"INCIDENCE AND PREDICTORS OF ACUTE KIDNEY INJURY IN LATE PRETERM AND TERM BIRTH ASPHYXIA"

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“INCIDENCE AND PREDICTORS OF ACUTE KIDNEY INJURY IN LATE PRETERM AND TERM BIRTH ASPHYXIA NEONATES “

B.L.D.E (DEEMED TO BE UNIVERSITY)VIJAYAPUR

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List of Abbreviations

BA- Birth asphyxia

AKI- Acute kidney injury

PBF-placental blood flow

Scr-serum creatinine

OPN- osteopontin

GFR- Glomerular filtration rate

TPN-total parenteral nutrition

IVH-intra-ventricular hemorrhage

ESPGHAN: European Society of Pediatric Gastroenterology, Hepatology and Nutrition Guidelines

RRT-Renal replacement therapy

INTRODUCTION

Birth Asphyxia is a sequence of events defined as failure of initiation and sustain breathing at birth and associated with reduction in the arterial oxygen(PaO2) tension, accumulation of carbon dioxide (CO2) and fall in blood P^H .Birth Asphyxia condition is mainly observed in 1st and 2nd stage of labour where there will be impaired gas exchange due to various factors leading to fetal acidosis, decrease in O2- hypoxemia and increase in CO2- hypercarbia .Incidence is 1-1.5% of total live births in developed countries. [1]

Initially termed as Acute Renal Failure (ARF) had been replaced by Acute kidney injury (AKI), and is defined as sudden (within hours) reduction in renal function, consisting of both injury (structural damage) and impairment (loss of function).[1] It is characterized by a increase in serum concentration of creatinine , nitrogenous waste products like urea etc implying renal dysfunctionin maintaining homeostasis of fluid and electrolyte.[1] The Acute Dialysis Quality Initiative (ADQI) group standardized the definition of AKI using the RIFLE criteria, a mnemonic for three levels of severity; Risk, Injury and Failure and two outcomes; Loss of kidney function and End-stage kidney disease.[1,2]

The Acute Kidney Injury Network (AKIN) proposed strata that defines AKI based on absolute increase in creatinine in relation to time , percentage increase, or documented oliguria.[3] A new definition merging the RIFLE criteria and the AKIN network definition has emerged from the Kidney Disease Improving Global Outcomes (KDIGO).[4] AKIN criteria shows close approximation to RIFLE stratification of patients and both schemes equate specific changes in serum creatinine to specific worsening of oliguria.[3,4]Increased morbidity correlates with increases in RIFLE and AKIN criteria.[3-5] The worldwide incidence in the paediatric

population of AKI is poorly known because of regional disparities ,under-reporting and differences in case definition. Studies from both resource-rich and poor regions of the world have showed high AKI incidence in children.[6,7]Varying from 1-56%[8]

AKI is a consequence of birth asphyxia.[9,10] In neonates , AKI incidence ranges from 30% to 56% of birth asphyxia cases.[9]

Acute Kidney Injury (AKI) is defined as the inability of the kidneys to excrete nitrogenous waste products and maintain fluid and electrolyte homeostasis.[10] Common in neonatal population and is one of the leading contributor of neonatal mortality and morbidity.[11,12] The exact prevalence in the neonates is still hidden, but the available data shows variable incidence of AKI in the Newborn Intensive Care Units (NICUs) ; ranging from 6-24 %.[13,14] Different retrospective single centre studies have shown high incidence and significant impact on mortality in different scenarios like : Extremely Low Birth Weight (ELBW), Very Low Birth Weight (VLBW), sepsis , asphyxia, and sick term/near term neonates.[15-19]

Simple but not the most accurate method to diagnose AKI is by measuring serum creatinine levels ,. At initial days of life (14days) serum creatinine concentration decreases from 1.1 mg/dl at birth (for preterm neonate: 1.3 mg/dl) to 0.4 mg/dl.[20]

Other causes of neonatal kidney injury are as follows : neonatal sepsis, urologic anomalies , heart failure, respiratory distress, dehydration etc .[21,22,23]But the real incidence of AKI is not well known, because we cannot suspect renal failure till a patient develops oliguria ,but 33% cases of AKI in neonates are of non -oliguric type.[23]

So the present study was taken with the objective to find out the incidence and predictors of AKI in late preterm and term neonates with Birth Asphyxia in our hospital setting.

OBJECTIVES

To Study late preterm and term neonates with Birth Asphyxia in terms of

- Incidence of acute kidney injury
- Predictors of acute kidney injury

Review of Literature :

This part of dissertation is discussed under following heads:

1. **Epidemiology of birth asphyxia**
2. **Epidemiology of AKI**
3. **Pathophysiology and management of AKI in preterm and term neonate**
4. **Studies conducted in the past on similar topic**

1. Epidemiology of birth asphyxia

Background

Globally estimated neonatal annual deaths are 2.5 million contributing nearly ~47% of the under-5 child mortality.[24,2526] In addition, an estimated 1.3 million newborns are reported to be "fresh stillborn" (FSB) suggesting intrapartum demise.[27,28]Birth asphyxia (BA), assumed to intrapartum events causing hypoxia-ischemia, accounts from 30 to 35 % of neonatal mortality. The first day and especially the first hour is critical to newborn survival with the highest risk of intrapartum-related neonatal deaths (60–70%), occurring within 24 h of birth. [24-26]

Defining Birth Asphyxia

Historically, asphyxia was categorized into two grades of severity; asphyxia pallida and livida, signifying varying degrees of disease pattern. Neonates with asphyxia pallida or pale asphyxia were more severely affected, requiring immediate resuscitation. This definition was, however, replaced by more objective measures such as the Apgar score, proposed in 1952.[11] It is universally accepted that a low APGAR score at 5 min can predict survival. But Apgar score correctly cannot diagnose perinatal asphyxia and predict long-term

neurodevelopmentalproblems.[12,13]

According to the American College of Obstetricians and Gynaecologists and the American Academy of Paediatrics, defined asphyxia if the following conditions are satisfied: (1) Umbilical cord arterial pH <7; (2) Apgar score of 0–3 for more than 5 min; (3) abnormal neurological manifestations (e.g.hypotonia seizures or coma); and (4) Multisystem organ dysfunction, e.g., renal system , gastrointestinal, haematological, cardiovascular or pulmonary system . Therefore ,neonate can be labelled demonstrates the 4 perinatal findings stated above and in whom other possible causes of neurological damage have been excluded. In the absence of such evidence, any neurological disability cannot be attributed to perinatal asphyxia or hypoxia.[27]

Perinatal Aphyxia in resource poor setting is defined as a failure to initiate or sustain spontaneous breathing at birth and in sometimes includes a 1-min Apgar score <7.00. [26]

And in resource rich settings BA is a biochemical definition, related to impaired gas exchange, due to interrupted placental blood flow (PBF) leading to progressive hypoxemia, hypercapnia, and acidosis(in cord umbilical arterial blood following delivery of the baby). Traditionally, asphyxia was defined as a cord umbilical arterial pH <7.20.[29] Using this definition, the risk for death or neuro developmental disability was exceedingly low.[30]

It has accepted that an umbilical arterial pH <7.00 (degree of acidosis) indicates severe fetal acidemia , where the neurodevelopmental sequelae risk is increased.[31,32] A cord pH <7.00 complicates ~0.3% of all deliveries, i.e., 3 / 1,000 term deliveries.[31] However, even with severe fetal acidemia, the likelihood of subsequent brain injury or mortality is low. Studies have shown >60 percent neonates with a cord pH

<7.00 have a normal intrapartum delivery course, initiates breathing shortly after delivery, are triaged to the regular care , and are being discharged within 24 h.[33]In most of the cases infants with severe fetal acidosis admitted to NICU care (mostly because of respiratory distress) exhibit a benign neurological course and low percentage of cases with moderate to severe encephalopathy has adverse outcome, i.e., either death or subsequent cerebral palsy(CP).[34-36] This observation shows the intrinsic resistance of the brain to severe asphyxia.

Physiology of Asphyxia

Circulatory Responses to Interruption of Placental Blood Flow to Preserve Cerebral Blood Flow

When there is utero placental insufficiency, the foetus redistributes cardiac output to the vital organs such as brain, heart, and adrenal gland to protect them at expense of flow to the kidney, skin and intestine. Factors contributing to this response including hypoxemia induced pulmonary vasoconstriction ,resulting in reduced pulmonary blood flow, left atrial blood return and a decrease in left atrial pressure.[37,38] There is an increase in right-to-left shunt across the foramen ovale, causing shunting of more oxygenated blood to the left heart which is then shunted to the brain and heart. And also , hypoxemia results in a decrease in cerebral vascular resistance (resistance can fall by as much as 50%), results in increase in cerebral blood flow. This compensates for the low blood oxygen content observed during the initial phase of asphyxia and when the asphyxia is prolonged and/or severe, systemic blood pressure falls to a point where the compensation fails and circulatory collapse starts. And this is called as critical threshold which differs among foetuses, and it is a point below which the cerebral circulation can no longer dilate to maintain flow.[39-41] At this point, cerebral oxygen delivery is unable to meet cellular demand, and brain injury ensues.

During initial phases of brain injury ,its temperature reduces and releases GABA neurotransmitter. At cellular level, neuronal injury in HIE is an evolving process and depends on both severity of insult and damage due to reperfusion. Following initial phase of energy failure, cerebral metabolism may recover but detoriates in secondary phase due to reperfusion starting at 6-24hours after initial injury characterised by cerebral edema and apoptosis . This phase is called as “delayed phase of neuronal injury “.

At biochemical level , a large number of excitatory amino acids such as glutamate and aspartate in cerebral cortex and basal ganglia causing neuronal death via receptors such as NMDA,AMPA and also local release of nitric oxide occurs . Activation of these receptors leads to opening of intracellular calcium channels causing increased intracellular calcium levels .Other important mechanism for ion pump destruction is by lipid peroxidation of cell membranes (Na/K channels) causing neuronal death .

Observed patterns of injury following hypoxic injury are :

- Cerebral edema in 24-48hrs.
- Selective neuronal necrosis
- Basal ganglia and brain stem – status marmoratus (marble like appearance)
- Para sagittal injury – affects cerebral cortex and sub cortical white matter .
- White matter injury – PVL in preterm babies.
- Focal cerebral infarction.

Sarnat and Sarnat clinical stages of HIE :

	State 1	**Stage 2**	**Stage 3**
Level of Consciousness	Hyperalert;irritable	Lethargic or obtunded	Stuporous,comatose
Neuromuscular Control	unhibited, over active	Diminished spontaneous Movement	diminished / absent spontaneous Movement
Muscle tone	Normal	Mild hypotonia	Flaccid
Posture	Mild distal flexion	Strong distal flexion	Intermittent decerebration
Stretch reflexes	Overactive	Overactive	Decreased or absent
Segmental myoclonus	Present or absent	Present	Absent

Complex Reflexes			
Suck	Weak	Weak or absent	Absent
Moro	Strong; low threshold	Weak; incomplete; high threshold	Absent
Oculovestibular	Normal	Overactive	Weak or absent
Tonic neck	Slight	Strong	Absent
Autonomic Function	Generalized sympathetic	Generalized parasympathetic	Both systems depressed
Pupils	Mydriasis	Miosis	Mid position; often unequal; poor light reflex
Heart Rate	Tachycardia	Bradycardia	Variable
Bronchial and Salivary Secretions	Sparse	Profuse	Variable
Gastrointestinal Motility	Normal or decreased	Increased; diarrhoea	Variable
Seizures	None	Common; focal or multifocal.(6-24 hrs of	Uncommon

		age)	(excluding decerebration)
Electroencephalogram Findings	Normal (awake)	Early: generalized low-voltage continuous delta and theta Later: periodic pattern (awake) Seizures: focal 1-to 1.5-Hz spike-and-wave	Early: periodic pattern with Isopotential phases Later: totally isopotential
Duration	<24 h	2-14	Hours to weeks
Out come	About 100% normal	80% normal; abnormal if symptoms more than 5 to 7 days	About 50% die ,remainder with severe sequele.

Respiratory Responses to Asphyxia

Additional to the cardiovascular changes as explained above associated with asphyxia, there occurs characteristic changes in the breathing pattern occurs. These cardio-respiratory changes associated with asphyxia have been described by Dawes et al[42] (Figure 1). Using the rhesus monkey, asphyxia was induced by umbilical cord ligation and covering the head with small bag of warm saline ,following which a characteristic series of changes were immediately noticed ,such as brief period of rapid rhythmic respiratory effort within 30 s noticed ultimately resulting in primary apnoea and bradycardia (heart rate (HR) >60 beats/min (bpm) in most cases.

But if the asphyxia was interrupted (usually within 30 to 90 s), the heart rate responded to basic resuscitation including drying, stimulation and/or bag mask ventilation . [42] If the asphyxia process was allowed to continue, then gasping ensues . Without any intervention, gasping ended for ~4 min, gradually became weak following which a terminal "last gasp" occurred. It was considered as secondary apnoea with a HR <60 beats/m and the pH <7.00. Without any intervention, death followed. Notably for every 1 min delay in initiating resuscitation at this stage of asphyxia, it took around2 min before gasping was observed, and 4 min until respirations became apparent. [42]

Pco_2	45	100	150	200	40
pH	7.3	7.0	6.8	6.75	7.1

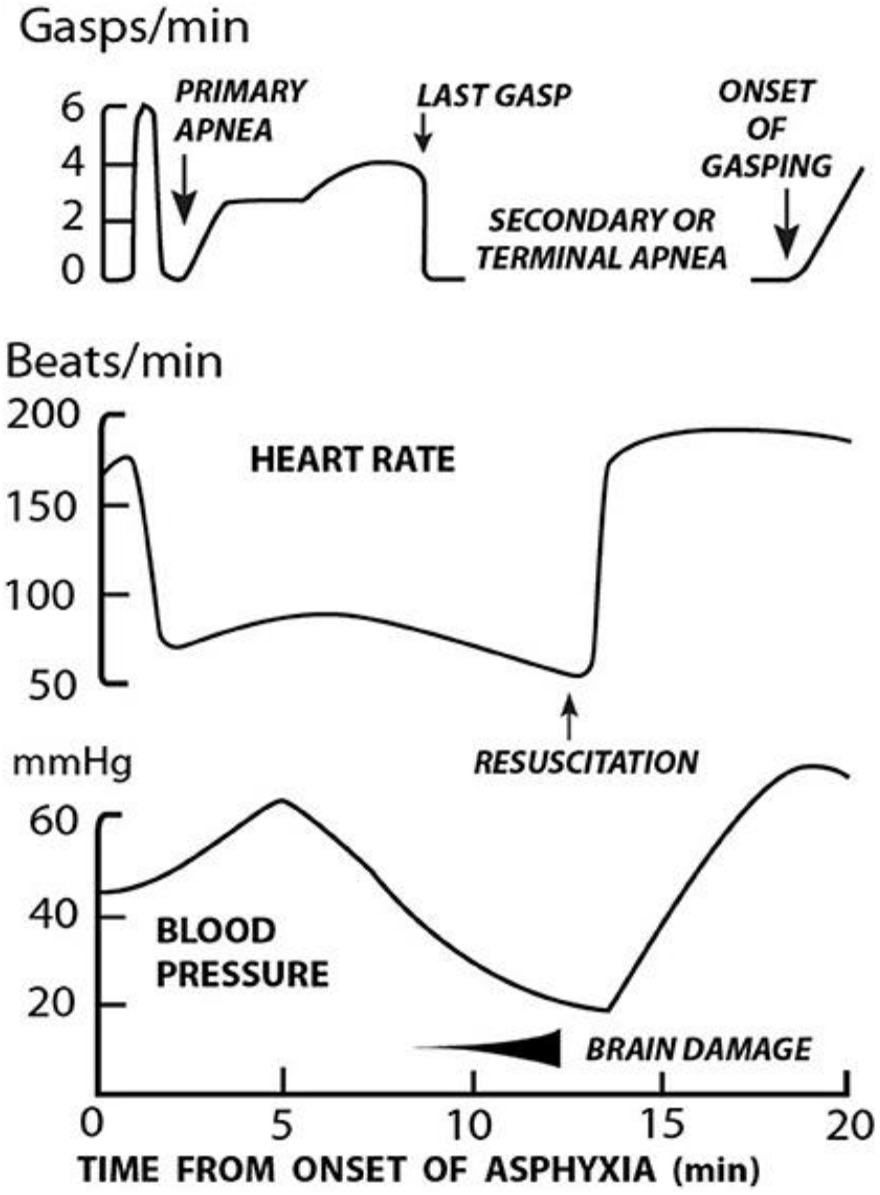


Figure1.

Relationship between respiration, heart rate, blood pressure, and acidosis in rhesus monkeys during asphyxia and resuscitation[42]

Transitional Circulation Changes at Birth

Transition from *in utero* to *ex-utero* life, there occurs simultaneous significant circulatory changes closely associated with respiratory changes. On cord clamping and removal of the placenta which has low resistance, systemic vascular resistance increases with subsequent raise in systemic blood pressure . On crying at birth, there occurs expansion of lungs resulting in drop in pulmonary vascular resistance and also within 10 to 25 s, following the initiation of breathing HR increases rapidly from 120 to 150 beats/min. All this results in significant raise in pulmonary vascular flow, and then reversal of right-to-left duct shunting as pulmonary arterial pressure falls below the systemic blood pressure. Following which there is increase in pulmonary venous return to left atrium, resulting in increase of left atria pressure. Ultimately causing foramen ovale to closefunctionally.[43]

Causes of Perinatal Asphyxia—Importance of Interruption of PBF

Interruption of placental blood flow at time of labour leads to perinatal asphyxia. Two components are important in this context, i.e., duration and the severity of the blood flow interruption.

Maternal conditions such as hypertension , preeclampsia, maternal hypotension due to a medications such as MgSO4 or spinal anaesthesia can alter placental vasculature resulting in compromised PBF. In one report spinal anaesthesia was the most common cause of an unanticipated cord arterial pH <7.00 related to maternal hypotension.[33]

Placental causes such as abruption (antepartum hemorrhage), feto-maternal hemorrhage, chorioamnionitis and funisitis compromise PBF and ultimately asphyxia.[33]

External umbilical cord compression such as a nuchal cord and cord prolapse.

In summary, methods for continuous HR monitoring for any abnormalities, is the first step toidentify the high-risk cases.

And the multiorgan failure following hypoxic-ischemia :

Renal	ARF, Myoglobinuria,Hematuria
Gastro intestinal	Abnormal motility and feed intolerance, necrotsing enterocolitis
Cardiovascular	Reduced ventricular function, myocardial infarction(ECG) papillary muscle necrosis.
Pulmonary	Meconium aspiration, persistent pulmonary hypertension, Apnoea.
Hematological	Dessiminated intravascular coagulation
Metabolic	Hyponatremia/SIADH,Hypoglycemia Hypocalcemia, Elevated liver enzymes, Elevated ammonia, Metabolic acidosis.

Epidemiology of AKI in preterm and term neonate[44]

Acute kidney injury (AKI) a.ka. acute renal failure, is defined by an acute and reversible increase in serum creatinine (SCr) value with or without reduction in urine output (oliguria/anuria). AKI is a complex disorder with clinical course ranging from mild to complete renal failure i.e., need of renal replacement therapy, peritoneal dialysis or haemodialysis.

Epidemiology of AKI has changed from the past few years, with rapid advances in technology. Recent studies shows that even small rise in serum creatinine (SCr) levels increases the risk of morbidity and mortality. And also it is demonstrated that

AKI has effects in long-term outcomes in childhood , compromising survival and increasing incidence of chronic kidney disease .

The prevalence of in-hospital AKI is high and of secondary to other systemic illness or medical treatment (nephrotoxic drugs) is more than that of primary renal disease. And it was difficult to estimate the AKI actual incidence, especially in paediatric age group. And also the advances in new renal biomarkers that increases clinical diagnosis and the initiation of early possible treatment have promoted the study of AKI in children. Inspite these advance technologies, the mortality rate from AKI remains high.

In neonates, AKI has more importance because neonatal kidneys are more vulnerable to hypoperfusion and have low glomerular filtration rate, high renal vascular resistance, high plasma renin activity, decreased intercortical perfusion, and decreased reabsorption of sodium in the proximal tubules. All these factors contribute neonates more vulnerable to renal injury in the first days of life. And also difficulties in SCr levels interpretation make it more difficult to achieve opinion regarding definition of AKI. [44]

Many studies have come up in recent years on epidemiology of AKI in older children, only a few have studied AKI incidence and clinical importance in neonates . Moreover, recent studies on AKI definition included only special neonatal groups as : post neonatal asphyxia, low birth weight(LBW) and post cardiac surgery. Limited Studies on AKI epidemiology in a general neonatal ICU has been studied scarcely. [44]

Critically ill neonates has higher risk of having AKI as they are exposed to nephrotoxic drugs like aminoglycosides and also frequent infections leading to multiorgan failure.[45]Older studies estimated that incidence of AKI in this neonatal population ranging from 8 - 24%[46] and a recent study, which includes Serum

creatinine and urine output, estimated an incidence of almost 20%. The importance of different definitions of AKI is highlighted by comparing with another new study that used only Serum Creatinine , where AKI was diagnosed in only 6.3% of neonates. [47]

Other neonatal population especially with high risk of having AKI is that with post neonatal asphyxia, after critically ill neonates. The incidence of asphyxia ranges from 1 and 10 / 1,000 live births and these babies are prone to multiorgan dysfunction as there will be redistribution of cardiac output to vitals organs such as cerebral, cardiac, and adrenal perfusion, while leading to renal hypoperfusion and ultimately ischemia.

AKI incidence in post neonatal asphyxia is reported in up to 30% to 56% of cases[48-51]. Neonates with AKI after post neonatal asphyxia have an grave prognosis, particularly those with oliguric AKI. [49]

Two new studies estimated AKI incidence in low-birth-weight neonates . Koralkar et al[52] performed a study in VLBW group (<1.500 g) and demonstrated that 18% of the VLBW neonates developed AKI with mortality rate 2.4 times higher than the others.

In one case-control study in VLBW infants[53], high mean airway pressure(MAP) , low blood pressure, and the use of drug cefotaxime were associated with AKI.

In a multicentre study, neonates on extracorporeal membrane oxygenation (ECMO) had an greater incidence(>80%) of AKI and 3.2 times higher mortality.[54]

3.Pathophysiology and management of AKI in preterm and term neonate

ETIOLOGY OF ACUTE KIDNEY INJURY[55]

Factors causing acute renal failure can be divided into 3 sub-categories – pre-renal, renal and post renal.

Pre-renal azotemia: Due to decreased blood flow to the kidney.

- **Decreased blood flow to kidney may be seen due to:**

1. Dehydration –Due to decreased preload and ultimately low cardiac output seen in increased loss as in diarrhoea, vomiting, increased trans-epidermal loss of free water, post-operative in gastro-intestinal surgeries or chest tube(ICD) losses.
2. Blood loss compromising circulatory volume – fetomaternal hemorrhage, perinatal blood loss
3. Capillary leak –Due to altered vascular endothelial permeability or due to decrease oncotic pressure as in infection, hydrops fetalis and low albumin levels
4. Increased abdominal pressure – Due to less abdominal compartment (post-operatively in gastroschisis, omphalocele, congenital diaphragmatic hernia CDH ; ascites and necrotizing enterocolitis NEC)
5. Decreased Cardiac output (cardiac failure)
6. Drugs affecting renal perfusion (Indomethacin and ACE inhibitors)

- **Renal causes - congenital and acquired causes :**

1. Acute tubular necrosis ATN (due to severe ischemia or toxins)
2. Infections (localized to the kidneys or part of severe systemic infections)
3. Vascular causes – renal artery or venous thrombosis or occlusion.
4. Nephrotoxic drugs -- Aminoglycosides, Indomethacin, Amphotericin B, radio-contrast dyes and acyclovir
5. Congenital malformations -- renal agenesis, dysplastic or polycystic

- **Post renal or obstructive causes**

Can be congenital /acquired and intrinsic / extrinsic obstruction.

It includes obstruction at various levels – prepuceal, urethral stenosis, posterior urethral valve, pelvi-ureteral junction obstruction.

Extrinsic obstruction may be due to sacrococcygeal teratoma or hematocolpos.

AKI IN PRETERM BABIES[56]

Preterm babies differ from the rest of the paediatric population as they are more vulnerable population and more prone to multi-organ injury is due to their immature immune system and incomplete organogenesis.

Higher incidence of asphyxia and occurrence of hyaline membrane disease HMD, intra-ventricular hemorrhage IVH, patent ductus arteriosus PDA ,sepsis and effects of nephrotoxic drugs like aminoglycosides and NSAIDS predispose them to multi-organ injury. Nephrogenesis is completed by 34 weeks. So any preterm baby born before 34 weeks has an immature renal system and at greater risk for ischemia, hypovolemia and hypotension; ultimately more prone to acute kidney injury (most common - pre-renal type)

In the developed countries ,incidence of premature birth rate was 12.8% of all live births. Risk factors : increasing maternal age, IVF pregnancies, multi-fetal pregnancies; complications like PIH, use of tobacco and alcohol in addition to spontaneous preterm labour.

In the developing countries, primi parity, young age, poor socio-economic status, lower educational status and poor maternal nutritional status were found to be some of the contributing factors to preterm labour by **Fathima et al** in a study in India.[60]

RISK FACTORS IN PRETERM BABIES PREDISPOSING TO AKI[61]

Asphyxia is a common risk factor in preterm neonates leading to hypoperfusion and increases risk of AKI. Accounts for almost 1/3rdof all asphyxiated babies .Prematurity – lower the gestational age and birth weight, Caesarean section are some of the factors associated with increased risk of resuscitation at birth.[62]

Hyaline membrane disease (otherwise known as Respiratory Distress Syndrome) : Most common complication in preterms. Higher incidence of HMD is seen in neonates born to mothers with PIH.[63] Use of antepartum steroids (Betamethasone /Dexamethasone), non-invasive ventilatory techniques and use of surfactant, the incidence of complications following HMD has been reduced in last few years. But still incidence is as high as 28% in a few centers.[64]

Sepsis : both early and late onset sepsis rates are higher in preterm. With use of intra-partum antibiotics, neonatal sepsis rates have drastically reduced in the West. Combined high risk of AKI in neonates with Hypotension ,hypoperfusion associated with sepsis.[65]

Necrotizing enterocolitis(NEC)is a disease of preterm that affects the gut and often associated with multi-organ dysfunction. A New South Wales study showed decreased trend of NEC following the use of antepartum steroids, early enteral feeding and gradual grading up of feeds.NEC incidence was 5% in this group.[66]

Other risk factors : usage of nephrotoxic drugs like Indomethacin, aminoglycosides, etc. Renal failure is mostly reversible following drugs toxicity. But long-term renal function was found to be normal following Indomethacin.[67]

The global incidence of AKI in neonates ranges from 3.4 to 24%. But data was not available on incidence in the Indian setting.

Ashraf etal done study of 80 asphyxiated neonates in Srinagarborn during March 2006 andFebruary 2007.Examination and history was collected by them . And investigations included urine examination, serum electrolytes, creatinine, urea, uric acid, USG abdomen and NSG. AKI noticed in 45% and of them non oliguric type was identified in majority i.e.,77%. Mortality rate was 11.1% and ultrasonography (USG) showed increased kidney echogenicity among all.[68]

A case control study done by Gupta etal in Rajasthan where 70 asphyxiated neonates and 28 healthy neonates were recruited. Investigations like urine microscopy, serum creatinine and urea were done . Oliguria (urine output <0.5 ml/kg/hour), Creatinine > 1mg/dl and urea > 40 were the criteria required to define AKI. AKI was seen in 47.1% and of them non-oliguric AKI was found in the majority of the (78%). Severe asphyxiated neonates had oliguria. Mortality rate was 7.1%. The baby survivors were called for follow up at 1 and 6 months and no baby had residual renal dysfunction.[69]

NEPHROGENESIS :

The fetal kidney develops from 3 mesodermal structures : pronephros, mesonephros and metanephros. Metanephros arises from the ureteric bud (branch of Wolffian duct). Interaction between mesenchyme of metanephros and epithelium of ureteric bud lead to "branching morphogenesis" results in formation of collecting system. Differentiation of metanephros occurs only by 5 weeks of gestation. First nephrons are formed only by 8 weeks and nephrogenesis is complete only by 34 weeks. Nephrons grow in size from 35 weeks till birth.[70]

Weight of the kidney increases with gestational age. Renal architecture can be appreciated as early as 20 weeks of gestation .The ratio between kidney and abdominal circumference (KC/AC) at the level of umbilical vein remains constant (0.27 to 0.3).

Preterms born before 34weeks has incomplete nephrogenesis ,sothat they have alesser renal volume and the impaired renal function. In addition to this, other risk factors also worsen the renal function. Therefore, it is crucial to diagnose AKI in neonatal period. And regular follow up with growth monitoring , blood pressure and renal function is needed. [71]

Along with ROP and OAE testing.

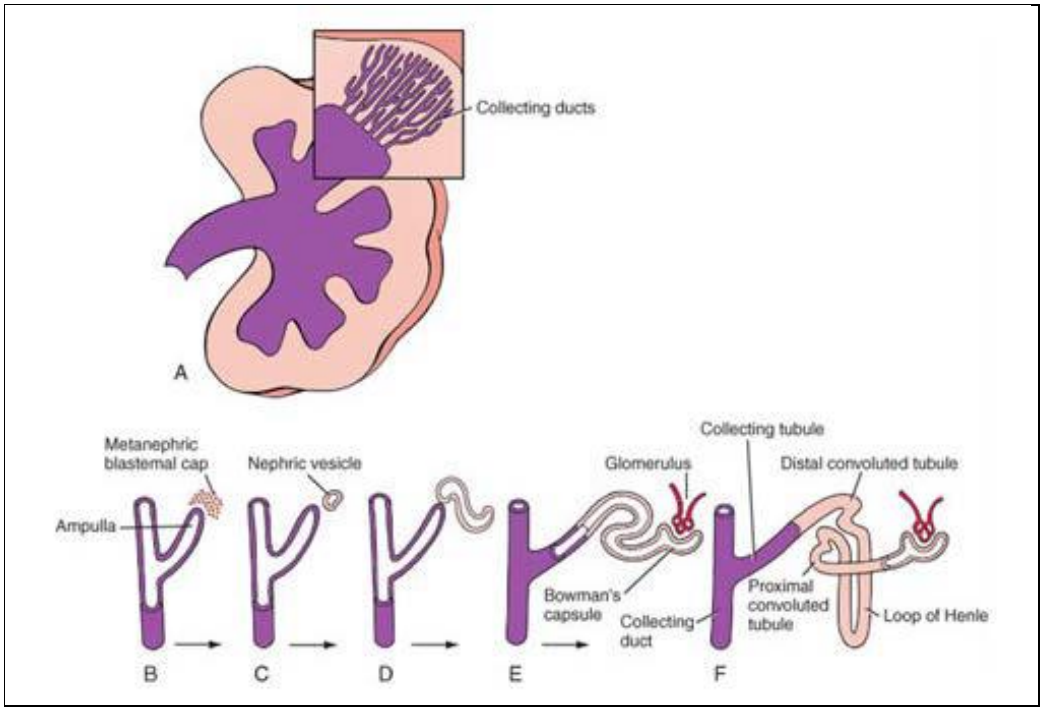


Figure 2: Nephrogenesis

Renal functional assessment in older children and adults can be done by monitoring urine output and serum creatinine levels. But cant be assessed in neonates due to various reasons. Creatinine measured within 72 hours of life reflects maternal creatinine values ,but in preterm babies persist as long as 15 days of life . Various factors that determine creatinine level are muscle mass, age, hydration status and gender. So not the ideal diagnostic tool for assessment of renal functional status.

Management of AKI

New Biomarkers in Neonatal Acute Kidney Injury[69]

Because of the high incidence of AKI and the poor outcome, research has been towards identifying new biomarkers that can anticipate the diagnosis of AKI in hours or even days before a oliguria/anuria or raised SCr detected. Early AKI diagnosis leads to early therapeutic intervention. Limited studies are available on neonatal AKI biomarkers and mainly performed in high risk population, such as VLBW, asphyxiated neonates and who underwent cardiac surgery with cardiopulmonary bypass (CPB). Studies on biomarkers predicting AKI in general in critically ill neonates are lacking.

There are many challenges in confirming AKI biomarkers. Large-scale observational multicentre studies are needed in critically ill neonates and healthy neonates to observe the course of SCr and biomarkers during period of AKI. Also, validation of new biomarkers in clinical practice and testing of markers as predictive factors for endpoints, such as LOS, needed for mechanical ventilation time ,renal replacement therapy, and mortality are needed.

One of the main difficulties is that the new biomarkers are generally tested against SCr. And also several studies have shown that some urinary biomarker levels depends on gestational age and birth weight just like SCr. And in premature neonates due to immature tubular reabsorption of these proteins can lead to different values in this neonatal group. Recent studies revelas early non-invasive AKI biomarkers : serum cystatin C (CysC), urinary interleukin-18 (IL-18), serum and urinary neutrophil gelatinase-associated lipocalin (N-GAL), kidney molecule-1 (KIM-1), osteopontin (OPN), and beta-2 microglobulin (B2mG)—Table 1. Another recent renalbiomarker is angiotensinogen. Urinary angiotensinogen and its association with

renin have been associated with severe AKI ; however, studies are lacking on neonatal AKI. Generally, renal biomarkers do not necessarily reflect a GFR reduction, because they are abnormally expressed in renal injury that can reflect lesion in nephron sites—Table 1.

Table 2: Biomarkers in neonatal acute kidney in

Author	Study design	AKI definition	Population	Biomarkers	Main findings
Askenazi et al. [43]	Nested case-control	AKIN	Very low birth weight infants (n = 30, AKI = 9)	Urine NGAL and OPN	Urine biomarkers were higher in those with AKI. No information about early AKI diagnosis.
Krawczeski et al. [44]	Prospective cohort	AKIN	374 infants (35 neonates, AKI = 8) undergoing cardiac surgery with CPB	Serum and urine NGAL	Serum and urine NGAL 2 h after CPB are early predictive biomarkers for AKI.
Askenazi et al. [37]	Nested case-control	SCr ≥1.7 mg/dL >72 h after birth or rising values >0.3 mg/dL within 48 h (AKIN)	Neonates birth weight > 2000 g, GA >34 weeks, 5-minute score Apgar ≤7 (n = 58, 9 neonates developed AKI)	Urine NGAL, OPN, uCysc, albumin, β2 microglobulin, epithelial growth factor, UMOD, and KIM-1	Urine CysC, UMOD, and epithelial growth factor were higher in those with AKI. No information about early AKI diagnosis.
Li et al. [45]	Prospective cohort	SCr >1.5 mg/dL or pRIFLE	Nonseptic critically ill neonates (n = 62, AKI = 11)	uCysC and uIL-18	Urine CysC and IL-18 are predictive of AKI in nonseptic critically ill neonates.
Sarafidis et al. [46]	Prospective cohort	SCr ≥1.5 mg/dL >24 h or rising values >0.3 mg/dL from DOL 1	13 asphyxiated neonates and 22 nonasphyxiated (n = 35, AKI = 8)	Serum CysC and NGAL Urine CysC, NGAL, and KIM -1	Serum NGAL and uNGAL and uCysC are higher in asphyxiated neonates, even in those not developing AKI. They had also provided an early AKI diagnosis.
Elmas et al. [47]	Case-control	pRIFLE or SCr ≥1.5 mg/dL on the first 3 days	Preterm neonates with RDS (n = 28, AKI = 8). Additional control group with 34 neonates without RDS nor AKI	Serum CysC	Serum CysC is an independent predictor of AKI in RDS neonates.

CPB: cardiopulmonary bypass; RDS: respiratory discomfort syndrome; CysC: serum cystatin C; sNGAL: serum neutrophil gelatinase-associated lipocalin; uCysC: urine CysC; uNGal: urine NGAL; KIM-1: kidney injury molecule-1; OPN: osteopontin; B2mG: beta-2 microglobulin; IL-18: interleukin-18; DOL 1: day of life; GA: gestational age; UMOD: uromodulin; PA: postmenstrual age; CPB: cardiopulmonary bypass; RDS: respiratory distress syndrome.

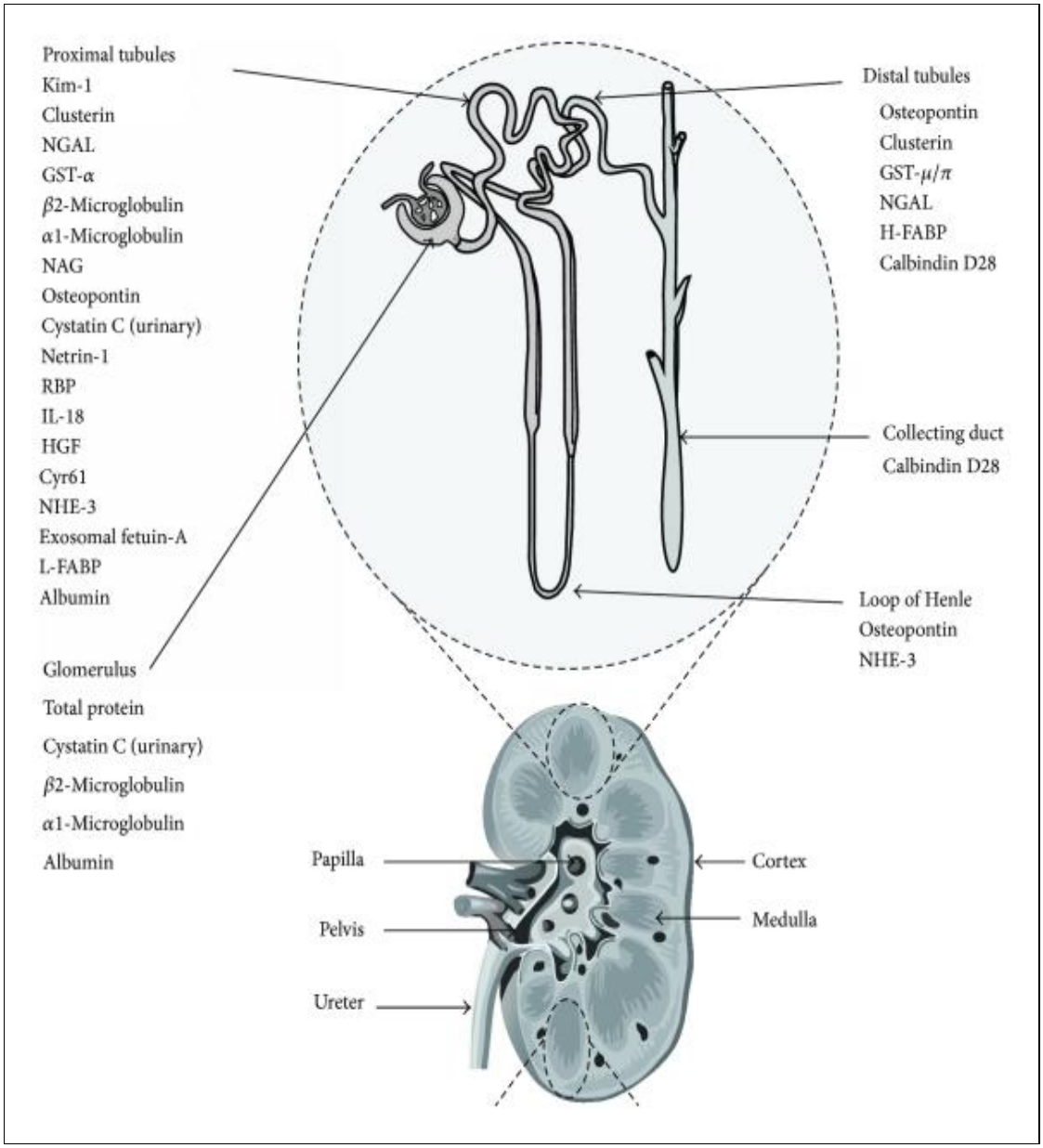


Figure 3: Nephron segment-specific biomarkers of kidney injury[69]

Cysteine proteinase inhibitor - Cystatin C (CysC) is expressed in all nucleated cells produced at a constant rate and excreted by the kidney , and reflects the renal function of the neonates in early postnatal life as it does not cross the placenta, regardless of body composition and size. One study was conducted in 62 preterm neonates with respiratory distress syndrome (RDS) and 34 control neonates without RDS by measuring serum CysC (sCysC) was identified as an earlier biomarker of AKI before there is increase in SCr. In non-sepsis critically ill neonates the

urinaryCysC (uCysC) was also predictive of AKI, and also small study was conducted , enrolling only 13 asphyxiated neonates, where uCysC was found to be sensitive and early AKI biomarker. And CystC levels were studied in older children but is difficult to compare their results to the neonatal population, because normal values of uCysC decrease with tubular maturation.

Interleukin-18 (IL-18) - proinflammatory cytokine that is cleaved by caspase-1 and is released in the proximal tubule after renal injury.

Li et al[70] enrolled 62 non-sepsis critically ill neonates and every 48–72 h urine samples were collected during the first 10 days of life. This study demonstrated that both urinary concentration of CysC (cited above) and IL-18 were associated with AKI, even after controlling for gestational and postnatal age, gender, birth weight, Apgar score, and neonatal acute physiology in non-septic critically ill neonates. But the advantage is uIL-18 is of not changing its normal value with increasing renal maturity with age but values can be altered by sepsis, reducing its ability to detect AKI.

One study evaluating OPN levels in neonates[71] was done. It is case-control study enrolling 30 neonates, only 9 neonates with AKI had higher OPN values than in controls. But studies are lacking to determine normal OPN value in diagnosing neonatal AKI. But no studies were found evaluating the role of KIM-1 specifically in AKI neonatal population.

Urinary NGAL - appears to be the most ideal AKI biomarker and it is the most upregulated gene and overexpressed protein in the kidney after ischemia. Many studies were done demonstrating increased urinary and serum NGAL capacity to predict AKI in both adults[72,73] and older children. [74,75]But in neonatal group ,both serum and urine NGAL were evaluated in patients after cardiopulmonary bypass

CPB surgery. Blood and urine samples for NGAL were collected 2 hours post CPB were able to predict the incidence of AKI with a sensitivity and specificity of nearly 90%. Another study evaluated for urinary NGAL at day of life 1 in preterm infants and it shows significantly associated with development of AKI . [71]

Another approach to diagnosis AKI is to combine multiple new biomarkers. **Askenazi et al**[71]enrolled 8 neonates for urinary biomarkers: NGAL, IL-18, KIM-1, OPN, B2mG, and CysC. They observed both isolated and combined abilities of these renal biomarkers to predict AKI and mortality in VLBW infants and showed the result was not good when combined all 3 biomarkers than their isolated use.But, this study conducted was only nested case-control type. Improving our ability to diagnose AKI, maybe with simultaneous use of multiple markers, will allow the implementation of more effective preventive and therapeutic measures to improve AKI prognosis.

Finally, some recent studies have included neonates and older children when evaluating AKI biomarkers. This can lead to inaccurate interpretations, as cut-off normal values can be different even in neonates with different gestational ages and birth weights.

Long-Term Consequences of Neonatal AKI[69]

Initially Acute kidney injury has been thought as a completely reversible condition. But, over few past years, a data from experimental animal and human studies have been demonstrated that AKI can results in permanent renal damage (i.e., chronic kidney disease—CKD) and may also results in nonrenal organs injury.[76-78] And also , mortality is greater in adults surviving an AKI episode.[79]

In older children, there are evidence of long term risk of renal sequelae associated with AKI caused by intrinsic renal parenchyma , such as Henoch-Schonlein

purpuraHSP or haemolytic uremic syndrome HUS.[80,81] But recently studies on long-term renal prognosis of AKI in children due to secondary renal disease were available. In a prospective cohort study, 126 children after 1st AKI episode were followed for up to 3 years. And among them 10% of patients developed CKD and this prevalence had a direct relation with AKI severity, i.e.,17% of children affected were with AKI stage 3. In this group, 30 patients had history of neonatal AKI and 5 (16.6%) developed CKD, suggesting that this neonatal group is at higher risk oflong term renal sequlae. In one study, evaluating long-term sequelae of AKI in newborn population after a 2-year follow-up, height was reduced in those with AKI. But studies evaluating for CKD on followup after first AKI episode in neonatal patients are lacking.

Approach to a neonate with renal failure[69]

History:

a) Prenatal history:

- Maternal History :H/O drug intake like ACE inhibitors(enalapril) , indomethacin which reduces glomerular filtration should be enquired.
- Maternal medical condition : Uncontrolled Diabetes is associated with genitourinary malformations.
- Oligohydramnios : due to fetal oliguria due to bilateral congenital renal disease, bilateral lower urinary tract obstruction.
- Polyhydramnios : defective urinary concentration . Hydrops may be the first sign of congenital nephrotic syndrome.

b) Family history: May be present in cases of polycystic kidney disease, renal tubular disorders and congenital nephrotic syndrome.

c) Natal history:

H/O Perinatal asphyxia (most common cause), respiratory distress, sepsis , shock may predispose the kidneys to anoxic injury leading to acute tubular necrosis ATN.

H/O Oliguria (asphyxia) due to prerenal failure via endothelin,intrinsic renal failure (ATN) , SIADH.

H/O Seizures that occur secondary to hypoxia(asphyxia) , intracranial hemorrhage, hypoglycaemia , hypocalcemia.

Micturition history: Nearly 7% babies do not void in the first 24 hours of life. Mostly due to inadequate renal perfusion.

But Intrinsic renal disorders and Urinary tract obstruction need to be ruled out.

Physical examination:

Assessment of hydration : edema/dehydration.

Vital signs :blood pressure

See for any dysmorphic features : Rule out Potter facies (low set ears, beaked nose ,epicanthal folds , downward slant of eyes, pulmonary hypoplasia ,limb deformities).

Any abdominal wall defects ,ambiguous genitalia, hypospadias etc which are associated with renal malformations.

Spontaneous pneumothorax may be associated with kidney abnormalities.

Any palpable Abdominal masses :suprapubic mass suggestive of palpable bladder.

Rule out posterior urethral valve : observation of the urine stream as dribbling ,thin stream, or post voidal residual bladder suggest

Table 3: Different Criterias for AKI[80]

KDIGO criteria for AKI

AKI stage	Serum creatinine (SCr)	Urine output
1	1.5-1.9 times baseline OR > 0.3 mg/dL increase	< 0.5 mL/kg/h for 6-12 hours
2	2.0–2.9 times baseline	< 0.5 mL/kg/h for > 12 hours
3	3.0 Times baseline OR Increase in SCr to > 4.0 mg/dL OR Initiation of RRT OR Decrease in eGFR to < 35 mL/min/1.73 m^2 in patients < 18 years	< 0.3 mL/kg/h for >24 hours OR Anuria for > 12 hours

Modified KDIGO for use in neonatal patients

AKI Stage	Serum Creatinine (SCr)
0	No change or rise <0.3 mg/dL
1	Increase SCr 0.3 mg/dL OR Increase SCr 150%-200% from previous trough value
2	Increase SCr 200%-300% from previous trough value
3	Increase SCr 300% from previous trough value OR 2.5 mg/dL OR Initiation of RRT

RIFLE, pRIFLE, and nRIFLE criteria for AKI

	Serum Creatinine (SCr)	Urinary Output and Duration		
		RIFLE	pRIFLE	nRIFLE
Risk (R)	SCr X 1.5	< 0.5 mL/kg/h (6 h)	< 0.5 mL/kg/h for (8 h)	< 1.5 mL/kg/h (24 h)
Injury (I)	SCr X 2.0	< 0.5 mL/kg/h (12 h)	< 0.5 mL/kg/h for (16 h)	< 1.0 mL/kg/h (24 h)
Failure (F)	SCr X 3.0 or > 4 or Acute rise > 0.5 mg/dL	< 0.3 mL/kg/h (24 h) OR Anuric (12 h)	< 0.3 mL/kg/h (24 h) OR Anuric (12 h)	< 0.7 mL/kg/h (24 h) OR Anuric (12 h)
Limitation (L)	Loss of kidney function for 4 weeks			
End stage (E)	Loss of kidney function > 3 months			

Table 4: Common nephrotoxic medications

Common nephrotoxic medication used in neonates

Medication	Toxicity	Monitoring Strategies	Uses
Aminoglycosides	Nephro/ototoxic	Trough levels should be routinely monitored	Antibiotics
Ibuprofen	Nephrotoxic	Serum Creatinine and urine output should be normal before starting therapy	Used for treating PDA
Vancomycin	Nephrotoxic	Levels should be monitored	Antibiotics
Indomethacin	Nephrotoxic	Serum Creatinine and urine output should be normal before starting therapy	Used for treating PDA

Hypotension and renal hypoperfusion in NICU population[80]

Systemic hypotension lead to renal hypoperfusion in the NICU population because of the shunting of blood to vital organs. Initially it is necessary to maintain normal intravascular volume status and vasopressors support to be started. Because unrecognized and untreated hypotension can lead to renal hypoperfusion, ultimately resulting in AKI. Birth asphyxia is another common cause of AKI in newborn infants.

Table 5: management of hypotension

Cause of hypotension	Mechanism/type of shock	Management
1. Hemorrhage (placental abruption, cord avulsion, massive intraventricular hemorrhage (IVH), adrenal hemorrhage, hepatic subcapsular hematoma, retroperitoneal bleeding, surgical blood loss)	Hypovolemia	- Intravenous fluids - Packed red blood cell (RBC) transfusion
2. Sepsis	Distributive or Cardiogenic	- Antibiotics - Correction of fluid deficits - Vasopressors
3. Patent ductus arteriosus	Diastolic run-off (low diastolic blood pressure)	- Medical/surgical closure
4. Adrenocortical insufficiency	Low Cortisol leading to vasopressor resistant hypotension	- Hydrocortisone
5. Necrotizing enterocolitis	Systemic inflammatory response leading to distributive shock	- Intravenous fluids - Vasopressors
6. Cardiogenic (congenital heart disease, myocarditis, pericardial effusion)	Cause specific	- Cause specific (inodilators, PGE2 if due to ductus dependent cardiac anomaly)

Management of Seizures :

When seizures occurs in neonatal HIE , loading dose of Phenobarbitone 20mg/kg is given as slow infusion rate IV ,followed by maintainance dose of 5mg/kg/day .But in case of next episode of seizures , mini loading dose 10mg/kg is given as IV stat.

If still seizures persists , Phenytoin is given as 2nd line of drug at 20mg/kg loading dose followed by 4-8mg/kg as maintainance dose . But before loading with anticonvulsants , rule out metabolic causes like hypoglycaemia ,hypocalcemia etc . And if seizures are resolved with normal neurological findings and normal EEG anti convulsant can be stopped.

But if anything is abnormal , then it should be continued till 3months of age .

Non-dialytic management of AKI in the newborn[80]

Goals

The main aim in management of Acute Renal Injury is to maintain fluid and electrolye homeostasis and also to maintain proper nutrition and correction of the acidosis till normal kidney function is regained. And also identification of etiology leading to renal injury to be established because to identify reversible causes. The causes of poor renal perfusion important cause for pre renal type of injury should be identified and corrected. Its crutial to look for any congenital anomalies of the kidney and urinary tract (CAKUT), renal vascular conditions and bladder outlet obstruction by renal ultrasound with Doppler studies .If an obstruction is identified, it should be immediately relieved by catheterizing (urethral or suprapubic) and also urological consultation should be given for further management. Once congenital anomalies are ruled out , careful assessment of the fluid balance should be made.

The following factors are taken into consideration to evaluate the intravascular volume in critically ill neonate :

1. Weight monitoring is needed twice daily to see for gain or loss. It should be weighed on a sensitive scale. The weight gain per day is quite variable in a neonates and depends on various parameters like gestational age, day of life , severity of illness, and nutritional status. Excessive weight gain (more than 20-30 g/day) in a sick neonate is indicative of fluid retention (rule out SIADH which is most common in Birth Asphyxia) and in same way weight loss is indicative of negative fluid balance.

2. Monitor vital Signs such as heart rate and blood pressure. Increased heart rate and low blood pressure are signs of low intravascular volume status -hypovolemia. Other causes of tachycardia like sepsis, fever, pain, medications, etc. should be looked for, and hypotension should be treated to maintain adequate renal blood flow .Serum and urinary levels of electrolytes and creatinine should be done. Monitoring of serum sodium is important marker for fluid status and is needed for appropriate management. The interpretation of serum sodium should be made carefully and take the following into consideration: sodium intake over the last few days, weight change, urinary output, serum BUN/Cr, urinary sodium and osmolarity. Hyponatremia due to dilution because of fluid retention also observed in SIADH; other common causes include excessive usage of diuretic and decreased amount of supplementation.

3. Combination of weight monitoring , estimation of previous few days' input and output charts , fluctuation in the vital signs, and the serum and urinary electrolytes ,creatinine is necessary to estimate the fluid status. Since major causes of oliguria are pre-renal (see above), response to 20-40 ml/kg of crystalloid may help differentiate between pre-renal azotemia and an established oliguric AKI. The urine output should be critically measured by placing an indwelling urinary catheter

(preferable) or neonatal urosac bag. If not possible in view of infections , careful weighing of wet diapers every 3 hours is a less sensitive , but acceptable method of determining the urinary output in ml/kg/h.

4. Alternative methods used to validate the intravascular fluid status include cardiac echo looking at the ventricular filling. The use of central venous pressure monitoring is difficult especially in very small neonates.

Estimation of fluid requirement

Main goal is to correct fluid and electrolyte imbalance and to provide adequate nutrition in an oliguric/anuric neonate till renal functions recover. During fluid management the following should be considered in newborns :

1. During 1st week of life, there will be shrinkage of the extracellular fluid(ECF) compartment in term babies leading to decrease in 5%-10% body weight .It will be up to 14% in neonates born prematurely .
2. Fluid should be restricted to the newborn is based on calculating the input and output i.e.,insensible water losses ,ongoing losses (e.g. ICD ,surgical drains) and previous day's urinary output. And daily fluid requirement in newborns will depends on the day of life and presence of any other congenital anomalies that in excessive fluid loss. The insensible water loss of fluid from skin and respiratory tract in term newborns is 25ml/kg/day.
3. In preterm infants, insensible losses are estimated based on the skin maturity (keratinization), postnatal age , and ongoing losses (drains, gastric losses and U/O), use of radiant warmers ,phototherapy etc. Based on the weights : newborns < 750 g : 100-150 ml/kg/day of insensible losses newbornsbetween 750 g to 1000 g : 60-70 ml/kg/day, Newborn between 1000-1250 g : 30-65 ml/kg/day of insensible losses.

4. Fluid overload can cause pulmonary edema, increased oxygen requirements, worsening of the PDA shunt and may also result in dilutional hyponatremia due to excessive free water. Because of massive fluids shifts, contraction of the extracellular fluids and natriuresis that accompanies the physiological weight loss during the first few days, sodium is not added to TPN for the first 48 to 72 hours. Thereafter, 2-3 mEq/kg/day can be added slowly to the fluids. It is important to account for the inadvertent administration of sodium along with umbilical arterial line fluid and other medications.

Management of electrolyte imbalances[80]

5. **Sodium**: Serum sodium should be monitored closely, based on basal requirements of 2-4 mEq/kg/day of sodium, and the daily provision adjusted based on estimated ongoing losses. Hyponatremia secondary to dilution is common in AKI and should be corrected by restricting the free water provision. In addition, sodium concentrations should be normalized prudently in order to prevent negative neurological outcomes.

   If serum sodium levels are ranging from 120-135mEq/L fluid restriction is sufficient ,but if it is lee than 120mEq/L with symptoms like seizures – immediate correction with 3%NS is needed .

6. **Potassium:** Hyperkalemia is common in the oliguric and anuric phase. Therefore, all potassium-containing fluids should be eliminated, or discontinued as soon as oliguria or Hyperkalemia is encountered. In the recovering polyuric phase, hypokalaemia can become an issue and must often be corrected. Commonly used strategies for treating Hyperkalemia have to be modified in preterm infants.

7. Hyperkalemia should be confirmed by venous sample, as hell-stick samples are often erroneous due to hemolysis. ECG changes can reflect potassium levels if ranging from 5.5-6.5mEq/L tall and peaked T waves , Prolonged PR interval with wide QRS complex if between 6.5-8mEq/L and absent P waves with bundle branch blocks and finally sine waves if >8mEq/L. Preterm infants tolerate hyperkalemia well, and therefore electrocardiogram (EKG) changes may not be reliable and may not be seen for high potassium levels. Kayexalate has been used as an exchange resin in neonates and can be administered rectally as an enema. There have been case reports documenting intestinal complications both with oral and rectal use. There have been concerns about its use as an enema since sorbitol, which is used for the suspension, results in high osmolarity leading to NEC and colonic perforation. Although the water suspension of Kayexalate is thought to be safe for enemas in preterm infants, there has been a reported case of colonic perforation. Bolus administration of sodium bicarbonate has been associated with sudden changes in the osmolarity and pH, leading to an increased incidence of intra-ventricular hemorrhage (IVH). Therefore, it should be used as a slow infusion and with great caution in preterm infants at risk for IVH.

Management of Hyperkalemia :

Medication	Level of K+ at which it is instituted	Dose	Mechanism	Onset of action
Calcium gluconate	ECG changes suggestive of hypokalemia	0.5 to 1 mL/kg over 5-10 min	Modifies myocardial excitability	5-10 min
Sodium bicarbonate	K+ - 6.0-6.5 mEq/L	1 mEq/kg over 10-30 min	Intracellular uptake of potassium	30 min
Glucose and insulin	K+ - 6.5-7.5 mEq/L	0.5g/kg/h of glucose and 0.2 U of regular insulin per g of glucose over 2 hr	Intracellular uptake of potassium	30 min.
Salbutamol IV infusion#	K+ - 6.5-7.5 mEq/L	4 µg/kg over 20 min	Intracellular uptake of potassium	1-2 h
Cation exchange resin (Na/Ca polystyrene sulfonate)*	K+ more than 6.0 mEq/L	1g/kg intrarectally q 6 h	Exchange of K for Na or Ca.	Minutes
Exchange transfusion	K+ more than 7.5 mEq/L	Washed RBC reconstituted with 5% albumin	Uptake of K by RBC.	Minutes
Peritoneal dialysis	K+ more than 7.5 mEq/L	Use a dialysate with low K+ concentration	Dialysis	Minutes

Calcium/Phosphate: Hyperphosphatemia is commonly seen in the acute phases due to renal insufficiency in addition to hypocalcemia. Phosphate intake should be curtailed during the anuric phase followed by careful monitoring and slow reintroduction after the establishment of urinary output. Secondary hyperparathyroidism is rarely seen in the neonatal population.

Renal trace elements: Traditionally, kidneys predominantly excrete trace elements, like selenium and iodine. Chromium may have adverse effects on renal functions and is eliminated from the total parenteral nutrition (TPN) in patients with renal insufficiency.

Nutrition

Protein intake

Conventionally, protein intake is restricted in patients with increasing BUN because restriction has been proven to decrease the BUN in adult patients. During the past decade, however, neonatal nutrition has undergone a paradigm shift with respect to protein intake, and it is commonly thought that the growth failure in preterm newborns can be prevented by the provision of 3-4.5 g/kg/day of protein. It has now become routine practice to administer 3-4 g/kg/day of protein beginning within a few hours of birth. Poor nutrition not only affects the somatic growth but also leads to undesirable neurodevelopmental outcomes. Protein intake should be adjusted at least to meet the basal growth requirements (1-2 g/kg/day) while keeping the BUN below the threshold for causing increase in the serum osmolarity.

Glucose

Hyperglycaemia should be avoided and may have to be treated with insulin. Due to the lack of hepatic reserves and gluconeogenesis, preterm infants require an infusion of glucose 4-6 mg/kg/min to meet the obligatory glucose requirement of the brain.

With fluid restrictions in place, infusion of a high concentration of glucose (> 12.5% Dextrose) can only be achieved via a central catheter. Parenteral glucose and intra-lipids are the predominant source of calorie intake in preterm infants. Additionally, in the absence of adequate calorie intake, dietary proteins are oxidized for energy instead of being used for tissue synthesis. This oxidation of proteins further contributes to the rising BUN. Hence, adequate caloric provision is not only important for anabolism but also for the rise of BUN. The daily caloric needs of infants should be calculated based on gestation and postnatal age. TPN should be tailored to meet both the fluid and caloric need.

Per the European Society of Paediatric Gastroenterology, Hepatology and Nutrition Guidelines (ESPGHAN), the basal energy requirements of a newborn are estimated to 50-60 kcal/kg/day. For optimal growth and protein accretion, a growing preterm infant would require 100-120 kcal/kg/day. The caloric requirements for infants who are on TPN are estimated to receive 90-100 kcal/kg/day due to a lack of fecal losses and diet induced thermogenesis. The caloric needs are met through the parenteral route since most of these infants are clinically unstable. Delivery of adequate calories in a fluid restricted neonate may require placement of a central line since the maximum concentration of dextrose that can be infused through a peripheral catheter is 12.5%.

Management of hypotension[80]

There is a lack of broad consensus about the management of BP in premature newborns. This is partly due to the scarcity of normative data and partly due to the lack of evidence of overall benefit in the treatment of borderline low BP in absence of signs of tissue hypoperfusion. The normal values of BP vary with gestational and postnatal age (hours after birth), but the most commonly used (although not always

accurate) method for determining normal mean arterial pressure (MAP) is the gestational age in weeks.

The cause of hypotension in the neonate would determine the treatment. Hypovolemia should be corrected carefully since rapid boluses have been associated with increased cerebral blood flow and may result in IVH. Dopamine has been traditionally used as the first line vasopressor, followed by dobutamine in non-responsive cases. Norepinephrine and epinephrine infusions are useful in cases of peripheral vasodilatory states like sepsis. Hydrocortisone has been shown to be effective in cases of vasopressor resistant hypotension. Random cortisol levels are of questionable significance in determining the cortisol response in a sick neonate. Cardiogenic shock has to be managed according to the etiology. Diastolic run off through the PDA leading to hypotension would be an indication for medical or surgical treatment of the PDA. The data is much more conclusive in cases of full-term infants.

BP can be monitored invasively by transducing an arterial catheter or non-invasively by using an automatic oscillatory BP instrument. Near infrared spectroscopy (NIRS) has been validated as accurate in determining the adequacy of cerebral and renal perfusion. Though not commonly used at present, it may become a non-invasive method of documenting tissue level hypoperfusion in the future.

Role of diuretics

As mentioned earlier, fluid overload has proven to be an independent risk factor associated with higher mortality in late preterm neonates. It is also one of the most common indications for RRT in addition to electrolyte imbalance and metabolic disorders. Osmotic diuretics should be avoided due to unintended consequences such as risks for IVH, although loop diuretics are commonly used in preterm infants to

treat bronchopulmonary dysplasia (BPD) and have a reasonably safe adverse effect profile.

Loop diuretics are used in the adult and paediatric population to treat fluid overload and convert oliguric renal failure to non-oliguric renal failure. Although the impact of loop diuretics on the outcomes of oliguric renal failure is debatable, urinary output allows the avoidance of fluid overload. Loop diuretics have also been proclaimed to be renal protective due to their effects on the redistribution of the renal blood flow resulting from the changes in the prostaglandin synthesis.

Loop diuretics should be used with caution due to their ototoxic potential (although reversible) and the risk of renal calculi with long-term usage. Due to brisk diuresis, loop diuretics may be associated with sudden decrease in the intravascular volume and electrolyte imbalances like hyponatremia, hypokalemia and hypocalcemia. There are only a handful of cases reporting the use of diuretics in neonates with oliguric AKI, and long-term outcomes have not been reported. Currently, the evidence suggests that loop diuretics should not be used to prevent AKI, although in cases of fluid overload with oliguria/anuria they do provide a reasonable therapeutic option in the absence of RRT.

Role of dopamine

Inotrope support mainly used in newborns population isDopamine . It is proven to be safe and efficacious as a 1st line choice of medication for treating hypotension in preterm neonates . Dopamine is a catecholamine and has dose dependent effects on the systemic and renal vasculature via D, Beta 1,2 and Alpha 1 receptors. At lower doses it has been shown to improve renal perfusion through the stimulation of D1, D2, and D4 receptors.At moderate dose 5-10mcg/kg/min : increases cardiac output and higher doses >10mcg/kg/min it has predominant pressor activity with minimal

inotropy .Although dopamine has not shown to have a substantial impact on the outcome in adult and pediatric populations, but shown transient improvement in urinary output and serum creatinine in newborns . Only a handful of studies have documented improvement in urinary output in healthy preterm infants. Furthermore, despite the lack of evidence for substantial clinical benefits, low dose dopamine is anecdotally used in newborns with low urinary output.

Role of dialysis

Use of Renal Replacement Therapy like dialysis to treat AKI especially in very low birth weight newborns– VLBW (<1500 g birth weight) , is technically challenging and is not routinely attempted. Advantages of Neonatal Peritoneal Dialysis is easy to perform ,disequilibrium syndrome is less likely , gradual correction of acid base and electrolyte imbalance and PD access placement is relatively easy. It is contraindicated in cases of associated abdominal wall defects .PD dialysate solution is available in standard hydrous dextrose concentrations of 1.5,2.5 and 4.25% .There are occasional reports describing RRT use in such newborn infants. The indications for RRT are not absolute and are listed in table 6

Table 6: Indications for Renal replacement therapy[80]

Indication	Peritoneal Dialysis efficacy	Hemodialysis efficacy
Fluid Overload: Resulting in increased ventilatory support, nutritional compromise due to fluid restriction.	Good	Excellent
Hyperkalemia non responsive to medical management	Fair	Excellent
Hyperammonemia	Fair	Excellent
High blood urea nitrogen (BUN) and creatinine	Fair	Excellent
Congenital anomalies resulting in end stage renal disease - including CAKUT, poly/multi -cystic kidneys, inborn errors of metabolism, oxalosis, angiotensin receptor blockade fetopathy	Can be used for short term use	Long term

3. **<u>Studies conducted in the past on similar topic</u>**

Pinar Isik Agras et al[81] conducted a retrospective study on 1311 newborns ,admitted in their Neonatal ICU during 42months in 2009 to find the course of illness, any therapeutic interventions, prognosis and riskfactors associated with development of AKI in the newborns .And among them 45 babies were diagnosed with AKI i.e.,if serum creatinine value is more than 1.5 mg/dL irrespective of the normal renal function of the mother. The information collected for each AKI case wereany risk factor contributing condition, cause and course of illness, gestational age , birthweight, age at the time of diagnosis, treatment, any perinatal risk factors andneed of oxygen requirement. And the prevalence of AKI is 3.4% Neonatal Intensive Care Unit during this 42 months period.And 31.1% of AKI cases were Premature new-borns. The mean birthweight in the group was 2863±1082 g, and the mean age at diagnosis was6.2±7.4 days. And cause for AKI was classified as 29 babies(64.4%) had prerenal cause,14 (31.1%) babies had renal and 2 babies(4.4%) had postrenal AKI. Non oliguric AKI is identified in 47% cases. And the contributing conditions

that leads to AKI were Asphyxia major cause (40.0%), followed by sepsis/metabolic disorders (22.2%) and feeding problems (17.8%). 77.8% of the AKI cases required supportive medical management and22.2% of the AKI cases needed dialysis. Mortality rate observed was 24.4% among AKI cases. Newborns with AKI who had Intrinsic renal failure, need for dialysis, and need for mechanical ventilation were associated with significantly high mortality($p<0.05$).But no statistical correlations was found between mortality rate, perinatal risk factors, oliguria, gestational age ,BUN and serum creatinine levels. And they identified ARF in the neonatal period is mostly associated with preventable conditions like asphyxia, sepsis and feeding problems in this study conducted at their institution. Conservative management is effective in most cases of AKI in newborns. Intrinsic Renal Failure, need for dialysis, and need for mechanical ventilation were identified as markers of poor prognosis in these neonates. Early recognition of risk factors and immediate treatment of contributing conditions will help to reduce the mortality in neonatal AKI cases.

Alaro Det al[82] in 2016conducted a prospective cohort study from from June 2012 to November 2012 that enrolled 60 full-term neonates admitted at the Kenyatta National Hospital newborn unit (NBU) in Nairobi with Birth Asphyxia. At day 3 of life newborns were investigated for serum creatinine levels. Serum creatinine above 1.3mg/dl was identified as AKI. Neurological examination was conducted daily tillbaby got discharged, death or till 7days of life. And based on Sarnat Classification ,60 (36.6%) cases diagnosed with HIE1 , 51.6% cases with HIE II and 11.8% cases with HIE III.11.7 % was the overall prevalence of ARF in this study. The overall risk of developing AKI is 15 times more in HIE stage 3 vs HIE stage 1, $p=0.034$. Mortality rate of perinatal asphyxia cases in association with AKI was 71.4 % i.e., 24 times greater risk of mortality in neonates with AKI, $p=0.001$. So,Birth Asphyxia

cases that are associated with AKI has grave prognosis. But larger studies are needed to see the association of maternal factors contributing to Birth Asphyxia -associated renal injury.

Shrikhande DYet al[83] in 2016 studied 152 newborns with asphyxia from duration September 2013 to August 2015 in Neonatal Intensive Care Unit of Rural Medical College of Pravara Institute of Medical Sciences, Loni, Ahmednagar, Maharashtra. It was an prospective observational hospital-based study.They investigated for serum creatinine levels, urea and urine output for assessing renal function .64% cases had kidney dysfunction manifested as increase in serum creatinine in 64% cases ,reduced urine output - oliguria in 22% and increased urea in 17%. And they found association of renal injury in birth asphyxia neonates.

Aslam M et al[84] in 2017 conducted a study in NICU during November 2014–October 2015with the objective to find the prevalence and predictors of renal injury in neonates with Perinatal asphyxia .It is conducted in a tertiary care centre. This is across‐sectional study conducted in the neonatal intensive care unit of a tertiary care centre in Northern India. All inborn neonates admitted with severe birth asphyxia based on mode of resuscitation and APGAR score were enrolled in this study. Neonates with congenital anomalies were excluded from the study. Next the neonates were investigated for renal dysfunction based on WHO definition i.e., by assessing serum creatinine levels ,urine output and were classified into 2 groups: Group A (newborns with severe birth asphyxia with associated AKI) and Group II (newborns with severe birth asphyxia without renal injury). Later these 2 groups were then compared. AKI network definition was used to define AKI. Theprevalence of AKI in neonates with asphyxia was 44.21% in this conducted study. No statistical signifance was found among prevalence of AKI among term and preterm asphyxiated newborns,

and in between 3 stages of HIE –Hypoxic Ischemia Encephalopathy. 95% asphyxiated neonates had nonoliguric type of AKI and only 5% with oliguric type of AKI. Among the enrolled cases ,92.8%patients recovered by the time of discharge and remaining cases recovered at 1 month follow-up after discharge. Among risk factors, H/O prolonged 1st and 2nd stages of labor and neonates presented with shock had advanced stages of renal failure and it was found to be significantly associated with AKI. So, Shock should be recognised early and should be aggressively treated with inotropic support if needed ,as it was significally associated with advanced stages of renal failure. Because neonatal AKI cases are difficult to diagnose based on the urine output (most cases manifest as non oliguric type of AKI or APGAR score , it is better to screen all perinatal asphyxia cases for renal failure so that they can be diagnosed early and managed accordingly. To diagnose AKI serial monitoring of serum creatinine and urea levels are needed as their single normal values cannot exclude AKI and can result in advance stage of renal failure.

Charlton JRet al[85] in 2019 conducted international retrospective observational cohort study carried to identify the risk factors and outcomes of neonatal AKI in the first postnatal week. All the neonates who received at least 48 hours of intravenous fluids admitted to a neonatalintensive care unit-NICU were included in this study. Based on KIDGO (KidneyDisease: Improving Global Outcomes)criteria ,early AKI was defined by an increase inserumcreatinine.0.3mg/dl or urine output less than 1ml/kg per hour on postnatal days 2–7. Assessed for the risk factors resulting in AKI and the association with duration of hospitalization and mortality rate. 21%Twenty-onepercent (449of 2110) cases were diagnosed with earlyAKI.Increased risk of AKI was associated the following factors such as : outborn babies ; need of epinephrine for neonatal resuscitation ,neonatal hyperbilirubinemia, neonates with inborn errors

of metabolism, or surgical cases ; so frequentrenal function monitoring is needed in these cases . These factors werefound to be associated with a lowerrisk for neonatal AKI were : multiplegestations,caesarean section-LSCS ,antimicrobials usage, usage of methylxanthines, diuretics,andvasopressors. Risk factors varied by gestational age strata. Increased risk of mortality rate was associated with earlyAKI(adjusted odds ratio 2.8; 95% confidence interval, 1.7 to 4.7) and longer duration of hospitalization (parameterestimate: 7.3 days 95% confidence interval, 4.7 to 10.0), adjusting for neonatal and maternal factors along withmedication(nephrotoxic drugs) exposures. So, early AKI in the 1stpostnatal week is most common and significantly associated with greater risk of mortality rate and prolonged duration ofhospitalization. The AWAKEN study demonstrates a number of specific risk factors that should serve as "redflags" for clinicians at the initiation of the neonatal intensive care unit course.

Katariya KL et al[86] conducted prospective observational study of one year duration period in 2019 at GMERS Medical College and General Hospital, Gotri, Vadodara, Gujarat,India. This study was conducted to evaluate renal profile in high-risk neonates admitted to neonatal intensive care unit-NICU.Criteria used for classification of acute kidney injury was for nRifle in this study for neonatal population.The incidence of AKI in this study among high-risk neonates admitted in NICU was found to be 52 (37.14%). Based on gender, male to female ratio in this current study was found to be 2.46 /1 . In this study ,44 (84.6%) of the newborn cases(majority) with AKI were found to be out born. The incidence of AKI was higher in full term neoantes. Mean birth weight of the cases in AKI group was 2048 grams. The highest incidence of AKI was found in Average for Delivery -AFD new-borns (57.69%). On investigating 52 newborns were diagnosed with AKI and based on nRIFLE criteria :27(51.9%) neonates were in R- risk category, 21 (40.4%) were

in I-injury group and 4 (7.7%) were in F-failure group based on serum creatinine levels and urine output adjusted for gestational age. The observed death rate in these groups were 5 (18.51%) in risk group, 7 (33.33%) in injury group and 3 (75%) in failure group. Among the contributing factors for neonatal AKI , Perinatal asphyxia was associated in majority of cases 18 (34.9%) followed by neonatal sepsis in 12 (23.1%) and with shock in 15 (28.5%). Non oliguric type of neonatal AKI was identified in 29 neonates (55.76%). And electrolyte disturbances in neonatal AKI cases were identified in 28 cases (53.8%)enrolled .So, this study concludes that early diagnosis of risk factors and therapeutic management of those factors accordingly can help in reduction of the neonatal AKI incidence and improved long term outcomes in them .

Gallo Det al[87]conducted a study in a cohort of neonates admitted in Neonatal Intensive Care Unit between January 2008 to December 2018in 2009 at Wilhelmina Children's Hospital/UMCUtrecht ,with the objectives to identify the incidence, etiology, and outcome of neonatesdeveloping AKI within the 1st postnatal week .Babies were investigated for renal dysfunction .Neonates diagnosed with early AKI were reassessed at time of discharge for renal dysfunction.AKI was defined as an absolute serumCr (sCr) value above 1.5 mg/dL (132 μmol/L) after thefirst 24 h or as stage 2–3 of the NIDDK neonatal definition.History ,course of illness and other clinical data and outcomes were collected from medical records available and were analyzed retrospectively. Total of 9,376 neonates were admitted in their Neonatal Intensive Care Unitduring that study period of 10years.Among them 139 were diagnosed with early AKI during the 1st post natal week. Among the neonatal AKI identified ,72 were full term neonates, the most commonetiology was perinatal asphyxia (72.2%), followed by congenitalkidney and urinary tract malformations

(CAKUT)(8.3%), congenital heart disease-CHD (6.9%), and sepsis (2.8%).And remaining 67 neonatal AKI cases were preterms that were associated with 27.2%of cases with HS-PDA hemodynamic significant PDA which took medical treatment followed by congenital kidney and urinary tract malformations – CAKUT in 21% cases, and birth asphyxia in 19.4%. The criteria for neonatal AKI diagnosis in preterm newborns and newborns with birth asphyxia was serum creatinine >1.5 mg/dL criterion.Among the AKI associated with acquired conditions cases ,76 neonates were improved at time of discharge . But neonates with stage 3 AKI showed increased serum creatinine values from baseline at time of discharge. Around 50% of these cases were diagnosed with congenital kidney malformations and evolved into chronic kidney disease (CKD) later in childhood life. Neurodevelopmental outcome(NDO) at 2 years was favorable in 93% of surviving neonates with detailed follow-up. During the first week after birth, AKI was seen in 1.5% of infants admitted toa level III NICU. Renal function at discharge had improved inmost neonates with acquired AKI but not in infants diagnosed with stage 3 AKI.Regular follow up of the neonatal AKI cases for long-term renal function is needed and neurological development appears to be good.

Ikpeme EEet al[88] conducted a study in the year 2020 for a duration of 8 months in Neonatal Intensive Care Unit the University of Uyo Teaching hospital, Uyo, Nigeria .It is a descriptive cross-sectional type of study . The sample size for this study was 104 newborns with provisional diagnosis of perinatal asphyxia based on the mode of resuscitation needed and APGAR score. All the recruited asphyxiated neonates that got admitted were investigated for serum creatinine levels within 6 hours of life and urine output monitoring . Serum creatinine levels were estimated using modified Jaffe method. Urine output was monitored by application of neonatal urosac bag to

the skin by adhesive patch without catheterising the baby. AKI is defined when serum creatinine level is more than 1.5mg/dl and oliguria is defined when urinary output less than 1.5ml/kg/hour. Among the total of 104 asphyxiated neonates enrolled into the study, 56 (53.8%) were males and 48 (46.2%) were females . The male : female ratio in this study was 1.2:1. Based on severity of asphyxia , 24 (23.1%) neonates were classified as mild perinatal asphyxia ,52 (50%) neonates had moderate perinatal asphyxia and 28 (26.9%) of the subjects had severe perinatal asphyxia. Total of 48 (46.1%) neonates had AKI ,among them 12(11.5%) was diagnosed based on serum creatinine levels and remaining 36 (34.6%) cases had AKI based on urinary output criteria . The mean urinary output (ml/kg/hr) for the newborn cases was 1.65±0.68 and the mean serum creatinine (mg/dl) level was 0.88±0.46.The overall incidence of AKI in the enrolled 104 perinatal asphyxia cases was 46.1% ,according to this study.

Bansal SC et al[89] carried out a study in the year 2020 for a duration of January 2008 to January 2010 . The sample size choosen for this study was 1745 neonates . It was a case control study . In this study they evaluated for the clinical course of the illness, identify the contributing and prognostic factors in neonates with AKI. Among the enrolled cases , 74 subjects were diagnosed with neonatal AKI . AKI is defined when serum creatinine level is more than 1.5mg/dl or urine output below <1ml/kg/hr criterion. Neonates with serum creatinine value <1.5 mg/dl was taken for choosing control group randomly from the hospital records of the neonates derived from the electronic registry .Among the two groups demographic variables like birth weight, gender, gestational age, age at time of admission ,growth restriction, APGAR scores, serum electrolyte levels and common clinical conditions like asphyxia, sepsis, meningitis, persistent pulmonary hypertension(PPHN), Necrotizing Enterocolitis

(NEC), mechanical ventilation, congenital heart disease (CHD) were compared amongst the both case and control groups. All the details regarding the maternal history was obtained from the hospital admission register, admission files, labour register of obstetrics and gynaecology department and electronic registry. Chi square/independent sample t-test as applicable and logistic regression were used to establish an association of various factors and outcome with AKI. The overall incidence of AKI in our study was 4.24%. Demographic variables more common in AKI group were inborn (p=0.011), male gender (p=0.032), term gestation (p=0.001), Appropriate for gestational age (0.001), higher birth weight (p<0.001), full term (p<0.001), sepsis (p<0.001), NEC (p=0.042), low APGAR scores at one minute (p=0.011) and five minutes (p=0.003). However, on multivariate logistic regression only male gender [Odds Radio (OR)=2.84, Confidence Interval (CI)=1.12-7.21] and Sepsis (OR=14.46, CI=4.5-46.46) were associated with AKI. Respiratory distress syndrome was more prevalent in the control group (p<0.003). Neonates with presence of shock and need of mechanical ventilation had poor prognosis for survival. The conclusion from this study was AKI continues to be of clinical significance in NICU . Further studies are needed to evaluate newer associations (like male gender and low APGAR scores).

Materials and Methods

Study setting: Level 3A NICU of Shri B. M. Patil Medical College, Hospital & Research Center, Vijayapur

Study population: All babies admitted in NICU of Shri B. M. Patil Medical College, Hospital & Research Center, Vijayapur, with H/o No cry/Delayed cry or Apgar below 7 at 5minutes. Both Inborn and Outborn late preterm and term babies are included.

Study period: Two years (From December 2019 to August 2021)

Study design: Descriptive observational study

Formula for sample size calculation :

With 95% confidence level and margin of error of +/-10%, a sample size of 65 subjects are included in the study to determine the incidence of acute kidney injury in term birth asphyxia neonates with finite population correction (N=200).

Formula used:

$$n = \frac{Z^2 p(1-p)}{d^2}$$

Where Z = z statistic at 5% level of significance

p = anticipated prevalence rate (50%)

d = Margin of error.

Sampling technique: Simple Random sampling method

Inclusion criteria:

1**. For Inborn Babies:** All late preterm and term (35-42wks) neonates born with Apgar score of 7 or <7 at 5minutes of birth

2. **For out born Babies:**

A new born is said to have suffered from birth asphyxia if she/he after birth has absent/ weak/delayed cry, or had absent or slow gasping respiration or any baby who needed resuscitation measures. Thus, if a neonate requires oxygen, bag and mask ventilation, drugs or intubation for initiation of respiration it will constitute birth asphyxia. Criteria followed for outborn babies.

Exclusion criteria:

The study excluded :

1. Babeis with gestational age below 35 weeks.

2. Neonates with renal anomalies (in antenatal scan)

Major congenital anomalies- h/o maternal nephrotoxic drugs intake are excluded from the study.

Methods of data collection:

After taking written informed consent from the parents and fulfilling inclusion and exclusion criteria, the neonates are be included in the study.

A **prospective cross-sectional study** involving late preterm and term neonates admitted in NICU. The Neonates with Birth Asphyxia are considered as **SUBJECTS.** After the baby fulfils the inclusion criteria, a detailed history has been taken from caregivers regarding Medical h/o, Ante-partum, Intrapartum, Fetal, placental risk factors. Blood samples for urea, creatinine, sodium,potassium,calcium,urinary sodium and urinary creatinine are collected after 72hrs of life to 96hrs of life. The incidence of acute kidney injury is assessed in neonates.

Statistical analysis:

Data is collected by using a structure proforma. Data entered in MS excel sheet and analysed by using SPSS 24.0 version IBM USA.Qualitative data is expressed in

terms of proportions. Quantitative data is expressed in terms of Mean and Standard deviation. Association between two qualitative variables will be seen by using Chi square/ Fischer's exact test. Descriptive statistics of each variable are presented in terms of Mean, standard deviation, standard error of mean.

A p value of <0.05 is considered as statistically significant whereas a p value <0.001 is considered as highly significant.

RESULTS

Table 1: Distribution of Parity

Parity	N	%
Multi	28	43
Primi	37	57
Total	65	100.0

We included total 65 cases in our study. Of that 37(57%) were primigravida and 28(43%) were multigravida.

Figure 1: Distribution of Parity

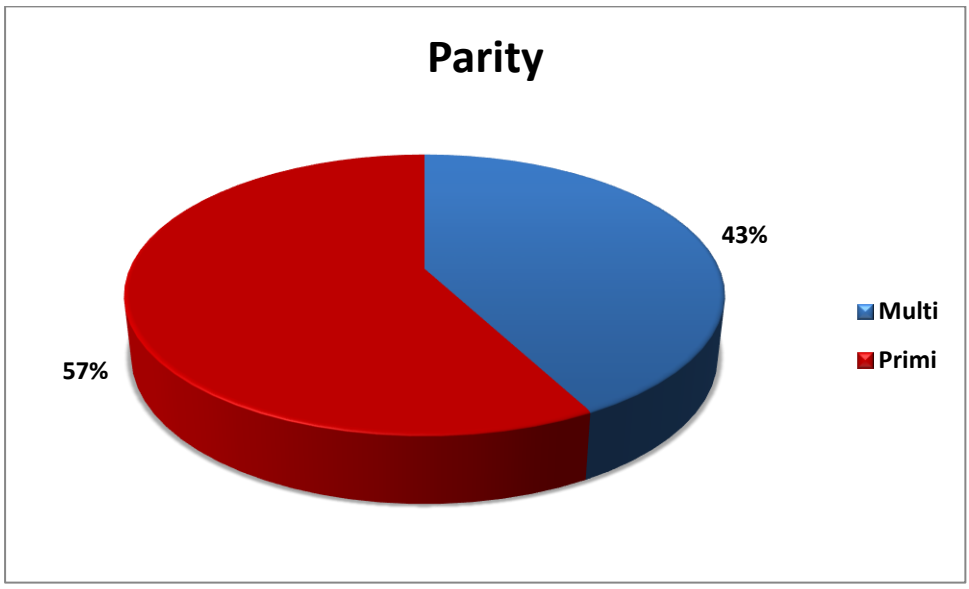


Table 2: Distribution of Socioeconomic status

Socioeconomic status	N	%
Low	55	84.7
Middle	10	15.3
Total	65	100.0

84.7% women were from lower SES and 15.3% were from middle SES

Figure 2: Distribution of Socioeconomic status

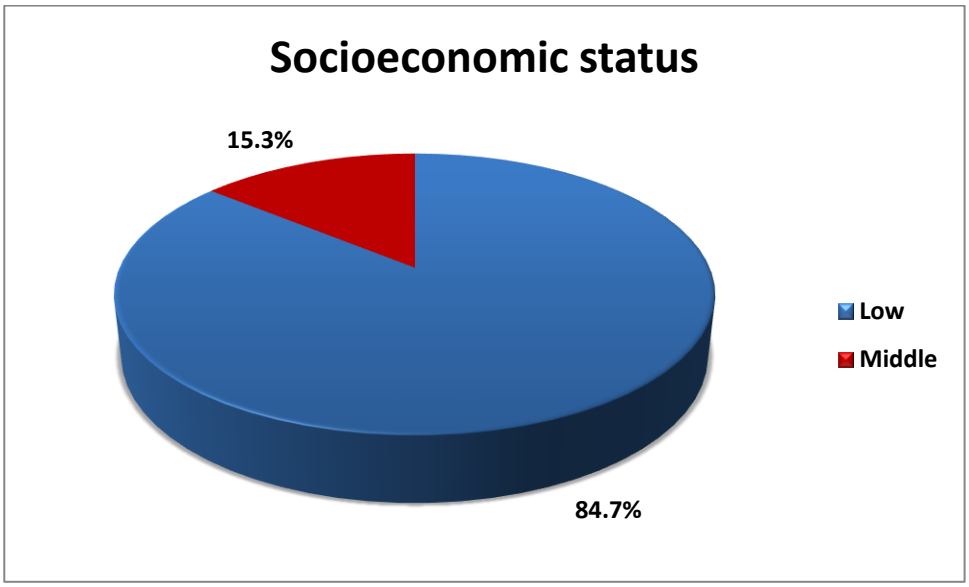


Table 3: Distribution of Antenatal history (number of mothers with positive antenatal risk factors)

Antenatal history (GDM/Eclampsia/HTN)	N	%
No	47	72.3
Yes	18	27.7
Total	65	100.0

27.7% of women has antenatal high risk factors like GDM/Eclampsia/HTN.

Figure 3: Distribution of Antenatal history

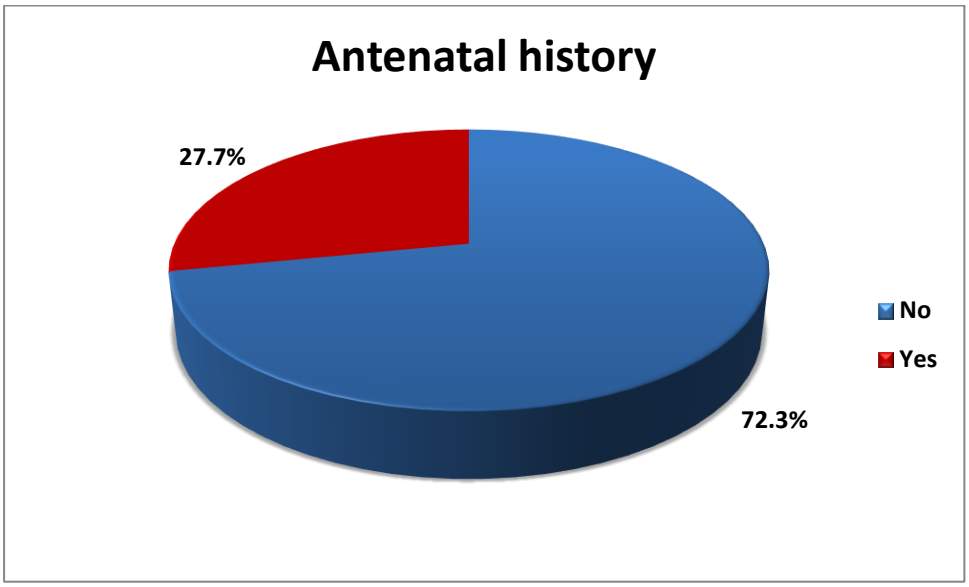


Table 4: Distribution of Mode of Delivery :

Mode of Delivery	N	%
LSCS	25	38.4
NVD	38	58.4
VBAC	2	3.2
Total	65	100.0

Mode of delivery in majority of the cases was normal vaginal delivery i.e. 38(58.4%) followed by 25(38.4%) with LSCS

Figure 4: Distribution of Mode of Delivery :

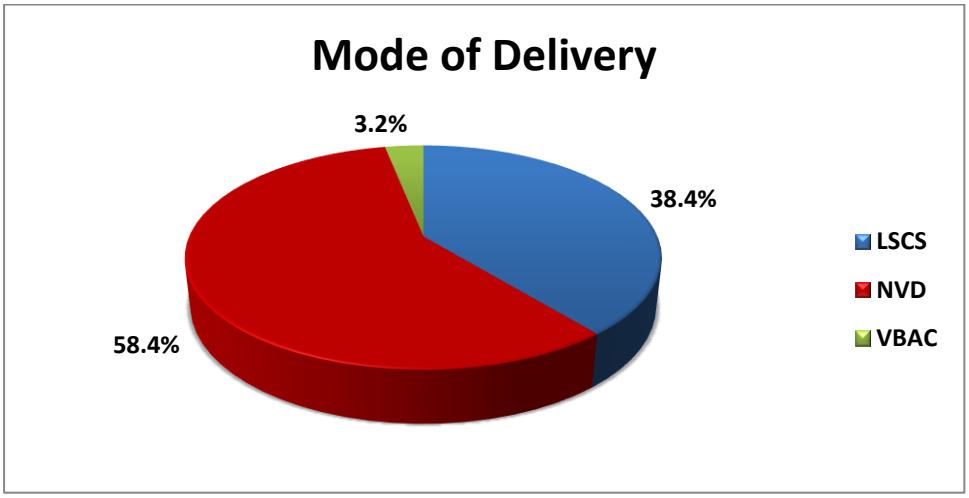


Table 5: Distribution of Age of mother between Study Groups

Parameters	Renal failure				p value
	Yes		No		
	Mean	SD	Mean	SD	
Age of mother(yrs)	22.7	2.0	22.5	2.4	0.782

Mean age of the mother with neonatal renal failure was 22.7±2.0 years and that of maternal age of remaining babies was 22.5±2.4 years. When we compared the mean age of the mothers between two groups, the difference was found to be non-significant (p>0.05)

Figure 5: Distribution of Age of mother between Study Groups

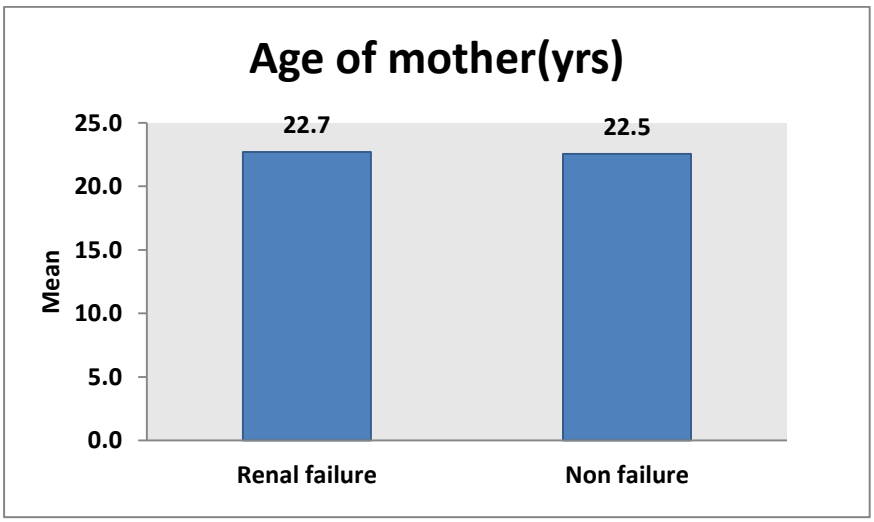


Table 6: Distribution of Parity between Study Groups

Parity	Renal failure				p value
	Yes		No		
	N	%	N	%	
Multi	7	31.8%	21	48.8%	0.224
Primi	15	68.2%	22	51.2%	
Total	22	100.0%	43	100.0%	

Incidence of neonatal renal failure in our study was 22(34.37%). Out of 22, 15 i.e. 68.2% were born to primigravida and remaining 7 i.e. 31.8% were born to multigravida. There was no association between renal failure and parity of mother

Figure 6: Distribution of Parity between Study Groups

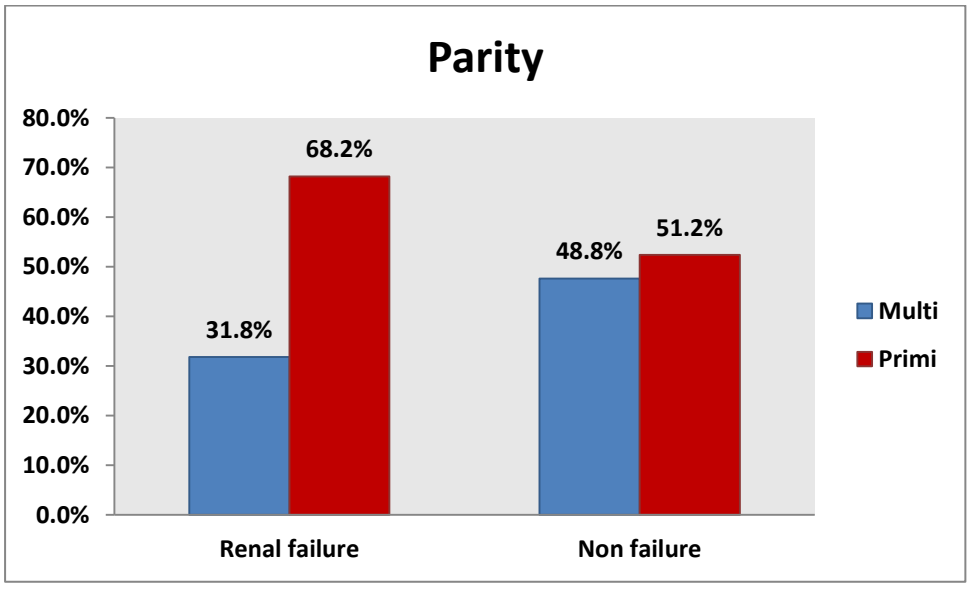


Table 7: Distribution of Socioeconomic status between Study Groups

Socioeconomic status	Renal failure				p value
	Yes		No		
	N	%	N	%	
Low	17	77.3%	38	88.4%	0.149
Middle	5	22.7%	5	11.6%	
Total	22	100.0%	43	100.0%	

Out of 22 renal failure cases : 17 neonatesare from Lower SES i.e., 77.3% and 5 neonates from middle SES i.e., 22.7%. And among neonates without renal failure :38 neonates (88.4%) are from Low SES and 5 neonates (11.6%) from Middle SES. This difference in the proportion of neonates with respect to SES was found to be statistically not significant in our study. It means there was no association between incidence of renal failure with SES.

Figure 7: Distribution of Socioeconomic status between Study Groups

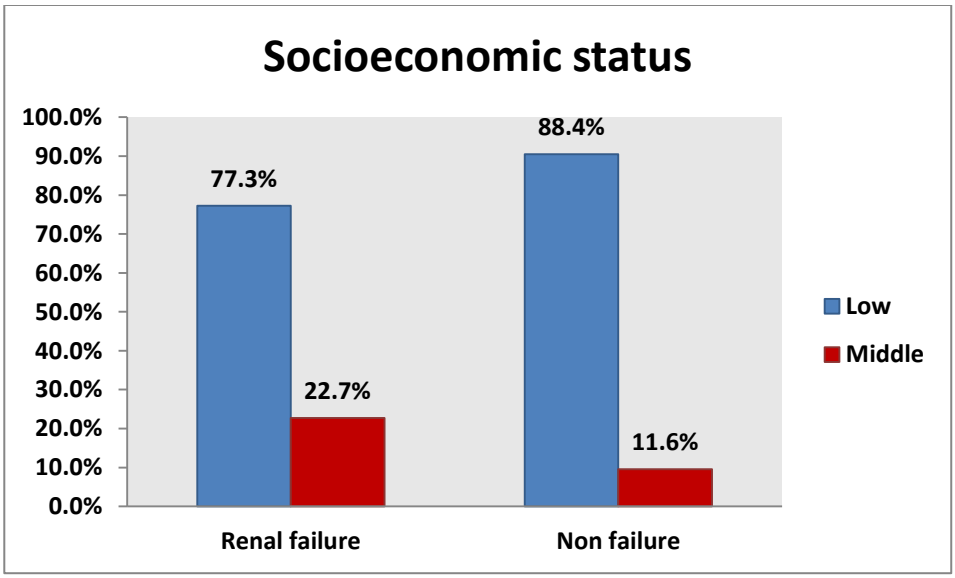


Table 8: Distribution of Antenatal history between Study Groups

Antenatal history (GDM, PIH, Eclampsia)	Renal failure				p value
	Yes		No		
	N	%	N	%	
No	15	68.2%	32	74.4%	0.634
Yes	7	31.8%	11	25.6%	
Total	22	100.0%	43	100.0%	

Proportion of neonates with renal failure having maternal antenatal history of GDM, PIH and eclampsia was 31.8% as compared to 25.6% non-renal failure with maternal antenatal history of GDM, PIH and eclampsia. This difference in the proportion of neonates with respect to antenatal maternal history of GDM, PIH and eclampsia was not found to be significant in our study. It means there was no association between incidence of renal failure with maternal history of of GDM, PIH and eclampsia.

Figure 8: Distribution of Antenatal history between Study Groups

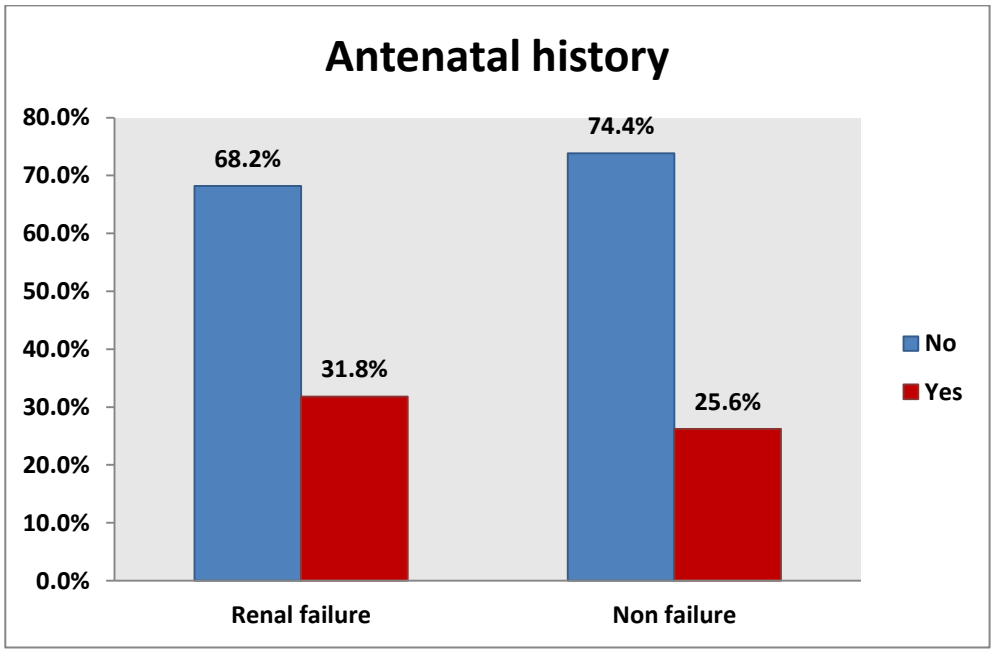


Table 9: Distribution of Mode of Delivery between Study Groups

Mode of Delivery	Renal failure				p value
	Yes		No		
	N	%	N	%	
LSCS	7	31.8%	18	41.9%	0.346
NVD	15	68.2%	23	53.4%	
VBAC	0	0.0%	2	4.7%	
Total	22	100.0%	43	100.0%	

31.8% neonates with renal failure were born by LSCS method ,68.2% renal failure neonates were born by NVD. And among non failure neonates : 41.9% via LSCS ,53.4% via NVDand 4.7% via VBAC. This difference in the proportion of neonates with respect to mode of delivery was not found to be significant in our study. It means there was no association between incidence of renal failure with mode of delivery.

Figure 9: Distribution of Mode of Delivery between Study Groups

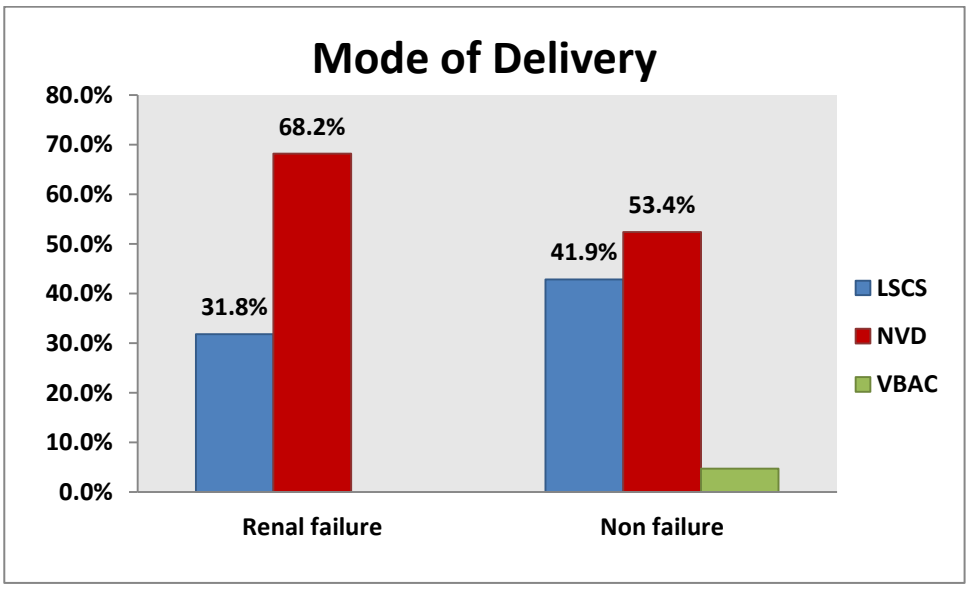


Table10: Distribution of Age of baby presented to NICU between Study Groups

Age in hrs	Renal failure				p value
	Yes		No		
	N	%	N	%	
1-2	4	18.2%	12	28%	0.506
3-5	6	27.3%	11	25.6%	
6-10	2	9.1%	8	18.6%	
11-24	4	18.2%	7	16.2%	
>24	6	27.3%	5	11.6%	
Total	22	100.0%	43	100.0%	

Out of 22 neonates with renal failure, majority were presented to NICU at> 24 hours age and 3-5 hrs age i.e. 27.3% each. This then followed by 18.2% from 1-2 hrs and 11-24 hrs each and 9.1% from 6-10 hrs.

Out of 43 neonates without renal failure, 28% neonates were presented at 1-2 hrs , 25.6% neonates at 3-5hrs , followed by 18.6% between 6-10 hrs age, 16.2% between 11-24 hrs and 11.6% at >24 hrs age.

Parameters	Renal failure				p value
	Yes		No		
	Mean	SD	Mean	SD	
Age in hrs	18.0	19.9	10.5	13.3	0.076

Mean age of the neonate having renal failure was 18±19.9 hrs and that of non failure neonate was 10.5±13.3 hrs. When we compared the mean age of the neonates between two groups, the difference was found to be non-significant (p>0.05)

Figure 10: Distribution of Age of baby between Study Groups

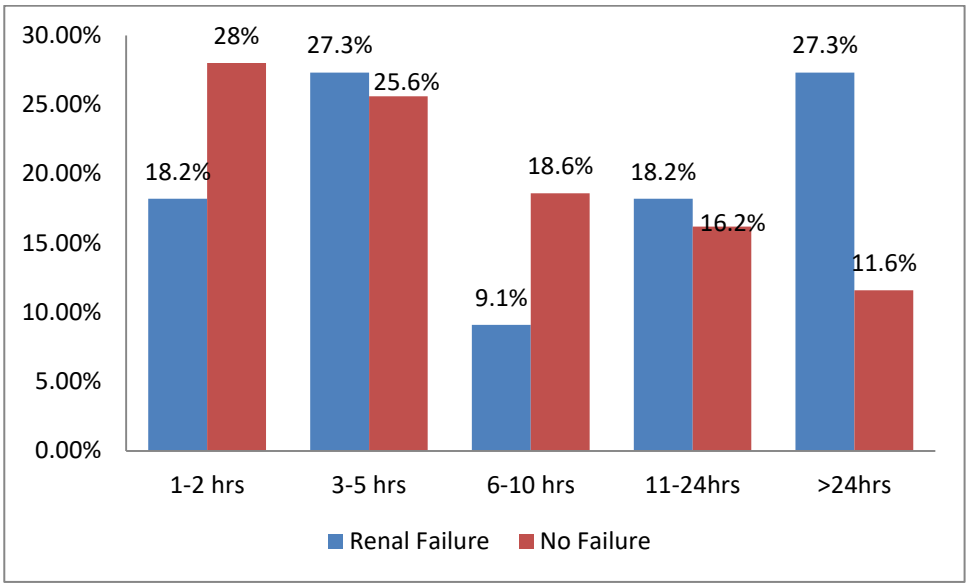


Table11: Demographic Parametersbetween Study Groups

Parameters	Renal failure				p value
	Yes		No		
	Mean	SD	Mean	SD	
Bwt (kg)	2.4	0.4	2.6	0.4	0.077
Length	48.1	1.5	48.8	1.4	0.065
HC	31.6	0.8	32.2	0.9	0.010*

Note: p value* significant at 5% level of significance (p<0.05)

Mean birth weight of the neonate having renal failure was 2.4±0.4 kg and that of non renal failure neonate was 2.6±0.4 kg. When we compared the mean birth weight of the neonates between two groups, the difference was found to be non-significant (p>0.05)

Mean length of the neonate having renal failure was 48.1±1.5 cm and that of non renal failure neonate was 48.8±1.4 cm. When we compared the mean length of the neonates between two groups, the difference was found to be non-significant (p>0.05)

Mean head circumference of the neonate having renal failure was 31.6±0.8 cm and that of non renal failure was 32.2±0.9 cm. When we compared the mean head circumference of the neonates between two groups, the difference was found to be statistically significant (p<0.05). It means head circumference was significantly less in the neonates with renal failure in our study.

Figure 11: Demographic Parametersbetween Study Groups

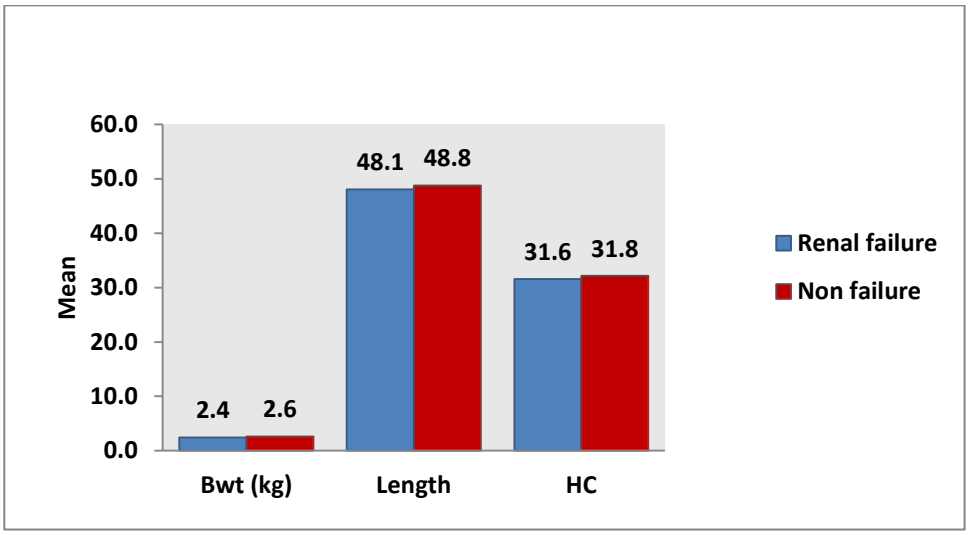


Table12: Mean parametersbetween Study Groups

Parameters	Renal failure				p value
	Yes		No		
	Mean	SD	Mean	SD	
HR	159.1	12.7	152.2	8.6	0.012*
RR	43.9	6.7	54.8	7.5	<0.001*
SpO2	95.6	2.0	96.8	0.8	0.002*

Note: p value* significant at 5% level of significance (p<0.05)

Mean HR of the neonate having renal failure was 159.1±12.7/ minute and that of non renal failure neonate was 152.2±8.6 /minute. Mean RR of the neonate having renal failure was 43.9±6.7 per minute and that of non renal failure was 54.8±7.5 per minute.

Mean SPO2 of the neonate having renal failure was 95.6±2% and that of non renal failure neonate was 96.8± 0.8%. When we compared the mean HR, RR and SPo2 of the neonates between two groups, the difference was found to be statistically significant (p<0.05). It means HR was significantly higher in neonates with renal failure as well as RR and SPo2 was significantly less in neonates with renal failure in our study.

Figure 12: Mean parametersbetween Study Group

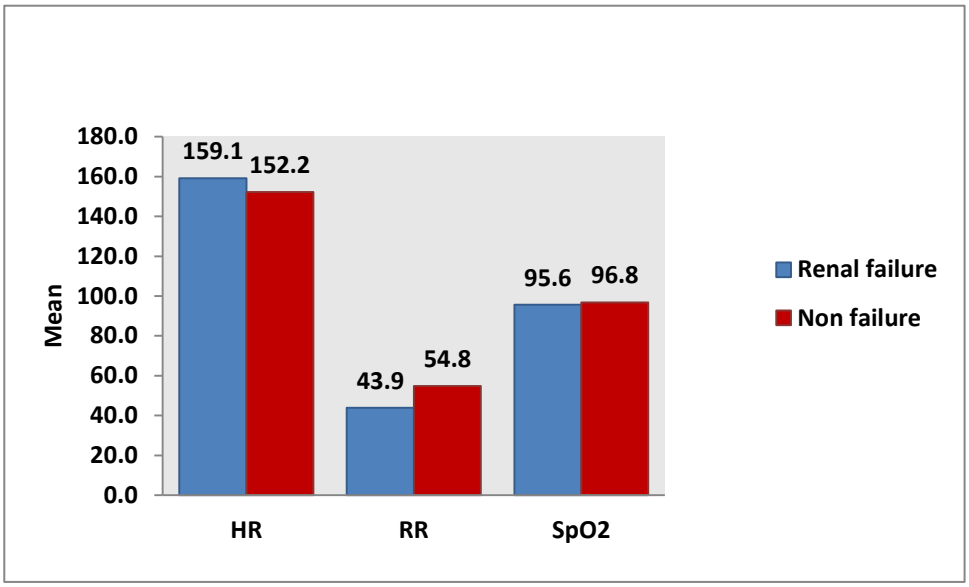


Table 13: Mean lab parametersbetween Study Groups

Parameters	Renal failure				p value
	Yes		No		
	Mean	SD	Mean	SD	
CRP	31.4	25.7	20.8	20.1	0.074
GRBS	93.1	23.9	91.6	20.9	0.791
UREA	56.5	31.8	33.4	13.7	<0.001*
SR.CREAT	1.7	1.6	1.0	0.3	0.005*
SR.Na	136.8	6.7	138.6	4.3	0.191
SR.K	4.7	0.8	4.3	0.7	0.042*
Sr.Cal	7.9	0.8	8.2	0.7	0.171
Ur.Na	54.9	20.3	33.2	17.7	<0.001*
Ur.Creat	28.2	16.6	27.5	15.0	0.870
FeNa	2.3	0.8	0.8	0.4	<0.001*

Note: p value* significant at 5% level of significance (p<0.05)

Mean CRP inneonate with renal failure was **56.5±31.8 and** that of non AKI neonate was **33.4±13.7.** Mean Sr. creatine in neonate having renal failure was **1.7±1.6** that of non AKI neonate was **1.0±0.3.** Mean Sr potassium in neonate having renal failure was **4.7±0.8** that of non AKI neonate was **4.3±0.7.** Mean Urine Na in neonate having renal failure was **54.9±20.3** that of non AKI neonate was **33.2±17.7.** Mean FeNa

value in neonate having renal failure was **2.3±0.8** that of non renal failure neonate was **0.8±0.4.** When we compared the mean CRP, Sr. creatine, Sr potassium, Urine Na, FeNa of the neonates between two groups, the difference was found to be statistically significant ($p<0.05$). It means CRP, Sr. creatine, Sr potassium, Urine Na, FeNa were significantly higher in neonates with renal failure.

Figure 13: Mean lab parametersbetween Study Groups

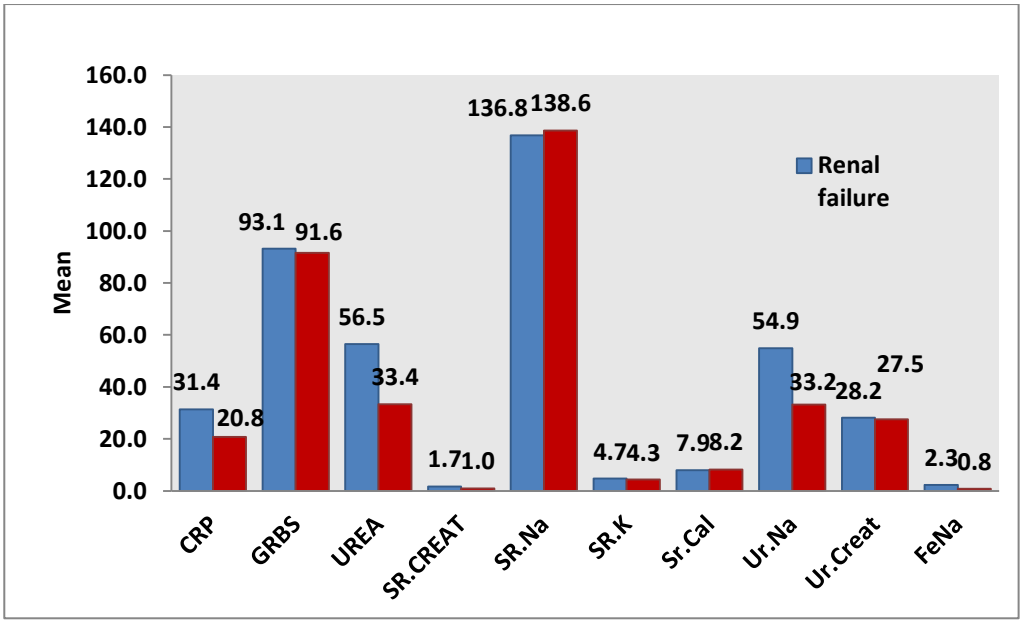


Table 14: Risk factor between Study Groups

Risk factor	Renal failure			
	Yes		No	
	N	%	N	%
MSAF	6	27.5%	17	39.4%
LOC	1	4.5%	4	9.3%
Eclampsia	1	4.5%	4	9.3%
PROM >48	2	9.1%	3	6.9%
prolong labor	3	13.6%	2	4.6%
Abruption	0	0.0%	2	4.6%
GDM	0	0.0%	2	4.6%
APH	0	0.0%	1	2.4%
Breech	1	4.5%	1	2.4%
Cord Prolapse	0	0.0%	1	2.4%
Difficult extraction	2	9.1%	1	2.4%
PIH	2	9.1%	1	2.4%
Hypothyroid	1	4.5%	0	0.0%
EOS	1	4.5%	0	0.0%
Others	2	9.1%	4	9.3%

Among neonates with renal failure ,MSAF was seen in 27.5 % ,LOC in 4.5%,eclampsia as risk factor in 4.5%, PROM >48hours in 9.1% , 13.6% of cases has prolonged labour ,4.5% with breech presentation ,difficult extraction of baby in 9.1/5 ,PIH in 9.1% ,hypothyroidism in 4.5% cases and 13.6% cases has more than 1 risk factor (MSAF + LOC/EOS/Breech).

Among non renal failure cases : 39.5% cases with h/o MSAF ,9.3% with LOC and eclampsia each,6.9% with PROM>48hours history ,4.6% with prolonged labour ,abruption and GDM each . Followed by 2.3% cases with APH ,Breech presentation ,cord prolapse, difficult extraction of baby and PIH . And no risk factors were identified in 4 cases.

PROM>48 hours, MSAF, prolonged labour, breech, difficult extraction, PIH and EOS were the risk factors for AKI identified in our study.

Figure 14: Risk factor between Study Groups

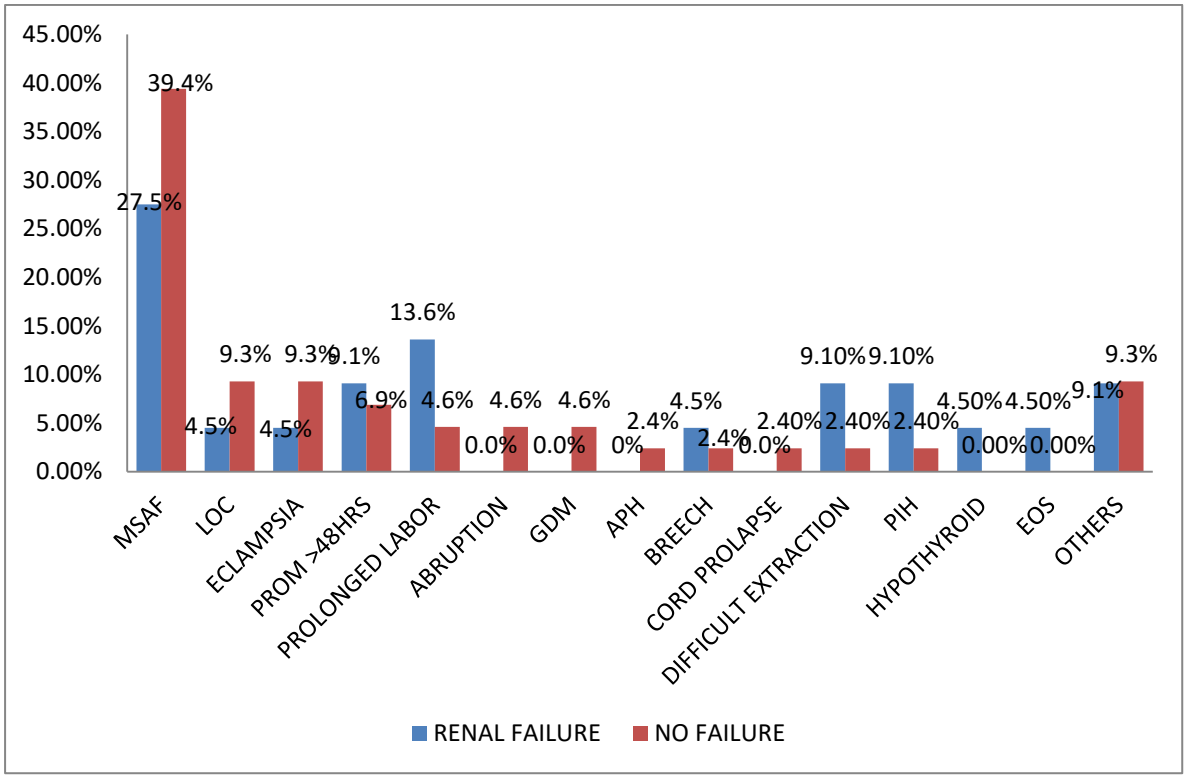


Table 15: Distribution of Gestational Age between Study Groups

Gestational age	Renal failure				p value
	Yes		No		
	N	%	N	%	
Late preterm	5	22.7%	5	11.7%	0.257
Term	17	77.3%	38	88.3%	
Total	22	100.0%	43	100.0%	

Prevalence of AKI in late preterm were 7.5% and in term were 25.7 %.And this relation of AKI among term and late preterm among two groups is not statistically significant in our study(p>0.05)

Figure 15: Distribution of Gestational Age between Study Groups

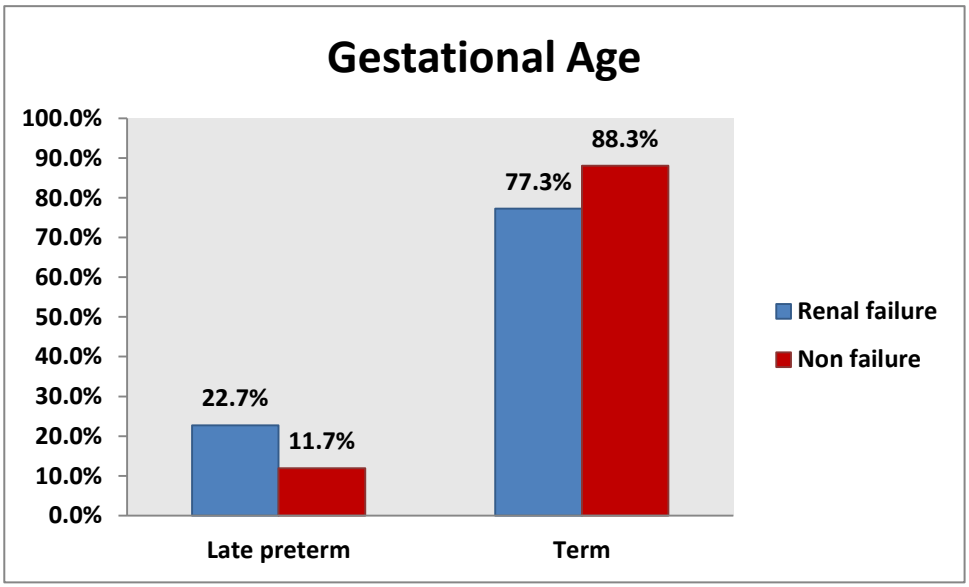


Table 16: Distribution of Sex of baby between Study Groups

Sex of baby	Renal failure				p value
	Yes		No		
	N	%	N	%	
Male	14	63.6%	31	72%	0.523
Female	8	36.4%	12	28%	
Total	22	100.0%	43	100.0%	

Proportion of male neonates with renal failure were 63.6% as compared to 72% without renal failure (p>0.05)Proportion of female neonates with renal failure were 36.4% as compared to 28% without renal failure(p>0.05)

Figure 16: Distribution of Sex of baby between Study Groups

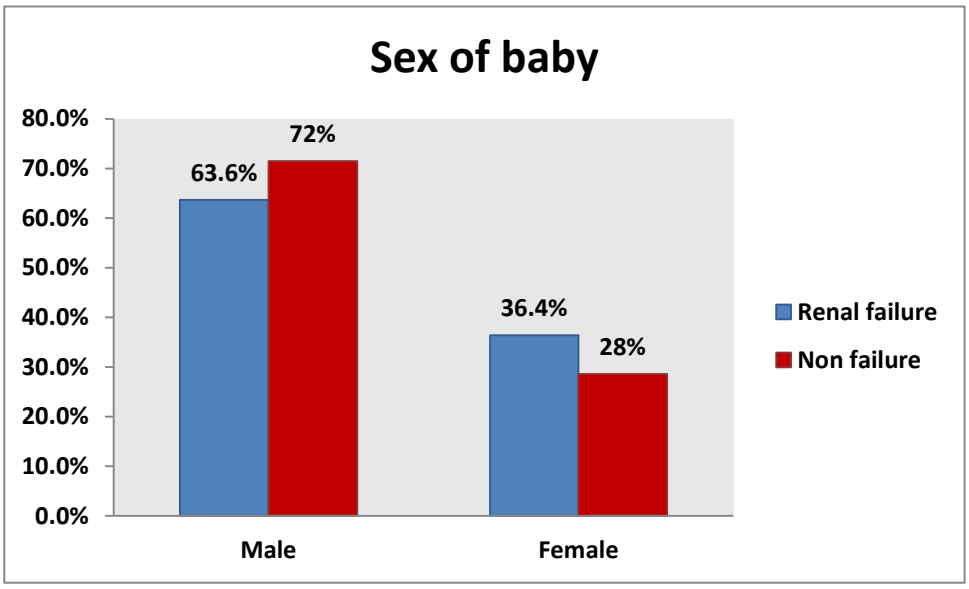


Table 17: Distribution of cyanosis between Study Groups

Colour	Renal failure				p value
	Yes		No		
	N	%	N	%	
Cyanosis	17	77.3%	11	26%	<0.001*
Pink	5	22.7%	32	74%	
Total	22	100.0%	43	100.0 %	

Note: p value* significant at 5% level of significance (p<0.05)

Cyanosis was present in 77.3% neonates with renal failure and in 26% neonates without renal failure.(p<0.05)

Figure 17: Distribution of cyanosis between Study Groups

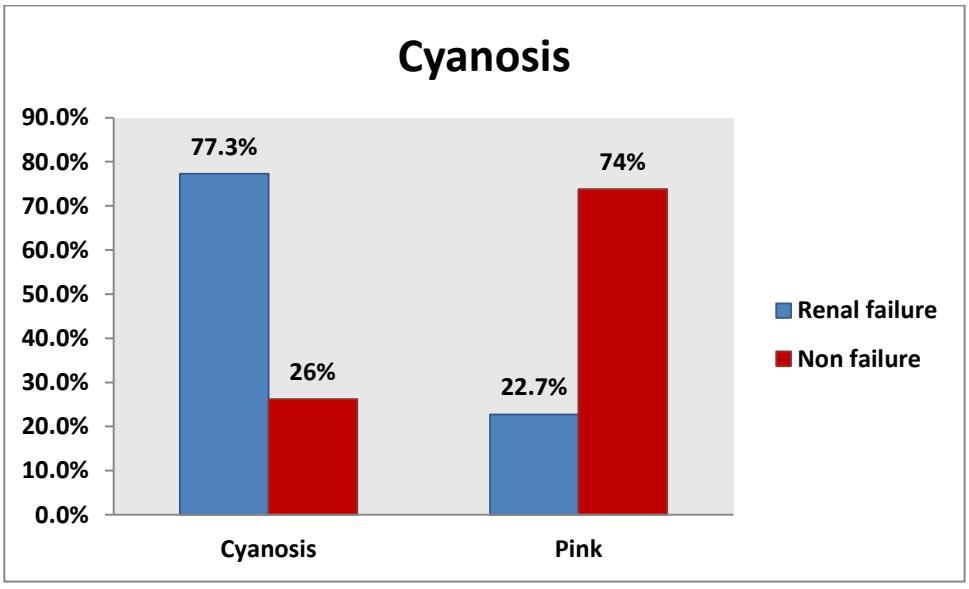


Table 18: Distribution of Activity between Study Groups

Activity	Renal failure				p value
	Yes		No		
	N	%	N	%	
Fair	10	45.5%	37	86%	<0.001*
Poor	12	54.5%	6	14%	
Total	22	100.0%	43	100.0%	

Note: p value* significant at 5% level of significance (p<0.05)

Activity was poor in 54.5% neonates with renal failure and 14% without renal failure(p<0.05)

Figure 18: Distribution of Activity between Study Groups

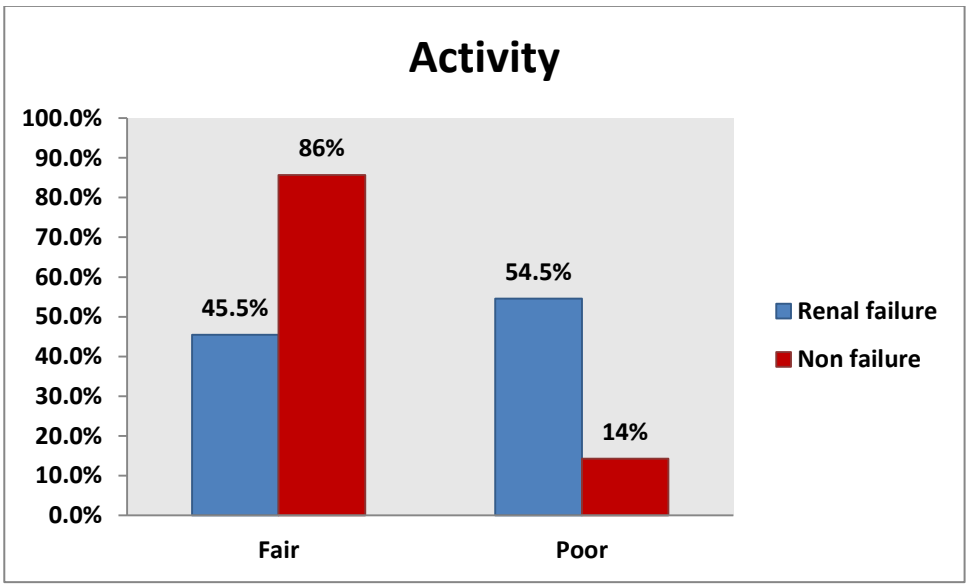


Table 19: Distribution of CFT between Study Groups

CFT	Renal failure				p value
	Yes		No		
	N	%	N	%	
<3	**8**	**36.4%**	**38**	**88.1%**	0.001*
>3	**14**	**63.6%**	**5**	**11.9%**	
Total	**22**	**100.0%**	**43**	**100.0%**	

Note: p value* significant at 5% level of significance (p<0.05)CFT was >3sec in 63.6% neonates with renal failure and 11.9% neonates without renal Failure (p<0.05)

Figure 19: Distribution of CFT between Study Groups

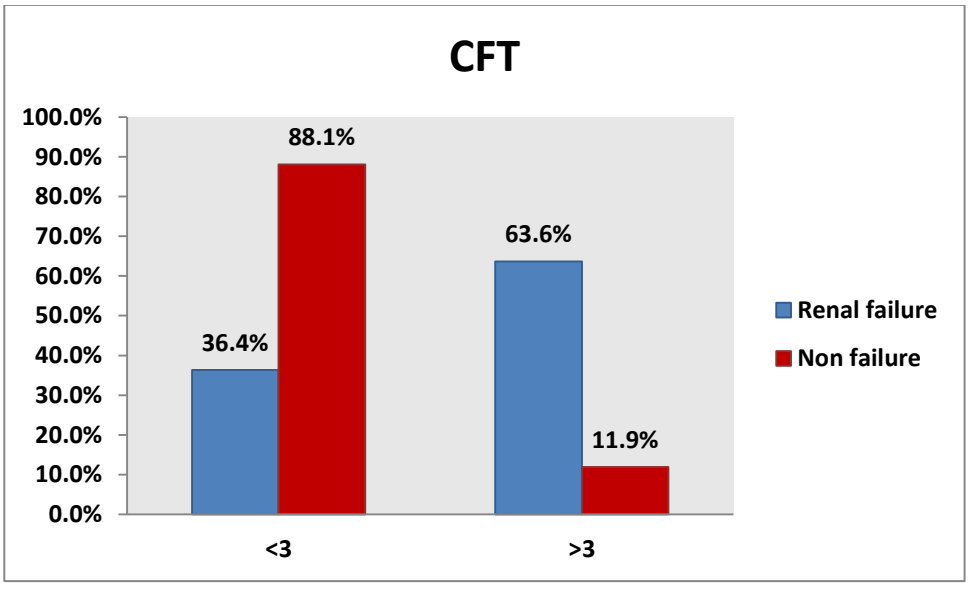


Table 20: Distribution of Shock between Study Groups

Shock	Renal failure				p value
	Yes		No		
	N	%	N	%	
No	7	31.8%	36	83.7%	<0.001*
Yes	15	68.2%	7	16.3%	
Total	22	100.0%	43	100.0%	

Note: p value* significant at 5% level of significance (p<0.05)

Incidence of shock was observed in 68.2% neonates with renal failure and 16.3% without renal failure where the difference in the incidence was found to be statistically significant (p<0.05).

Figure 20: Distribution of Shock between Study Groups

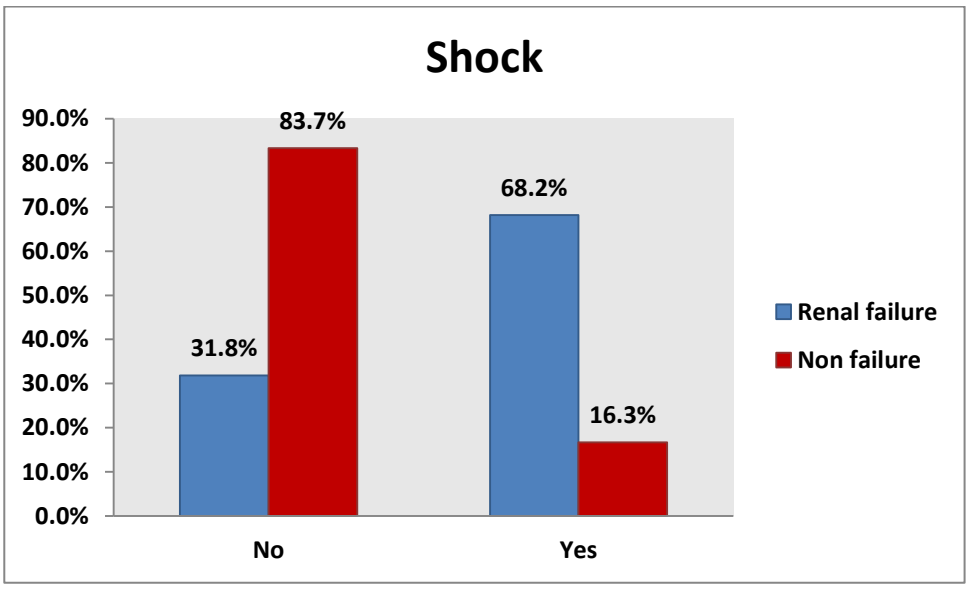


Table 21: Distribution of Urine output between Study Groups

Urine output(ml/kg/hr)	Renal failure				p value
	Yes		No		
	N	%	N	%	
<1	17	77.3%	4	9.4%	<0.001*
>1	5	22.7%	39	90.6%	
Total	22	100.0%	43	100.0%	

Note: p value* significant at 5% level of significance (p<0.05)

Urine output<1ml/kg/hr was seen in 77.3% neonates with renal failure and 9.4% without renal failure where the difference in the incidence was found to be statistically significant (p<0.05).

Figure 21: Distribution of Urine output between Study Groups

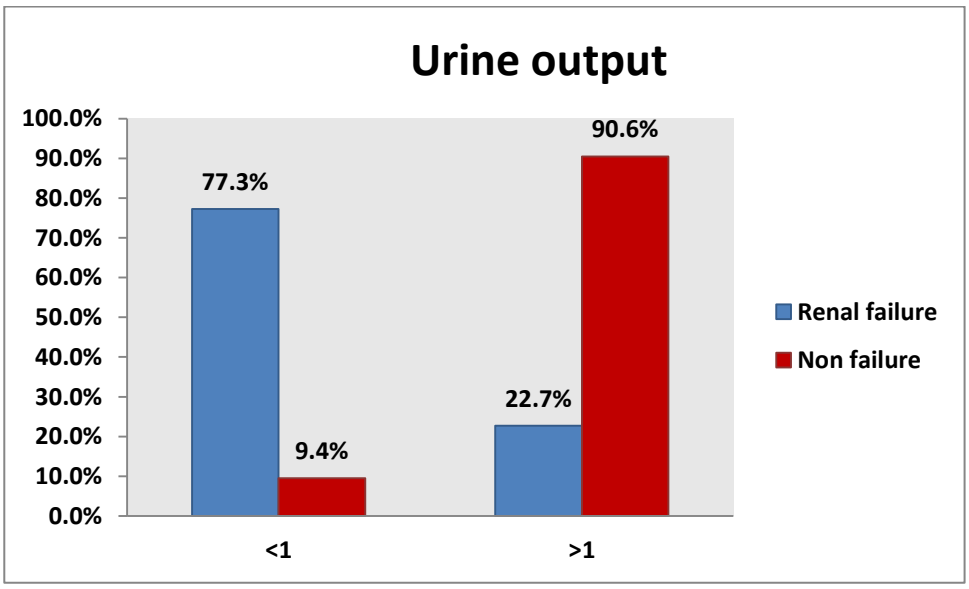


Table 22: HIE grade between Study Groups

HIE grade	Renal failure				p value
	Yes		No		
	N	%	N	%	
I	1	4.5%	21	48.8%	<0.001*
II	9	40.9%	20	46.5%	
III	12	54.5%	2	4.7%	
Total	22	100.0%	43	100.0%	

Note: p value* significant at 5% level of significance (p<0.05)

HIE grade III was seen in 54.5% neonates with renal failure and 4.7% without renal failure where the difference in the incidence was found to be statistically significant (p<0.05).

Figure 22: HIE grade between Study Groups

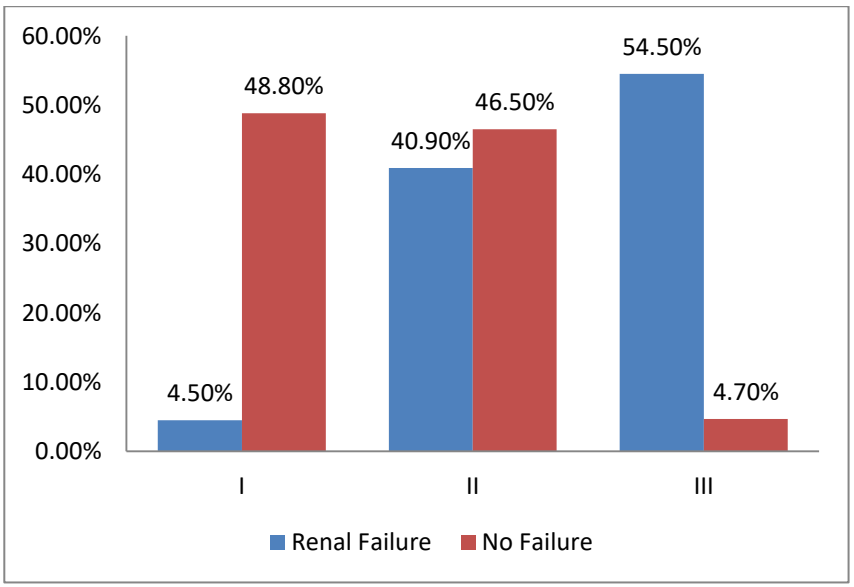


Table 23: Distribution of O2 support given between Study Groups

O2 support	Renal failure				p value
	Yes		No		
	N	%	N	%	
HFNC	2	9.1%	6	14.3%	<0.001*
Hood	2	9.1%	32	73.8%	
Ventilator	18	81.8%	5	11.9%	
Total	22	100.0%	43	100.0%	

Note: p value* significant at 5% level of significance (p<0.05)

81.8% neonates with renal failure were on ventilator as compared to 11.9% without renal failure (p<0.05)

Figure 23: Distribution of O2 support given between Study Groups

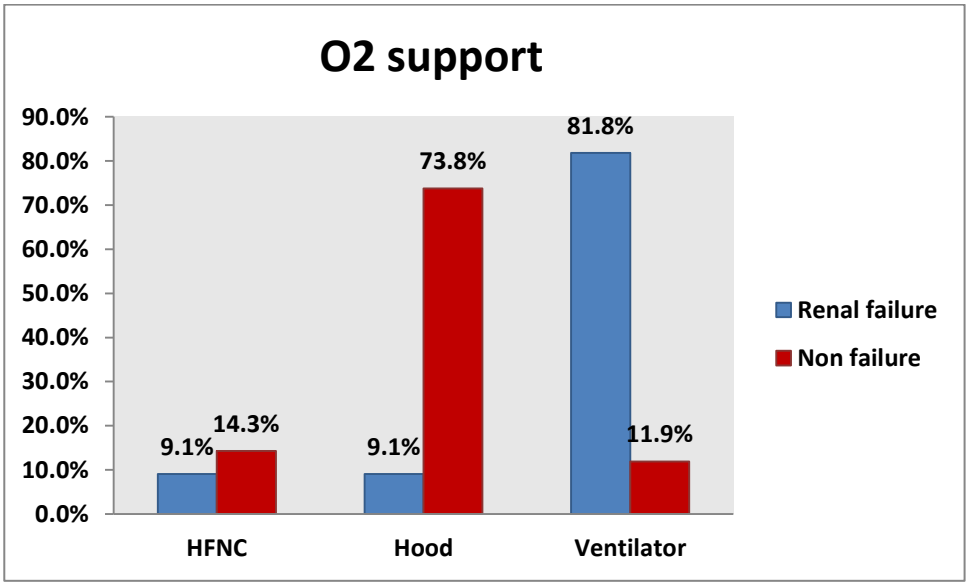


Table 24: Distribution of Inotropes usage between Study Groups

Inotropes	Renal failure				p value
	Yes		No		
	N	%	N	%	
Yes	18	81.8%	9	21%	<0.001*
No	4	18.2%	34	79%	
Total	22	100.0%	43	100.0%	

Note: p value* significant at 5% level of significance (p<0.05)

81.8% neonates with renal failure were given inotropes as compared to 21% without renal failure (p<0.05)

Figure 24: Distribution of Inotropes usage between Study Groups

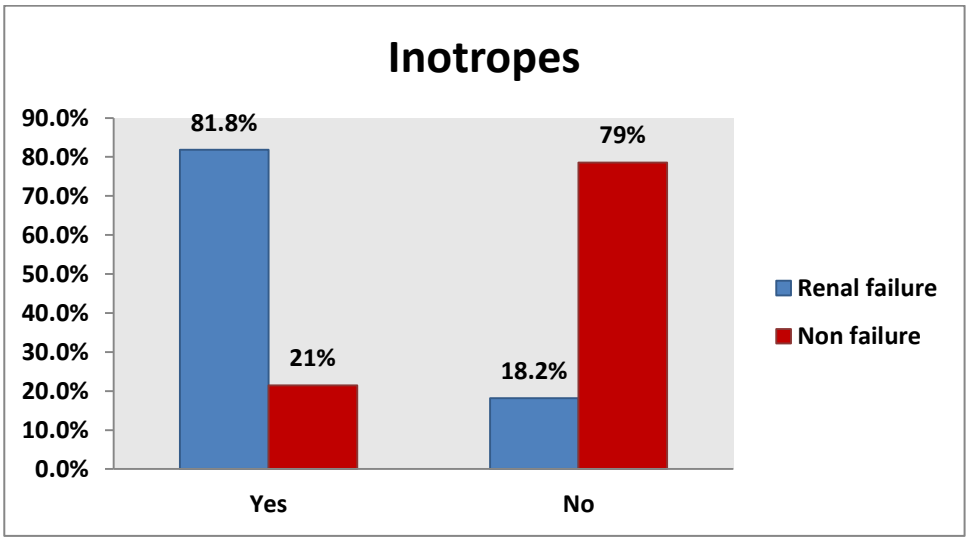


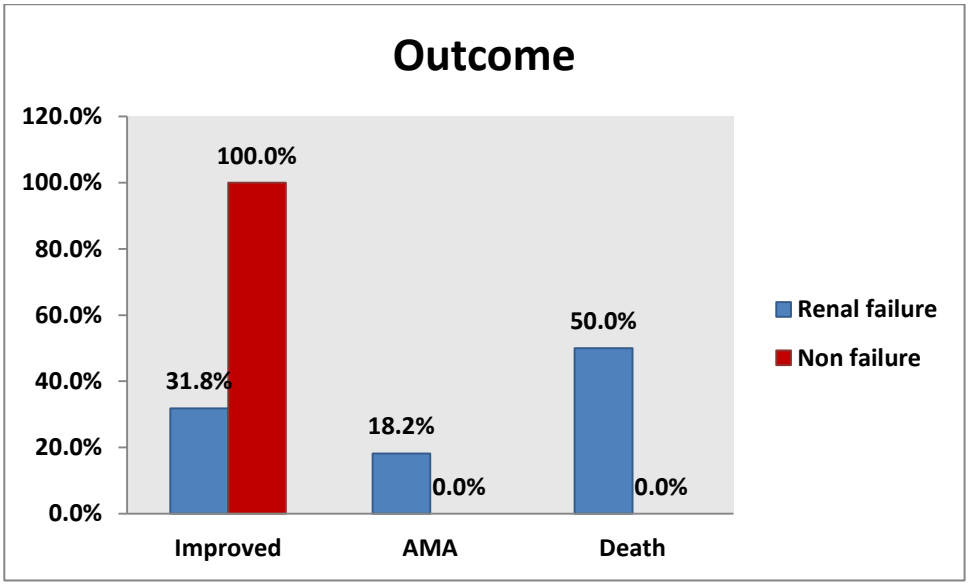
Table 25: Outcome between Study Groups

Outcome	Renal failure				p value
	Yes		No		
	N	%	N	%	
Improved	7	31.8%	43	100.0%	<0.001*
AMA	4	18.2%	0	0.0%	
Death	11	50.0%	0	0.0%	
Total	22	100.0%	43	100.0%	

Note: p value* significant at 5% level of significance (p<0.05)

Out of 22 AKI neonates, 11 died accounting for mortality rate of 50% in in our study.

Figure 25: Outcome between Study Groups



Discussion

Incidence of neonatal renal failure

Incidence of neonatal renal failure in our study was 34.7%.

Bansal SC et al[89] evaluated the clinical profile, identify associated and prognostic factors in new-borns with AKI. Total 1745 newborns were admitted, of which 74 babies had AKI. The incidence of AKI in their unit was 4.24 % during the study period.

Katariya KL et al[86]reported the incidence of AKI as 37.14%. **Katariya KL et al[86]**reported that Occurrence of AKI was observed to be significant in outborn neonates ($p < 0.05$). In this study, the incidence of AKI was higher in term newborns.

Aslam M et al[84]reported the incidence of AKI as 37.14% which is slightly higher than our study findings.

Aggarwal A et al[90] in his study reported the incidence of AKI in newborns to be 3.9 in 1000 live births and 34.5 in 1000 newborns admitted in the NICU. A Turkish study using criterion of serum creatinine >1.5 mg/dl showed an incidence of AKI as 3.4%.[91]

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. [92,93]

Most of the published studies, especially older, have used arbitrary definitions of AKI; one frequently used is absolute serum creatinine >1.5 mg/dl,[91,94,95] 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. [94]

AKI and gender

Proportion of male neonates with renal failure were 63.6% as compared to 72% without renal failure (p>0.05). Proportion of female neonates with renal failure were 36.4% as compared to 28% without renal failure (p>0.05). Predominance of male gender is observed in our study.

Bansal SC et al[89] in their study reported that male: female ratio of 1.69:1 was observed in the admissions during the study period (1096 males; 649 females). The female gender was less associated with AKI (28.9% v/s 47.3 %; p=0.032). They observed predominance of male newborns (n= 61; 82.4%) in the AKI group, in accordance with our study findings.

Katariya KL et al[86]reported that male to female ratio in current study was 2.46:1. Majority of neonates with AKI were out born 44 (84.6%). The incidence of AKI was higher in term new-borns.

Our findings of male predominance are consistent with previous study. [96]

Another recent NICU study although reported higher prevalence of AKI among females.[97]

Present study was in agreement with **Pradhan SK et al[98], and Gharenbhaghi MM et al[99]** who reported a male-female ratio of 2.03:1 and with **Airede A et al[100]**, with a male-female ratio of 3.3:1 in neonates with AKI.

Mode of delivery and renal failure

Mode of delivery in majority of the cases was normal vaginal delivery i.e. 38(58.4%) followed by 25(38.4%) with LSCS. 31.8% neonates with renal failure were born by

LSCS method as against 42.9% neonates without renal failure. This difference in the proportion of neonates with respect to mode of delivery was not found to be significant in our study. It means there was no association between incidence of renal failure with mode of delivery.

Bansal SC et al[89] in their study reported that out of 74 neonates, 20 were inborn, 61 were male and 52 were born through vaginal delivery.

AKI and birth weight

In our study, mean birth weight of the neonate having renal failure was 2.4±0.4 kg and that of normal women was 2.6±0.4 kg. When we compared the mean birth weight of the neonates between two groups, the difference was found to be non-significant (p>0.05). AKI is commonly observed in VLBW/ELBW new-borns in our study.

Bansal SC et al[89] reported that one baby out of 22 babies <1500 gm had AKI, 30 babies out of 84 babies between birth weights 1500 - <2500 gm had AKI, and 39 out of 59 babies with birth weight 2500 gm or more had AKI.

Various studies suggest that AKI is common in VLBW/ELBW newborns and is associated with poor prognosis.[101,102,103]

Koralkar et al[101] reported incidence of AKI using modified KDIGO criteria to be 18% amongst 229 VLBW infants. They also reported higher mortality in the AKI group (p-value <0.001).

Katariya KL et al[86]reported that occurrence of AKI increased with increasing gestational age (p <0.05). Mean weight of study was 2018 grams. Mean weight in AKI group was 2048 grams. In this study, only 4 VLBW neonates had AKI, while 18 neonates (34.61%) in weight band 1500-2500 developed AKI.

VishwanathanS et al[102] and Carmody JB et al[103] also reported similar findings.

A previous study from India showed that the percentage of babies with birth weight of <2500 gm in AKI group was higher than in healthy neonates.[104,105] 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.

Neonatal mortality

Out of 22 AKI neonates, 11 died accounting for mortality rate of 50% in in our study. **Bansal SC et al[89]** reported that out of those 74 neonates, 21(28.4%) were discharged, 38(51.3%) newborns went Discharge against Medical Advice (DAMA) and 15(20.3%) newborns died.

Risk factors for AKI

Prevalence of late preterm were 7.5% and term were 25.7% having AKI. PROM>48 hours (9.1%), MSAF (27.5%), prolonged labour (13.6%), breech (4.5%), difficult extraction (9.1%), PIH (9.1%) ,EOS (4.5%) , >1 risk factor (13.6%) were the risk factors for AKI identified in our study.

Less head circumference, high serum urea, creatine, serum sodium, potassium, low levels of SPO2, low APGAR score were the clinical factors for AKI identified in our study.

Bansal SC et al[89] in their study reported that AKI was more common in term babies (54.1% v/s 28.4 %; p=0.001), outborn babies (p=0.011) and low APGAR score at one minute and five minute Appropriate for Gestational Age (AGA) newborns had more chances of AKI than Small for Gestational Age (SGA)(53.7% v/s 28.9%; p=0.001).

Several previous studies have found birth asphyxia to be the most common cause of AKI of neonatal period.[91,106,107] Perinatal asphyxia is associated with acute tubular injury which is the most common cause of intrinsic AKI. Two recent studies reported

an association between asphyxia and AKI using modern definition for AKI.[108,109]**Selewski DT et al**[110] reported an incidence of 38% of AKI and **Kaur S et al**[111] reported 41.67%. The second study was conducted amongst neonates undergoing therapeutic hypothermia for perinatal asphyxia.

A recent study by **Esfandier N et al**[112] mentions hyaline membrane disease (HMD), using mechanical ventilation, the need to use surfactant, low Apgar score, high blood PCO2, high serum creatinine level, and low birth weight being related to mortality.

Aslam M et al[84]reported that the AKI group had prolonged labor more often than the non‑AKI group, and the difference was statistically significant ($P < 0.05$). In addition, the two groups did not differ significantly in terms of gestational age, low birth weight, and appropriate for gestational age (AGA)/small for gestational age (SGA)/large for gestational age. Antibiotic usage either in the mother during the last week or in the neonate was also not found to be significantly different between the two groups.

Aslam M et al[84]reported that the neonates in the two groups had a significantdifference in initial blood urea and creatininevalues at the time of admission. Contrary to theexpectation, the values were lower in asphyxiatedneonates with AKI, the difference being statisticallysignificant ($P < 0.05$). This signifies that an initialnormal blood urea/serum creatinine value cannotrule out AKI and underlines the important of serialmonitoring.

Summary and Conclusion

Summary

The present Descriptive observational study was conducted at NICU of Shri B. M. Patil Medical College, Hospital & Research Center, Vijayapur involving 65 babies admitted in NICU of Shri B. M. Patil Medical College, Hospital & Research Center, Vijayapur, with H/o No cry/Delayed cry or Apgar below 7 at 5 minutes. Both Inborn and Outborn late preterm and term babies will be included. The study was carried out with the objective to study late preterm and term neonates with Birth Asphyxia in terms of incidence of acute kidney injury and predictors of acute kidney injury.

The results of our study are summarised as follows:

- We included total 65 cases in our study. Of that 37(57%) were primigravida and 28(43%) were multigravida.
- 84.7% women were from lower SES and 15.3% were from middle SES
- 27.7% women have history of antenatal risk factors like GDM/HTN/Eclampsia.
- Mode of delivery in majority of the cases was normal vaginal delivery i.e. 38(58.4%) followed by 25(38.4%) with LSCS
- Mean age of the mother having neonatal renal failure was 22.7±2.0 years and that of normal women was 22.5±2.4 years. When we compared the mean age of the mothers between two groups, the difference was found to be non-significant ($p>0.05$)
- Prevalence of neonatal renal failure in our study was 22(34.37%). Out of 22, 15 i.e. 68.2% were born to primigravida and remaining 7 i.e. 31.8% were born to multigravida. There was no association between renal failure and parity of mother
- Proportion of neonates with renal failure from Lower SES were 77.3% and88.4% neonates without renal failure from same class. Proportion of neonates with renal

failure from middle SES were 22.7% as compared to 11.6% neonates without renal failure from same class. This difference in the proportion of neonates with respect to SES was found to be statistically not significant in our study. It means there was no association between prevalence of renal failure with SES.

- Proportion of renal failure with maternal antenatal history of GDM, PIH and eclampsia was 31.8% as compared to 25.6% non-renal failure cases with maternal antenatal history of GDM, PIH and eclampsia. This difference in the proportion of neonates with respect to antenatal maternal history of GDM, PIH and eclampsia was not found to be significant in our study. It means there was no association between prevalence of renal failure with maternal history of of GDM, PIH and eclampsia.
- 31.8% neonates with renal failure were born by LSCS method as against 41.9% neonates without renal failure. This difference in the proportion of neonates with respect to mode of delivery was not found to be significant in our study. It means there was no association between prevalence of renal failure with mode of delivery.
- Out of 22 neonates with renal failure, majority were from more than 24 hours age and 3-5 hrs age i.e. 27.3% each. This then followed by 18.2% from 1-2 hrs and 11-24 hrs each and 9.1% from 6-10 hrs.
- Out of 43 neonates without renal failure, majority were from 1-2 hrs with 28% followed by25.6% presented between 3-5 hrs age group followed by 18.6% from 6-10 hrs age, 16.2% from 11-24 hrs and 11.6% from more than 24 hrs age.
- Mean age of the neonate having renal failure was 18±19.9 hrs and that of normal women was 10.5±13.3 hrs. When we compared the mean age of the neonates between two groups, the difference was found to be non-significant ($p>0.05$)

- Mean birth weight of the neonate having renal failure was 2.4±0.4 kg and that of non renal failure neonate was 2.6±0.4 kg. When we compared the mean birth weight of the neonates between two groups, the difference was found to be non-significant ($p>0.05$)
- Mean length of the neonate having renal failure was 48.1±1.5 cm and that of non failure neonate was 48.8±1.4 cm. When we compared the mean length of the neonates between two groups, the difference was found to be non-significant ($p>0.05$)
- Mean head circumference of the neonate having renal failure was 31.6±0.8 cm and that of non failure neonate was 32.2±0.9 cm. When we compared the mean head circumference of the neonates between two groups, the difference was found to be statistically significant ($p<0.05$). It means head circumference was significantly less in the neonates with renal failure in our study.
- Mean HR of the neonate having renal failure was 159.1±12.7 per minute and that of non failure failure was 152.2±8.6 per minute. Mean RR of the neonate having renal failure was 43.9±6.7 per minute and that of non failure neonate was 54.8±7.5 per minute.
- Mean SPO2 of the neonate having renal failure was 95.6±2% and that of non failure neonate was 96.8± 0.8%. When we compared the mean HR, RR and SPo2 of the neonates between two groups, the difference was found to be statistically significant ($p<0.05$). It means HR was significantly higher in neonates with renal failure as well as RR and SPo2 was significantly less in neonates with renal failure in our study.
- Mean CRP in neonate having renal failure was 56.5±31.8 and that of non failure neonate was 33.4±13.7. Mean Sr. creatine in neonate having renal failure was

1.7±1.6 that of non failure neonate was 1.0±0.3. Mean sr potassium in neonate having renal failure was 4.7±0.8 that of non failure neonate was 4.3±0.7. Mean urine Na in neonate having renal failure was 54.9±20.3 that of non failure neonate was 33.2±17.7. Mean Fe Na in neonate having renal failure was 2.3±0.8 that of non failure neonate was 0.8±0.4. When we compared the mean CRP, Sr. creatine, sr potassium, urine Na, Fe Na of the neonates between two groups, the difference was found to be statistically significant ($p<0.05$). It means CRP, Sr. creatine, sr potassium, urine Na, Fe Na were significantly higher in neonates with renal failure as well as RR and SPo2 was significantly less in neonates with renal failure in our study.

- MSAF was seen in 27.5% neonates with renal failure and in 39.4% neonates without renal failure. LOC was seen in neonates with renal failure and in 4.5% and in 9.3% neonates without renal failure. Eclampsia was seen in neonates with renal failure in 4.50% and in 9.3% neonates without renal failure. PROM >48 was seen in neonates with renal failure and in 9.10% and in 6.9% neonates without renal failure. Prolong labor was seen in neonates with renal failure and in13.60% and in 4.6% neonates without renal failure. Abruption was seen in neonates with renal failure and in 0.00% and in 4.6% neonates without renal failure. GDM was seen in neonates with renal failure and in 0.00% and in 4.60% neonates without renal failure. APH was seen in neonates with renal failure and in 0.00% and in2.40% neonates without renal failure. Breech was seen in neonates with renal failure and in 4.50% and in 2.40% neonates without renal failure. Cord Prolapse was seen in neonates with renal failure and in0.00%and in 2.40% neonates without renal failure. Difficult extraction was seen in neonates with renal failure and in9.10% and in 2.40% neonates without renal failure. PIH was

seen in neonates with renal failure and in 9.10%and in 2.40% neonates without renal failure. hypothyroid was seen in neonates with renal failure and in 4.50% and in 0.00% neonates without renal failure. EOS was seen in neonates with renal failure and in 4.50% and in 0.00% neonates without renal failure. And >1 risk factor is seen in 13.6% neonates with renal failure and 9.3% in neonates without renal failure.

- Proportion of neonates with renal failure among late preterm were 22.7% as compared to 11.7% without renal failure. ($p>0.05$)
- Proportion of male neonates with renal failure were 63.6% as compared to 72% without renal failure. ($p>0.05$)
- Proportion of female neonates with renal failure were 36.4% as compared to 28% without renal failure. ($p>0.05$)
- Cyanosis was present in 77.3% neonates with renal failure and 26% without renal failure
- Activity was poor in 54.5% neonates with renal failure and 14% without renal failure
- CFT > 3 in 63.6% neonates with renal failure and 11.9% without renal failure
- Prevalence of shock was observed in 68.2% neonates with renal failure and 16.3% without renal failure where the difference in the prevalence was found to be statistically significant ($p<0.05$).
- CNS was poor in 50% neonates with renal failure and 11.7% without renal failure
- Urine output <1ml/kg/hr was seen in 77.3% neonates with renal failure and 9.4% without renal failure where the difference in the prevalence was found to be statistically significant ($p<0.05$).

- HIE grade III was seen in 54.5% neonates with renal failure and 4.7% without renal failure where the difference in the prevalence was found to be statistically significant ($p<0.05$).
- 81.8% neonates with renal failure were on ventilator as compared to 11.9% without renal failure
- 81.8% neonates with renal failure were given inotropes as compared to 21% without renal failure ($p<0.05$)
- Mortality rate was 50% in neonates with renal failure in our study.

CONCLUSION

Incidence of neonatal AKI in our study is **34.7%.**

From the present study, it can be inferred that it is difficult to predict AKI based on clinical features, oliguria, or Apgar score, and it is better to screen all the babies of birth asphyxia for AKI so that they can be detected early and managed accordingly. In addition, a single normal value of blood urea/serum creatinine cannot exclude AKI, and serial monitoring is important. Shock should be detected early and treated aggressively as shock is associated with advanced stages of AKI.

Episodesof AKI were generally transient and self-limiting and weremainly diagnosed by serum creatinine value ,urine output and FeNa ratio.

Among AKI cases, 90.9% neonatal AKI cases were referred from other centers at late stage of shock with >24hours of life at time of presentation time to NICU.So early diagnosis and management is required.And 50% mortality mostly from HIE stage 3 were observed and all are referred from other centers.

And non oliguric AKI was seen in 22.7% cases .

PROM>48 hours (9.1%), MSAF (27.5%), prolonged labour (13.6%), breech (4.5%), difficult extraction (9.1%), PIH (9.1%) and EOS (4.5%) were the risk factors for AKI identified in our study.

Less head circumference, high serum urea, creatine, serum sodium, potassium, low levels of SPO2, low APGAR score were the clinical factors for AKI identified in our study.

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B.L.D.E. (DEEMED TO BE UNIVERSITY)
(Declared vide notification No. F.9-37/2007-U.3 (A) Dated. 29-2-2008 of the MHRD, Government of India under Section 3 of the UGC Act, 1956)
The Constituent College
SHRI. B. M. PATIL MEDICAL COLLEGE, HOSPITAL AND RESEARCH CENTRE

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The ethical committee of this college met on 13-11-2019 at 3-15 pm to scrutinize the synopsis of Postgraduate students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected and revised version synopsis of the Thesis has been accorded Ethical Clearance

Title: Incidence and predictors of acute kidney injury in late preterm and term birth asphyxia neonates.

Name of PG student: Dr Pulapa Mounica, Department of Paediatrics

Name of Guide/Co-investigator: Dr S S Kalyanshettar Professor Department of Paediatrics

DR RAGHVENDRA KULKARNI
CHAIRMAN
Institutional Ethical Committee
BLDEU's Shri B.M. Patil
Medical College,BIJAPUR-586103

Following documents were placed before Ethical Committee for Scrutinization:

1. Copy of Synopsis / Research project
2. Copy of informed consent form
3. Any other relevant documents.

B.L.D.E.(Deemed to be University)
SHRI B.M.PATIL MEDICAL COLLEGE,VIJAYAPUR-586103
INSTITUTIONAL ETHICAL COMMITTEE

Date : 13-11-2019

1. Name of UG/PG Students/Researcher: Dr Pulapa Mounica
2. Department: Pediatrics
3. Title : Incidence and predictors of acute kidney injury in late preterm and term birth asphyxi neonates
4. Guide/Co-Guide/Principle Researcher:, Dr S S Kalyanshettar Professor
5. Date of Admission (PG Only) :

Observation :

- Elaborate Statistical analysis
- Revise and submit

I.E.C. Remarks : Ethical Clearance accorded/be Chairman after corrected revised version is submitted by stipulated time.
1. Any alternation in Synopsis protocol should be intimated to E.C. in writing for review & approval.
2. Any adverse effects to subject of the study should be intimated in writing to E.C.
3. If study is stopped or an included patient is out of study inform E.C. the same with reason.

Signature of the Committee Members :

1. Dr Raghavendra Kulkarni, Chairman
2. Dr Tejaswini Vallabha
3. Dr Akram Naikawadi
4. Dr P.B.Jaju
5. Dr Chandrashekhar Bhuyyar
6. Dr Pranesh Jahagirdar
7. Dr Manjunatha Aithala
8. Dr Satish Patil
9. Dr Mohammed Shannawaz

ANNEXURE VI

RESEARCH INFORMED CONSENT FORM

BLDE(DEEMED TO BE UNIVERSITY) Shri B.M.PATIL Medical College, Hospital & Research Centre, Vijayapur-586103.

TITLE OF THE PROJECT :" INCIDENCE AND PREDICTORS OF ACUTE KIDNEY INJURY IN LATE PRETERM AND TERM BIRTH ASPHYXIA NEONATES "

GUIDE : Dr.S.S.KALYANSHETTAR ,MD

PROFESSOR & HOD

DEPARTMENT OF PAEDIATRICS

PG STUDENT: DR.PULAPA MOUNICA

PURPOSE OF RESEARCH:

I have been informed that the present study will help in assessing the incidence of acute kidney injury and its predictors .

PROCEDURE:

I understand that after having obtained a detailed clinical history, thorough clinical examination and relevant investigations, a final follow up of the birth asphyxia neonate and its outcome is planned. **RISK AND DISCOMFORTS:**

None

BENEFITS:

I understand that my participation in the study will have no direct benefit to me other than the potential benefit of the research and education.

CONFIDENTIALITY:

I understand that the medical information produced by this study will become a part of hospital records and will be subject to the confidentiality. Information of sensitive personal nature will not be part of the medical record, but will be stored in the investigations research file.

If the data are used for publication in the medical literature or for teaching purpose, no name will be used and other identifiers such as photographs will be used only with special written permission. I understand that I may see the photograph before giving the permission.

REQUEST FOR MORE INFORMATION:

I understand that I may ask more questions about the study at any time; Dr.PulapaMounica at the department of Paediatrics is available to answer my questions or concerns. I understand that I will be informed of any significant new findings discovered during the course of the study, which might influence my continued participation. A copy of this consent form will be given to me to keep for careful reading.

REFUSAL FOR WITHDRAWAL OF PARTICIPATION:

I understand that my participation is voluntary and that I may refuse to participate or may withdraw consent and discontinue participation in the study at any time without prejudice. I also understand that **Dr. S.S.KALYANSHETTAR** may terminate my participation in the study after he has explained the reasons for doing so.

INJURY STATEMENT:

I understand that in the unlikely event of injury to my baby resulting directly from baby's participation in this study, if such injury were reported promptly, the appropriate treatment would be available to the baby. But, no further compensation would be provided by the

hospital. I understand that by my agreements to participate in this study and not waiving any of my legal rights.

I have explained to _____the purpose of the research, the procedures required and the possible risks to the best of my ability.

_____ _____

Dr. PULAPA MOUNICA Date

(Investigator)

PARENTS / GUARDIAN CONSENT STATEMENT:

We confirm that Dr. PULAPA MOUNICA is doing a study on "INCIDENCE AND PREDICTORS OF ACUTE KIDNEY INJURY IN LATE PRETRM AND TERM BIRTH ASPHYXIA NEONATES" Dr.PulapaMounica, has explained to us the purpose of research and the study procedure. We are willing to give as much as information required for the study and consent for investigations and the possible discomforts as well as benefits. We have been explained all the above in detail in our ownlanguage and we understand the same. Therefore we agree to give consent for baby's participate as a subject in this research project.

_____ _____

(Parents / Guardian) Date

_____ _____

(Witness to signature) Date

ANNEXURE- VII

PROFORMA

1.MATERNAL HISTORY

Name: B/o IP No:

Age DOA

Parity DOD

2.ANTENATAL HISTORY :

3.BIRTH HISTORY :

M.O.D

If LSCS :emergency /elective Indication

APGAR : 1min 5min

Mode of resuscitation

Risk factors

4.NEONATE :

Gestational age

Sex

Age in hours

Birth weight

Length

Head circumference

Cry Colour Activity

5.VITALS :

HR :RR : CFT : SPO2

SHOCK :present /absent

6.HEAD TO TOE EXAMIANTION :

Head AF Face

Ears

Nose oral cavity neck

Spine

Orifice count

Any obvious congenital anomalies or dysmorphic features :

7.SYSTEMIC EXAMINATION :

CVS

RS

P/A

CNS

8.URINE OUTPUT :

9.MECONIUM :

10.DIAGNOSIS :

11.INVESTIGATIONS :

CRP

GRBS

BLOOD UREA

SERUM CREATININE

SERUM ELECTROLYTES

Na :

K :

Ca :

URINARY EXCRETION OF SODIUM

URINE EXCRETION CREATININE

FRACTIONAL EXCRETION OF SODIUM

12.TREATMENT :

IVF type and dose

Antibiotics

Anti convulsants

Transfusion :

Outcome :

Type of renal injury if present :

NAME : DR.S.S.KALYANSHETTAR

DOB : 17-01-1974

EDUCATION : MBBS, MD(PEDIATRICS)

KMC REGISTRATION NUMBER : 45576

WORK EXPERIENCE : 15 years

MEMBERSHIP : INDIAN ACADEMY OF PEDIATRICS

PRESENTLY WORKING AS : PROFESSOR

DEPARTMENTOF PEDIATRICS

SHRI B M PATIL MEDICAL COLLEGE HOSPITAL

VIJAYAPUR – 586103

INVESTIGATOR BIODATA

NAME :Dr. PULAPA MOUNICA

QUALIFICATION : MBBS

NRI MEDICAL COLLEGE AND HOSPITAL

MANGALAGIRI ANDHRA PRADESH.

REGISTRATION NO :

KMC:ANP 2019 0001623 KTK

ADDRESS FORCORRESPONDANCE :

DEPARTMENT OF PEDIATRICS

SHRI B M PATIL MEDICAL COLLEGE HOSPITAL,

VIJAYAPUR – 586103.

Name	IP NO	Phone	Age	DOA	Parity	DOD	Socioeconomic status	Antenatal history	MOD	Place	LSCS eme	LSCS ele	APGAR 1	APGAR 5	MOR	Risk factor	Gest age	sex	age in hrs
B/O Basamma	2193	9980941947	24	9/1/2020	G2P1L1		low	G2P1L1 ,41+3 ,PIH	NVD	outside	_	_	_	_	embu	MSAF ,LOC	41+3	male	8hrs
B/O Pooja	1806	9284339580	20	9/1/2020	Primi		low	Primi , 39 wks	NVD	outside	_	_	_	_	embu	MSAF	39	male	46hrs
B/O Jyothi pujari	2966	22114433	23	9/3/2020	primi		low	primi , term	NVD	outside	_	_	_	_	embu	2 LOC	term	male	4hrs
B/O Sangeetha	2768	7496378072	26	9/2/2020	primi		low	primi , term	NVD	outside	_	_	_	_	embu	MSAF	term	male	3hrs
B/O Gayatri Patil	18847	9980450575	24	8/15/2020	primi mother		low	primi ,term	NVD	outside	_	_	_	_	intubated	PROM>48	term	male	48hrs
B/O Manjuladevi	18674	9449741631	23	8/12/2020	G8P7L7		low	G8P7L7 ,term	NVD	outside	_	_	_	_	embu	Cord Prolapse	term	male	3hrs
B/O Renuka S	4232	9632397832	24	9/8/2020	primi		middle	primi ,term	NVD	outside	_	_	_	_	?	prolong labor	term	male	90hrs
B/O Surendra	4497	9732490216	23	9/9/2020	primi		low	primi,term	LSCS	outside	yes	_	_	_	intubated	MSAF	term	female	16hrs
B/O Jabeena	18729	9449756956	24	8/13/2020	primi		low	primi,term	NVD	outside	_	_	_	_	intubated	MSAF	term	male	13hrs
B/O Rekha Rathod	18645	8105180262	24	8/12/2020	primi		low	primi,term	NVD	outside	_	_	_	_	embu	LOC	term	male	10hrs
B/O Pooja	18458	9900458614	24	8/10/2020	primi		low	primi,term	NVD	outside	_	_	_	_	intubated	prom>48	term	male	48hrs
B/O Asma	18444	740381312	26	8/9/2020	G2P1L1		low	G2P1L1,35+4	LSCS	outside	yes	_	_	_	intubated	MSAF	late pre	male	20hrs
B/O Chetra	26039	9611855363	23	12/11/2020	G3		low	G3P1L1A1,term	NVD	outside	_	_	_	_	intubated	hypothyroid	term	male	52hrs
B/O Ashwini	15689	9465277024	27	11/4/2020	G4P3L3		low	G4P3L3,term,	LSCS	outside	yes	_	_	_	_	APH	term	male	5hrs
B/O laksmi	15701	7877078944	24	11/2/2020	primi		low	primi,term	LSCS	outside	yes	_	_	_	_	obstructed labor	term	male	4hrs
B/O Sharada	15129	9949624252	23	10/30/2020	G3P2L2		low	G3P2L2,35+5	LSCS	outside	yes	_	_	_	_	LOC,MSAF	late pre	male	12hrs
B/O Asma	14788	8152847540	20	27-102020	G2P1A1		low	G2P1A1,term	NVD	outside				_	intubated	2nd stage prolong	term	male	5hrs
B/O Kutumbi	12820	8660546264	24	10/17/2020	Primi		low	primi,term,breech	NVD	BLDE			apgar 5	7	embu	Breech	term	female	1hr
B/O Savitri	12675		21	10/16/2020	Primi		middle	primi,term	NVD	outside	_	_	_	_	intubated	MSAF	term	male	49HRS
B/O Sangeetha	12253		20	10/14/2020	Primi		low	primi,term	LSCS	outside	yes	_	_	_	_	PROM >48	term	male	59hrs
B/O Manjula	149101	8971593112	26	3/20/2021	Primi		middle	primi,term	NVD	outside	_	_	_	_	embu	MSAF	term	male	18hrs
B/O Akshata	124113		21	2/20/2021	Primi		low	primi,term	NVD	outside	_	_	_	_	_	MSAF	term	male	4hrs
B/O Gurubai		9342562520	22		G2P1L1		middle	G2P1L1 ,Term	LSCS	outside	yes	_	_	_	embu	prolong labor	term	male	2hrs
B/O shilpa	49648	9632891912	24	1/9/2021	primi		low	primi,LP,eclampsia	LSCS	outside	yes	_	_	_	intubated	prolong labor	late pre	male	18hrs
B/O surramdevi T2	46560	8722054842	24	1/7/2021	G2P3L1		middle	G2P3L1,Twin,PIH,35+5	LSCS	outside	yes	_	_	_	intubated	Difficult extraction	late pre	male	2hrs
B/O Surramdevi T1	46564	8722054842	24	1/7/2021	G2P3L1		middle	G2P3L1,Twin,PIH,35+5	LSCS	outside	yes	_	_	_	intubated	Difficult extraction	late pre	female	2hrs
B/O Padmasree	42421	9144256129 5	19	1/11/2021	G2P1L1		low	G2P1L1,term	NVD	outside				_		MSAF	term	female	2hrs
B/O Sumitra	35946	8162541360	19	1/6/2021	G2P1L1		middle	G2P1L1,term	NVD	outside				_		MSAF	term	female	2 hr
B/O Mahadevi	43702	9146251421	22	1/6/2021	Primi		middle	primi,term,eclampsia	LSCS	BLDE	yes	_	4	5	intubated	MSAF	term	male	1hr
B/O Rameeza	42430	9845281811	20	1/4/2021	G2P1L1		middle	G2P1L1,LP	NVD	outside	_	_	_	_	_	_	36	male	4Hrs
B/O Shanta	40675	8971021870	20	1/3/2021	G2P1L1		low	G2P1L1,term	NVD	BLDE	_	_	6	7	embu	_	term	female	1hr
B/O Jyothi	43825		21	1/6/2021	primi		low	primi,term,polyhydramnios	NVD	BLDE	_	_	5	6	embu	MSAF	term	male	1HR
B/O Asma	28006		19	12/19/2021	Primi		low	primi,term	NVD	outside	_	_	_	_	intubated	MSAF	term	female	13hrs
B/O Renuka c	28832		20	12/22/2020	Primi		low	primi,term,eclampsia	LSCS	BLDE	yes	_	5	7	embu	Eclampsia	term	male	1hr
B/O Devamma	28618	8462174132	20	12/17/2020	Primi		low	primi,term,eclampsia	LSCS	outside	yes	_	_	_	_	Eclampsia	term	male	26hr
B/O Neelamma	27626	9146261519	21	12/17/2020	G2P1D1		low	G2P1D1,term	NVD	BLDE	_	_	3	4	intubated	MSAF	term	female	1hr
B/O Sangeetha	26385	6465034621	19	12/8/2020	Primi		low	primi,term	LSCS	outside	yes	_	_	_	_	PROM>48	term	male	3hrs
B/O Mahanandа	28627	8197348287	21	12/20/2020	Primi		low	primi,term	NVD	outside				_	intubated	LOC	term	male	4hrs
B/O Bhimmavva	20658	8125163421	19	12/20/2020	G2P1L1		low	G2P1L1,term,PIH	NVD	outside	_	_	_	_	embu	PROM>48	term	male	8hrs
B/O Vijayalakxmi	18787	9648523351	22	12/8/2020	Primi		low	primi,term	LSCS	outside			_	_	embu	GDM	term	female	8hrs
B/O Basamma	24984	9902334925	24	12/8/2020	G2P1L1		low	G2P1L1,term	VBAC	outside	_	_	_	_	embu	_	term	female	6hrs
B/O Veena	24612	9480634442	22	12/6/2020	Primi		low	primi,term,pih	VBAC	BLDE	_	_	6	7	embu	PIH	term	male	1hr
B/O Anitha	24541	8197862512	25	12/6/2020	G3P2L2		low	G3P2L2,term	NVD	BLDE			5	6	embu	Abruption	term	female	1hr
B/O Ashwini	24520	9164821552	23	12/5/2020	primi,term		low	primi,term,eclampsia	LSCS	BLDE	yes	_	6	7	embu	Eclampsia,MSAF	term	male	1hr
B/O Asha	24632	9663299756	24	12/7/2020	primi		low	primi,term	LSCS	outside	yes	_	_	_	_	LOC ,MSAF	term	female	7hr
B/O Chandrakala	23371	9900343439	26	11/23/2020	G2P1L1		low	G2P1L1,term	LSCS	outside	_	_	_	_	embu	MSAF	term	female	8hrs
B/O Manjula	24035	8762887498	24	12/4/2020	G2P1L1		low	G2P1L1,term	NVD	outside	_	_	_	_	_	MSAF	term	female	8hrs
B/O Yamanewwa	15151	772994190	26	10/20/2020	primi		low	primi,term	LSCS	outside	yes	_	_	_	_	Difficult extraction	term	male	10hrs
B/o Nagamma	18717	8251265192	23	10/13/2020	primi		low	primi,term	NVD	outside	_	_	_	_	intubated	LOC	term	male	46hrs
B/O laxhmi pujari	17128	9611254713	23	11/6/2020	G3P2L2		low	G3P2L2,term	NVD	outside	_	_	_	_	_	LOC ,MSAF	term	male	26hr
B/O Parvati	16968	9591084813	27	11/5/2020	G3P2L2		low	G3P2L2,term,breech	NVD	outside	_	_	_	_	_	Breech	term	male	4hrs
B/O Annapurna	16990	7892942517	23	11/6/2020	G2P1L1		low	G2P1L1,term,GDM	LSCS	outside	yes	_	_	_	_	GDM,obstructed labor	term	male	4hrs
B/O Vijayalakxmi	19032	9623001628	24	8/19/2020	G3P2L2		low	G3P2L2,LP	NVD	outside			_	_	embu	_	late pre	female	2hrs
B/O Karishma	18985	9307456956	23	8/18/2020	primi		low	primi,LP,PIH	NVD	outside	_	_	_	_	intubated	PIH	late pre	female	3hrs
B/O Poojа ch	19110	7760130160	24	8/20/2020	primi		low	primi,term	NVD	outside	_	_	_	_	embu	MSAF	term	male	3hrs
B/O Bouramma	19187	8861164199	24	8/22/2020	primi		low	primi,term,eclampsia	LSCS	outside	yes	_	_	_	embu	Eclampsia	term	male	6hrs
B/O Sana	154038	9491567324	23	1/12/2021	primi		low	primi,term,	NVD	outside	_	_	_	_	intubated	prolong labor	term	male	11hrs
B/O Jayasree	18230	8125692341	24	7/9/2020	G2P1L1		low	G2P1L1,late preterm,PIH	LSCS	outside	yes	_	_	_	embu	PIH	late pre	female	5hrs
B/O aishwarya	18505	6261568345	24	7/12/2020	G2P1D1		low	G2P1D1 ,term,female	NVD	outside	_	_	_	_	embu	MSAF	term	female	14hrs
B/O shilpa	49648	9632891912	20	1/9/2021	primi		low	primi,late preterm on venti	LSCS	outside	yes	_	_	_	intubated	eclampsia	late pre	male	24hr
B/O Kurshibanu	18326	8123811348	19	8/9/2020	G3P2L2		low	G3P2L2,term	LSCS	outside	yes	_	_	_	embu	MSAF	term	male	16hrs
B/O Bouramma	19187	8861161199		1/20/1900	primi		low	primi,term	LSCS	outside	yes	_	_	_	embu	eclampsia	term	female	4hrs
B/O laxmi k	2020-583	9945766996	20	9/3/2020	primi		low	primi,term	NVD	outside			_	_	intubated	EOS	term	male	DOL 4
B/O Asha	24632	9663299756	19	12/7/2020	primi		low	primi,term	NVD	outside	_	_	_	_	intubated	MSAF	term	female	46hrs
B/O Padmasree	234678	9876354267	19	12/7/2020	multi		middle	G3p2l2,term	NVD	BLDE			5	6	embu	nil	term	male	1

Bwt	length	HC	cry	color	activity	HR	RR	CFT	SpO2	Shock yes	Shock no	head to toe	CVS	RS	P/A	CNS	Urine	Meconium	Diagnosis	CRP
2.3	47	32.5	weak	pink	fair	146	52	<3	97	_	no	Normal	SI\S2 +	B/LAE	Soft	c/T/A fair	P (1.2ml/kg/hr)	P	T/A/M/HIE2/3	89
2.5	49	32	weak	pink	fair	140	50	<3	98	_	no	Normal	SI\S2 +	B/LAE	Soft	c/T/A fair	P (1.4ml/kg/hr)	P	T/A/M/HIE2/3	23
2.7	49	32.5	weak	pink	fair	150	52	<3	98	_	no	Normal	SI\S2 +	B/LAE	Soft	c/T/A fair	P (1.8ml/kg/hr)	P	T/A/M/HIE1/2	9.9
2.7	48	32	weak	pink	fair	152	54	<3	97	_	no	Normal	SI\S2 +	B/LAE	Soft	c/T/A fair	P (1ml/kg/hr)	P	T/A/M/HIE1/2	23
2.5	50	32	_	cyanosis	poor	140	50	>3	96	yes	_	AF bulged	SI\S2 +	B/LAE	Soft	T/A poor	P (0.4ml/kg/hr)	P	T/A/M/HIE3/subdural hematoma	37
3.5	49	32	weak	pink	fair	150	54	<3	97	_	no	Normal	SI\S2 +	B/LAE	Soft	c/T/A fair	P(1.8ml/kg/hr)	P	T/A/M/HIE2/3	24
2.7	49	32	poor	cyanosis	poor	160	40	>3	95	yes	_	Normal	SI\S2 +	B/LAE	Soft	T/A poor	P(0.8ml/kg/hr)	P	T/A/M/HIE3/MAS/Cerebraledema	16.9
2.4	49	32.5	_	cyanosis	fair	150	40	>3	97	yes	_	Normal	SI\S2 +	B/LAE	Soft	T/A poor	P(1.3ml/kg/hr)	P	T/A/F/HIE2/3/MAS	11
2.4	48	31	_	cyanosis	fair	146	40	>3	97	yes	_	Normal	SI\S2 +	B/LAE	Soft	T/A poor	P(<1ml/kg/hr)	P	T/A/M/HIE2/3/MAS	16
2	46	31.5	weak	cyanosis	fair	170	60	>3	97	yes	_	Normal	SI\S2 +	B/LAE	Soft	T/A fair	P(<1ml/kg/hr)	P	T/A/M/HIE2	64
2.6	50	32	_	cyanosis	poor	170	40	>3	97	yes	_	Normal	SI\S2 +	B/LAE	Soft	T/A fair	P(<1ml/kg/hr)	P	T/A/M/HIE3/EOS/DIC/MAS	>90
2.2	47	32	_	cyanosis	poor	175	40	>3	97	yes	_	Normal	SI\S2 +	B/LAE	Soft	T/A poor	P(<1ml/kg/hr)	P	LP/A/M/HIE3/MAS	18
2.6	48.5	32.5	_	cyanosis	fair	170	40	>3	97	yes	_	Normal	SI\S2 +	B/LAE	Soft	T/A fair	P(<1ml/kg/hr)	P	T/A/M/HIE2/MAS	60
2.4	49	32	weak	pink	fair	160	50	<3	97	_	no	Normal	SI\S2 +	B/LAE	Soft	T/A fair	P(1.6ml/kg/hr)	P	T/A/M/HIE1/2	5
2.2	47	32	weak	pink	fair	146	60	<3	96	_	no	Normal	SI\S2 +	B/LAE	Soft	T/A fair	P(1.7ml/kg/hr)	P	T/A/M/HIE1/2	11.8
2.4	49	32	weak	pink	fair	156	50	<3	97	_	no	Normal	SI\S2 +	B/LAE	Soft	T/A fair	P(2ml/kg/hr)	P	LP/A/M/HIE2	7.6
3.3	50	32.5	weak	cyanosis	fair	153	40	>3	97	yes	_	Normal	SI\S2 +	B/LAE	Soft	T/A fair	p(<1ml/kg/hr)	P	T/A/M/HIE2/3/MAS/SEPSIS	37.8
2.6	49	32	weak	pink	fair	146	55	<3	97	_	no	Normal	SI\S2 +	B/LAE	Soft	T/A fair	P(<1ml/kg/hr)	P	T/A/F/HIE2	75.7
2.6	49	32	_	cyanosis	poor	160	40	>3	90	yes	_	Normal	SI\S2 +	B/LAE	Soft	T/A poor	P(<1ml/kg/hr)	P	T/A/M/HIE3/Severe MAS	90
2.4	47	33	fair	pink	fair	156	52	<3	97	_	no	Normal	SI\S2 +	B/LAE	Soft	T/A fair	P(2.2ml/kg/day)	P	T/A/M/HIE2/3/EOS	20
2.9	47	31	weak	pink	fair	140	55	<3	97	_	no	Normal	SI\S2 +	B/LAE	Soft	T/A fair	P(2ml/kg/hr)	P	T/A/M/HIE2/MAS	7.2
2.6	49	32	weak	pink	fair	146	52	<3	97	_	no	Normal	SI\S2 +	B/LAE	Soft	T/A fair	P(1.9ml/kg/hr)	P	T/A/M/HIE1/2	5
2.7	48	32	weak	pink	fair	150	56	<3	96	_	no	Normal	SI\S2 +	B/LAE	Soft	T/A fair	P (2.8ml/kg/hr)	P	T/A/M/HIE1/2	13.9
1.8	48	32	_	cyanosis	poor	160	40	3	97	yes	_	Normal	SI\S2 +	B/LAE	Soft	T/A poor	P(1.7ml/kg/hr)	P	LP/S/M/HIE3	8.4
2	47	32	_	cyanosis	poor	156	40	<3	96	_	NO	Normal	SI\S2 +	B/LAE	Soft	T/A poor	P(1ml/kg/hr)	P	LP/A/M/HIE3/Severe MAS	37.6
1.9	47	31	_	cyanosis	poor	156	40	<3	96	_	NO	Normal	SI\S2 +	B/LAE	Soft	T/A poor	P(>1ml/kg/hr)	P	LP/A/F/HIE3/severe MAS	31
2.4	49	32	fair	pink	fair	140	50	<3	97	_	no	Normal	SI\S2 +	B/LAE	Soft	T/A fair	P(2.7ml/kg/hr)	P	T/A/F/HIE1	37.4
2.6	48	31	fair	pink	fair	160	52	<3	96	_	no	Normal	SI\S2 +	B/LAE	Soft	T/A fair	P(2.4ml/kg/hr)	P	T/A/M/HIE1/MAS	29.3
2.5	48	32	_	cyanosis	poor	160	40	>3	97	yes	_	Normal	SI\S2 +	B/LAE	Soft	T/A poor	P(<1ml/kg/hr)	P	T/A/M/HIE2/3/MAS	15.2
2.4	48	32	weak	pink	fair	158	60	<3	97	_	no	Normal	SI\S2 +	B/LAE	Soft	T/A fair	P(2ml/kg/hr)	P	LP/A/M/HIE2	6.3
2.3	49	32	weak	cyanosis	poor	140	54	<3	97	_	no	Normal	SI\S2 +	B/LAE	Soft	T/A fair	P(2.2ml/kg/day)	P	T/A/F/HIE2	41
3	48	32	weak	cyanosis	fair	146	49	<3	98	_	no	Normal	SI\S2 +	B/LAE	Soft	T/A fair	P(1.9ml/kg/hr)	P	T/A/M/HIE1/2/	5
2.5	49	31	_	cyanosis	fair	170	40	>3	92	yes	_	Normal	SI\S2 +	B/LAE	Soft	T/A fair	P(<1ml/kg/hr)	P	T/A/F/HIE3/MAS/Severe PAH	5
1.9	49	32	weak	cyanosis	poor	146	60	<3	97	_	no	Normal	SI\S2 +	B/LAE	Soft	T/A poor	P(2.1ml/kg/hr)	P	T/S/M/HIE1/2	9.5
2.6	51	32	weak	pink	poor	152	64	<3	96	_	no	Normal	SI\S2 +	B/LAE	Soft	T/A poor	P(2.1ml/kg/hr)	P	T/A/M/HIE2/3	9
2.9	47	33	_	cyanosis	poor	136	40	>3	94	yes	_	Normal	SI\S2 +	B/LAE	Soft	T/A poor	P(1.6ml/kg/hr)	P	T/A/F/HIE3	9.3
2.5	50	32	weak	pink	fair	150	52	<3	97	_	no	Normal	SI\S2 +	B/LAE	Soft	T/A fair	P(2.4ml/kg/hr)	P	T/A/M/HIE1/EOS	50
1.6	44	30	_	cyanosis	fair	170	40	<3	94	_	no	Normal	SI\S2 +	B/LAE	Soft	T/A fair	P(>1ml/kg/hr)	P	T/S/M/HIE3/PPHN	5
2.2	49	33	weak	pink	fair	136	60	<3	96	_	no	Normal	SI\S2 +	B/LAE	Soft	T/A fair	P(2.1ml/kg/hr)	P	T/A/M/HIE1/2	9.2
3.2	53	34	weak	pink	fair	160	62	<3	94	_	no	Normal	SI\S2 +	B/LAE	Soft	T/A fair	P(1ml/kg/hr)	P	T/A/F/HIE2	6.2
2.9	51	32	fair	pink	fair	164	64	<3	96	_	no	Normal	SI\S2 +	B/LAE	Soft	T/A fair	P(2ml/kg/hr)	P	T/A/F/HIE1/2	18
2.7	49	34	fair	pink	fair	164	69	<3	97	_	no	Normal	SI\S2 +	B/LAE	Soft	T/A fair	P(1.2ml/kg/hr)	P	T/A/M/HIE1/2/Moderate MAS	12
2.5	51	32	fair	cyanosis	fair	150	62	<3	97	_	no	Normal	SI\S2 +	B/LAE	Soft	T/A fair	P(1.9ml/kg/hr)	P	T/A/F/HIE1/2	5.7
2.8	49	32	fair	cyanosis	fair	160	69	3	97	yes	_	Normal	SI\S2 +	B/LAE	Soft	T/A fair	P(1.7ml/kg/hr)	P	T/A/M/HIE1/2/MAS	30.4
2.8	50	32	weak	pink	fair	136	53	3	97	yes	_	Normal	SI\S2 +	B/LAE	Soft	T/A fair	P(1.4ml/kg/hr)	P	T/A/F/HIE3/MAS	15
2.4	47	32	weak	pink	fair	146	56	<3	97	_	no	Normal	SI\S2 +	B/LAE	Soft	T/A fair	P(>1ml/kg/hr)	P	T/A/F/HIE1/2 /BL CTEV	5
2.5	48	32	weak	pink	fair	153	54	<3	97	_	no	Normal	SI\S2 +	B/LAE	Soft	T/A fair	P(>1ml/kg/hr)	P	T/A/F/HIE2/3/MAS	5
2.9	49	32	weak	pink	fair	160	55	<3	97	_	no	Normal	SI\S2 +	B/LAE	Soft	T/A fair	P(>1ml/kg/hr)	P	T/A/M/HIE2/3	90
3	50	32	_	cyanosis	fair	160	40	>3	97	yes	_	Normal	SI\S2 +	B/LAE	Soft	T/A fair	P(1.4ml/kg/hr)	P	T/A/M/HIE2/3	12.6
3	50	33	weak	pink	fair	146	59	<3	97	_	no	Normal	SI\S2 +	B/LAE	Soft	T/A fair	P(>1ml/kg/hr)	P	T/A/M/HIE2/3	12.4
3.1	50	33	weak	pink	fair	150	50	<3	97	_	no	Normal	SI\S2 +	B/LAE	Soft	T/A fair	P(1.4ml/kg/hr)	P	T/A/M/HIE2	14.7
3.6	52	34	weak	pink	fair	138	59	<3	97	_	no	Normal	SI\S2 +	B/LAE	Soft	T/A fair	P(1ml/kg/hr)	P	T/A/M/HIE2/3/IDM	27
2.1	48	33	weak	cyanosis	fair	164	64	>3	97	yes	_	Normal	SI\S2 +	B/LAE	Soft	T/A fair	P(>1ml/kg/hr)	P	LP/A/F/HIE1/2	5
1.9	46	32	_	cyanosis	poor	160	40	>3	97	yes	_	Normal	SI\S2 +	B/LAE	Soft	T/A fair	P(1.3ml/kg/hr)	P	LP/A/F/HIE2/3	12
2.4	48	32	weak	pink	poor	150	64	<3	97	_	no	Normal	SI\S2 +	B/LAE	Soft	T/A fair	P(>1ml/kg/hr)	P	T/A/M/HIE2/MAS	65
3	49	33	weak	pink	fair	160	56	<3	97	_	no	Normal	SI\S2 +	B/LAE	Soft	T/A fair	P(1.5ml/kg/hr)	P	T/A/M/HIE2/3	35
2.6	49	32	_	pink	poor	150	40	>3	95	yes	_	Normal	SI\S2 +	B/LAE	Soft	T/A poor	P(<1ml/kg/hr)	P	T/A/M/HIE2/3	26.2
2.3	47	30	fair	pink	fair	157	58	<3	97	_	no	Normal	SI\S2 +	B/LAE	Soft	T/A fair	P(<1ml/kg/hr)	P	LP/A/F/HIE1/2	28
2.5	48	31	fair	pink	fair	160	57	<3	97	_	no	Normal	SI\S2 +	B/LAE	Soft	T/A fair	P(>1ml/kg/hr)	P	T/A/F/HIE1/2	66
2.4	47	30	_	pink	fair	158	40	<3	97	_	no	Normal	SI\S2 +	B/LAE	Soft	T/A fair	P(>1ml/kg/hr)	P	LP/A/M/HIE1/2	8.4
2.6	48	30	fair	pink	fair	160	57	<3	97	_	no	Normal	SI\S2 +	B/LAE	Soft	T/A fair	P(>1ml/kg/hr)	P	T/A/M/HIE2/3	15
2.5	47	30	fair	cyanosis	fair	156	58	<3	97	_	no	Normal	SI\S2 +	B/LAE	Soft	T/A fair	P(<1ml/kg/hr)	P	T/A/F/HIE2/3	35
2.5	48	31	_	cyanosis	poor	179	40	>3	92	yes	_	Normal	SI\S2 +	B/LAE	Soft	T/A poor	P(<0.5ml/kg/hr)	P	T/A/M/HIE3/Shock	25.7
2.6	48	31	_	cyanosis	poor	185	40	>3	94	yes	_	Normal	SI\S2 +	B/LAE	Soft	T/A poor	P(<1ml/kg/hr)	P	T/A/F/HIE3/B/L cerebral edema	15
2.5	49	32	fair	pink	fair	136	54	<3	97	_	no	Normal	SI\S2 +	B/LAE	Soft	T/A fair	P(>1ml/kg/hr)	p	T/A/M/HIE1	8

GRBS	UREA	SR.CREAT	SR.Na	SR.K	Sr.Cal	Ur.Na	Ur.Creat	FeNa	ECHO	IVF ,volume	Antibiotic	Anti convulsant	O2 support	Inotropes	Transfusion	Outcome	TYPE
80	70	1.5	136	3.6	8.3	50	25	2.1	large PDA	100-->EP	piptaz ,meropenam	gradinal	hood	nil	nil	Improved	RENAL
80	40	1	132	5.2	8.6	28	15	1.4	_	EP	Piptaz	gardinal	hood	nil	nil	Improved	
82	25	1	141	4.4	8.8	50	40	0.9	ASD	100-->EP	piptaz	nil	hood	nil	nil	Improved	
74	38	0.6	141	4.1	9	45	20	0.9	ASD	100-->EP	piptaz	nil	hood	nil	nil	Improved	
82	68	1.7	150	5	9.3	65	21	2.6	_	EP	piptaz ,meropenam	gardinal	ventilator	adrenaline	FFP ,WB	death	RENAL
90	50	0.9	138	4.5	7.5	68	29.5	1.5	Mod PAH	100-->EP	piptaz,amikacin	gardinal	HFNC	nil	nil	Improved	
120	100	1.4	147	6	8.4	19.3	10	1.6	_	EP	Mero ,vanco	levera gardinal	ventilator	adrenaline	nil	AMA	RENAL
96	50	1.2	132	3.3	8.3	12.2	45	0.3	_	100-->EP	piptaz	gardinal	HFNC	dopamine	nil	Improved	
69	32	2	130	5	8	70	25	4	_	100-->EP	piptaz	levera gardinal	ventilator	adrenal dopamine	nil	death	RENAL
82	36	1.2	138	3.4	9.1	30	30	0.9	_	100-->EP	piptaz ,meropenam	gardinal	hood	dopamine	nil	Improved	
74	59	1.2	142	4.3	8.2	75	39.5	1.6	Severe PAH,PDA 2	EP	piptaz ,meropenam	gardinal	ventilator	adrenaline	FFP	death	RENAL
86	52	0.7	141	4.7	7	60	9.9	3	Severe PAH	EP	PIPTAZ	gardinal	ventilator	adrenaline	nil	DEATH	RENAL
76	50	1.2	141	4	9	80	28	2.4	PDA,ASD,PAH	EP	piptaz ,meropenam	gardinal	ventilator	adrenaline ,sildenafil	nil	Improved	RENAL
80	35	1	144	3.5	8.6	36	40	0.6	_	100-->EP	piptaz	nil	hood	nil	nil	Improved	
90	35	1	145	4.4	7.6	24	41.4	0.5	_	100-->EP	Piptaz	nil	hood	nil	nil	Improved	
84	30	1	135	5.2	8.4	12	30.8	0.3	_	100-->EP	piptaz	gardinal	hood	nil	nil	Improved	
140	70	2.5	141	3.6	8.2	46	44.5	1.8	PDA,PAH,EF 55	100-->EP	Mero ,vanco	gardinal	ventilator	adrenaline dopamine	nil	AMA	RENAL
96	65	2	135	5.2	8.2	30	57.3	0.7	_	100-->EP	piptaz ,meropenam	nil	hood	nil	nil	Improved	PRERENAL
82	170	8.7	139	4.3	6	40	67.5	3.7	PDA,PAH	EP	piptaz	gardinal	ventilator	adrenaline dopamine	nil	AMA	RENAL
96	20	0.5	135	4.8	8	17	8	0.8	_	EP	Piptaz	gardinal	hood	nil	nil	Improved	
88	20	0.7	137	3.5	8.6	50	25	0.9	_	100-->EP	piptaz	gardinal	hood	nil	nil	Improved	
90	40	1.1	134	4.8	8.2	24	19	0.9	_	100-->EP	Piptaz	nil	hood	nil	nil	Improved	
96	24	0.6	138	4	8.4	24	12	0.8	_	100-->EP	piptaz	nil	hood	nil	nil	Improved	
79	31	1.1	135	4.6	9.3	50	30.3	1.3	_	100-->EP	Piptaz	nil	ventilator	adrenaline	nil	Improved	
156	43	0.9	135	4.7	7.9	42	15.5	1.7	PDA,PAH,LV DYS	100-->EP	piptaz ,meropenam	nil	ventilator	adrenaline dopamine	nil	death	RENAL
96	44	1	144	5.5	8.2	89	20	2.7	PDA,PAH,LV DYS	100-->EP	piptaz ,meropenam	nil	ventilator	adrenaline dopamine	nil	death	RENAL
140	39	1	141	4.7	8.2	50	33.4	1.1	_	100-->EP	piptaz	nil	hood	nil	nil	Improved	
76	18	0.5	134	5	8.5	50	39.5	0.5	_	100-->EP	piptaz	nil	hood	nil	nil	Improved	
96	60	1.6	131	4.8	7.9	44	20	2.5	_	100-->EP	Piptaz	levera	ventilator	dopamine	nil	Improved	RENAL
72	12	0.6	137	4.8	7.6	30	13.4	0.9	PFO	100-->EP	piptaz	gardinal	hood	nil	nil	Improved	
92	49	1.3	144	4.6	8.4	44	33	1.1	PDA,PAH	100-->EP	piptaz ,meropenam	gardinal	HFNC	adrenaline	FFP	Improved	
116	30	1	146	4.5	9.1	33	14	1.4	_	100-->EP	piptaz	nil	hood	nil	nil	Improved	
126	40	1.5	146	4.3	7.2	48	20	2.4	PAH	100-->EP	piptaz	levera	ventilator	adrenaline dopamine	FFP	death	RENAL
113	23	1.1	137	3.7	7	40	58	0.5	PFO	100-->EP	piptaz	nil	hood	nil	nil	Improved	
86	30	1	145	4.2	9.7	50	68	0.6	_	EP	piptaz	gardinal	HFNC	nil	nil	Improved	
116	12	1	131	4.6	7	20	17.3	0.8	PFO,PAH	100-->EP	piptaz	gardinal	ventilator	adrenaline dopamine	FFP	Improved	
72	50	0.7	132	4.5	7.9	53	36	0.6	_	100-->EP	piptaz	nil	hood	nil	nil	Improved	
96	64	1.7	127	3.5	6.3	30	16	2.6	PAH,PDA	100-->EP	piptaz	levera	ventilator	adrenaline	nil	Improved	RENAL
90	16	0.7	139	3.1	8.8	17	10.3	0.8	_	100-->EP	piptaz	nil	hood	nil	nil	Improved	
72	27	1.2	139	4	6.9	90	38.7	2	PDA	100-->EP	piptaz	levera	hood	nil	nil	Improved	
140	30	0.8	139	3.5	8.3	26	26.2	0.5	PDA,ASD,PAH	100-->EP	piptaz	nil	hood	nil	nil	Improved	
86	78	2.4	143	4.2	6.4	12	13.6	0.01	PFO	100-->EP	piptaz	nil	HFNC	nil	nil	Improved	
106	43	1	144	4.2	7.6	13	37.6	0.26	_	100-->EP	piptaz	nil	hood	nil	nil	Improved	
96	24	0.8	138	3.6	8	41	10.03	0.2	_	100-->EP	piptaz	nil	hood	nil	nil	Improved	
80	14	1.2	130	5.2	8.5	85	49	1.6	PDA,PAH	100-->EP	piptaz	gardinal	ventilator	adrenaline dopamine	nil	death	RENAL
80	10	0.8	136	3.6	8.7	30	31.9	0.6	_	100-->EP	piptaz	nil	hood	nil	nil	Improved	
69	29	1	134	3.8	7	28	29.7	0.7	PDA,PAH	100-->EP	piptaz	gardinal	hood	nil	nil	Improved	
78	47	1	143	4.3	7.5	35	25	1	PDA	100-->EP	mero ,vanco ,colistin	gardinal	hood	nil	nil	Improved	
70	45	0.8	138	4.3	8.3	41	22.5	1	ASD	EP	Meropenam	levera	ventilator	adrenaline	nil	Improved	
89	29	1.5	144	4.7	7.8	10	14.3	0.7	_	EP	piptaz	levera	hood	nil	nil	Improved	
113	28	0.9	142	3.6	8.2	20	54.7	0.2	_	100-->EP	piptaz	gardinal	hood	nil	nil	Improved	
82	60	1.6	142	5	8	10	54.9	0.2	PDA,ASD,PAH	100-->EP	piptaz ,meropenam	gardinal	ventilator	adrenaline	nil	Improved	
90	24	0.7	144	6	8.9	20	9.1	1	LV dysfunction	100-->EP	Piptaz	nil	hood	adrenaline	nil	Improved	
64	44	0.9	130	4.9	8.3	60	15	2.7	PDA,VSD	100-->EP	piptaz	gardinal	ventilator	dopamine	nil	death	RENAL
84	34	1.1	136	4.6	8.5	20	10	1.4	ASD,PAH	100-->EP	piptaz ,meropenam	gardinal levera	hood	nil	nil	Improved	
166	36	1.2	137	4.3	7	17	10	1.5	_	100-->EP	Piptaz	gardinal	HFNC	dopamine	nil	Improved	
112	42	2	131	6.9	7.7	54	28	2.9	_	100-->EP	piptaz,meropenam	gardinal	ventilator	adrenaline	nil	AMA	RENAL
73	47	0.6	136	4.3	8.3	65	18.5	1.5	ASD	100-->EP	piptaz ,meropenam	nil	HFNC	nil	nil	Improved	RENAL
70	50	0.6	144	6.2	8.3	56	18	1.2	_	100-->EP	piptaz,amikacin	nil	hood	nil	nil	Improved	
100	31	1.1	135	4.6	9.3	52	30.3	1.3	PAH	100-->EP	piptaz	nil	ventilator	nil	nil	Improved	
96	24	0.8	132	4.1	8.8	15	9	1	_	100-->EP	piptaz	gardinal	hood	nil	nil	Improved	
78	59	1.5	137	4.3	6.8	17	6.8	2.7	PDA,	100-->EP	piptaz,meropenam	gardinal ,levera	HFNC	nil	nil	Improved	RENAL
89	35	1.1	134	4.3	7.9	68	31	1.8	LV EF 40	EP	meropenam	gardinal,levera	ventilator	adrenaline	FFP	death	RENAL
78	14	1.2	126	5.6	8.5	71	52	1.2	Severe PAH,PDA,40?%	EP	piptaz,3%ns	gardinal	ventilator	adrenaline,sildenafil	nil	death	RENAL
79	20	0.7	137	3.5	8.9	50	25	0.8	_	100-->EP	Piptaz	nil	hood	nil	nil	Improved	