Thyroidectomy	2 (3%)	**HR:** Tachycardia Bradycardia	3 (4.5%) 55 (82.1%)

Thalassemia Minor	1 (1.5%)	Pallor	1 (1.5%)
Placental Insufficiency	1 (1.5%)	**Systolic BP (mm/hg)** Mean ± SD Median (Range)	68.34 ± 11.8 65 (50- 101)
		Diastolic BP (mm/hg) Mean ± SD Median (Range)	40.75 ± 10.9 40 (28 - 75)
		Generalized Oedema	39 (58.2%)
		Lower Limb Oedema	45 (67.2%)

Presentation of neonatal sepsis in studied patients showed that hypothermia, delayed capillary refill time, bradycardia, and skin mottling were the most common visible manifestations, mean systolic blood pressure was (68.34 ± 11.8) mmHg, and mean diastolic BP was (40.75 ± 10.9) mmHg. Lab findings of the studied patients showed that 25 (37 %) of cases were anemic (means hemoglobin less than 13.5 g/d), 28 (42%) had leukocytosis, 9 (13.4%) were leucopenic, and 38 (56.7%) of cases were thrombocytopenic. 38 (56.7%) of cases had positive CRP and only 3 (4.5%) of cases had elevated creatinine > 1.5 mg/dl, (Table.5)

Table 5. Laboratory Findings of the studied Patients

Variable	n = 67	Variable	n = 67
HGB (g/dl) Mean ± SD Median (Range)	14.10 ± 2.6 14.5 (6.5 – 20.5)	**Clarity/Turbidity** Yes	6 (9%)
WBC.s $*10^3$ Mean ± SD Median (Range)	14.28 ± 11.3 11 (2.5 – 63.5)	**Specific Gravity** Mean ± SD Median (Range)	1024.30 ± 7.1 1025 (1015 - 1040)
PLT $*10^3$ Mean ± SD Median (Range)	189.28 ± 13.9 160 (21 - 516)	**Pus Cells** Mean ± SD Median (Range)	16.37 ± 13.8 10 (3 - 55)
ESR 1st hour Mean ± SD Median (Range)	20.90 ± 14.1 15 (5 - 80)	**RBCs** Mean ± SD Median (Range)	13.08 ± 13.1 10 (3 - 75)
ESR 2nd hour Mean ± SD Median (Range)	37.36 ± 21.6 31 (10 - 110)	**Urate Crystals** ● No ● +1	0 (0%) 24 (35.8%)
CRP (Positive)	38 (56.7%)	● +2 ● +3	39 (58.2%) 4 (6.0%)
Blood Urea Mean ± SD Median (Range)	54.69 ± 28.5 50 (14 - 179)	**Epithelial Cells** ● No ● +1	5 (7.5%) 46 (68.7%)

Serum Creatinine			● +2	15 (22.4%)
Mean ± SD	0.97 ± 0.2		● +3	1 (1.5%)
Median (Range)	1 (0.5 – 1.9)			

Comparison of septic neonates with and without AKI showed that there was significance between two groups regarding weight, positive blood culture, and mortality, while there was insignificance between two groups regarding gestational age, sex, mode, and place of delivery. Maternal obstetric disorder showed that only PROM significantly higher in cases with AKI (Table6 and 7).

Table 6. Comparison of Septic Neonates with and Without AKI regarding demographic data

	AKI (No=45)	Without AKI (No=22)	P-value
Gestational Age/weeks	35.98 ± 3.3	36.55 ± 2.7	= 0.461*
● **< 37 weeks**	17 (37.8%)	9 (40.9%)	= 0.505**
● **≥ 37 weeks**	28 (62.2%)	13 (59.1%)	
Weight/kg	2.38 ± 0.8	2.76 ± 0.8	**= 0.044***
● **< 2.5 kg**	21 (46.7%)	8 (36.4%)	= 0.297**
● **≥ 2.5 kg**	24 (53.3%)	14 (63.6%)	
Sex ● **Female** ● **Male**	18 (40%) 27 (60%)	8 (36.4%) 14 (63.6%)	= 0.495**
Mode of delivery ● **VD** ● **CS**	9 (20%) 36 (80%)	4 (18%) 18 (82%)	
In/Out-hospital delivery **In-hospital delivery** **Out-hospital delivery**	32 (71.1%) 13 (28.9%)	17 (77.3%) 5 (22.7%)	= 0.411**
Culture ● **Negative** ● **Positive**	34 (75.6%) 11 (24.4%)	10 (45.5%) 12 (54.5%)	**= 0.015***
Mortality ● **Alive** ● **Death**	22 (48.9%) 23 (51.1%)	17 (77.3%) 5 (22.7%)	**= 0.027***

*T-test was used to compare the difference in means between the two groups

**Chi-square analysis was used to compare the difference in proportions
--Significance level is considered when p ≤ 0.05

Table 7. Comparison of Septic Neonates with and Without AKI regarding obstetric complications

	AKI (No=45)	Without AKI (No=22)	P-value*
PROM	7 (15.6%)	0 (0%)	**= 0.015**
Preeclampsia	6 (13.3%)	3 (13.6%)	= 0.623
Antepartum Haemorrhage	2 (4.4%)	0 (0%)	= 0.315
Gestational Diabetes	2 (4.4%)	1 (4.5%)	= 0.701
Thalassemia Minor	0 (0%)	1 (4.5%)	= 0.150
Thyroidectomy	1 (2.2%)	1 (4.3%)	= 0.523
Placental Insufficiency	1 (2.2%)	0 (0%)	= 0.481

*Chi-square analysis was used to compare the difference in proportions
**NA=Not Applicable
--Significance level is considered when p ≤ 0.05

Prognostic factors in neonatal acute kidney injury showed that gestational age, weight, and positive blood culture were significantly lower in dead than living neonates. Low birth weight (LBW) was insignificantly higher in dead than living neonates. There was an insignificant relationship between the living and dead neonates with AKI regarding sex, mode, place of delivery, neonatal anemia, abnormal WBCs (leucopenia or leucocytosis), and thrombocytopenia. CRP was Positive in half of living patients vs. more than 2/3 of dead patients; also, CRP, ESR 1st-hr, and ESR 2nd -hr were significantly higher in dead than living cases. Blood Urea > 20 mg/dl presented in all living and dead patients. Serum Creatinine > 1.5 mg/dl was 4.3% in dead patients only with insignificant P-value (Table.8 and 9)

Table 8.Prognostic factor in neonatal acute kidney injury (Alive vs. Dead) regarding demographic data

	Survival (No=22)	Death (No=23)	P-value
Gestational Age/weeks	36.59 ± 2.8	35.39 ± 3.8	**= 0.032***
● **< 37 weeks**	6 (27.3%)	11 (47.8%)	= 0.133**
● **≥ 37 weeks**	16 (72.7%)	12 (52.2%)	
Weight/kg	2.64 ± 0.8	2.13 ± 0.7	**= 0.029***
● **< 2.5 kg**	8 (36.4%)	13 (56.5%)	= 0.145**
● **≥ 2.5 kg**	14 (63.6%)	10 (43.5%)	
Sex			
● **Female**	8 (36.4%)	10 (43.5%)	= 0.428**
● **Male**	14 (63.6%)	13 (56.5%)	
Mode of Delivery			
● **CS**	16 (72.7%)	20 (87%)	= 0.207**
● **VD**	6 (27.3%)	3 (13%)	
In/Out-hospital delivery			
● **In-hospital delivery**	17 (77.3%)	15 (65.2%)	= 0.288**

● **Out-hospital delivery**	5 (22.7%)	8 (34.8%)
Culture		
● **Positive**	14 (63.6%)	9 (39.1%)	**= 0.019****
● **Negative**	8 (36.4%)	14 (60.8%)

***T-test was used to compare the difference in means between the two groups**
****Chi-square analysis was used to compare the difference in proportions**
--**Significance level is considered when p ≤ 0.05**

Table 9. Prognostic factor in neonatal acute kidney injury (Alive vs. Dead) regarding lab abnormalities

	Alive (No=22)	Dead (No=23)	P-value
HGB (g/dl) (< 13.5)	8 (36.4%)	9 (39.1%)	0.546*
WBCs *10^3 (<5/>12)	16 (72.7%)	15 (65.2%)	0.413*
PLT *10^3 (<10)	5 (22.7%)	8 (34.8%)	0.288*
CRP Positive	11 (50%)	16 (69.6%)	**0.039****
Abnormal ESR 1st-hr	7 (31.8%)	11 (47.8%)	**0.042****
Abnormal ESR 2nd-hr	18 (81.8%)	18 (78.3%)	0.530**
Blood Urea > 20	22 (100%)	23 (100%)	NA
Serum Creatinine > 1.5	0 (0%)	1 (4.3%)	0.511**

***T-test was used to compare the difference in means between the two groups**
****Chi-square analysis was used to compare the difference in proportions**
--**Significance level is considered when p ≤ 0.05**

Discussion

Acute Kidney Injury is the kidneys' inability to excrete nitrogenous waste products and maintain fluid and electrolyte homeostasis. It is relatively common in the newborn population and is a significant contributor to neonatal mortality and morbidity (**Coca et al., 2012**).

Our study included 67 neonates, ≥ 28 weeks with proved neonatal sepsis. Growth in blood culture presented in about one-third of cases. This result was in agreement with **Jagrawal et al., (2016)** as they reported growth in 27% of their neonates. In contrast to **Holda et al. (2015),** they reported growth in 65.9% of their cases.

More than two-thirds of our cases with neonatal sepsis had AKI, diagnosis based on oliguria presence as oliguria presented in 67.2% of patients with neonatal sepsis. This prevalence is higher than that reported by **Mathur et al., (2006);Salahet al., (2010); Pradhan et al., (2014);Holda et al., (2015);Jagrawal et al., (2016); Durga and Rudrappa, (2017),** the prevalence of AKI in their septic neonates was 26%, 31.6%, 27.2%, 23.3%, 31.7%, and 24% respectively. **Mathur et al., (2006); Holda et al., (2015);Jagrawal et al., (2016);Nickavar et al., (2017)** reported the prevalence of oliguria in neonates with sepsis was only 15%, 13.5%, 8%, and 22.6% respectively. As we see, 67% of our cases had oliguria while

only 4.5% of them had raised creatinine and so, it is crucial to follow-up urine output regularly in patients with neonatal sepsis for early detection and prevention of acute kidney injury

The mean gestational age of affected AKI cases was (35.98 ± 3.3) weeks, with 62% of them full-term. In agreement with our study, **Mathur et al., (2006); Mortazavi et al., (2009);Salahet al., (2010),** as they observed that the rate of AKI in their cases was 61.5%, 70.2%, and 56.7% in full-term infants. In contrast to our study, **Alaro et al., (2014);Jagrawal et al., (2016);Weintraub et al., (2016)**, as they found that the prevalence of AKI was 42%, 29.5%, and 42% in full-term neonates.

Sex distribution of the studied cases showed male predominance with 60 %of neonates with AKI were males. In agreement with **Holda et al., (2015), Nickavar et al., (2017); Bansal et al., (2017)** as theyconcluded that the male gender was more associated with AKI (61.5%, 61.5%, and 47.3%)**.** In contrast to**Durga and Rudrappa, (2017),** the male percentage in their study was 34%. The high frequency of AKI in boys can be explained based on increased vulnerability of boys to some perinatal disorders for example as sepsis and respiratory distress syndrome. It can also be due to more number of male neonates presented with neonatal sepsis in our study and seeks medical treatment compared to females due to the gender bias persisting in our society.

The mean weight of cases of AKI was (2.38 ± 0.8) kg, with 47% were LBW. In agreement with **Jagrawal et al., (2016),** they reported that 32% of patients with AKI were less than 2.5 kg. In contrast to **Mathur et al., (2006);Holda et al.,**

(2015); Kumar et al., (2017) found that 86.5%, 87.5 and 68.4% of septic infants with AKI were below 2.5 kg. **Durga and Rudrappa (2017)** found no significant difference in the incidence of AKI in sepsis in AGA and SGA neonates of both the groups, so they concluded that birth weight was not a significant factor contributing to AKI in sepsis.

Regarding the place of delivery in our study, In-hospital delivery presented in 71% of cases, **Bansal et al., (2017)** reported that out-hospital delivery (73%) is more than in-hospital delivery (27%) in neonates with AKI. This result may be due to our strategy in our hospital is to give priority to in-hospital delivery admission than to out-hospital delivery, and so the number of admissions is more in in-hospital delivery

Regarding mode of delivery, C.S was fourfold that of vaginal delivery (V.D) in patients with AKI. Similar to that found by **Bolat et al., (2013**) and **Askenazi et al.,(2009)**, who reported that CS was 54% in patients with AKI.

Growth in blood culture was significantly lower in patients with AKI in which it was positive in 24.4% in patients with AKI and 54.5% in patients without AKI. In agreement with **Mathur et al., (2006);Jagrawal et al., (2016),** they reported that blood culture was positive in 15.6% and 32.35% of neonates with AKI. In contrast to**Holda et al., (1015); Durga and Rudrappa, (2017)**, they found that 51.9% and 80% of neonates with a positive blood culture developed AKI compared to only 10% with negative blood culture.

Pre-eclampsia was the most frequently encountered maternal obstetric disorders among studied cases, followed by PROM then Gestational DM, while in cases with

AKI, PROM was the first, followed by preeclampsia. **Durga and Rudrappa, (2017)** found that 62.2% of septic patients with PROM developed AKI. Previous study results showed that PROM was significantly associated with the risk of neonatal sepsis **(Gebremedhin et al., 2017)**. Although PROM treatment with antibiotics during pregnancy may contribute to newborns' exposure to nephrotoxic agents, PPROM itself is an intrauterine insult **(Bolat et al., 2013)**.AKI in NICUs mostly occurs because of perinatal conditions such as placental insufficiency, that present in cases of preeclampsia and PROM **(Beth and Katherine, 2011)**. Some mothers with acute renal failure may receive more drugs during pregnancy and delivery (mainly anti-hypertensive and NSAIDs). NSAIDs interference with endogenous renal prostaglandin production will increase angiotensin-II dependent vasoconstriction, leading to reduced GFR and renal insufficiency **(Holdaet al., 2015)**.

The presentation of the studied patients in our study revealed that hypothermia, delayed capillary refill time, skin mottling, and bradycardia were the most prominent presentations, while a small number of neonates were presented by tachypnoea, tachycardia, hypoactivity, and pallor. More than half of the patients were presented by generalized or lower limb edema, while blood pressure was more or less normal. **Baltimore, (2003**), concluded in their study that the early signs of neonatal sepsis include respiratory distress, temperature instability, breathing difficulty, lethargy, reluctance to feed, and hypoactivity. **Gebrehiwot et al., (2012)** found that clinical characteristics such as failure to suck, fast breathing, lethargy, and seizure were found to be significantly associated

with neonatal sepsis. The newborns with sepsis may be predisposed for AKI because of hypotension secondarily to sepsis and a direct damaging effect on renal microvasculature **(Selewskiet al., 2015)**.

Our patients' lab findings showed that more than one-third of cases were anemic, and more than half of them were thrombocytopenic**,** 42% had leukocytosis, 13.4% were leucopenic. CRP was positive in more than half of the cases. Like **Mel-Setand El-Sayed, (2009); El-Dinet al., (2015),** CRP was positive in 85.3% of cases.In contrast to **Siddaiah et al., (2017),** CRP was positive in 22% of their patients.

Regarding to outcome in neonatal acute kidney injury, mortality was significantly higher in patients with AKI as it was 51.1% in patients with AKI and 22.7% in patients without AKI. In agreement with **Salah et al., (1010); Pradhan et al., (1014);Jagrawal et al., (2016)** where they found the mortality rates in septic neonates with AKI to be 50%, 70.2% and 56.5%, respectively. In contrast to **Agras et al., (2004);Timovska et al., (2015),** they reported a mortality rate of 35.4%, and 44.4% in neonates with AKI. In neonatal AKI, the prognosis showed that gestational age and weight were significantly lower in dead than living cases. LBW was insignificantly higher in dead than living cases. Similar to **Mathur et al., (2006); Nickavar et al., (1017)** in contrast to **Jagrawal et al., (2016); Bansal et al., (2017)** as they reported that there were no significant differences in gestational age nor weight between dead and living neonates with AKI. There was an insignificant relationship between the living and dead patients with AKI regarding sex, mode and place of delivery,

similar to the results of studies done by **Bansal et al., (2017);Nickavar et al., (1017)**.

Blood culture was positive in 61% in dead patients and 90% in living patients with significant P value, in contrast to **Mathur et al., (2006); Jagrawal et al., (2016)**, where they reported that blood culture was positive in 10.7%, 23% in dead patients and 21.4%, 3.8% in living patients.

There was an insignificant relationship between the living and dead patients with AKI regarding neonatal anemia, abnormal WBCs (leucopenia or leucocytosis), and thrombocytopenia. CRP was Positive in half of living patients vs. more than 2/3 of dead patients; in addition, CRP, ESR 1st-hr, and ESR 2nd -hour were significantly higher in dead than living cases. **Nickavar et al., (1017)** concluded in their study that cases with AKI has higher WBC, fewer platelets, and the same hemoglobin level than cases without AKI, 1.8% of cases with AKI had positive CRP. **Agras et al., (2004)** demonstrated that intrinsic AKI and need for dialysis were associated with higher mortality rates, whereas no significant correlation was found between mortality rate and prematurity, creatinine levels, blood urea nitrogen, and perinatal factors. **Esfandiar et al., (2013)** described high serum creatinine level and LBW as related to mortality; they observed an association between mortality and smaller gestational age, oliguria, and smaller weight in neonates with AKI. **Mathur et al., (2006)** studied the significance of various prognostic factors in predicting fatality in cases of neonatal AKI, and they found that gestational age, weight, culture positivity, early-onset sepsis, nephrotoxic drugs, and oliguria all were not associated with increased mortality.

Previous studies demonstrated that the predisposing factors of mortality include underlying etiology, female gender, birth asphyxia, low birth weight, multiorgan failure, hypotension, septicemia, profound acidosis, shock, oligoanuria, nephrotoxic drugs, vasopressor treatment, mechanical ventilation, and peritoneal dialysis **(Andreoli, 2004; Momtazet al., 2014)**.

Conclusion

The present study revealed that 67% of neonates with sepsis had AKI based on oliguria presence. Gestational age and weight were less in patients with AKI, with more than half of patients with AKI were full-term and $\geq$ 2.5 kg. Gender was not a significant risk factor for AKI in sepsis. Mortality was significantly higher in patients with AKI. Mortality was high full-term and in low birth weight baby. Dead cases with acute kidney injury were less anemic, less leucopenic, and more thrombocytopenic than living neonates. Acute kidney injury complicating neonatal sepsis is predominantly oliguric.

We recommend screening all septic neonates for AKI by estimating urine output as it is a straightforward, inexpensive, and non-invasive method**.** Early detection of oliguria and renal function monitoring are imperative to reduce mortality and morbidity in neonatal AKI.Early recognition of risk factors for AKI and rapid effective correction of contributing conditions. Early treatment of sepsis for the prevention of AKI. Good monitoring for and improvement of nutritional status as the low birth weight was associated with high mortality in neonates with AKI**.**

Abbreviations:

AKI: Acute kidney injury

CBC: complete blood count

CRP: C-reactive protein

CS: cesarean section

DM: diabetes millets

ESR: erythrocyte sedimentation rate

GFR: Glomerular filtration rate

LBW: Low birth weight

NICU: Neonatal intensive care units

NSAIDs: Nonsteroidal anti-inflammatory drugs

PROM: Premature rupture of membrane

SCr: serum creatinine

VD: vaginal delivery

WBC: white blood cells

Conflict of interest: None

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