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FREQUENCY OF ACUTE KIDNEY INJURY IN TERM NEONATES WITH PERINATAL ASPHYXIA

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Abstract:

Background: *Acute kidney injury is defined as an abrupt reduction in kidney function measured by rapid decline in glomerular filtration rate. Acute kidney injury is an independent predictor of mortality in critically ill neonates even after controlling other co-morbidities.*

Objective: *To determine frequency acute kidney injury in term neonates with Perinatal asphyxia*

Setting: *Neonatal intensive care unit of a National institute of Child Health, Karachi.*

Duration: *Six months October 2017 to April, 2018*

Study Design: *Descriptive, Cross sectional study*

Material And Methods: *In this study 96 participants fulfilling the inclusion criteria were selected. Informed consent was taken from parents after explaining purpose of study. History regarding maternal age, parity, maternal illness (gestational diabetes and gestational hypertension), antenatal care, mode and place of delivery were taken. Weight of the baby was checked. 2cc blood sample for serum urea and creatinine were taken on 3rd day of birth by trained technician to assess acute kidney injury.*

Results: *Forty (41.7%) neonates were female and 56(58.3%) were male. Forty-four (45.8%) of asphyxiated neonates were found to have acute kidney injury (AKI).*

Conclusion: *AKI is common among asphyxiated neonates. It should be suspected in all sick newborns as early recognition and prompt management prevent severe kidney injury.*

Key Words: *Acute kidney injury, perinatal asphyxia, neonates."*

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INTRODUCTION:

Acute renal injury is an unexpected decline in renal functions determined by rapid decrease in the rate of glomerular filtration. [1] In neonates, perinatal asphyxia is a key causative factor of acute renal injury, [4] with prevalence of 50.0-72.0% in full-term neonates with asphyxia; [5,6,7] leading to ischemia that results in neonatal kidney failure [8]. Following initial event of renal ischemia and shock, a transient ischemic state sensitive to O_2 deprivation occurs. In case of ischemic event, renal insufficiency occurs; which if persisted can result in medullary necrosis and circulatory cortical [9]. Acute renal injury is an independent forecaster of mortality among seriously ill newborns yet after regulating further co-morbidities. [2,3] Neonatal asphyxia can cause multi-organ failure and redistribution of cardiac-output to maintain adrenal, cardiac and cerebral perfusion while potentially compromising gastrointestinal, renal and skin perfusion. [10,11] In spite of neonatal asphyxia provoked acute renal injury being often faced in intensive care nursery, very inadequate local data is existing regarding it. Thus, the rationale of current study is to identify fact regarding local incidence of neonatal (perinatal) asphyxia provoked acute renal injury. This will assist in making strategies concerning early screening as well as application of certain prophylactic policies to avoid acute renal injury provoked mortality and morbidity among neonates.

MATERIALS AND METHODS:

This cross sectional descriptive study was performed in intensive care nursery (NICU) of a National institute of Child Health Karachi, within the time period of 6 months. Following ethical approval and well-versed consensus of parents, this study was carried out on 96 term neonates with neonatal asphyxia through non-probability consecutive sampling technique. The parents refusing for study, neonates with congenital renal abnormalities (dysplastic/ hypo plastic/ absent kidney) or Twin pregnancy were excluded. Acute kidney injury was defined as, asphyxiated neonates is considered to have acute kidney injury; if following criteria are noted; Serum creatinine > 1 mg/dl and Blood urea > 40 mg/dl.[6] Neonatal Asphyxia was defined as failure to start and maintain breathing at birth[4] with APGAR score of below 7 at 5 minutes.[5] Data was collected through a Performa especially designed for this study from all the participant of study. Statistical data analysis was done by SPSS software version 17.0. Post stratification chi square test were employed by considering P-values ≤0.05 as significant.

RESULTS:

Overall 96 asphyxiated term newborns were enrolled to study. Mean gestational age was found as 38.2±1.9 weeks and 3.38±0.54 kilograms of birth weight was found. 40 (41.7%) were female newborns and male were 56(58.3%). Forty (43.8%) women had primiparious and 54(56.2%) were multiparous 39(40.6%) patients had gestational diabetes mellitus, 71(73.9%) females had gestational hypertension, booking status revealed that 68(70.8%) had unbooked status. 29(30.2%) females had vaginal delivery and 67(69.8%) had c/section. 50(85.4%) women delivered in hospitals and 46(47.9%) women delivered in home or by non-doctor and paramedic staff. 14(14.6%) subjects had IUGR. low birth weight was noted in 54(56.3%) neonates, 44(45.8%) females were aged below 25 years.

Forty-six (45.8%) of asphyxiated neonates were found to have AKI. Eighteen patients (45%) were female, twenty-six (46.4%) male, with insignificant difference between the gender and AKI occurrence (p-value = 0.89).

Twenty-one (54.8%) mothers of neonates with AKI were multiparous and 23(54.8%) were primiparous (p-value = 0.12).

Thirty-eight (71.8%) of asphyxiated neonates with AKI were from mothers with gestational diabetes (GDM), while 16 (28.1%) with no GDM (p-value = 0.001).

Thirty-nine (54.9%) of asphyxiated neonates with AKI were from mothers with gestational hypertension(GHTN), while 5 (20%) with no GHTN (p-value = 0.003).

Home deliveries were reported in 18 (39.1%) babies, while 26(52%) were delivered in hospital (p-value = 0.21).

Vaginal deliveries were reported in 8 (27.6%) babies, while 36(53.7%) were delivered through C/section (p-value = 0.018).

Table: 1: Descriptive statistics variables (n=96)

Variables	Mean	SD
Gestational age	38.2	1.9
Maternal age	28	4.5
Birth weight	3.38	0.54

Table: 1: Demographic characteristics of patients n=96

Variables	Total
Gender	
Male	56(58.3%)
Female	40(41.7%)
Parity	
Multiparity	54(56.2%)
Primiparity	42(43.8%)
Gestational Diabetes mellitus	
No	57(59.4%)
Yes	39(40.6%)
Gestational Hypertension	
No	25(26.1%)
Yes	71(73.9%)
Mode of delivery	
C/Section	67(69.8%)
Vaginal delivery	29(30.2%)
Booking status	
Un booked	68(70.8%)
Booked	28(29.2%)
IUGR	
No	82(85.4%)
Yes	14(14.6%)
Place of delivery	
Hospital	50(52.1%)
Home/non-medical	46(47.9%)
Birth weight	
>2.5 kgs	42(43.7%)
</=2.5 kgs	54(56.3%)
Maternal age	
>25 years	52(54.2%)
</=25 years	44(45.8%)

Table: 3: Distribution of acute kidney injury in term neonates with perinatal asphyxia (n=96)

Acute kidney injury	Frequency	Percentages
No	52	54.2%
Yes	44	45.8%
Total	96	100%

Table: 4. Stratification for acute kidney injury with respect to effect modifiers

Variables		Acute kidney injury		Total	P-Value
		No 52(54.2%)	Yes 44(45.8%)		
Gender	Female	22(55%)	18(45%)	40(100%)	0.89
	Male	30(53.6%)	26(46.4%)	56(100%)	
Parity	Multiparous	33(61.1%)	21(38.9%)	54(100%)	0.12
	Primiparous	19(45.2%)	23(54.8%)	42(100%)	
Gestational Hypertension	Yes	32(45.1%)	39(54.9%)	71(100%)	0.003
	No	20(80%)	5(20%)	25(100%)	
Gestational Diabetes mellitus	Yes	11(28.2%)	28(71.8%)	39(100%)	0.001
	No	41(71.9%)	16(28.1%)	57(100%)	
Mode of delivery	Vaginal delivery	21(72.4%)	8(27.6%)	29(100%)	0.018
	C/Section	31(46.3%)	36(53.7%)	67(100%)	
Booking status	Booked	8(28.6%)	20(71.4%)	28(100%)	0.001
	Un booked	44(64.7%)	24(35.3%)	68(100%)	
Place of delivery	Home/non-medical	28(60.9%)	18(39.1%)	46(100%)	0.21
	Hospital	24(48%)	26(52%)	50(100%)	
IUGR	Yes	5(35.7%)	9(64.3%)	14(100%)	0.13
	No	47(57.3%)	35(42.7%)	82(100%)	
Maternal age	</=25 years	24(54.5%)	20(45.5%)	44(100%)	0.94
	>25 years	28(53.8%)	24(46.2%)	52(100%)	
Birth weight	</=2.5 kgs	26(48.1%)	28(51.9%)	54(100%)	0.18
	>2.5 kgs	26(61.9%)	16(38.1%)	42(100%)	
Gestational age	37-39	27(56.2%)	21(43.8%)	48(100%)	0.68
	40-42	25(52.1%)	23(47.9%)	48(100%)	

DISCUSSION:

As stated by the Acute Kidney Injury Network (AKIN), Acute renal injury is an absolute rise in creatinine of ≥ 26.4µmol/l (or rising rate of serum creatinine up to at least 50%) over two successive days. [12] Creatinine rate in a normal neonate at term is 79 µmol / l at day 1 and declines to 44 µmol / l, by Schwartz) at day 5. [11] Earlier than 48 hours of life, the serum creatinine reflects that of the mother. [13] Reports by Jayshree [14], Nouri [15] and Gupta [16] documented the threshold of 90 µmol / l at 48 hours of life for serum creatinine. Studies by Karlowicz [17] Kaur [18] documented the 133 µmol/l threshold level for serum creatinine at 48 hours to make a

diagnosis of acute renal injury. In current study, the threshold of 133 µmol / l for creatinine at 72 hours of life was taken so as to intensify our likelihood of diagnosis as there would be a noticeable decline in the maternal creatinine level by then. There is a high incidence of AKI among the asphyxiated term infants (7 – 72%). [16,17] AKI after perinatal asphyxia was noted in 42% of cases for Martin-Ancel 4, 47% to Gupta [16] 68% for Aggrawal [13] ,70% to Gluckman [19], 17.2 % Nouri [15] and 33% in our study. Current study noted an incidence rate of 11.7%; hence lying within the range of majority of the studies done. The incidence rate can possibly have been considerably greater contrasted to the study of Tunisia, if serum creatinine was sampled at 48 hours and 90 µmol / l of threshold level used. The existing studies exhibit that the incidence rates were alike in both poor-resource and rich-resource regions; denoting that acute renal injury in neonatal asphyxia is a worldwide problem. The existence of neonatal asphyxia and its severity seems to associate with rising prevalence of acute renal injury [16,20] Nouri [15] who had 2/3 of neonates with acute renal injury (AKI) with grade II and 1/3 neonates had AKI with grade III. Though, no renal injury was noted in neonates with grade-I, in his study. There was no significant difference (p = 0.13). Gupta, however revealed that serum creatinine and blood urea were significantly greater in HIE and asphyxiated babies contrasted to the control group ($P < 0.05$) and ($P < 0.001$) respectively thus exhibiting the association amid HIE and AKI. Kaur[18] exhibited that AKI developed within 1 out of eleven (9.1%) neonates with moderate asphyxia and in 12 of 25 (56%) with severe asphyxia. Current study noticed a 15-fold raised risk of AKI development in HIE-III contrasted to HIE-I, p=0.034 with 95% CI (1.2–183.6). Though, no correlation was found amid HIE-I and HIE-II (p=0.50), and this could possibly be explained by the small sample size. AKI was greatest in the newborns with HIE-III (42.9%) on day 3 of life and lowest within the newborns with HIE-I (4.8%). The small sample sizes in majority of studies have been a main obstacle in grasping correlations between AKI and maternal or neonatal characteristics. Some authors have exhibited a significant correlation amid low Apgar score at the 5th and AKI, with as low level of significance as, p = 0.0013, by Nouri. [20,21] In current study 14% of subjects with severe Apgar score had AKI whereas most of (86%) subjects with moderate asphyxia had acute renal injury. This could possibly be explained by the statement that most of the severe asphyxiated neonates die earlier than day 3 of life and thus were excluded from the study. Though, we established no significant association amid AKI and Apgar (p=0.473). The rates of mortality of neonatal asphyxia-related AKI varies from 2% to 20 % (p=0.11). [16,15,22] Our study showed a mortality rate of 71.4 % ,(p=0.001); and an average death at 4 days. There was 24-fold raised risk of deaths in AKI, p=0.001 with 95% CI (3.7–157). The wide confidence interval and a high mortality rate could have been contributed to by the small sample size. Acute renal injury (AKI) is not usually a direct reason for death. [14] The reason for death among AKI diagnosed patients can possibly not be the similar to the cause of acute renal injury. The mortality rate relies on further correlated conditions, such as other organs failure, mainly cardiac failure, serious infection and HIE, thus the it is problematic to mention the exact values for mortality rates secondary to AKI in current study and the earlier ones.

1 out of every 8 newborns with severe and moderate perinatal asphyxia is likely to develop acute renal injury with 5 out of 7 of these newborns likely to die by day 4 of life. AKI associates with HIE, and the risk of AKI development is greater with a further severe form of HIE. The newborns with HIE-III have a 15-fold raised risk of AKI development. The newborns with AKI developed, have a 24-folds raised risk of death. 1 neonate out of 7, who developed AKI was released from hospital by the day 7 of life. Clinicians should thus attempt to diagnose AKI and establish appropriate measures from day 3 of life. Larger studies are required to be performed to compare neonatal asphyxia and maternal factors-associated acute kidney injury.

Contrasted to older kids, neonates are further susceptible to AKI since they have low rate of glomerular filtration, high rates of plasma renin activity, high renal vascular resistance and reduced sodium reabsorption in the proximal tubules. Furthermore, problems in interpretation of serum creatinine make it further problematic to achieve an agreement in terms of AKI definition. [23]

The epidemiology of acute renal injury has shifted in the past few decades, with quick improvements in medical technology. Fresh studies recognized that even small rises in levels of serum creatinine raise mortality and morbidity [24,25] This study from Sudan is the first to report from its region that focuses on the prevalence of acute renal injury in asphyxiated newborns and applying pRFILE taxonomy for diagnosis and outcome.

Our study exhibited that acute renal injury was a common concern among 46 (54.1%) asphyxiated newborns, it is highly common at stage-II in 29(63%) neonates and this finding is paralleling the study carried out in Austria which exhibited that 56% of

asphyxiated newborns had AKI. It is as-well comparable to the research work carried out in Saudi Arabia which established AKI among 18 out of 32 (56.25%) asphyxiated neonates with considerably high levels of serum creatinine and serum urea on day 3 of life [26]. Our study exhibited that 69.4% mothers underwent systematic antenatal care and the prevalence of home delivery among asphyxiated newborns was 39.2% which is estimated high. This is similar to a study performed in Pakistan, where 64% mothers underwent systematic ANC, though home delivery was noted among 56%, which is even greater and this is possibly because of the beliefs of grandparents and parents. [27] Our study exhibited that 56.7% asphyxiated neonates underwent spontaneous vaginal deliveries, 16.5% underwent assisted vaginal deliveries and C/S in 27.1% cases, these findings differ from a study of Indonesia which found spontaneous vaginal delivery among 43%, assisted vaginal delivery among 10% and C/S among 47% cases. This greater C/S rate would impact the fetal outcome. [28]

Current study exhibited that the highly common HIE stage was stage-II among 54.1% cases, this is comparable to a study carried out in Kenya, showing Stage-II among 30 (50%) out of 60 neonates. [29]. Non-oliguric AKI was noted among 65% of asphyxiated newborns in current study which is comparable to a USA's study which underlines the insensitivity of oliguria to forecast AKI among newborns. [30] and again it is similar to a study that was done in India where the non-oliguric renal failure represented 78% of asphyxiated neonates. [31] In contrast a study from New Delhi reported oliguric renal failure in 69% of asphyxiated neonates.

In the present study all neonates with AKI as a result of birth asphyxia received supportive treatment with good outcome where 91.3% of babies had full recovery and death occurred in 8.7%. A higher mortality rate was reported in a recent Indian study where 18.75% of neonates with AKI died. [32]

CONCLUSION:

The overall prevalence of AKI in neonates with perinatal asphyxia was noted to be similar to other studies. The prevalence of AKI in neonatal asphyxia is high (45.8%). The more severe degree of neonatal asphyxia, the more severe AKI stage and the lower median GFR.Acute kidney injury (AKI) is common among asphyxiated neonates. It should be suspected in all sick newborns as early recognition and prompt management prevent severe kidney injury.

REFERENCES:

1. Khan M, Khan KMA, Chachar S, Memon AA. Association and outcome of acute renal failure in neonates in a tertiary care hospital. Pak pediatr J 2014; 38(2):96-101.
2. Askenazi DJ, Griffin R, McGwin G, Carlo W, Ambalavanan N. Acute kidney injury is independently associated with mortality in very low birthweight infants: a matched case-control analysis. Pediatr Nephrol 2009; 24:991-7.
3. Koralkar R, Ambalavanan N, Levitan EB, McGwin G, Goldstein S, Askenazi D. Acute kidney injury reduces survival in very low birthweight infant. Pediatr Res 2010; 69:354-8.
4. Alaro D, Bashir A, Musoke R, Wanaiana L. Prevalence and outcome of acute kidney injury in term neonate with perinatal asphyxia. Afr Health Sci. 2014; 14(3):682-8.
5. Mehta R, Kellum J. Acute Kidney Injury Network (AKIN): report of an initiative to improve outcome in acute kidney injury. Crit Care. 2007; 11:31-32.
6. Gupta B, Pramod S. The incidence of renal failure in asphyxiated neonates and to correlate severity and type of renal failure with Apgar score and hypoxic ischemic encephalopathy (HIE) grading of the neonates. Indian Pediatrics 2005; 42:928-34.
7. Kaur S, Jain S, Saha A, Chawla D, Parmar VR, Basu S, Kaur J. Evaluation of glomerian and tubular renal function in neonate with birth asphyxia. Ann Trop Paediatr. 2011;31(2):129-34.
8. Ashraf M, Ahmed N, Choudary J, Saif RU. Acute Renal Failure: Nephrosonographic findings in asphyxiated neonates. Saudi J Kidney Dis Transpl. 2011; 22(67):1187-92.
9. Perinatal morbidity. Report of the health care committee expert panel on perinatal morbidity. National Health and Medical Research Council. Australian Govt. Publishing Service; 1995.
10. Karlo J, Bhat BV, Koner BC, Adhisivam B, Evaluation of renal function in term babies with perinatal asphyxia.Indian J Paediatr. 2014; 81:243-7.
11. Durkan AM, Alexander RT. Acute kidney injury post neonatal asphyxia. J Pediatr.2011;5.
12. Mehta R, Kellum J. Acute Kidney Injury Network (AKIN): report of an initiative to improve outcome in acute kidney injury. Crit Care. 2007; 11:31–32.
13. Aggarwal A, Kumar P, Chowdhary G, et al. Evaluation of renal functions in asphyxiated newborns. J Trop Pediatr. 2005; 51:295–299.
14. Jayashree G, Dutta AK, Sarna MS, et al. Acute renal failure in asphyxiated newborns. Indian Pediatr. 1991; 28:19–23.
15. Nouri S, Mahdhaoui N. Acute renal failure in

full term neonates with perinatal asphyxia. Prospective study of 87 cases. Arch Pediatr. 2008; 15:229–235.
16. Gupta B, Pramod S, et al. The incidence of renal failure in asphyxiated neonates and to correlate severity and type of renal failure with Apgar score and hypoxic ischemic encephalopathy (HIE) grading of the neonates. Indian Pediatrics. 2005; 42: 928–934.
17. Karlowicz M, Adelman R. Nonoliguric and oliguric acute renal failure in asphyxiated term neonates. Pediatr Nephrol. 1995; 9:718–722.
18. Kaur S, Jain S. Evaluation of glomerular and tubular renal function in neonates with birth asphyxia. Ann Trop Paediatr. 2011; 31:129–134.
19. Gluckman P, Wyatt J, Azzopardi D, et al. Selective head cooling with mild systemic hypothermia Effective neonatal encephalopathy: multicentre randomized trial. Lancet. 2005; 365:663–670.
20. Martin-Ancel A, Garcia-Alix A, Gaya F, et al. Multiple organ involvement in perinatal asphyxia. J Pediatr. 1995; 127:786–793.
21. Jim Cassidy; Donald Bissett; Roy A. J. Spence; Miranda Payne (1 January 2010). Oxford Handbook of Oncology. Oxford University Press. p. 706.
22. Schwartz GJ, Feld LG, Langford DJ. A simple estimate of glomerular filtration rate in full-term infants falling on the first year of life. J Pediatr. 1984;104:849–854.
23. Libório AB, Castello Branco KMP, de Melo Bezerra CT. Acute Kidney Injury in Neonates: From Urine Output to New Biomarkers, BioMed Research International 2014; 2014:1–8Article ID 601568.
24. Zappitelli M, Bernier PL, Saczkowski RS, Tchervenkov CI, Gottesman R, Dancea A, et al. A small postoperative rise in serum creatinine predicts acute kidney injury in children undergoing cardiac surgery. Kidney International 2009; 76:885–892.
25. Alkandari O, Eddington K A, Hyder A, Gauvin F, Ducruet T, Gottesman R, et al. Acute kidney injury is an independent risk factor for pediatric intensive care unit mortality, longer length of stay and prolonged mechanical ventilation in critically ill children: a two-center retrospective cohort study. Critical Care 2011; 10;15:R146.
26. Roy B, Mandal GJ. Renal failure in Babies with perinatal asphyxia. J Pediatr Suadi Arabia 2013. December; 33:9.
27. Majeed R, Menon Y, Majeed F, Shaikh NP, Rajar UDM. Risk factors for birth asphyxia. J Ayub Med Coll Abbottabad 2007; 19:67–71.
28. Amardiyanto R, Trihono PP, Rundjan L, Pusponegoro HD. Acute Kidney injury in Asphyxiated neonates. Paediatr Indones2013; 53:232–8.
29. Alero D, Wainaing L. Incidence and short outcomes of AKI in term neonates with perinatal asphyxia. Kenya14th Annual Conference 16th-20th April.
30. 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 (Berlin, Germany) 2009; 24:265–274.
31. Karlowicz MG, Adelman RD. Nonoliguric and oliguric acute renal failure in asphyxiated term neonates. Pediatr Nephrol 1995; 9:718–22.
32. Gopal G. Acute Kidney Injury (AKI) in perinatal asphyxia. Indian J Pharm Biol Res 2014; 2:60–65.