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A clinical study of acute kidney injury in high risk neonates

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Abstract
Introduction: Acute kidney injury (AKI) is a common occurrence in the neonatal intensive care unit (NICU). In recent years, our knowledge of the incidence and impact of neonatal AKI on outcomes has expanded exponentially. Currently, the diagnosis of AKI is solely made by rise in serum creatinine or decrease in urine output. Unfortunately, serum creatinine is considered as a suboptimal biomarker as it is a marker of kidney function, not damage or injury; thus, rise in serum creatinine is observed after 48–72 h of insult. By the time serum creatinine is raised, a significant amount of function has already been lost.
Objective of the study:
1. To estimate the proportion of Acute Kidney Injury in high-risk neonates.
2. To study the risk factors and outcome of acute kidney injury in these neonates.

Material and Methods: This is a prospective observational cohort of 200 high risk neonates admitted in NICU, SIMS, Hyderabad over a period of 2 years. All high-risk neonates with 2 or more serum creatinine values were included in this study and neonates with death within 48 hours after birth, less than 1 day of measured urine output (UOP) on days 2 to 7 after birth, and fewer than 2 Serum Creatinine measurement were excluded.
Results: Among the 200 neonates enrolled, the occurrence of AKI was 30% (60/200 patients): 56 neonates fulfilled the modified neonatal KDIGO definition of AKI according to the Serum Creatinine criteria, 31 neonates fulfilled the modified neonatal KDIGO definition of AKI according to the UOP criteria, and 28 neonates fulfilled both the Serum creatinine and UOP criteria of the modified neonatal KDIGO definition of AKI. This resulted in a total of 60neonates with AKI. When classified according to the neonatal modified KDIGO stages: 28 (56%), 22 (44%) and 10 (20%) neonates fulfilled the criteria of AKI stage 1, 2, and 3, respectively. There were 3 deaths (5.36%) and 3 were discharged against medical advice (5.36%). The remaining 94.64% were discharged well.
Conclusion: AKI is a life threatening condition with still high mortality rate. Early recognition of the risk factors and the rapid effective treatment of the contributing conditions will reduce AKI in the neonatal period.

Keywords: Acute kidney injury, neonatal, continuous renal replacement therapy, fluid overload, premature (babies), N ICU, renal failure, kidney support therapy

Introduction
Acute kidney injury (AKI; previously called acute renal failure) is defined as a rapid, potentially reversible deterioration in renal functions sufficient to result in accumulation of nitrogenous wastes in the body (Uraemia)
An increase in serum creatinine of >/= 0.3mg/dl within 48hrs; or Also it is seen an increase in serum creatinine of >/= 1.5 times baseline, which is known or presumed to have occurred within the prior 7 days; or Urine volume <0.5ml/kg per hour for more than six hours.
Assessment of Worldwide Acute Kidney Injury Epidemiology in Neonates (AWAKEN) study demonstrated that 30% of neonates admitted to a neonatal intensive care unit (NICU)developed AKI and that those with AKI had 4.8 times higher adjusted odds of mortality compared with neonates without AKI [2]. Increased morbidity and mortality due to acute kidney injury occurs frequently in preterm neonates [3, 4]. Under normal circumstances, the kidney adopt to various endogenous and exogenous stresses, However, in sick neonates and stressful conditions like sepsis and shock the adaptive capacities of the kidney may be overcome leading for renal dysfunction [5]. The incidence of AKI in children appears to be increasing and the aetiology of AKI over the past decades has shifted from primary renal disease to multifactorial causes, particularly in hospitalized children. Recent advances in neonatal intensive care have resulted in improved patient survival, but this had not been paralleled by improved outcomes for neonates with AKI.

Compared to older infants, neonates have certain physiological characteristics that increase the risk of AKI, including higher susceptibility to hypo perfusion, higher vascular resistance, elevated plasma renin activity, and decreased reabsorption of sodium in the proximal tubules. Identification of risk factors associated with acute kidney injury will contribute in prevention of acute kidney injury in neonates and improve the outcome. This study is an attempt to identify the risk factors and their effect on outcome of the neonates [6].

The exact prevalence of AKI among neonates is unknown and incidence varies from 6% to 24% in neonatal intensive care units (NICUs) worldwide [4]. Risk factors for neonatal AKI include very low birth weight (<1.5 kg), a low 5-min APGAR score, maternal drug administration (Nonsteroidal anti-inflammatory drugs and antibiotics), intubation at birth, respiratory distress syndrome, patent ductus arteriosus, sepsis, phototherapy and neonatal medication administration (Nonsteroidal anti-inflammatory drugs, antibiotics, diuretics, etc.) [5]. The kidneys of neonates are particularly susceptible to hypoperfusion because of high renal vascular resistance, high plasma renin activity, low glomerular filtration, decreased intracortical perfusion rate, and decreased reabsorption of sodium in the proximal tubules in the first few days of life [6].

Definition of AKI

The first international definition for AKI was implemented in 2004 with the RIFLE classification, soon followed by the AKIN classification. AKI definitions have since then been refined and modified to account for children. The KDIGO classification, successor to RIFLE and AKIN, is currently the most widely used AKI definition, and is applicable to children and in patients with chronic kidney disease (CKD).

AKI is now defined as an abrupt change in glomerular filtration rate (GFR), reflected by an increase in serum creatinine (SCr) for up to 7 d or a decrease in urine output over 6 to 24 h. The amplitude of SCr rise from its baseline or the severity and duration of compromised urine output is used for staging (Table 1). Increasing KDIGO stages of AKI are associated with worse outcomes (e.g., mortality, need for renal replacement therapy, CKD and length of stay)

Table 1: Definition of Acute Kidney Injury [1]

Stage	Serum creatinine (SCr)	UOP during the past 24h
0	No change in SCr or rise <0.3 mg/dl	>1ml/kg/h
1	SCr rise≥0.3 mg/dl within 48 h or SCr rise between ≥1.5 and 1.9 times reference SCr within 7 d	Between >0.5 and ≤1ml/kg/h
2	SCr rise between ≥2 and 2.9 times Reference SCr	Between >0.3 and ≤0.5 ml/kg/h
3	SCr rise ≥3 times reference SCr orSCr≥2.5 mg/dl or receipt of dialysis	≤0.3 ml/kg/h

Abbreviation: UOP- urine output Reference SCr is the lowest prior SCr value

This value is lower than the original Kidney Disease: Improving Global Outcomes (KDIGO) definition because an SCr value of 2.5mg/dl in neonates suggests an estimated glomerular filtration rate less than 10 ml/min/1.73 m^2

Aims and Objectives

1. To estimate the proportion of acute kidney injury in high-risk neonates.
2. To study the risk factors and outcome of acute kidney injury in these neonates.

Materials and Methods

All high-risk neonates admitted to Neonatal Intensive Care Unit (NICU), around 200 neonates are taken as sample size. And it is a prospective cohort study, conducted over a period of 2 years. Inclusion criteria: All High risk neonates admitted to Neonatal intensive care unit (NICU). Exclusion criteria: Infants who have less than two serum creatinine measurements, death within the first 48hrs after birth, Presence of congenital renal anomalies and presence of lethal chromosomal anomaly. After obtaining Institutional Ethical Clearance, all those babies who fulfilled the inclusion Criteria and had none of the Exclusion criteria were recruited. After counselling the parents and getting consent from them, the study proformas were filled in.

Demographic data including sex, gestational age, and duration of admission, antenatal history including maternal age, maternal illnesses (diabetes, hypertension, cardiac disease, anaemia, bronchial asthma, immune thrombocytopenic purpura), obstetric problems like antepartum hemorrhage, premature rupture of membranes, oligohydramnios, multiple gestation, MSAF, TORCH infection and urinary tract infection), and maternal drug intake [antibiotics, steroids, low-molecular-weight heparin and treatment of diabetes mellitus (DM),and hypertension], natal history including mode of delivery, whether normal vaginal delivery or caesarean section as well as place of delivery, whether at home or at a hospital, and postnatal history including cyanosis, jaundice, respiratory distress, perinatal asphyxia and h/oneonatal transport and associated contributing conditions, including (a) peri- natal asphyxia, (b) sepsis, (c) respiratory distress syndrome, (d) mechanical ventilation and its duration). (e) dehydration due to feeding problems, (f) oliguria, (g) heart failure, (h) nephrotoxic drug administration and its duration, (i) urologic anomalies, and (j) history of surgical operation and reason for surgery.

All neonates were subjected to general examination including anthropometric measures (weight, length, and head circumference), vital signs (heart rate, respiratory rate, blood pressure, and temperature), skin examination (for pallor, oedema, sclerema, and poor perfusion), and urine output. Systemic examination was performed for all neonates including respiratory system examination (for the presence of respiratory distress), cardiovascular examination (for the presence of cardiac failure and poor perfusion), abdominal examination (for the presence abdominal distension, hepatomegaly, full bladder, and fullness of renal angle), and neurological examination (including assessment of the conscious level and neonatal reflexes).

All cases were subjected to the following investigations: Laboratory testing: basic investigations like complete blood count, C-reactive protein, Serum creatinine, BUN, serum electrolytes, calcium, and arterial blood gases. Radiological assessment when needed (renal imaging studies) to aid in the diagnosis of AKI(defined as plasma creatinine level higher than 1.5 mg/dL or BUN level higher than 20 mg/dL on two separate occasions at least 12 h apart, while maternal renal function was normal).

Sufficient data was defined as having at least two measurements of serum creatinine after the first 72 h of life or the data of the minimum of 1-day record of UOP documented every 6 h. Baseline Serum creatinine was defined as the lowest recorded Serum creatinine value after the first 72 h of life. Kinetic- spectrophotometric determination of Serum creatinine was conducted using the Jaffe reaction. UOP will be calculated at 6, 12, and 24 h to accurately monitor UOP. Infants were classified as having AKI based on either Serum creatinine criteria, UOP, or both criteria. Infants will be prospectively followed up during the NICU stay, and the events will be documented.

Data on kidney function and the last measured Serum creatinine before discharge will be recorded.

- Perinatal depression was defined as the need for resuscitation beyond gentle stimulation.
- Probable sepsis is defined as the case with clinical signs and symptoms of sepsis with one or both of these criteria; presence of a total leukocytes count of over 30000/cu mm3 or under 5000/mm3; CRP level > 6 ug /ml; existence of predisposing factors i.e. maternal fever or foul smelling liquor or prolonged rupture of membranes (> 12 hours) or presence of gastric polymorphonuclear leukocytes (5 or more polymorphonuclear cells/ high power field).
- Sepsis was defined as a positive blood culture during hospital stay.

AKI staging was based on the modified neonatal KDIGO definition. (Table-1) According to the modified neonatal KDIGO definition, AKI was classified into three stages based on the following criteria: absolute increase in SCr from a previous trough, decrease in UOP or both serum creatinine increase and UOP decrease.

Results

This is a prospective observational cohort of high-risk neonates admitted in NICU, SIMS, Hyderabad, Telangana from September 2015 to January 2017.

A total of 200 neonates were enrolled in this study, of which 60% were male and 40% were female. Majority of the participants were preterm (74%) with gestational age between 33-36 +6 months of gestational age (41.1%) had birth weight between 1500-2499g (45%) and most of them were inborn (81.1%).

Table 2: Socio-demographic characteristics of study participants (n = 200)

Demography	N (%)
Sex	
Male	120 (60%)
Female	80 (40%)
Birth weight	
<1000g	10 (5%)
1000-1449g	40 (20%)
1500-2499g	90 (45%)
>2500g	50 (25%)
Mean ±SD	1.80 ±0.52
Gestational Age	
<28 wks	10 (5%)
28-32+6 wks	52 (26%)
33-36+6 wks	66 (33%)
>37 wks	72 (36%)
Inborn/Outborn	
Inborn	158(79%)
Out born	42(21%)
Preterm/Term/Postterm	
Preterm	140(70%)
Term	44(22%)
Post term	16(8%)

AKI among critically ill neonates

Among the 200 neonates enrolled, the occurrence of AKI was 30% (60/200 patients): 56 neonates fulfilled the modified neonatal KDIGO definition of AKI according to the Serum Creatinine criteria, 31 neonates fulfilled the modified neonatal KDIGO definition of AKI according to the UOP criteria, and 28 neonates fulfilled both the Serum creatinine and UOP criteria of the modified neonatal KDIGO definition of AKI. This resulted in a total of 60neonates with AKI. When classified according to the neonatal modified KDIGO stages: 28 (56%), 22 (44%) and 10 (20%) neonates fulfilled the criteria of AKI stage 1, 2, and 3, respectively.

Table 3: AKI Stages based on Serum Creatinine (KDIGO)

	AKI
Stage 1	28(56%)
Stage 2	22(44%)
Stage 3	10(20%)

Our study revealed non oliguric variety of AKI is seen in 60% as compared to oliguric AKI (40%). In our study, there was male sex predominance and the male– female ratio was 2.3:1 with P-value of 0.038, and it is statistically significant.

In our study majority of cases were Inborn (83%), but there is no much difference between neonates with AKI (84%) and without AKI (80.4%) and it is statistically not significant.

In our study maximum number of AKI cases was seen in >37 weeks (56%), then 28-32+6(32%), 33-36+6(10%)), followed by <28 weeks (5%). There is a significant difference in gestational age between AKI and without AKI neonates with a P- value of <0.001.

In our study majority of AKI cases are seen in >2500g (39.3%) neonates and there is a significant difference in birth weight between with and without AKI cases with P-value of 0.04.

Table 4: Comparison of neonates with Perinatal Risk Factors

Mother's details	With AKI (n=60)	Without AKI (n=140)	Total (n=200)	P value
Age in years				
20-25	28(31.6%)	55(46.5%)	83(38%)	0.198
26-30	18(54.4%)	50(27.9%)	68(43%)	
31-35	10(10.5%)	14(20.9%)	24(15%)	
36-40	6(3.5%)	2(4.7%)	8(4%)	
Mean ±SD	28.26±3.22	27.58±4.12	28.55±4.21	
Gravida para living abortions				
Primi	23(48%)	55(43.55%)	78(44.44%)	0.650
Multi	32(52.6%)	70(56.45%)	100(55.56%)	
H/o drug intake antibiotics/steroids/LM WH				
No	30(53.6%)	82(67.7%)	112(62.22%)	0.117
Yes	26(46.4%)	42(32.26%)	68(37.78%)	
H/O radiation exposure				
No	56(100%)	124(100%)	180(100%)	1.000
Yes	0(0%)	0(0%)	0(0%)	
H/o fever during Pregnancy				
No	50(92%)	106(88.2%)	92(52%)	0.487
Yes	6(11%)	14(14.52%)	20(17.3%)	
H/o any medical problem				
Normal	52(52.6%)	48(65.1%)	141(58%)	
Abnormal	27(46%)	15(32%)	42(42%)	0.210
Hypertension	18(30.35%)	30(21%)	47(27%)	0.383
Diabetics	8(14.4%)	6(5.03%)	14(7.8%)	0.011
Cardiac disease	2(3.57%)	3(3.3%)	5(3%)	0.663

Compared to non AKI neonates, AKI neonates are born to mothers who had risk factors like hypertension, diabetes, cardiac diseases, had h/o drug intake and fever during pregnancy.

In our study H/o medical problems like Diabetes Mellitus has significant statistical difference between AKI and non-AKI cases with P-value 0.011.

Table 5: Comparision of Obstetric problems with and without AKI

h/o obstetric problems	With AKI (n=60)	Without AKI (n=140)	Total (n=200)	p-value
Anaemia	10(19%)	15(12.1%)	28(20%)	0.300
APH	8(12%)	17(13.7%)	26(18%)	0.555
PPROM	20(37%)	24(18.6%)	44(26.4%)	0.017
Multiple gestation	22(41%)	17(15.31%)	36(20%)	<0.001
Oligo	10(19.2%)	20(18.3%)	30(16.67%)	0.721
UTI	8(16%)	13(12.8%)	21(13.67%)	0.455
Previous LSCS	12(17%)	19(18.32%)	28(16%)	0.877
Toxoplasmosis	3(3.7%)	4(2.31%)	4(2.2%)	0.399
MSAF	7(18%)	10(9.8%)	18(10.56%)	0.014

Although risk factors like Anemia, APH, PPROM, multiple gestation, Oligohydramnios, UTI, previous LSCS, Toxoplasmosis and MSAF are more in neonates with AKI, only PPROM, multiple gestation and MSAF are statistically significant.

Table 6: Comparision of Natal history with and without AKI

Natal history	With AKI n=60(%)	Without AKI n=140 (%)	Total n=200 (%)	P value
Preterm/term/postterm				
Preterm	26(48.4%)	92(71.7%)	120(63.89%)	<0.001
Term	32(55.7%)	35(28.22%)	80(36.11%)	
Delivery: vaginal/LSCS				
Vaginal	24(42.85%)	34(27.42%)	58(32.22%)	0.902
LSCS	32(57.15%)	90(72.58%)	122(67.78%)	
Resuscitation				
Required	24(35.1%)	23(30.2%)	47(32%)	0.041*
Not required	35(64.9%)	95(72.1%)	130(68%)	
Any congenital Anomalies				
No	58(98.2%)	123(97.7%)	178(98%)	0.562
Yes	1(1.8%)	1(2.3%)	2(2%)	

In our study most of the neonates with AKI are term (55.7%) as compared to (48.4%). And there is statistically significant difference between gestation and occurrence of AKI with P- value<0.001.

Compared to neonates with no AKI, resuscitation in labour room required more for neonates with AKI and had low APGAR score. These results are statistically significant with P-value of 0.048.

In our study AKI risk factors like Perinatal Asphyxia, RDS, Mechanical Ventilation, Sepsis, nephrotoxic drugs, Shock, Dehydration fever had statistically significant difference between AKI and non-AKI group. Whereas no significant difference was seen between NEC, oedema, DIC, KUB anomaly and babies undergoing surgeries.

Table 7: Investigations

Investigations	With AKI (n=60)	Without AKI (n=140)	Total (n=200)	P value
Hb				
Anemia	10(18.29%)	22(18.3%)	32(22.22%)	0.57
Normal	45(80.1%)	115(82.7%)	168(77.78%)	
TLC				
Normal	40(79%)	100(80%)	140(79.4%)	0.862
Leucocytosis	10(17.0%)	22(17.74%)	32(18.22%)	
Leucopenia	4(7%)	2(1.8%)	6(4%)	
Platelets				
Normal	45(81.9%)	90(72.9%)	135(80.67%)	0.297
Thrombocytopenia	10(14.29%)	30(24.19%)	40(22.1%)	
Thrombocytosis	2(1.8%)	3(2.2%)	5(2.8%)	
Serum sodium				
Normal	40(74.43%)	120(88.7%)	160(86.33%)	0.014*
Hyponatremia	12(23%)	10(8.06%)	22(12.22%)	
Hypernatremia	4(7.14%)	4(3.22%)	8(4.44%)	
Serum potassium				
Normal	40(73.21%)	113(87.1%)	158(82.78%)	0.039*
Hyperkalemia	11(20%)	11(12.9%)	22(17.22%)	
Serum chloride				
NORMAL	56(100%)	124(100%)	180(100%)	1.000
ABNORMAL	0(0%)	0(0%)	0(0%)	
CRP				
Negative	32(58.1%)	90(72%)	124(67.2%)	0.05
Positive	24(44%)	35(28.3%)	59(32.7%)	
Blood C/S				
growth	8(16%)	6(7.3%)	14(12%)	0.066
no growth	50(84%)	120(88%)	17(87%)	
ABG				
NORMAL	42(76%)	120(83.9%)	162(85.2%)	0.029
Metabolic acidosis	15(25%)	20(14.1%)	35(18.1%)	

Hyponatremia (23%) and hyperkalaemia (20%) found to be common electrolyte disturbances associated in the present study. There is a statistic significant difference seen with hyponatremia and hyperkalaemia between AKI and Non-AKI groups with P-value of 0.014 and 0.039 respectively.

There were 3 deaths (5.36%) and 3 were discharged against medical advice (5.36%). The remaining 94.64% were discharged well.

Discussion

Burden of neonatal morbidity among critically ill neonates in lower- and middle- income countries is usually attributed to neonatal sepsis, prematurity and perinatal asphyxia, these conditions also account for high neonatal mortality. These conditions may lead to short term and long-term complications including acute kidney injury.

This study has demonstrated that AKI is very common among critically ill neonates with an occurrence of 31% (56/180) patients based on modified KDIGO criteria. This rate is similar to findings from other studies including a multicentre (AWAKEN) study [2] which reported a rate of 27% among neonates in intensive care units in developed countries and one conductedby Abdel Raheem *et al.* in Sudan[12]. Naomi A *et al.* [14] also showed similar results with prevalence of 31.5%.

In contrast, Youssef *et al.* [12] reported a lower prevalence of 10.8%, whereas a Turkish study reported a still lower prevalence of 3.4%. The wide variability of incidence of AKI in the available data from different units can be attributed to demographic characteristics of population studied, and secondly no consensus definition of AKI was used. There have been two recent studies in similar population (critically ill neonates); one using urine output with serum creatinine as the criteria and the other one only using serum creatinine.

The incidence of AKI was 20% and 6.3% respectively; highlighting the importance of having fixed definitions of AKI. Most of the published studies, especially older, have used arbitrary definitions of AKI; one frequently used is absolute serum creatinine >1.5 mg/dl [1], other studies have used risk, injury, failure, loss of kidney function, and End-stage kidney disease (RIFLE) and Acute Kidney Injury Network (AKIN) criteria, which are not meant for neonatal population[8]. Recently, Jetton JG and Askenazi [1] proposed anew definition modified KDIGO guidelines. It graded severity of AKI using changes in serum creatinine and urine output. Subsequently, in April 2013 the group of neonatologists and paediatric nephrologists at the National Institute of Health (NIH) neonatal AKI workshop recommended the use of this definition [2].

In our study, there was male sex predominance and the male–female ratio was 2.3:1 with P-value of 0.038, and it is

statistically significant. This is similar to other studies done by Mortazavi *et al*. [11] which showed male to female ratio of 2:1 and Airede *et al*. [16], who reported male to female ratio of 3.3:1 in neonates with AKI. The reason for such high incidence among males may be due to higher number of male neonates admission during the period of study and in partly to the general population attitude of seeking more active care for male neonates as compared to female neonates.

In our study majority of AKI cases are seen in >2500g (25%) neonates and there is a significant difference in birth weight between with and without AKI cases. Various studies suggest that AKI is common in VLBW/ELBW newborns and is associated with poor prognosis. Koralkar *et al*., [14] reported incidence of AKI using modified KDIGO criteria to be 18% amongst 229 VLBW infants.

Vishwanathan S *et al*. [16], and Carmody JB *et al*., [12] also reported similar findings. Interestingly, we observed higher incidence in term babies, this could be attributed to the fact that a major portion of full term neonates catered in our study were referred for sepsis or asphyxia, which also form a high risk group for AKI.

In our study maximum number of AKI cases was seen in term neonates (56%) and it is statistically significant. In a study carried out by Jayashree *et al*. [54] found that 63.72% of babies where in 36-38 weeks gestational age. Mortazavi *et al*. [11] reported that preterm cases (25.2%) were less frequently accompanied by AKI than those who were full term (70.2%). This may be because of a large number of term babies admitted to our NICU because of sepsis, asphyxia and meconium-stained amniotic fluid.

Although risk factors like Anemia, APH, PPROM, multiple gestation, Oligohydramnios, UTI, previous LSCS, Toxoplasmosis and MSAF are more in neonates with AKI, only PPROM, multiple gestation and MSAF are statistically significant.

Compared to non AKI neonates, AKI neonates are born to mothers who had risk factors like hypertension (30.35%), diabetes(14.29%), cardiac diseases (3.57%), had h/o drug intake (46.4%) like antibiotics, steroids or LMWH and h/o fever during pregnancy (10.71%).

Diabetes Mellitus has significant statistical difference between AKI and non-AKI cases with P-value of 0.013.

Similarly, Doaa Youssef *et al*. [12] showed that PROM, Diabetic mother and pre-eclampsia were the risk factors in neonatal AKI. Griffin *et al*. found that 4.7% babies born to diabetic mother had ARF in their study. The cause for acute kidney injury in babies born to diabetic mother was attributed to renal vein thrombosis secondary to polycythemia.

Although, Obstetric problems like Anemia, APH, PPROM, multiple gestation, Oligohydramnios, UTI, previous LSCS, Toxoplasmosis and MSAF are more in neonates with AKI, only PPROM, multiple gestation and MSAF are statistically significant in our study.

APH and PPROM (>24hours) predisposed to neonatal sepsis which is a risk factor for AKI.MSAF is thought to indicate a state of intrauterine stress and hypoxia, which could lead to increased vulnerability of kidneys.

Mode of delivery included normal vaginal, Caesarean section, low forceps and breech. Caesarean section was the mode of delivery in more than half of them (57.15%) followed by normal delivery (42.85%). Indication for Caesarean section included both maternal and neonatal factors – severe pre-eclampsia, failed induction, fetal distress and abnormal doppler. The higher rate of Caesarean section may be due to the fact that ours is a tertiary care center with more referrals for safer delivery in cases of complicated pregnancies.

Neonatal risk factors included those who needed resuscitation at birth.

Resuscitation included bag and mask ventilation and/or intubation. The indications for resuscitation included depressed at birth with low Apgar scores, secondary apnoea and poor perfusion.

In our study resuscitation required in 35.1% of AKI cases and perinatal asphyxia (35.1%) have been associated with a higher risk of AKI. Several previous studies done by Aggarwal A *et al*. [20], and Gupta *et al*. [21], have found birth asphyxia to be the most common risk factor for AKI of neonatal period. Two recent studies Kaur S *et al*., [17] reported an association between asphyxia and AKI in 38% and 41.67% respectively. Perinatal asphyxia is associated with acute tubular injury which is the most common cause of intrinsic AKI.

The leading risk factor of neonatal AKI in developing countries like India was perinatal Asphyxia followed by sepsis. This doesn't hold true for our present study, which showed sepsis as the primary risk factor of AKI (73.21%). Sepsis has been consistently associated asa risk factor for development of AKI in various studies conducted around the world contributing to as high as 78% cases in some neonatal studies. The possible mechanisms were: Shock due to gram negative septicaemia and Direct damage to blood vessels leading to DIC and renal ischemia.

Nephrotoxic drugs is the second most risk factor of AKI in our study (70.74%). Various nephrotoxic drugs used in our NICU are aminoglycosides and Ionotropes for babies with sepsis and shock. Various studies done by Naomi A *et al*. [14]showed 30.5% of neonates who used nephrotoxic drugs developed AKI. Timovska *et al*. [23] reported use of nephrotoxic drugs in 92% of neonates in their study. Nephrotoxic drugs is known to cause acute tubular injury which is the most common cause of intrinsic AKI.

Mechanical ventilation is the third most common risk factor of AKI in our study (67.86%).

Several theories have been proposed in support of this hypothesis. A recent NICU study from Turkey also reported similar association. Major mechanisms involved are compromised renal blood flow because of hypercapnia or hypoxemia; and barotrauma induced pulmonary inflammatory reaction leading to secondary systemic inflammatory reaction.

We found RDS to be more common in AKI group (49%). The limited literature supports a positive association between AKI and RDS. A recent study by Momtaz HE *et al*., [8] reported RDS as a third most common association with AKI (34.6%) after sepsis and dehydration.

Sepsis (73.21%), nephrotoxic drugs (69%), mechanical ventilation (67.86%), RDS (50%), perinatal asphyxia (35.1%), dehydration fever (32.14%), shock (25%), NEC (10.7%) and Oedema (7.14%) are the risk factor for AKI in our study.

Similar findings were seen in Askenazi *et al*. [8] who reported predisposing factors for AKI to be sepsis, RDS, mechanical ventilation, perinatal asphyxia, dehydration, and surgical operations in 63%, 55.6%, 51.9%, 18.5%, 14.8%, and 11.1%, respectively. Doaa Youssef *et al*. [12] showed

that most common predisposing factors for AKI were sepsis (63%), RDS (55.6%) and Mechanical ventilation (51.9%).

In neonates with AKI, hyponatremia (serum sodium ≤135 mg/dL), hyperkalaemia (serum potassium >5.5 mg/dL) and metabolic acidosis (pH <7.0), were seen in 12(23%), 11(20%), and 14(25%) neonates, respectively.

Hyponatremia (23%) and hyperkalaemia (20%) found to be common electrolyte disturbances associated in the present study. Similar results were seen in study done by Deepti Damayanty *et al.* [25] who reported hyponatremia, hyperkalemia and metabolic acidosis in 28 (56%), 18 (36%) and 9 (18%) neonates with AKI, respectively.

In our study 60 neonates fulfilled the modified neonatal KDIGO definition of AKI according to the Serum Creatinine criteria, 31 neonates fulfilled the modified neonatal KDIGO definition of AKI according to the UOP criteria, and 28 neonates fulfilled both the Serum creatinine and UOP criteria of the modified neonatal KDIGO definition of AKI. This resulted in a total of 56(31%) neonates with AKI.

Among the 200 neonates enrolled, the occurrence of AKI was 30% (60/200 patients): 56 neonates fulfilled the modified neonatal KDIGO definition of AKI according to the Serum Creatinine criteria, 31 neonates fulfilled the modified neonatal KDIGO definition of AKI according to the UOP criteria, and 28 neonates fulfilled both the Serum creatinine and UOP criteria of the modified neonatal KDIGO definition of AKI. This resulted in a total of 60neonates with AKI. When classified according to the neonatal modified KDIGO stages: 28 (56%), 22 (44%) and 10 (20%) neonates fulfilled the criteria of AKI stage 1, 2, and 3, respectively.

Aggarwal, *et al*., [20] and Gupta *et al*., [21] reported that non oliguric AKI was the most common type of AKI associated with perinatal asphyxia in full term infants. Doaa Yousef etal[12] showed that non oliguric AKI was more frequent than oliguric AKI. There were 3 deaths (5.36%) and 3 were discharged against medical advice (5.36%). The remaining 94.64% were discharged well.

Conclusion

Acute kidney injury (AKI) is a major contributor toward neonatal mortality and morbidity. The kidneys of neonates are particularly susceptible to hypo perfusion because of high renal vascular resistance, high plasma renin activity, low glomerular filtration, decreased intracortical perfusion rate, and decreased reabsorption of sodium in the proximal tubules inthe first few days of life.

AKI has a frequency of occurrence of one in three high risk neonates admitted to our NICU (31%), with the non oliguric renal form being the most common, with variable contributing factors of which sepsis, nephrotoxic drugs and mechanical ventilation were the most common. We conclude that early recognition of risk factors for developing AKI and timely intervention may reduce the risk of its occurrence.

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Conflict of interest

None

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