

Clinical Audit of Acute Kidney Injury in Critically Ill Obstetric Patients

Rekha Sachan ¹, Himani Singh ², Munna Lal Patel ³, Radhey Shyam ⁴

¹Professor, Department of Obstetrics and Gynaecology, King George Medical University Lucknow, Uttar Pradesh, India.

²Senior Resident, Department of Obstetrics & Gynaecology, King George Medical University, Lucknow, Uttar Pradesh, India.

³Professor, Department of Medicine, King George Medical University Lucknow, Uttar Pradesh, India.

⁴Additional Professor, Department of Geriatric Mental Health, King George Medical University Lucknow, Uttar Pradesh, India.

*Corresponding Author: Prof. Rekha Sachan; drrekhasachan@gmail.com

Abstract

Background: Pregnancy-related acute kidney injury (PRAKI) has a bimodal distribution. Study aimed to analyze epidemiological factors causing AKI in critically ill obstetric women and required early interventions. **Materials and Methods:** The study was conducted in an Obstetrics intensive care unit over a year. Total 447 obstetric patients admitted in critical care unit were recruited, 162 critically ill women who developed AKI were enrolled and followed for 3 months for renal outcome, AKI defined as per KDIGO guidelines. Data was collected through a structured questionnaire, medical records, and daily follow-ups until discharge. Analyses included ABG, complete blood count, serum urea, creatinine, PT/INR, and electrolytes. Critical illness was evaluated using the APACHE II score. **Results:** AKI incidence was 36.2%, hypertensive pregnancy disorders being the major cause (50.6%). Sepsis was most common mortality factor (27.16%), followed by hemorrhage (20.73%). 19.4% women died. Those patients who developed AKI, 70% recovered completely, 6.4% partially, 4.4% progressed to end stage renal disease. 71.6% cases of AKI were of antenatal. After 3 months of follow up, complete recovery significantly higher in Stage I AKI (96.4%) and Stage-II (81.3%) while rate of partial recovery and deaths were higher in Stage III AKI vs stage II (36.8%&15.8%). Higher APACHE II score (19.72 ± 5.00) was associated with stage III AKI. Duration of ICU stay (4.56 ± 4.82), duration of intubation (3.74 ± 5.31) and requirement of vasopressor support significantly associated with adverse outcome. **Conclusion:** Higher stages of acute kidney injury (AKI) resulted in higher mortality, morbidity, APACHE II score, intervention and intubation requirements, and ICU stay.

Keywords: Acute kidney injury, APACHE II score, Hypertensive disorders of pregnancy, obstetric, ICU, sepsis, renal recovery.

Introduction

Acute kidney injury (AKI) is a frequent cause for admission to the intensive care unit (ICU), affecting approximately 10-30% of patients in these critical care settings [1]. Pregnancy-associated acute kidney injury (PRAKI) constitutes a significant portion of the overall AKI burden, contributing 15% to 20% of AKI cases in developing countries [2]. In India, a concerning prevalence of pregnancy-associated acute kidney injury (PRAKI) is observed, with an incidence of 1 in 50 pregnancies. This translates to PRAKI accounting for a significant proportion, up to 20%, of all diagnosed cases of acute kidney injury (AKI) within the country [3]. Conversely, the incidence of AKI in developed nations has exhibited a dramatic reduction, with a decrease from 1 per 2,000 pregnancies to a significantly lower rate of 1 in 20,000 pregnancies. Limited high-quality research on AKI in critically ill pregnant women is a major gap in knowledge. Managing critically ill pregnant women presents

a unique challenge. Physiological adaptations during pregnancy, coupled with the presence of a fetus, complicate diagnosis and treatment of the underlying critical illness. Furthermore, specific pregnancy-related conditions (e.g., pre-eclampsia) may arise, necessitating a multidisciplinary approach with both obstetric and critical care expertise [4]. Obstetrics causes accounts for up to 2% of all general ICU admissions [5]. Serum creatinine is typically lower in pregnancy due to hyper-filtration. In a systematic review conducted by Wiles et al., (2018), concluded that, a serum creatinine of $>77 \mu\text{mol/l}$ (0.87 mg/dl) should be considered outside the normal range for pregnancy [6]. The Kidney Disease Improving Global Outcomes (KDIGO) definition and staging system is a recent and preferred definition [7]. Thus this study was planned with the aim to analyze epidemiological factors causing kidney injury, required intervention (dialysis, intubation, vasopressor support), duration of ICU stay and maternal outcome.

Methods

This prospective observational study was carried out in Obstetrics intensive care unit, Department of Obstetrics & Gynecology, King Georges Medical University, Lucknow, U.P., India, over a period of one year. After informed consent and ethical clearance from institutional ethics committee (ref.no. XIV-PGTSC-IIA/P19), total 447 obstetric patients were recruited for this study who were admitted in critical care unit, out of 447, 162 critically ill women who developed AKI were enrolled for this study and followed for 3 months-postpartum to evaluate renal outcome, AKI defined as per KDIGO guidelines 2012. Two patients were lost to follow up before analysis. Data was collected in structured questionnaire. Information regarding the patient's history and examination was obtained from patients and attendants. Demographic characteristics were obtained from medical record sheets and patients were followed daily till discharge from hospital or death and 3 months after discharge. ABG, complete blood count, serum urea, serum creatinine, LFT, PT/INR, serum electrolytes were analyzed. Critical illness was evaluated by APACHE II score. In those patients who required dialysis, hemodialysis was carried out by B. Brawn machine. The severity of AKI was graded as per the KDIGO guidelines. According to KDIGO 2012 guidelines, Acute Kidney Injury (AKI) is defined as increase in S Creatinine by 0.3 mg/dl or 26.5 μ mol/l within 48 hours, an increase to 1.5 times from baseline within 7 days, or an urine output below 0.5 ml/kg/h for 6 hours.

Results

Age of women enrolled in the study ranged between 19 & 44 year, although majority of women (n=125; 77.2%) were aged up to 30 years, mean age was 27.28 $\pm$ 5.22 year. Stage III AKI was found more in primipara while stage II AKI was more among multipara and stage I AKI was significantly higher in nullipara on applying chi square test (p=0.008). Out of 159, maximum women were referred from district hospitals (32.7%) followed by from private hospitals of Lucknow (25.79%) and private hospitals other than Lucknow (23.9%). 7.4% were referred from CHC/PHC and 10.1% patients from medical colleges. Out of 162 women enrolled in the study, majority (71.6%) were in Antenatal period, 6.2% were in post abortion phase and 22.2% in postpartum period. Higher proportion of postabortion and postpartum women developed Stage III AKI due to sepsis and hemorrhage. Antenatal women mostly developed stage I AKI. Though proportion of women without ANC visits was higher for Stage III AKI as compared to Stage I & II AKI (47.4% vs. 39.3% & 38.8%), women who had less than 4 ANC visits mostly developed stage II AKI and women who had more than 4 ANC visits mostly had Stage I AKI (**Table 1**).

Most common etiological factor was hypertensive disorders of pregnancy (HDP). HDP was more commonly associated with AKI

Stage I and Stage II as compared to AKI Stage III (57.1%, 51.0% vs. 43.9%) but this difference was not significant.

Hemorrhage was associated in higher proportion of Stage III AKI as compared to Stage I & II AKI (24.6% vs. 19.6% & 18.4%) but difference was not significant.

Sepsis was found in higher proportion of Stage III AKI patients as compared to Stage I & II AKI (42.1% vs. 14.3% & 24.5%). This association was statistically significant (p=0.004).

Heart disease as etiological factor, associated with Stage I AKI and Stage II AKI more as compared to Stage III AKI (26.8% & 18.4% vs. 12.3%). HELLP showed strong association with Stage III AKI as compared to Stage I & II (12.3% vs. 3.6% & 8.2%) (**Table 2**).

Duration of hospital stay ranged from 1 day to 35 days, mean duration of hospital stay was 9.29 $\pm$ 6.00. Though duration of hospital stay was minimum for Stage I AKI followed by Stage II AKI and maximum in AKI Stage III women.

Duration of ICU stay was ranged from 1 to 35 days, mean duration was 4.56 $\pm$ 4.82 days. Duration of ICU stay was maximum in Stage III AKI (6.47 $\pm$ 7.21 vs. 3.39 $\pm$ 1.78 & 3.65 $\pm$ 2.62 days) and this association was statistically significant on applying Friedman test (p=0.001).

Duration of intubation also showed significant association with AKI stage. Significantly higher duration of ventilatory support was required in AKI Stage III (6.05 $\pm$ 8.05 days) as compared to Stage I (2.38 $\pm$ 2.24) and Stage II AKI (2.54 $\pm$ 1.50 days) (p=0.001).

APACHE-II score of Stage III women was significantly higher as compared to Stage II & I (19.72 $\pm$ 5.00 vs. 17.45 $\pm$ 2.29 & 17.29 $\pm$ 2.96) (p=0.001) (**Table 3**).

After 3 months of follow up, out of 160 patients, 70% completely recovered, 6.3% had partial recovery, 4.4% had End stage renal disease and 19.4% expired during the hospital stay or during follow up. 2 patients who took LAMA were lost to follow up.

Complete recovery in Stage I & II AKI was significantly higher as compared to Stage III AKI (96.4%, 81.3% vs. 35.1%). Mortality rate of stage III AKI patients was higher as compared to Stage I & II (36.8% vs. 3.6% & 16.7%). Partial recovery and end stage renal disease was higher in stage III AKI (15.8% & 12.3%). This association was statistically significant (p<0.001) (**Figure 1**).

Hypertensive disorders, Hemorrhage, Sepsis, Dialysis, intubation, transfusion, pH abnormality and Potassium levels, Urine output and APACHE-II at admission were significantly associated with outcome of the women.

Among survivors and non survivors, hypertensive disorder, Dialysis, acidosis and hospital stay were significantly associated with mortality. (p=0.023), (p=0.022) (p=0.003) and (p=0.004) respectively.

Sepsis, need of intubation, vasopressor support, reduced urine output and higher APACHE II strongly associated with mortality on applying ANOVA test. (p<0.0010), (p<0.001), (p<0.001) and (p<0.001) respectively (**Table 4**).

Table 1: Association of AKI stages with demographic profile of patients (N=162)

	Stage I (n=56)	%	Stage II (n=49)	%	Stage III (n=57)	%	Total (n=162)	%
Age $\chi^2=7.471$; p=0.487	27.68 $\pm$ 5.83 (19-44)		27.61 $\pm$ 5.06 (19-41)		26.61 $\pm$ 4.71 (20-39)		27.28 $\pm$ 5.22 (19-44)	
Parity $\chi^2=13.922$; p=0.008								
Nullipara	30	53.6	17	34.7	19	33.3	66	47.4
Primipara	9	16.1	11	22.4	24	42.1	44	27.16
Multipara	17	30.4	21	42.9	14	24.6	52	32.09

Referred(n=159) $\chi^2=6.414$; $p=0.601$								
CHC/PHC	12	4	7.5	5	10.2	3	5.3	
District Hospital	52	18	34.0	19	38.8	15	26.3	
Medical Colleges	16	6	11.3	3	6.1	7	12.3	
Pvt Hospital, Lucknow	41	16	30.2	11	22.4	14	24.6	
Period of pregnancy $\chi^2=7.049$; $p=0.133$								
Antenatal	45	80.4	37	75.5	34	59.6	116	71.6
Postabortion	3	5.4	3	6.1	4	7.0	10	6.1
Postpartum	8	14.3	9	18.4	19	33.3	36	22.2
Trimester of pregnancy $\chi^2=3.671$; $p=0.452$								
14-28 weeks	1	2.2	3	8.1	4	11.8	8	6.89
29-40 weeks	43	95.6	33	89.2	30	88.2	106	91.37
Post-dated	1	2.2	1	2.7	0	0.0	2	1.2
ANC visits $\chi^2=2.887$; $p=0.576$								
0	22	39.3	19	38.8	27	47.4	68	41.97
1-3	25	44.6	26	53.1	23	40.4	74	45.67
≥ 4	9	16.1	4	8.2	7	12.3	20	12.3

Table 2: Association of AKI stages with etiological factors (N=162)

Etiological factors	Total (n=162)	Stage I AKI(n=56)		Stage II AKI (n=49)		Stage III AKI(n=57)		Statistical significance	
		No.	%	No.	%	No.	%	χ^2	'p'
Hypertensive disorders	82	32	57.1	25	51.0	25	43.9	1.999	0.368
Hemorrhage	34	11	19.6	9	18.4	14	24.6	0.703	0.704
Sepsis	44	8	14.3	12	24.5	24	42.1	11.304	0.004
Heart disease	31	15	26.8	9	18.4	7	12.3	3.868	0.145
HELLP	13	2	3.6	4	8.2	7	12.3	2.905	0.234

HELLP- hemolysis, elevated liver enzyme, low platelet count

Table 3: Association of AKI stage with hospital stay, ICU stay, duration of intubation and APACHE II score

	STAGE 1	STAGE 2	STAGE 3	MEAN
HOSPITAL STAY(DAYS) $F = 1.128$; $p=0.326$	8.52	9.12	10.19	9.29
ICU STAY (DAYS) $F = 7.583$; $p=0.001$	3.39	3.65	6.47	4.56
DURATION OF INTUBATION (DAYS) $F = 7.130$; $p=0.001$	2.38	2.54	6.05	3.74
APACHE II SCORE $F = 7.708$; $p=0.001$	17.45	17.29	19.72	18.20

Table 4: Requirement of critical care with renal outcome

SN	Variables	Total	Complete recovery (n=112)	%	Partial Recovery (n=10)	%	ESRD (n=7)	%	Expired (n=31)	%
1-	Intubation $p=0.005$	121	77	68.8	8	80.0	5	71.4	31	100.0
2-	Vasopressor ($p=0.004$)									
	Noradrenaline	34	19	17.0	3	30.0	1	14.3	11	35.5
	Noradrenaline +Vasopressor	6	1	0.9	0	0.0	1	14.3	4	12.9
3-	Dialysis $p<0.001$	25	2	1.8	7	70.0	7	100.0	9	29.0
4-	Transfusion $p=0.031$	108	68	60.7	8	80.7	7	100.0	25	80.6

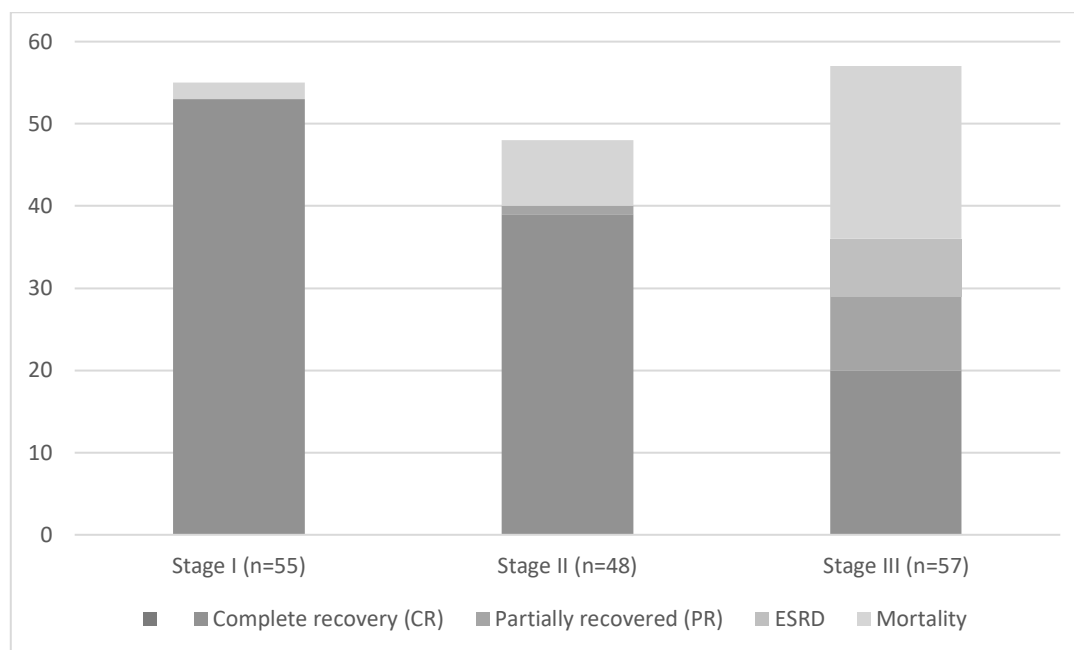


Figure 1: AKI Stage wise renal outcome after 3 months of follow up (N=160)

Discussion

In our study mean age of the study population was 27.28 ± 5.22 years. While other authors [8,9] reported mean age 25 years and 27.70 years. Our study found a statistically significant relationship ($p=0.008$) between parity and the stages of AKI. Specifically, we observed higher rates of stage I AKI in nulliparas, stage III AKI in primipara, and stage II AKI in multipara.

In another study 30% patients were primigravida and 70% were multigravida. Most of the patients in other study were multipara (49.3%) and in stage III AKI 53.0% were multipara [10], other authors reported PRAKI more common in multipara, 62%, 61.1%, and 79.6% respectively [9,11,12], while two studies reported PRAKI more common in primipara (52%) [13,14].

Patients referred from private hospitals outside Lucknow, mostly developed AKI stage III, possibly due to late diagnosis, longer duration of transportation and a greater number of referrals.

Patients referred from CHC/PHC and district hospitals mostly landed in AKI stage II, possibly due to non-availability of ICU facilities or expert doctors, late diagnosis and late referrals.

Most of the antenatal women developed AKI in the third trimester of pregnancy, none of the patient had AKI in 1st trimester, due to better understanding and management of hyperemesis gravidarum and better antenatal workup at our tertiary center.

Women who had less than 4 ANC visits mostly developed stage II AKI and women who had more than 4 ANC visits mostly had Stage I AKI.

In present study, the most common risk factor associated with AKI was Hypertensive disorders of pregnancy (severe preeclampsia, antepartum and post-partum eclampsia) in 50.65% cases and was significantly associated with development of AKI ($p=0.041$). Similarly in a study hypertensive disorders of pregnancy was present in 56% [8] and other studies reported 33.3% and 32.5% [9,12]. One more study reported preeclampsia, and eclampsia in 56% [15,16].

Hypertensive disorders increase the risk of kidney disease by multiple mechanisms include endothelial dysfunction, accelerated accumulation of comorbidities, and podocyte damage [17].

In present study, sepsis was present in 27.2% which was significantly associated with stage III AKI ($p=0.004$) and strongly associated with mortality ($p<0.001$) and was responsible for 54.8% of total maternal deaths. Recent evidence shows that microvascular dysfunction, inflammation, and metabolic reprogramming are 3 fundamental mechanisms that may play a role in the development of S-AKI [18].

Some studies have reported sepsis rates around 59%, while others have found sepsis in approximately 50% and 41.7% [9,10,15,19]. One study also identified sepsis as the leading cause of mortality in 20% of their cases [20]. In current study 71.60% developed AKI in antenatal period, out of which 66.66% had AKI in third trimester, 4.9% patients developed AKI in second trimester, none of the patients developed AKI in first trimester, possibly because of better understanding and management of hyperemesis gravidarum. In our study hemorrhage was the etiological factor in 20.8%. Placental rupture and hemorrhage are other causes of prerenal AKI, while posing a considerable risk for maternal mortality. Due to the hypercoagulable nature of pregnancy, women have a high risk of acute cortical necrosis in the setting of severe hypotension.

In our study 41.9% patients had no antenatal visit to the hospital, out of which 39.7% cases landed in AKI stage III while 45.6% had 1-4 antenatal visits, out of which 35.1% cases were in stage II AKI, only 12% cases had more than 4 antenatal visits, out of which 45% had AKI stage I. Hence antenatal care plays an important role in prevention of AKI.

In one similar study, 88% patients were postpartum and 12% were antepartum [16]. Another author found that 82% developed AKI in postpartum period and 15.3% women developed during pregnancy [11].

In our study mean duration of hospital stay was significantly higher (9.46 days) in completely recovered patients as compared to non survivors (6.48 days) ($p=0.001$), mean ICU stay was significantly shorter in completely recovered cases (3.74 days) as compared to non survivors ($p<0.001$). Out of 162 enrolled patients, 75.9% patients underwent endotracheal intubation, mean duration of intubation was 2.68 days in completely recovered cases and 5.13 days in non survivors which was statistically significant ($p=0.001$) with the development of AKI. Although all patients were critically but the duration of ICU stay was short in completely recovered patients as compared to patients who developed stage III AKI and

with higher APACHE II score and patients who did not survive. Another study found mean duration of hospital stay (days) 15 days in survivors 11 days in non survivors. Duration of ICU stay 7 days in survivors and 9 days in non survivors ^[15].

Conclusion

Our study reveals a high incidence of AKI (36.2%) among critically ill obstetric patients in the ICU, highlighting a significant challenge in maternal care. The disproportionate prevalence of stage 2 and 3 AKI in primiparas, coupled with the high referral rate and lack of antenatal care in a substantial proportion of these patients, suggests potential gaps in primary and secondary care. The strong association of postpartum/postabortal AKI with severe disease and mortality underscores the need for heightened vigilance and specialized management in this vulnerable population. While hypertensive disorders of pregnancy were identified as the most common risk factor and its association with stage I AKI, the stronger link between sepsis and mortality emphasizes the critical importance of prompt sepsis recognition and treatment. The study's finding that stage 3 AKI is strongly linked to poor outcomes, including mortality, and the identification of key clinical indicators associated with mortality (intubation, vasopressors, dialysis, etc.) provide valuable prognostic information. However, the study would benefit from further exploration of the specific causes of AKI within each trimester and postpartum/postabortal period, as well as a more detailed analysis of the impact of different management strategies. Further research is also needed to understand the factors contributing to the lack of antenatal care in a significant proportion of these patients and to develop targeted interventions to improve maternal outcomes.

Declarations

Conflict of Interest

None

Ethical clearance

Approved in Institutional Ethics Committee, King Georges Medical University, Lucknow Ref. Code: Ref. code XIV-PGTSC-IIA/P9, date 15.02.2023

This study was approved by the institutional review board/ethics committee at King George's Medical University, Lucknow, India (Ref. code XIV-PGTSC-IIA/P9). The authors followed the applicable EQUATOR Network guidelines, specifically the STROBE and reporting participation in case control studies Guidelines, during the conduct of this research project.

Author Contribution

Prof. Rekha Sachan- Concept design and Manuscript writing
Prof. Munna Lal Patel - Management, Editing, Final Drafting
Dr. Rashi Rastogi - Manuscript writing, data collection,
Dr. Radhey Shyam - Help of Patient enrollment, Case management

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