Original Article

Causes of Acute Kidney Injury (AKI) in Pregnancy at Tertiary Care Center

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ABSTRACT

Objective: To find the frequency of common contributing factors of AKI during pregnancy.
Study Design: Descriptive, cross-sectional study.
Place and Duration of Study: This study was conducted at the Department of Nephrology and Obstetrics & Gynaecology, Fatima Memorial Hospital Lahore from 20th December 2020 to 19th June 2021.
Materials and Methods: One hundred and twenty female pregnant patients were any trimesters having acute kidney injury with ages between 18-45 years were included. Patients with renal transplantation and diagnosed CKD cases were excluded. Serum creatinine was measured at baseline along with complete blood count (CBC), peripheral blood smear, urine analysis, serum LDH, Coomb's test, ultrasound abdomen and pelvis, ABGs to determine the common contributing factors of AKI.
Results: The frequency of common contributing factors of acute kidney injury were found to be sepsis in 68 (56.7%), pre-eclampsia/eclampsia in 55 (45.83%), pre-renal/ischemic ATN in 45 (37.50%), acute glomerulonephritis in 11 (9.2%) and TTP/HUS in 08 (6.67%) patients.
Conclusion: Sepsis is the most common contributing factor of acute kidney injury in pregnancy followed by pre-eclampsia/eclampsia and pre-renal/ischemic ATN.

Key Words: Acute kidney injury, Pregnancy, Sepsis, Pre-eclampsia.

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INTRODUCTION

Renal hemodynamic adaptation mechanisms come into play as pregnancy starts. There is a 40% rise in glomerular filtration rate (GFR) and renal plasma flow in the first trimester which falls gradually in the third trimester and touches normal baseline value as pregnancy ends, however, these changes may persist 6-8 weeks after delivery.[1] Clinically these changes can be observed by looking at serum creatinine (S. Cr) value which shows an average fall of 0.4mg/dl from baseline in pregnancy. To supply adequate nutrition to mother and fetus, maternal blood volume increases up to 1.2 liters.[2]

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In case there's an unexpected sudden or progressive decrease in blood volume, it'll lead to diminished renal blood flow and acute kidney injury (AKI). In the early phase of pregnancy hyperemesis gravidarum is one of the main causes of AKI.[3] However in later phases of pregnancy especially in the third trimester various medical ailments like high blood pressure, thrombotic microangiopathies (TMA), severe sepsis, antepartum, or postpartum uterine bleeding, fatty infiltration of the liver, and autoimmune disorders contribute to AKI.[4] In developing countries pregnancy-related AKI (P-AKI) frequency is nearly 5 to 20% which has declined altogether from 20 to 40% recorded in the 1960 decade. This improvement is because of the accessibility of better antenatal and post-pregnancy health care services yet underdeveloped nations are a long way behind in medical care as shown by <1% incidence of P-AKI cases in developed nations.[5] Among all the causes,90% of cases of P-AKI are due to sepsis, pre-eclampsia, and antepartum/post-partum hemorrhages.[6,4]

Clinical conclusion of AKI depends upon the serum creatinine rise of≥0.3 mg/dl and decreased urine output of <0.5 ml/kg/h for 6–12 h inside a week duration. Assuming kidney illness is irreversible and lingers for over 90 days, then at that point, the clinical diagnosis of chronic kidney disease (CKD) is labeled.[7]However, the naming of kidney illness that persists for one to three months is yet an issue of debate, and terminology of acute kidney disease (AKD) has been proposed for such

issues.[8] Customarily RIFLE and AKIN criteria are utilized for the determination of AKI. To keep away from disarray and contrasts between these two AKI classification systems, Kidney Disease Improving Global Outcomes (KDIGO) proposed a unified classification system of AKI.[9] In pregnancy utilization of these classifications of AKI arenot accurate however without any characterized P-AKI analytic framework, KDIGO AKI criteria have right now been utilized around the world.[10]

Sepsis is the leading cause of P-AKI in developing countries whereas it holds the fourth number in the USA. Diagnosis of sepsis becomes difficult in pregnancy as WBCs count rises normally up to 25,000 mm^3.[11] Clinicians mainly rely on SIRS (systemic inflammatory response syndrome) and SOFA (Sepsis-related Organ Failure Assessment) criteria for sepsis diagnosis in wards and ICU settings, but results based on these criteria overestimated clinical diagnosis of sepsis and its associated mortality rates. Recently sepsis in obstetrics (SOS) score has been developed with 64% sensitivity and a negative predictive value of 98% for exclusion of sepsis. Abortions, pyelonephritis, bronchopneumonia, and pelvic inflammatory diseases are major causes of sepsis in pregnant females.[12] Pre-eclampsia progressively develops into eclampsia and HELLP syndrome which in a significant number of cases leads to P-AKI enhancing maternal & fetal mortality.[13] Haemorrhages occurring before or after the delivery may precipitate hypotension which is a risk factor for ischemic acute tubular necrosis.[14] Other causes like TTP/HUS, acute glomerulonephritis, acute fatty liver of pregnancy may contribute to P-AKI but these conditions are not frequently encountered.[5]

Availability of the limited number of local studies on contributing factors of P-AKI, this study was carried out to ascertain the frequency of causes leading to P-AKI.

MATERIALS AND METHODS

This Descriptive, cross-sectional study was conducted at the Department of Nephrology & Obstetrics & Gynecology, Fatima Memorial Hospital Lahore from 20th December 2020 to 19th June 2021. A sample size of 120 cases was calculated with a 95% confidence level and 4.5% margin of error while taking the expected frequency of pre-eclampsia as6.8%.[15] Using Non-probability, consecutive sampling, female patients aged 18-45 years having pregnancy of any trimester were included. Female patients with renal transplantation and already diagnosed as CKD were excluded. After taking permission from the institutional ethical review board, patient information was taken using history, physical examination, and review of the previous record. Serum creatinine was measured at baseline along with complete blood count (CBC), peripheral blood smear, urine analysis, Serum LDH, Coomb's test, ultrasound abdomen & pelvis and ABGs to determine the common contributing factors of AKI. For the diagnosis of AKI, KDIGO guidelines were utilized.[9] Data was collected and compiled in the computer SPSS-20. Data was stratified for age and weeks of gestation. Post-stratification Chi-Square test was used and a p-value ≤ 0.05 was considered significant.

RESULTS

The age range between 18 to 45 years with mean age was 26.47±5.03 years. Most of the patients 104 (86.7%) were between 18 to 32 years of age. Mean gestational age was 25.12±7.97 weeks. Mean baseline serum creatinine was 0.55±0.18 mg/dL and mean baseline eGFR was 127.88±21.45 ml/min. Mean serum creatinine at diagnosis was 2.04±1.28 mg/dL and mean eGFR at diagnosis was 47.01±25.65 ml/min. The frequency of common contributing factors of acute kidney injury in pregnant females was found to be sepsis in 68 (56.7%) patients followed by pre-eclampsia/eclampsia in 55 (45.83%), Ischemic Pre-renal/ATN in 45 (37.50%), acute glomerulonephritis in 11 (9.17%) and TTP/HUS in 08 (6.67%) patients. Stratification of common contributing factors concerning age and gestational age.

Table No.1: Stratification of the contributing factors concerning age groups (n=120)

Contributing factors		Age (years)		Total	P value
		18-32 (n=104)	33-45 (n=16)		
Sepsis	Yes	55 (52.9%)	13 (81.2%)	68 (56.7%)	0.05
	No	49 (47.1%)	3 (18.8%)	52 (43.3%)	
Pre-Eclampsia/Eclampsia	Yes	50 (48.1%)	5 (31.2%)	55 (48.8%)	0.283
	No	54 (51.9%)	11 (68.8%)	65 (54.2%)	
Ischemic Pre-renal/ATN	Yes	37 (35.6%)	8 (50.0%)	45 (37.5%)	0.281
	No	67 (64.4%)	8 (50.0%)	75 (62.5%)	
Acute glomerulonephritis	Yes	10 (9.6%)	1 (6.2%)	11 (9.2%)	1.000
	No	94 (90.4%)	15 (93.8%)	109 (90.8%)	
TTP/HUS	Yes	8 (7.7%)	-	8 (6.7%)	0.595
	No	96 (92.3%)	16 (100%)	112 (93.3%)	

Table No.2: Stratification of the contributing factors concerning gestational age (n=120)

Contributing factors		Gestational age (weeks)		Total	P value
		≤20 (n=41)	>20 (n=79)		
Sepsis	Yes	11 (26.8%)	57 (72.2%)	68 (56.7%)	0.001
	No	30 (73.2%)	22 (27.8%)	52 (43.3%)	
Pre-Eclampsia/Eclampsia	Yes	20 (48.8%)	35 (44.3%)	55(45.8%)	0.701
	No	21 (51.2%)	44 (55.7%)	65 (54.2%)	
Ischemic Pre-renal/ATN	Yes	20 (48.8%)	25 (31.6%)	45 (37.5%)	0.076
	No	21 (51.2%)	54 (68.4%)	75 (62.5%)	
Acute glomerulonephritis	Yes	5 (12.2%)	6 (7.6%)	11(9.2%)	0.507
	No	36 (87.8%)	73(92.4%)	109(90.8%)	
TTP/HUS	Yes	1 (2.4%)	7 (8.9%)	08 (6.7%)	0.262
	No	40 (97.6%)	72 (91.1%)	112(93.3%)	

When the data was stratified concerning gestational age, a statistically significant correlation was found in sepsis with a p-value of 0.0001, however, no statistically significant correlation was present with Pre-eclampsia/eclampsia, ischemic pre-renal/ATN, acute glomerulonephritis, and TTP/HUS with p-values 0.701, 0.076, 0.507, and 0.262 respectively. A statistically significant correlation was found in sepsis with a p-value of 0.05, however, no statistically significant correlation was present with pre-eclampsia/eclampsia, ischemic pre-renal/ATN, acute glomerulonephritis and TTP/HUS with p-values 0.283, 0.281, 1.000, and 0.595 respectively (Tables 1-2).

DISCUSSION

Previously, AKI was viewed as a reversible condition however, studies have proved that AKI might expand the danger of creating persistent kidney damage. The frequency of P-AKI has diminished notably overall during the lasthalf-decade, likely due to a change in obstetric and pre-birth care and a decrease in the rate of illicit abortions. Even though the occurrence of PR-AKI has been declining, it stays a significant issue because of its relationship with maternal and fetal morbidity and mortality. As indicated by some researchers, the incidence of maternal mortality in patients with P-AKI has ascended to 30- 60% especially in developing countries.[16]

Sepsis is one of the major causes of AKI not only in the general population but also in pregnancy. Among hospitalized patients, almost 5-30% of individuals develop AKI secondary to sepsis. Sepsis-induced AKI has complex pathogenesis. Relative hypotension secondary to sepsis-induced vasodilatation is the initial pathology seen in the pre-renal stage of AKI. If sepsis remained untreated inflammatory molecules such as damage-associated molecular patterns (DAMPs) are released that exhibit their binding affinity to Toll-like receptors that are present on endothelial cells and renal tubular epithelial cells, resulting in damage and necrosis of glomerular vasculature and tubules.[12] Recently role of an individual's immune response and programming for tolerance has been identified as an important factor for sepsis-induced AKI.[17] In our study 56.7% of patients developed P-AKI secondary to sepsis. Sepsis as a cause of P-AKI has been almost abolished in western countries but it is quite prevalent in Asian and African countries. In India, 15.4% sepsis-related P-AKI has been recorded including puerperal and septic abortion. Another study from Indian reported a decline in the rate of septic abortion-related AKI from 59% (1976), 20% (2008) to 6% (2014). However puerperal sepsis is still a leading aetiology accounting for 40-61.4% of cases of P-AKI.[18] In Pakistan situation is not different from India having reported percentages of 47-50% of sepsis-related AKI.[4] This high figure of sepsis is most likely due to handling of home deliveries by traditional non-professional ladies called "Dai's".

Preeclampsia and eclampsia (PE&E) are the biggest causes of P-AKI in Uruguay, South Africa, China, and Turkey with 47%, 48%, 21.2%, and 75% respectively.[19,20] Preeclampsia and eclampsia accounts for 12 to 16.6% in Pakistan and 15 to 30.5% in India.[19,21] In our study PE&E occurred in 45.83% of P-AKI cases. Diagnosis of PE&E is not as simple as it is thought to be, especially if antepartum hemorrhage, intrauterine death, sepsis, and DIC are present simultaneously. Because of overlapping features of all these conditions presumptive diagnosis of PE&E as the cause of P-AKI is usually made which in true sense is not correct. Whatever the reason, the presence of PE&E requires urgent termination of pregnancy, and reversal of P-AKI due to acute tubular necrosis is usually seen in the majority of cases.[5] Ischemic pre-renal/ATN secondary to uterine hemorrhages is the third major cause of P-AKI in our study. Placenta previa and abruptio placenta are common causes of antepartum haemorrhages which in most cases lead to volume depletion and pre-renal AKI, however, prolonged hypotension may cause acute tubular necrosis. The reported prevalence of antepartum haemorrhage (APH) is 11.5% in Malawi,[22] 4.8% in Pakistan,[15] 15% in Kashmir,[23] and 20% in India,[18] whereas postpartum hemorrhage (PPH) isseen in 10.2% to 41%of cases.[15,6] In our study pre-renal/ischemic ATN is present in

37.50% cases, this high frequency is because we have included all cases of uterine hemorrhages (APH, PPH), vomiting, and diarrhea. In our study, other causes include acute glomerulonephritis in 19.17% and TTP/HUS in 6.67% of patients. Almost similar reports with little variations have been reported from other parts of Pakistan and India.[15,18]

CONCLUSION

Sepsis is the most common contributing factor of acute kidney injury in pregnancy followed by pre-eclampsia/eclampsia and Pre-renal/ischemic ATN.

Author's Contribution:

Concept & Design of Study:	Kinza Karim
Drafting:	Omer Sabir, Shahid Anwar
Data Analysis:	Hafiz Tahir Usman, Mateen Akram, Zahid Anwar
Revisiting Critically:	Kinza Karim, Omer Sabir
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Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Odutayo A, Hladunewich M. Obstetric Nephrology: Renal Hemodynamic and Metabolic Physiology in Normal Pregnancy. CJASN 2012; 7(12):2073–80.
2. Hytten F. Blood volume changes in normal pregnancy. Clin Haematol 1985;14(3):601–12.
3. Jim B, Garovic VD. Acute Kidney Injury in Pregnancy. Semin Nephrol 2017;37(4):378–85.
4. Haroon F, Dhrolia MF, Qureshi R, Imtiaz S, Ahmed A. Frequency of pregnancy-related complications causing acute kidney injury in pregnant patients at a tertiary care hospital. Saudi J Kidney Dis Transpl 2019;30(1):194–201.
5. Prakash J, Ganiger VC. Acute kidney injury in pregnancy-specific disorders. Indian J Nephrol 2017;27(4):258.
6. Gopalakrishnan N, Dhanapriya J, Muthukumar P, Sakthirajan R, Dineshkumar T, Thirumurugan S, et al. Acute kidney injury in pregnancy - a single center experience. Renal Failure 2015;37(9): 1476–80.
7. Levey AS. Defining AKD: The Spectrum of AKI, AKD and CKD. Nephron 2021; 24:1–4.
8. Chawla LS, Bellomo R, Bihorac A, Goldstein SL, Siew ED, Bagshaw SM, et al. Acute kidney disease and renal recovery: consensus report of the Acute Disease Quality Initiative (ADQI) 16 Workgroup. Nat Rev Nephrol 2017;13(4):241–57.
9. Alseiari M, Meyer KB, Wong JB. Evidence Underlying KDIGO (Kidney Disease: Improving Global Outcomes) Guideline Recommendations: A Systematic Review. Am J Kidney Dis 2016; 67(3):417–22.
10. Ferreira DP, Amorim FF, Matsuura AJ, de Sousa JL, Santana AR, de Souza JA, et al. Pregnancy-related acute kidney injury: mortality and survival of patients treated at a maternal intensive care unit. J Nephrol 2020; 33(6):1361–7.
11. Çintesun E, Incesu Çintesun FN, Ezveci H, Akyürek F, Çelik Ç. Systemic inflammatory response markers in preeclampsia. J Lab Physicians 2018;10(3):316–9.
12. Bridwell RE, Carius BM, Long B, Oliver JJ, Schmitz G. Sepsis in Pregnancy: Recognition and Resuscitation. West J Emerg Med 2019;20(5): 822–32.
13. Duhig K, Vandermolen B, Shennan A. Recent advances in the diagnosis and management of pre-eclampsia. F1000 Res 2018;7:242.
14. Trikha A, Singh PM. Management of major obstetric haemorrhage. Indian J Anaesth 2018; 62(9):698–703.
15. Khattak MI, Sabir S, Khattak SN, Tahir N. Spectrum of Acute Kidney Injury (AKI) in Pregnancy. JRMC 2014;18(2):267-9.
16. Bentata Y, Housni B, Mimouni A, Azzouzi A, Abouqal R. Acute kidney injury related to pregnancy in developing countries: etiology and risk factors in an intensive care unit. J Nephrol 2012;25(5):764–75.
17. Gómez H, Kellum JA, Ronco C. Metabolic reprogramming and tolerance during sepsis-induced AKI. Nat Rev Nephrol 2017;13(3): 143–51.
18. Aggarwal RS, Mishra VV, Jasani AF, Gumber M. Acute renal failure in pregnancy: our experience. Saudi J Kidney Dis Transpl 2014;25(2):450–5.
19. Arrayhani M, El Youbi R, Sqalli T. Pregnancy-Related Acute Kidney Injury: Experience of the Nephrology Unit at the University Hospital of Fez, Morocco. ISRN Nephrol 2012;2013: e109034.
20. Huang C, Chen S. Acute kidney injury during pregnancy and puerperium: a retrospective study in a single center. BMC Nephrol 2017;18(1):146.
21. Sivakumar V, Sivaramakrishna G, Sainaresh VV, Sriramnaveen P, Kishore CK, Rani CS, et al. Pregnancy-related acute renal failure: a ten-year experience. Saudi J Kidney Dis Transpl 2011; 22(2):352–3.
22. Cooke WR, Hemmilä UK, Craik AL, Mandula CJ, Mvula P, Msusa A, et al. Incidence, aetiology and outcomes of obstetric-related acute kidney injury in Malawi: a prospective observational study. BMC Nephrol 2018;19(1):25.
23. Najar MS, Shah AR, Wani IA, Reshi AR, Banday KA, Bhat MA, et al. Pregnancy related acute kidney injury: A single center experience from the Kashmir Valley. Ind J Nephrol 2008;18(4): 159–61.