(International Print/Online Journal)

SJIF IMPACT FACTOR: 5.565
PUBMED-National Library of Medicine ID-101739732

ISSN (Print): 2209-2870
ISSN (Online): 2209-2862

International Journal of Medical Science and Current Research (IJMSCR)
Available online at: www.ijmscr.com
Volume 5, Issue 3, Page No: 981-987
May-June 2022

IJMSCR

Prevalence and Risk Factors of Acute Kidney Injury In Very Low Birth Weight Infants

Dr. Presha Desai[1*], Dr. Poonam Singh[2], Dr. Amita Surana[3]
[1]Senior Resident, [2]Professor, [3]Associate Professor
Department of Paediatrics, Surat Municipal Institute of Medical Education & Research,
Umarwada, Sahara Darwaja, Surat, Gujarat, India

***Corresponding Author:**
Dr. Presha Desai
Senior Resident, Department of Paediatrics, Surat Municipal Institute of Medical Education & Research,
Umarwada, Sahara Darwaja, Surat, Gujarat, India

Type of Publication: Original Research Paper
Conflicts of Interest: Nil

ABSTRACT

Background: Preterm infants are more likely to develop Acute Kidney Injury (AKI) as they usually require intensive care, are more prone to develop sepsis and hypotension, in addition to being exposed to potentially nephrotoxic medications.

Methods: All admitted VLBW (Very Low Birth Weight) infants who stayed >48 hours in neonatal unit were included in the study. They were categorised using Acute Kidney Injury Network (AKIN) criteria. Baseline serum creatinine at 48 hours of life then twice weekly till 4 weeks of postnatal age or discharge whichever was earlier and maternal & neonatal risk factors were evaluated.

Results: Prevalence of AKI was found to be 2.5% with male gender, gestational age <32 weeks and birth weight <1.2 kg at higher risk of developing AKI. Maternal factors, pre- eclampsia, chorioamnionitis and Premature rupture of membranes (PROM) were significant risk factors associated with AKI. Neonatal comorbidities, Severe Respiratory Distress Syndrome (RDS) [p <0.05] and culture positive sepsis [p <0.05] were significant risk factors associated with AKI. Mean day of life at which AKI was detected in our study was 8.9 ± 2.7 days. Mean values of serum creatinine progressively increased in 2nd week in both groups but was statistically significant in patients of AKI [p <0.05]. Mortality was 100 % in patients with AKI & 11.4 % in those without AKI.

Conclusion: AKI was associated with increased risk of mortality hence close monitoring of serum creatinine levels and urine output is needed in making an early diagnosis.

KEYWORDS: AKI, Risk Factors, VLBW infants

INTRODUCTION

AKI is characterized by a clinical syndrome in which a sudden deterioration in renal function results in the inability of the kidneys to maintain fluid and electrolyte homeostasis. AKI has been shown to be an independent risk factor for morbidity and mortality in VLBW neonates.[1] Preterms have accelerated renal maturation, a higher percentage of morphologically abnormal glomeruli and a higher glomerular volume (which is suggestive of renal hyperfiltration) which suggest that the kidneys of these babies have fewer functional nephrons, which increase their vulnerability to impaired renal function.[2] Preterm infants are more likely to develop AKI as they usually require intensive care admission, are more prone to develop sepsis and hypotension, in addition to being administered potentially nephrotoxic medications.[3] An elevated or rising serum creatinine is an indicator of a reduction in GFR, which is the hallmark of AKI.[4] Glomerular filtration rate (GFR) at birth is lower in the most

premature infants and rises after birth depending on the degree of prematurity.

There is a dearth of studies reflecting prevalence of AKI and risk factors associated with its development from India. Keeping this in mind this study was therefore carried out to assess prevalence and risk factors of AKI in VLBW infants at a medical college in tertiary NICU setup in western India. We used AKIN criteria for diagnosing AKI in these babies. A major advantage of AKIN criteria is not using the individual's baseline creatinine rather it uses two measurements:- an initial baseline and another obtained after 48 hours. It was hoped that the results of the present study will contribute to know the magnitude of AKI and associated modifiable risk factors in VLBW infants.

MATERIALS AND METHODS:

Study type, setting & design: Prospective hospital based observational study conducted at tertiary health care center over period of 15 months.

Inclusion & exclusion criteria: All admitted VLBW infants with duration of stay for > 48 hours in neonatal unit during study period were included in the study. Neonates whose parents did not give consent, who expired or left against medical advice and/or transferred to other hospital within 48 hours of birth and those diagnosed with congenital renal anomalies antenatally and postnatally were excluded from the study.

Institutional ethical committee (IEC) clearance [I.E.C./Outward no.-20; Date – 03/09/2019] and written consent from parents were taken for the study.

Data collection: Data collection was done by using a structured case recording form. The demographic data (gestational age, birth weight, gender), and maternal risk factors including prenatal exposure to corticosteroid, mode of delivery, pre-eclampsia, PROM, chorioamnionitis were recorded. Neonatal co-morbidities like RDS, intraventricular haemorrhage (IVH), Necrotising enterocolitis (NEC), culture positive sepsis, interventions like need for antibiotics & their duration, Continuous Positive Airway Pressure (CPAP) support, mechanical ventilation and inotropic medications were documented. AKI was defined by AKIN criteria[5] and patients were categorised into 2 groups AKI and No AKI. The baseline blood samples for serum creatinine levels were collected after 48 hours followed by twice weekly till 4 weeks of postnatal age or discharge whichever is earlier. Urine output of patients was measured by weighing diapers with digital weighing scale with precision of ±5 grams. Estimated Glomerular Filtration Rate (eGFR) was calculated using Schwartz formula.[6] An AKI diagnosis was made only after the first 48 hours of life, which avoided calling the expected low urine output during the first 2 days of life of an infant as AKI. Final outcome data included survival of VLBW infants in relation with AKI.

Sample size estimation: It was calculated by using OPENEPI software by considering 7% proportion of VLBW admission and 5% allowable error with 95% level of significance.

The calculated sample size was a total of 120 neonates.

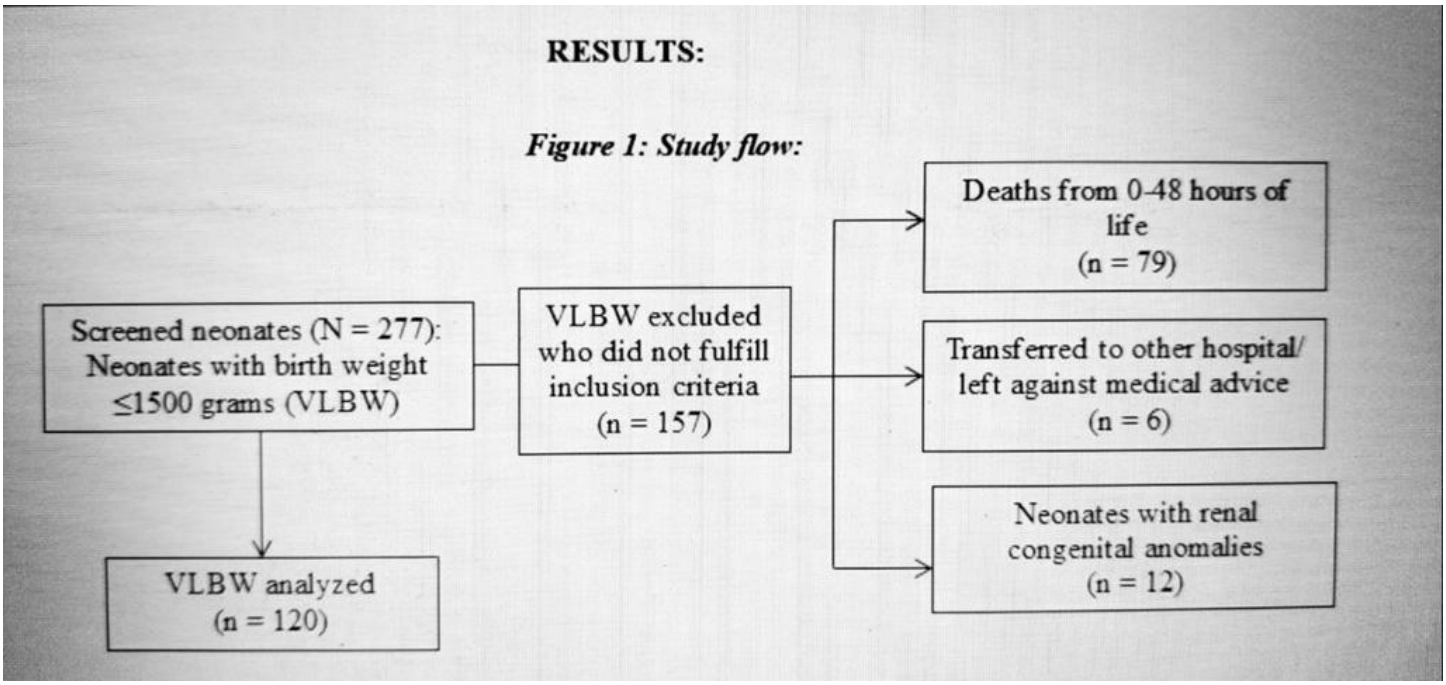
Statistical Analysis:

1. Descriptive statistics for intergroup comparison was used where qualitative data was depicted in percentage and quantitative data was depicted in mean and standard deviation.
2. Z test of proportion was applied to observe significant difference between 2 independent groups of qualitative data.
3. Chi-square test was applied to know the association between two independent qualitative variables.
4. Independent T-test was applied to observe significant difference between 2 independent groups of quantitative data.
5. A p value of < 0.05 was considered significant

Volume 5, Issue 3; May-June 2022; Page No 981-987

RESULTS:

Figure 1: Study flow:



Demographic Profile:

3 infants met the definition of AKI according to AKIN criteria. Therefore, in our study, period prevalence of AKI in VLBW babies was 2.5%, all falling in AKI stage-1. Males were 2.1 times likely to develop AKI than females. Gestational age <32 weeks and birth weight <1.2 kg were at higher risk of developing AKI. [Table 1]

AKI & Maternal risk factors and Neonatal comorbidities:

Amongst all the maternal risk factors in our study, pre-eclampsia, chorioamnionitis and PROM were found to be at higher risk for developing AKI. Among neonatal comorbidities included in our study, severe RDS, culture positive sepsis, IVH and NEC were at higher risk for developing AKI. [Table 1]

Mean drug duration, interventions and final outcome in relation with AKI:

Amongst various drugs given to patients in the study group, mean duration of antibiotics like cefotaxime, netilmycin, piperacillin and levofloxacin was longer in patients with AKI than that of patients without AKI, but there was no statistical significance. All 3 patients (100%) with AKI were given ionotropic and ventilatory support, mean duration of which was much longer and statistically significant. Amongst 120 patients in our study, mortality was 100 % in patients with AKI and 11.4 % in patients without AKI. [Table 1]

AKI and Renal parameters:

Mean day of life at which AKI was detected in VLBW infants in our study was 8.9 ± 2.7 days. Mean values of serum creatinine progressively increased from day 3 to 21 in both groups but was statistically significant in patients of AKI [$p < 0.05$]. Urine output was lower in patients with AKI though none had oliguria i.e. < 1 ml/kg/hr.[7] Mean values of eGFR in patients with AKI gradually decreased till 3rd week of life which was statistically significant [Table 2].

DISCUSSION:

The present study was conducted to determine the prevalence and risk factors for AKI in VLBW infants. Prevalence of AKI in VLBW babies in our study was 2.5%. AKI was seen in babies having risk factors like maternal PROM, pre-eclampsia and chorioamnionitis. Male gender and lower gestational age were significant demographic factors. Comorbidities and mortality (100%) were higher in babies with AKI. We provided a descriptive overview of AKI in newborns that were admitted to Neonatal intensive care unit (NICU).

The prevalence of AKI in our study was 2.5 % which was lower than that in the study by Timovska et al [6.5 %], Fatih et al [8] [8.4 %] and Deepti damayanty [9] et al [7.4 %]. Prevalence is higher in Fatih et al [8]

Volume 5, Issue 3; May-June 2022; Page No 981-987

as they included all babies admitted in NICU irrespective of their weight. More recent studies [9, 11] are showing a lower rate of AKI probably due to better understanding of neonatal care. Our study also showed that most neonatal AKI were mild and classified as stage 1 of AKIN similarly Ankana Daga et al showed milder AKI was more common than more severe stages of AKI.

This study showed that pre-eclampsia [66.7%], PROM [33.3%] and chorioamnionitis [33.3%] were observed to be the significant maternal risk factors for AKI similar to Fatih et al [8] which showed pre-eclampsia [19.6%] and PROM [23.8 %] in AKI groups. During intrauterine life infections, intrauterine growth restrictions, placental insufficiency can affect kidney function more in premature infants. Fetal programming hypothesis suggests that adverse intrauterine milieu causes structural, hormonal and metabolic adaptation in fetus.[8] Pre-eclampsia is found to be a protective effect against AKI in some studies[12] relating to conditioning of fetal kidney or medications for control of BP.

In this study, severe RDS [100 %] and sepsis [66.6 %] were the most important neonatal comorbidities associated with AKI similar to Ankana Daga et al study, which also showed RDS [96%] and sepsis [71 %] as most common comorbidities associated to AKI. It has been proposed that sepsis and RDS requiring ventilatory support can enhance AKI by compromising blood flow and release of inflammatory mediators.[9]

Mean day of life at which AKI was detected in VLBW infants in our study was 8.9 ± 2.7 days (2nd week) in comparison to study by Deepti damayanty et al [9] in which AKI was detected at

4.24 ± 2.58 days (1st week). Mean serum creatinine levels in our study [1.01 ± 0.08] were comparable to Emad E. Ghobrial et al [10] which showed [1.06 ± 0.6]. Mean urine output in our study [1.86 ± 0.36] was comparable to Deepti damayanty et al [9] which showed [1.9 ± 0.6]. None of the patients who developed AKI had oliguria in our study similar to Ankana Daga et al. This result is consistent with the fact that AKI in newborns is generally non-oliguric.[11]

In our study a higher proportion of neonates with AKI received ionotropic [100 %] and ventilatory support [100 %] in comparison to that of patients without AKI [11.9 %, 26.4 %] similar results were also seen with Chein Chung et al [12] [86 %, 81 %] and Fatih et al [8] [19 %, 88 %] for ionotropic and ventilatory support respectively in patients with AKI. In our study, the duration of ventilatory support given to the neonates with AKI [14.6 ± 5.6] was observed to be longer than that of the patients without AKI [4.9 ± 4.3] which was similar to Fatih et al [8] [AKI - 12 ± 4.8; No AKI - 5.2 ± 2.1].

The mortality in our study was higher in patients with AKI [100 %] as compared to those without AKI [11.4 %] which was comparable to Naomi et al [13] [AKI - 70.6 %; No AKI - 29.4%] and to Maisa Al Malla et al [14] [AKI - 54 % ; No AKI - 14 %].

Limitation:

Regression analysis could not be done due to less sample size.

CONCLUSION:

Prevalence of AKI using AKIN criteria was 2.5 % in VLBW infants in our study. VLBW babies are at risk of AKI especially male gender, gestational age <32 weeks and birth weight < 1.2 kg. Maternal risk factors also contributed significantly to development of AKI. Early diagnosis of AKI in VLBW infants is crucial which can be done by high index of suspicion specially in those who have risk factors. Baseline creatinine and close monitoring of serum creatinine levels with urine output can be helpful in making an early diagnosis. Efforts to prevent and ameliorate the impact of AKI are likely to improve the outcomes in this vulnerable population. Early diagnosis of AKI in VLBW infants is crucial which can be done to avoid progression.

REFERENCES:

1. Koralkar R, Ambalavanan N, Levitan EB, McGwin G, Goldstein S, Askenazi D. Acute kidney injury reduces survival in very low birth weight infants. Pediatric research. 2011 Apr;69(4):354- 8.
2. Sutherland MR, Gubhaju L, Moore L, Kent AL, Dahlstrom JE, Horne RS, Hoy WE, Bertram JF, Black MJ. Accelerated maturation and abnormal morphology in the

Volume 5, Issue 3; May-June 2022; Page No 981-987

preterm neonatal kidney. Journal of the American Society of Nephrology. 2011 Jul 1;22(7):1365-74.
3. Askenazi DJ, Ambalavanan N, Goldstein SL. Acute kidney injury in critically ill newborns: what do we know? What do we need to learn?. Pediatric nephrology. 2009 Feb;24(2):265-74.
4. Auron A, Mhanna MJ. Serum creatinine in very low birth weight infants during their first days of life. Journal of perinatology. 2006 Dec;26(12):755-60.
5. Section 2: AKI Definition. Kidney inter, Suppl. 2012;2(1):19-36.
6. Schwartz GJ, Work DF. Measurement and estimation of GFR in children and adolescents. Clinical Journal of the American Society of Nephrology. 2009 Nov 1;4(11):1832-43..
7. Srisawat N, Hoste EE, Kellum JA. Modern classification of acute kidney injury. Blood Purif 2010;29:300-7.
8. Bolat F, Comert S, Bolat G, Kucuk O, Can E, Bulbul A, Uslu HS, Nuhoglu A. Acute kidney injury in a single neonatal intensive care unit in Turkey. World Journal of Pediatrics. 2013 Nov;9(4):323-9.
9. Pradhan DD, Meher BK, Panda SK, Samal D. Prevalence and factors affecting prognosis in neonates with acute kidney injury in a neonatal intensive care unit. Journal of Clinical Neonatology. 2018 Oct 1;7(4):237.
10. Andreoli SP. Management of Acute Kidney Injury in Children. Pediatric Drugs. 2008 Nov;10(6):379-90.
11. Jetton JG, Askenazi DJ. Update on acute kidney injury in the neonate. Current opinion in pediatrics. 2012 Apr;24(2):191.
12. Lee CC, Chan OW, Lai MY, Hsu KH, Wu TW, Lim WH, Wang YC, Lien R. Incidence and outcomes of acute kidney injury in extremely-low-birth-weight infants. PLoS One. 2017 Nov 6;12(11):e0187764.
13. Mwamanenge NA, Assenga E, Furia FF. Acute kidney injury among critically ill neonates in a tertiary hospital in Tanzania; Prevalence, risk factors and outcome. Plos one. 2020 Feb 13;15(2):e0229074.
14. Al Malla M, Varghese NV, AlAbdullatif M, Narchi H, Khassawneh M. Prevalence and outcome of acute kidney injury, as defined by the new Kidney Disease Improving Global Outcomes guideline, in very low birth weight infants. World Journal of Nephrology. 2017 Sep 6;6(5):229.

TABLES:

Table 1: Characteristics of VLBW infants in relation to AKI

Total enrolled			**120 [N (%)]**		
No AKI			117 (97.5)		
AKI			3 (2.5)		
AKI Stage 1			3 (100)		
AKI Stage 2			0		
AKI Stage 3			0		
Demographic variables		**AKI (N = 3) (%)**	**No AKI (N = 117) (%)**	**p - value**	**OR (95% CI)**
Gender	Male	2 (66.7)	57 (48.7)	0.26	2.105 (0.18 - 23.85)
	Female	1 (33.3)	60 (51.3)		

Volume 5, Issue 3; May-June 2022; Page No 981-987

Birth weight	< 1.2 Kg	1 (33.3)	27 (23.0)	0.33	1.667 (0.145 - 19.09)
	> 1.2 Kg	2 (66.7)	90 (77.0)		
Gestational age	< 32 weeks	2 (66.7)	33 (28.2)	0.07	5.09 (0.44 - 58.05)
	> 32 weeks	1 (33.3)	84 (71.8)		
Maternal Risk Factors	**AKI (N=3) (%)**	**No AKI (N=117) (%)**	**Total (N=120) (%)**	**p - value**	**OR (95% CI)**
1) Antenatal steroids	1 (33.3)	80 (68.3)	81 (67.5)	0.07	0.231 (0.020 – 2.631)
2) Chorioamnionitis	1 (33.3)	21 (17.9)	22 (18.3)	*0.009*	2.286 (0.198 - 26.39)
3) Pre-eclampsia	2 (66.7)	26 (22.2)	28 (23.3)	*0.000*	7 (0.610 - 80.28)
4) PROM	1 (33.3)	4 (3.4)	5 (4.1)	*0.000*	14.13 (1.05 - 190)
5) Caesarean delivery	1 (33.3)	55 (47)	56 (46.6)	0.08	0.563 (0.049 – 6.388)
Neonatal Comorbidities					
1) RDS	3 (100)	14 (11.9)	17 (14.1)	*0.000*	_
2)Culture positive sepsis	2 (66.6)	28 (23.9)	30 (25)	*0.00*	6.357 (0.555 - 72.76)
3) IVH	1 (33.3)	13 (11.1)	14 (11.6)	*0.00*	4.0 (0.338 - 47.22)
4) NEC	1 (33.3)	10 (8.5)	12 (10)	*0.00*	5.35 (0.445 - 64.29)

	Mean duration of drugs (in days)		
Drug Administered	**AKI (N=3)**	**No AKI (N=117)**	**p - value**
1) Cefotaxime	5	4.37 ± 2.38	0.6
2) Netilmycin	6.6 ± 2.8	5.5 ± 2.75	0.4
3) Amikacin	0	8 ± 8.4	-
4) Meropenem	4.6 ± 1.5	6.7 ± 3.9	0.3
5) Colistin	6.6 ± 6.2	9.7 ± 4.7	0.2
6) Piperacillin	7.5 ± 3.5	5.7 ± 3.3	0.3
7) Levofloxacin	7.3 ± 5.1	6.9 ± 3.9	0.8
8) Vancomycin	0	6.5 ± 5.7	-
9) Fluconazole	4	5.1 ± 3.9	0.6
Interventions in relation to AKI	**AKI (N=3) (%)**	**No AKI (N=117) (%)**	**p - value**
1) Ionotropic support	3 (100)	14 (11.9)	0.000

Volume 5, Issue 3; May-June 2022; Page No 981-987

2) CPAP support	Number of patients	2 (66.7)	24 (20.5)	*0.000*
	Mean duration (Days)	2.5 ±1.3	2.3 ± 0.7	0.6
3)Ventilatory support	Number of patients	3 (100)	31 (26.4)	*0.000*
	Mean duration (Days)	14.6 ± 5.6	4.9 ± 4.3	*0.000*

Outcome in relation to AKI	**AKI (N=3) (%)**	**No AKI (N=117) (%)**
1) Discharge	0	78 (66.6)
2) DAMA	0	26 (22.2)
3) Death	3 (100)	13 (11.4)

Table 2: AKI & renal parameters

Variables (Mean ± SD)	**Day of life**	**AKI (N=3)**	**No AKI (N=117)**	**p - value**
Serum creatinine (mg/dl)	Day 3-7	0.71 ± 0.11	0.72 ± 0.14	0.9
	Day 8-14	1.01 ± 0.08	0.74 ± 0.11	*0.000*
	Day 15-21	1.28 ± 0.09	0.75 ± 0.12	*0.000*
Urine output (ml/kg/hr)	Day 3-7	1.76 ± 0.29	1.87 ± 0.39	0.6
	Day 8-14	1.86 ± 0.36	2.01 ± 0.46	0.5
	Day 15-21	1.89 ± 0.38	2.10 ± 0.49	0.4
eGFR (ml/min/1.73m^2)	Day 3-7	19.3 ± 1.5	20.4 ± 4.7	0.6
	Day 8-14	18.1 ± 1.9	22.3 ± 4.9	0.1
	Day 15-21	17.2 ± 2.2	25.4 ± 5.2	*0.007*

[DAMA – Discharge Against Medical Advice

SD – Standard Devaiation

OR – Odd's Ratio

CI- Confidence interval]

Volume 5, Issue 3; May-June 2022; Page No 981-987