Original Article

Risk Factors and Prognosis of Acute Kidney Injury in Pre-Eclampsia

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ABSTRACT

Objective: To explore the risk factors and clinical outcomes in women with preeclampsia who developed AKI.
Study Design: A prospective observation study
Place and Duration of Study: This study was conducted at the gynecology department of Bakhtawar Amin Trust Teaching Hospital Multan from June 2020 to June 2021.
Materials and Methods: The study was conducted on pregnant women admitted to the hospital with pre-eclampsia. Women with maximum creatinine ≥90 μmol/L during admission were assessed for pre-pregnancy serial creatinine level. Kidney Disease Improving Global Outcomes criteria were adopted to evaluate the renal injury and its recovery. Predetermined risk factors, maternal and neonatal outcomes were contrasted between AKI stages.
Results: Among the total of 50 women with pre-eclampsia, 13 (26%) women qualified for the AKI KDIGO criteria. Of these, 7 (14%) had AKI stage 1, 4 (8%) had stage 2, and 2 (4%) had stage 3. Women with AKI (Stages 1-3) had a significantly higher incidence of stroke (risk ratio (RR), 15.5; 95% CI, 1.5- 157.7; p=0.012), eclampsia (RR, 1.6; 95% CI, 1.1-2.5; P=0.003) and were likely to die more (RR, 3.9; 95% CI, 1.2-12.3; P=0.002) than the woman who didn't develop AKI. Similarly, women with AKI were more prone to experience a stillbirth (RR, 1.9; 95% CI, 1.6-2.6; P<0.01) and neonatal death (RR, 2.3; 95% CI, 2.2-2.5; p=0.001). Hypertensive disorder in a previous pregnancy was the strongest predictor of the development and severity of AKI. It was found that the recovery rate reduced with an increase in the severity of the disease.
Conclusion: Conclusively, AKI was found to be a common complication in women with pre-eclampsia and resulted in considerable maternal and neonatal mortality. The failure to acquire absolute recovery of the affected population requires serious consideration of risk factors.

Key Words: AKI, pre-eclampsia, renal outcomes, pregnancy

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INTRODUCTION

Globally, the prevalence of pregnancy-associated acute kidney injury (AKI) has declined over the last few decades due to betterment in reproductive health care [1]. However, it remains a major factor behind dialysis initiation in low developing states [2,3], including Pakistan, and contributes to increasing rates of neonatal and maternal morbidity and mortality[2,4]. The situation is majorly due to the scarce understanding of contributing risk factors that limits the utilization of available resources. Additionally, the majority of studies published on this subject have contradicted due to reliance on diverse AKI definitions and only a few document incidence as per Kidney Disease Improving Global Outcomes (KDIGO) criteria [3].

Regardless of pregnancy, AKI is a strong risk factor for chronic kidney disease (CKD) [5,6] and the literature suggests a higher incidence of CKD in low-income states. The incidence of CKD in women of reproductive age is twice in low-income states as that of high-income states (9% vs 5.9%, respectively) [7], but the association between pregnancy-associated AKI and consequent CKI is largely unknown in developing states.

Across the world, hypertensive disorders during pregnancy are majorly recognized as the cause of pregnancy-associated AKI [4,2,8,9]. However, to the best of our knowledge, no study in Pakistan has yet investigated the association between the two conditions. Therefore, this study was designed to explore the risk factors and clinical outcomes in women with preeclampsia who developed AKI.

MATERIALS AND METHODS

A prospective observational study was conducted at the gynecology department of Bakhtawar Amin Trust Teaching Hospital Multan for 1 year between 5th June

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2020 to 5th June 2021. All women diagnosed with preeclampsia were consecutively enrolled according to a predetermined sample size of 50, calculated considering 95% confidence interval and 80% power of the study. Written consent was acquired from all enrolled women and ethical approval was sought from the ethical committee of the hospital. At admission, age, parity, body mass index (BMI), systolic blood pressure (SBP) and diastolic blood pressure (DBP), serum creatinine levels, and results of urine analysis through dipstick were recorded. Women with serum creatinine ≥90 μmol/L were asked to provide serial pre-pregnancy creatinine reports and were also evaluated for hematological and other biochemical indicators. Women who failed to provide previous medical data were excluded from the study.

Following potential risk factors for AKI were assessed: BMI, maternal age, parity, gravidity, various comorbidities, including anemia (Hb <9g/dL), chronic hypertension, and HIV, and history of former pregnancy with the hypertensive disorder. The KDIGO creatinine criteria were used to classify AKI stages and to determine kidney recovery at the day of discharge and during follow-up in all women with maximum creatinine ≥90 μmol/L while admitted for pre-eclampsia. Baseline creatinine was referred to lowest creatinine level <90 μmol/L before pregnancy whereas, if no such pre-pregnancy creatinine value is found, the lowest creatinine level at pregnancy was considered baseline creatinine. Maximum creatinine referred to highest creatinine value ≥90 μmol/L while admitted in the hospital. Discharge and follow-up creatinine was characterized as single minimum creatinine at the day of discharge and during follow-up after discharge, respectively. Maximum to baseline creatinine ratios were calculated according to KDIGO staging criteria. Ratios higher than 1.5, 2, and 3 denoted 1, 2, and 3 stages, respectively. Creatinine levels were evaluated during the first 48 hrs. After admission to assess minimum and maximum values. Minimum creatinine at discharge or follow-up to baseline ratios <1.5 determined recoveries at discharge and follow-up.

SPSS (version 17) was used for statistical analysis. Logistic regression analysis determined the relationship between baseline data and clinical conditions and the incidence & severity of AKI. Outcome data were categorized as: no AKI, max creatinine ≥90 μmol/L but not satisfying AKI criteria, AKI stage 1, AKI stage 2, AKI stage 3. Kruskal-Wallis test was used for simple comparisons between study groups.

RESULTS

A total of 50 women with pre-eclampsia were enrolled in the study. Among them, 16 (32%) women reported a maximum creatinine level ≥90 μmol/L during admission. Further, of these 16 women, Serial changes in creatinine level of 13 (26%) women qualified the AKI KDIGO criteria. Of these, 7 (14%) had AKI stage 1, 4 (8%) had stage 2, and 2 (4%) had stage 3. In these 13 women, urea, creatinine, and white blood cells were found to be raised whereas hemoglobin levels were reduced. Among 2 women with AKI stage 3, 1 (50%) required dialysis for a median duration of 5 days (range 2-6).

Table 1 presents the demographics and admission characteristics of patients whereas maternal and neonatal outcomes are described in Table II. Women with AKI (Stages 1-3) had a significantly higher incidence of stroke (risk ratio (RR), 15.5; 95% CI, 1.5-157.7; p=0.012), eclampsia (RR, 1.6; 95% CI, 1.1-2.5; P=0.003) and were likely to die more (RR, 3.9; 95% CI, 1.2-12.3; P=0.002) than the woman who didn't develop AKI. There were 2 (2%) maternal deaths in the AKI group and no statistical difference was found between 3 sub-groups based on AKI stages. However, the incidence rate of stroke and eclampsia were significantly different between the groups. Similarly, women with AKI were more prone to experience a stillbirth (RR, 1.9; 95% CI, 1.6-2.6; P<0.01) and neonatal death (RR, 2.3; 95% CI, 2.2-2.5; p=0.001). The incidence rate of stillbirth and neonatal death increased with the severity of AKI; however, no significant difference was found between these sub-groups.

Individual and step-wise logistic regression of predicted risk factors indicated that age, gravidity, parity, chronic hypertension, the hypertensive disorder in a previous pregnancy, admission SBP, and DBP at maximum SBP significantly played role in the incidence and severity of AKI (Table 3).

Table IV presents the recovery rate among women with AKI. It was found that the recovery rate reduced with an increase in the severity of the disease.

Table No.1: Demographics and admission characteristics of participants

Variable	No AKI		AKI		
	Max Cr <90 (n=37)	Max Cr ≥90 but AKI criteria reached (n=3)	Stage 1 (n=7)	Stage 2(n=4)	Stage 3(n=2)
Baseline creatinine umol/L, mean (SD)	-	-	72 (21)	60 (40)	58 (32)
Time at which creatinine was measured					
Prepregnancy			2 (1.9)	3 (4.5)	1 (1.6)
During admission			86 (80.4)	45 (67.2)	52 (82.5)

Following discharge			1 (0.9)		
Maternal demographics					
Age (years), mean (SD)	26.3 (5.2)	25.1 (6.5)	27.3 (5.8)	27.1 (5.5)	26.9 (5.8)
Body mass index (kg/m^2), mean (SD)	29.5 (6.9)	26.3 (5.9)	30.4 (6.9)	29.4 (5.8)	27.6 (6.2)
Primiparous, n (%)	14 (37.8%)	2 (66.6%)	2 (28%)	1(30.5%)	1 (50%)
Admission characteristics					
Admission SBP (mmHg), mean (SD)	143 (18)	145 (16)	149 (19)	151 (23)	159 (29)
Admission DBP (mmHg), mean (SD)	94 (15)	94 (13)	97 (20)	103 (17)	106 (22)
Admission urine dipstick, n (%)*					
1+	9 (13%)	-	1 (14.2%)	-	
2+	12 (32%)	2 (66.6%)	2 (28.5%)	1 (25%)	1 (50%)
3+	10 (27%)	1 (33.3%)	4 (57.1%)	2 (50%)	1 (50%)
Negative	6 (16.2%)	-	-	1 (25%)	

*= statistical significance between groups ($p<0.05$)

Table No.2: Maternal and neonatal outcome of study groups

Variable	**No AKI**		**AKI**		
	Max Cr <90 (n=37)	Max Cr ≥90 but AKI criteria reached (n=3)	Stage 1 (n=7)	Stage 2(n=4)	Stage 3(n=2)
Maximum SBP* (mmHg), mean (SD)	169 (15.5)	171 (16)	177 (17)	180 (20)	185 (23)
Maximum DBP* (mmHg), mean (SD)	99 (15)	103 (17)	110 (17)	112 (19)	112 (22)
Mode of delivery					
Caesarean section	27 (72.9%)	2 (66.6%)	5 (71.4%)	3 (75%)	2 (100%)
Vaginal delivery	10 (27%)	1 (33.3%)	2 (28.5%)	-	-
Eclampsia*	3 (11.1%)	-	-	1 (25%)	1 (50%)
Stroke*	1 (2.7%)	-	1 (14.2%)	-	-
Maternal death*	1 (2.7%)		1 (14.2%)	-	1 (50%)
ICU admission*	10 (27%)	1 (33.3%)	3 (42.8%)	2 (50%)	2 (100%)
Neonatal outcomes (n=54), n (%)					
No. Of babies	37	4	7	4	3
Still birth*	5 (13.5)	-	3 (42.8%)	2 (50%)	1 (50%)
Neonatal death*	2 (5.4)	1 (33.3%)	1 (14.2%)	-	1 (50%)

*= statistical significance between groups ($p<0.05$)

Table No.3: Logistic regression of predicted risk factors of development and severity of AKI

Risk factors	**Odd ratio**	**95% CI**	**Z-score**	**P-value**
Anemia	1.21	0.45–2.99	0.38	0.71
HIV	1.30	0.61–2.23	0.76	0.42
Primiparous	.70	0.43–1.16	-1.37	0.23
Parity (ascending)	1.23	1.00–1.48	2.12	0.02
Gravidity (ascending)	1.20	1.02–1.39	2.23	0.03
Chronic hypertension	1.90	1.12–3.43	2.47	0.013

Hypertensive disorder in a previous pregnancy	2.0	1.22–3.54	2.81	0.004
BMI	0.90	0.78–1.14	-0.81	0.32
Age	1.01	1.04–1.11	2.75	0.007
Admission SBP	0.94	.98– .99	-2.12	0.02
DBP at maximum SBP	1.01	1.0–1.04	2.41	0.012

DISCUSSION

The study found out that 26% of women with pre-eclampsia developed pregnancy-associated AKI according to KIDGO standard. Moreover, stillbirths, stroke, maternal death, and eclampsia were raised in women with AKI than their counterpart. It was unique to find out the significant impact of hypertensive complication in previous pregnancy on the development and severity of AKI. 84% of patients recovered fully after the completion of follow-up.

The significant association of AKI with stillbirths and maternal deaths reported in this study is in alliance with the description given in a related meta-analysis [3]. However, it is challenging to compare the incidence reported in different studies due to the adoption of various pregnancy-associated AKI[4,10]. Only a few previous related studies followed KIDGO AKI criteria[7]. In similar studies, less than 20% of AKI experiencing cases suffered maternal death while the need for dialysis ranged from 0-54.6% [11, 12, 13] with absolute renal recovery in 69.4% [4], 89.4%[2], and 84.6% [13] cases. Another study reported that 1.25% of cases were dependent on dialysis [4]. These contradicting outcomes are majorly due to variable definitions of AKI and different etiologies. The high incidence of eclampsia in our study complies with a South African study[14]. Given this high eclampsia rate, a higher cesarean section was expected since most of the women experienced preterm pre-eclampsia that is mostly linked with placental dysfunction that commonly hinders birth through vaginal route [15].

The literature considers cardiovascular diseases, diabetes mellitus, hypertension, renal insufficiency, and high gestational age as likely risk factors for the development of AKI in non-pregnant cases[16,17]. However, it seems to be scare when it comes to risk factors of pregnancy-related AKI. Our study found a significant association of history of hypertension in a previous pregnancy was significantly associated with AKI development and this risk factor remained independent of other risk factors. It has recently been proposed that individuals having reduced renal reserve are more prone to develop AKI as they can't respond to protein loading[18]. Subsequently, it is predicted that hypertensive disorder in previous pregnancy likely reduces renal reserve and thus the capacity to deal with psychological changes of the subsequent pregnancy. Moreover, it is found that pre-eclampsia incidence increases by 4 fold in women with a former pregnancy with AKI despite the recovery. Thus, non-apparent sub-clinical renal disease likely influence the incidence of pre-eclampsia and AKI.

Our study found out that 15.3% of women failed to recover fully after the follow-up period which is higher than reported in the previous study (9.5%) [12]. This might be due to the difference in the severity of the disease and the follow-up scheme. The recovery rate of non-pregnant women is found to be lower than that of pregnant probably due to any protective effect of pregnancy[19].

CONCLUSION

Conclusively, AKI was found to be a common complication in women with pre-eclampsia and resulted in considerable maternal and neonatal mortality. The failure to acquire absolute recovery of the affected population requires serious consideration of risk factors.

Author's Contribution:

Concept & Design of Study:	Muhammad Muzammil
Drafting:	Asim Iqbal Qureshi
Data Analysis:	Humaira Imran
Revisiting Critically:	Muhammad Muzammil, Asim Iqbal Qureshi
Final Approval of version:	Muhammad Muzammil

Conflict of Interest: The study has no conflict of interest to declare by any author.

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