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Pregnancy-Associated Acute Kidney Injury: Incidence and Risk Factors at a Tertiary Hospital in Bangladesh

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Abstract

Background: *Pregnancy-related acute kidney injury (PRAKI) still remains an important cause of maternal and fetal morbidity and mortality, although the last three decades have witnessed a dramatic decrease in its incidence in developing countries. The present study was conducted to explore the incidence, clinical characteristics and risk factors of AKI during pregnancy and puerperium in the context of Bangladeshi women.*

Method: *This was a cross-sectional study conducted among 180 pregnant women and women who were at puerperium. The study of this participants were categorized into two groups; group I included the pregnant women who developed Acute Kidney Injury (AKI) and group II included the apparently healthy pregnant women who did not develop AKI.*

Result: *About 34.4% of the pregnant women developed PRAKI. Pregnant women with PRAKI were significantly more likely to experience pregnancy induced hypertension (PIH) (69.7% vs 1.7%), Eclampsia (22.6% vs 1.7%), Sepsis (48.4% vs 2.6%) and PPH (46.8% vs 1.7%) compared to those without PRAKI (p<0.001). Multivariate regression analysis revealed that being older (≥30 years) [OR(95%CI)= 1.12(1.02-1.89),p=0.048], having PIH [OR(95%CI)= 1.10(1.00-2.00),p=0.049], developing sepsis OR(95%CI)= 1.87(1.03-3.00),p=0.038] and having post-partum hemorrhage [OR(95%CI)= 1.22(1.01-3.23),p=0.035] were significant risk factors of developing acute kidney injury among pregnant women.*

Conclusion: *In addition to recognizing the risk factors of PRAKI, it is essential to comprehend the physiological renal adaptations occurring during pregnancy. This understanding is pivotal for early identification, diagnosis, and effective management to mitigate obstetric complications.*

Keywords: *Acute Kidney Injury; Pregnancy-Related Acute Kidney Injury; Pregnancy-Induced Hypertension; Post-Partum Hemorrhage; Bangladesh*

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I. Introduction

Acute kidney injury (AKI) during pregnancy poses a dual threat to both the mother and fetus, primarily stemming from potentially preventable obstetric complications. Historically, AKI was a substantial contributor to maternal mortality and morbidity, globally [1-3]. However, the incidence of pregnancy-related acute kidney injury (PRAKI) has markedly decreased in developed nations due to the legalization of abortion and advancements in antenatal care, currently estimated at 1 in 20,000 pregnancies [4,5] However, in developing countries, PRAKI persists as a significant contributor to fetal mortality and maternal morbidity, leading to the development of end-stage renal diseases (ESRD) [6.7] Third-trimester and postpartum PRAKI show a high incidence (39%) of fetal/neonatal mortality [8] Despite a notable reduction in AKI incidence in pregnant women worldwide, it still remains a major concern, especially in developing and underdeveloped countries [9], which is mainly due to environmental, socioeconomic, and healthcare system differences between developing and developed countries [10,11].

Pregnancy-Related Acute Kidney Injury (PRAKI) is increasingly acknowledged as a condition that is both preventable and manageable, often with straightforward and cost-effective interventions [12]. The primary causes of AKI in pregnancy stems from obstetric complications, including septic abortion, preeclampsia,

thrombotic microangiopathy (TMA), heart failure, and postpartum hemorrhage. Additionally, it can occur due to abruption placentae, intrauterine fetal death (IUD), and puerperal sepsis in women with previously healthy kidneys [13]. The pathophysiology of obstetric AKI is traditionally viewed as bimodal, with distinct patterns for the early and late stages of gestation and the postpartum period. During the first trimester, septic shock frequently contributes to the development of AKI [14] In the third trimester and immediate puerperium, AKI is associated with conditions such as pre-eclampsia/eclampsia, antepartum hemorrhage (APH), postpartum hemorrhage (PPH), puerperal sepsis, hemolytic uremic syndrome (HUS), disseminated intravascular coagulation, and HELLP (hemolysis, elevated liver enzymes, low platelet levels) syndrome [15] This comprehensive understanding of the diverse etiologies of obstetric AKI underscores the importance of tailored interventions throughout different stages of pregnancy.

Data from South Asia suggested that PRAKI continues to account for 10% of total AKI cases and that mortality rates remain as high as 20% [16]. The incidence of PRAKI reported in Chinese population ranged from 0.02 to 1.84 % in recent years [17]. The prevalence of PRAKI was 3-7% in Indian sub-continent context [18]. In Bangladesh, acute renal failure contributes to 25% of maternal mortality [19]. To comprehend the current landscape, the present study was undertaken to explore the incidence, clinical characteristics, and risk factors associated with Acute Kidney Injury (AKI) during pregnancy and the puerperium, specifically within the Bangladeshi women.

II. Materials Methodology

Study design and sample

This single-centre cross-sectional study was conducted among 180 pregnant women and women who were at puerperium attending the Department of Obstetrics & Gynaecology, Dhaka Medical college hospital, Dhaka. Study participants were recruited consecutively by convenience sampling and were categorized into two groups: a pregnant woman at any gestational age or a woman in puerperium having PRAKI was assigned in group-I; while those without were considered as group-II. Pregnant women with chronic kidney disease (CKD), End-stage kidney disease, history of renal stone, small size echogenic kidneys and recent history of urological intervention were excluded from the study. This study adhered to ethical guidelines, obtaining clearance from the Institutional Review Board/Ethical Review Committee of American International University - Bangladesh (AIUB). All participants willingly agreed to take part in the research, expressing their consent through a detailed informed consent form integrated into the initial page of the questionnaire. Additionally, no incentives were provided to the participants, and their involvement was entirely voluntary, with no coercion involved in the recruitment process.

Diagnostic definition of Pregnancy-Related Acute Kidney Injury (PRAKI)

The diagnostic criteria for renal diseases in pregnancy lack uniformity and vary widely in the literature [20] making the establishment of a validated definition for Pregnancy-Related Acute Kidney Injury (PRAKI) challenging. The application of the risk, injury, failure, loss of kidney function, and end-stage kidney disease (RIFLE) classification in pregnant women requires further investigation and lacks consensus. While the prognostic utility of the RIFLE system has been demonstrated in non pregnant women [21] limited studies have explored its effectiveness in pregnancy [22]. Pregnancy induces a physiological increase in Glomerular Filtration Rate (GFR) and plasma volume, leading to a normal decline in serum creatinine, potentially masking mild AKI. In pregnancy, a creatinine level of ≥1 mg/dl or a rapid rise (defined within 48 hours) of 0.5 mg/dl above baseline is investigated for the diagnosis of AKI. Understanding these physiological adaptations is crucial in a clinical context, as levels of serum creatinine and blood urea nitrogen that are typically deemed normal (1.0 mg/dl and 13 mg/dl, respectively) in non-pregnant individuals may indicate renal impairment in pregnant women [23]. With no agreed-upon definition for PRAKI), the current diagnostic approach relies on an elevation in serum creatinine level. For our study, the diagnostic criteria for AKI in pregnant women encompassed of any of the following: (1) a sudden increase in serum creatinine exceeding 1 mg/dl, (2) oliguria/anuria, or (3) the necessity for dialysis [10].

Questionnaire development and data collection

Upon admission of pregnant women, comprehensive demographic, obstetric, and clinical histories were meticulously obtained, accompanied by necessary clinical examinations. Maternal blood samples were collected for essential biochemical analyses, placed in plain tubes, and then centrifuged at 3000 rpm for 10 minutes within a 2-hour window of collection. The study was conducted in person by trained volunteer physicians who explained the study's objectives to participants and secured written informed consent. Verification and supplementary information were acquired from patient medical records and collateral history from relatives as needed. Participants were recruited based on the clinical diagnosis of acute kidney injury by the attending obstetrician, with all details recorded in a structured questionnaire.

Data management and analysis

Descriptive statistics were completed relating to respondent's characteristics which were expressed as frequencies and percentages for categorical variables and means and standard deviations for continuous variables. Pearson's Chi-square test and independent student t-test analysis was performed to determine the factors associated with development of PRAKI. Risk factors responsible for PRAKI were assessed using univariate and multivariate logistic regression. Data was analyzed using the Statistical Package for Social Sciences (SPSS) version 25. A p value <0.05 was considered statistically significant in the analysis.

III. Result

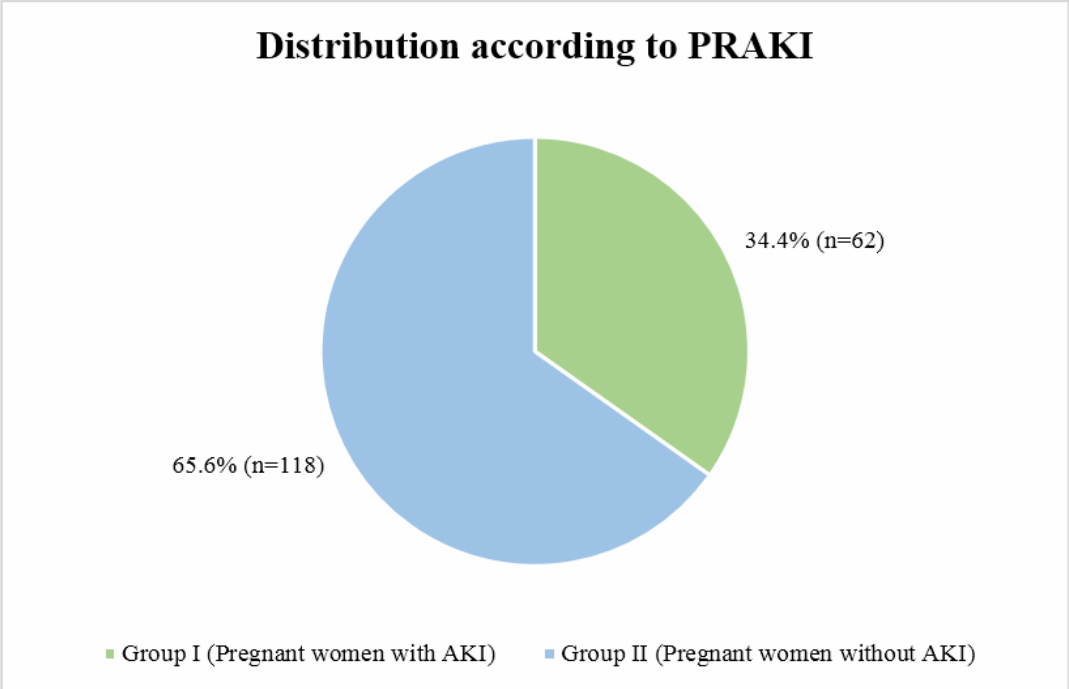

Figure 1: Distribution of study patients according to Pregnancy with Acute Kidney Injury (PRAKI) (n=180).

Demographic profile and incidence of PRAKI among study population

Among 180 pregnant women, 34.4% (n=62) developed PRAKI and 65.6% did not develop PRAKI (n=118)**.** The mean age of the women with PRAKI was 37.6±6.2 (SD) years and BMI was 28.5±3.2 kg/m^2. Age and BMI was significantly different in women with PRAKI and women without PRAKI (p<0.001). Pregnant women with PRAKI have significantly higher mean blood pressure compared to those without PRAKI (p<0.001). Pregnant women with PRAKI have a higher incidence of pregnancy-induced hypertension (PIH), and intrauterine death (IUD) compared to those without PRAKI (p<0.001) **(Table-1 and Figure 1).**

Table-1 Demographic and obstetric profile of the study population (n=180)

	Group I n=62 n(%)	**Group II n=118 n(%)**	**p-value***
Age (years)			0.010
<30	11 (17.7)	42 (36.2)	
≥30	51 (82.3)	76 (63.8)	
Mean±SD	37.6±6.2	30±7	<0.001**
Monthly family income(BDT)			0.085
≤15000	48(77.4)	104(88.1)	
>15000	14(22.6)	14(11.7)	
BMI(kg/m^2)			<0.001**
Mean±SD	28.5±3.2	25.5±3.6	
Blood pressure (mmHg)			

SBP, mean±SD	152.6±14.1	123.1±11.7	<0.001**
DBP, mean±SD	104.5±8.2	80.8±1.8	<0.001**
Gestational period			0.131
1st trimester	0 (0)	1 (0.7)	
2nd trimester	6 (9.7)	24 (20.7)	
3rd trimester	26 (41.9)	50 (43.1)	
Puerperium	30 (48.4)	41 (35.3)	
Gravidity			0.122
Primigravida	36 (58.1)	65 (56)	
Multigravida	26 (41.9)	51 (44)	
Past obstetric history			<0.001
Abortion	1 (1.6)	8 (6.9)	
Ectopic pregnancy	1 (1.6)	3 (2.6)	
PIH	11 (17.7)	0 (0)	
IUD	4 (6.5)	2 (1.7)	

Abbreviations: *BMI: Body mass index, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, PIH: Pregnancy induced hypertension, IUD: Intra uterine death*
p value was determined by *Chi-square test and **Independent sample t test.
Group I: *Pregnant women with PRAKI*
Group II: *Pregnant women without PRAKI*

Laboratory profile of study population

Pregnant women with PRAKI had a significantly higher total leucocyte count (11.9×10^9 vs 8.8×10^9), serum creatinine (1.8mg/dl vs 0.7mg/dl), D-dimer (1296.1ng/ml vs 775.6ng/ml), prothrombin time (10.3 secs vs 9.3 secs) and activated partial thromboplastin time (31.1secs vs 25.4 secs) compared to those without PRAKI ($p<0.01$). significantly lower serum haemoglobin (7.43gm/dl vs 11.1gm/dl) and platelet count (135×10^9 vs 195.4×10^9) were observed in PRAKI women compared to women without PRAKI ($p<0.01$) **(table 2).**

Table 2: Laboratory findings among the study population (n=180)

	Group I n=62 mean±SD	Group II n=118 mean±SD	p-value*
Serum Hb (gm/dl)	7.43 ±0.89	11.07±1.0	<0.01
Total leucocyte count (TLC)/10^9	11.88±1.90	8.85±0.61	<0.01
Platelet Count (PC) /10^9	134.98±28.7	195.40±23.1	<0.01
Serum Creatinine (mg/dl)	1.80±0.35	0.68±2.1	<0.01
D-dimer (ng/ml)	1296.1±172.8	775.7±224.5	<0.01
AST (U/L)	24.68± 8.93	22.46±6.59	0.062
ALT (U/L)	20.08±7.86	17.94±7.51	0.078
Total bilirubin (µmol/L)	0.61±0.13	0.59±0.10	0.273
PT (seconds)	10.35±1.10	9.28±1.07	<0.01
APTT (seconds)	31.14± 3.10	25.36±4.75	<0.01

Abbreviations: *ASR: Aspartate amino transferase, ALT: Alanine amino transferase, PT: Prothrombin time, APTT: Activated partial thromboplastin time.*
p value was determined by *Independent sample t test.
Group I*: Pregnant women with PRAKI*
Group II*: Pregnant women without PRAKI*

Distribution of Maternal complications

Maternal complications were more common in pregnant women with PRAKI (group I) compared to women without PRAKI (group II). Pregnant women with PRAKI were significantly more likely to experience PIH (69.7% vs 1.7%), Eclampsia (22.6% vs 1.7%), Sepsis (48.4% vs 2.6%) and PPH (46.8% vs1.7%) compared to those without PRAKI ($p<0.001$). 23 out of 62 PRAKI women had pre-eclampsia whereas none of the pregnant women without PRAKI were reported to have pre-eclampsia **(table 3).**

Table 3: Maternal complications among the study populations (n=180)

	Group I n=62 n(%)	Group II n=118 n(%)	p-value*
PIH	37 (69.7)	2 (1.7)	<0.01
Pre-eclampsia	23 (37.1)	0	-
Eclampsia	14 (22.6)	2 (1.7)	<0.01
Sepsis	30 (48.4)	3 (2.6)	<0.01
PPH	29 (46.8)	2 (1.7)	<0.01
Gestational diabetes mellitus	7 (9.7)	6 (5.2)	0.079
UTI	8 (12.9)	9 (7.8)	0.112
Ante Partum Hemorrhage	4 (6.4)	2 (1.7)	0.092
Hyperemesis gravidarum	4 (6.4)	2 (1.7)	0.092
HELLP syndrome	1 (1.6)	0	0.348
Acute diarrheal disease	1 (1.6)	0	0.348

Abbreviations: *HELLP syndrome: Hemolysis, Elevated Liver enzymes and Low Platelets syndrome PIH: Pregnancy induced hypertension, PPH: Post-partum haemorrhage, UTI-urinary tract infection*
****p value was determined by Chi-square test***
Group I: *Pregnant women with PRAKI*
Group II: *Pregnant women without PRAKI*

Risk factors of PRAKI in pregnant women

Multivariate regression analysis revealed that being older (≥30 years) [OR(95%CI)= 1.12(1.02-1.89),p=0.048], having pregnancy induced hypertension [OR(95%CI)= 1.10(1.00-2.00),p=0.049], developing sepsis [OR(95%CI)= 1.87(1.03-3.00),p=0.038] and having post-partum hemorrhage [OR(95%CI)= 1.22(1.01-3.23),p=0.035] were significant risk factors of acute kidney injury among pregnant women **(table 4).**

Table 4: Regression analysis for identifying risk factors that influence PRAKI in pregnant women (n=62)

	Univariate model		Multivariate model	
	OR(95%CI)	**p-value**	**OR(95%CI)**	**p-value**
Age (≥30 years)	2.63(1.24-5.59)	0.012	1.12(1.02-1.89)	0.048
BMI(>24.9)	0.78(0.70-0.87)	<0.01	1.80(0.49-2.00)	0.508
PIH	84.4(19.1-373)	<0.01	1.10(1.00-2.00)	0.049
Sepsis	35.3(10.1-123.3)	<0.01	1.87(1.03-3.00)	0.039
PPH	50(11.3-221)	<0.01	2.22(1.92-3.00)	0.038

Abbreviations: *BMI: Body mass index, PIH: Pregnancy induced hypertension, PPH: Post-partum haemorrhage*

IV. Discussion

Pregnancy-Related Acute Kidney Injury (PRAKI) is one of the most challenging and serious complications of pregnancy which imposes a heavy burden of maternal morbidity and mortality if its diagnosis and treatment are delayed. Despite a decline in developed countries, PRAKI continues to be a major contributor to maternal mortality and adverse fetal outcomes in developing countries [24]. PRAKI is a diverse condition arising from various underlying causes, representing a critical obstetric complication with substantial morbidity and mortality risks [25]. Identifying pregnant women with AKI or at risk is crucial, and understanding PRAKI risk factors is essential for effective management. This study aimed to ascertain the prevalence of PRAKI and identify associated risk factors with among Bangladesh pregnant women.

In our study, the incidence of PRAKI was documented at 34.4%. A study by Hassan et al. from Pakistan reported a comparable incidence of PRAKI at 30% Hassan et al. [26]. However, a prospective study in Bangladesh revealed an incidence more than three times higher (9.2%).[27] Globally, there has been a noticeable decrease in the incidence of PRAKI over the last five decades [28,29]. Studies have indicated that PRAKI incidence ranged from 1.0% to 2.8% in developed nations compared to 4% to 26% in developing nations [30,31]. This decline in developed nations is linked to improved antenatal care and a decrease in septic abortion due to legalization.[24]The high prevalence of PRAKI in our study may be influenced by socioeconomic factors,

including poverty, inadequate obstetric care, limited healthcare facilities and awareness, delayed referral processes, and population growth [19,32].

In the present study, the average age of women with PRAKI was in their late thirties, and those above 30 years were considered at risk for developing PRAKI. Similar findings were reported by Shah et al. (2020), [33] who identified increased age as a significant risk factor for PR-AKI. Wang et al. (2011) [34] also noted a mean age of 30±5 (SD) years for PR-AKI patients, while Li et al. (2021) [17] reported a lower mean age of 27.7±5.6 years, contrasting with the findings of our current study. Additionally, our study revealed a predominant occurrence of primigravida women with PRAKI, aligning with findings from Makusidi et al.[35] and Eswarappa et al.[36] who likewise observed a higher susceptibility among primigravida individuals. The majority of patients in our study had a monthly income below 15,000 BDT, potentially serving as a contributing factor to the development of AKI. Low socioeconomic status has been consistently identified as a factor leading to underutilization or insufficient utilization of antenatal services [37]. Moreover, Grams et al. [38] identified low socioeconomic status as a risk factor for AKI in the general population.

This study found that in pregnant women with PRAKI, maternal complications were notably more prevalent compared to those without PRAKI. The incidence of Pregnancy-Induced Hypertension (PIH) was a significant risk factors for the development of PRAKI in pregnant women. Several studies have identified PIH as the predominant cause of Pregnancy-Related Acute Kidney Injury (PRAKI) [37]. The susceptibility to hypertensive disorders during pregnancy is highest among young primigravida and older multiparous women. Hypertensive disorders in pregnancy encompass chronic hypertension, preeclampsia, eclampsia, gestational hypertension, and preeclampsia superimposed on chronic hypertension. Notably, preeclampsia and eclampsia have been consistently reported as the primary contributors to PRAKI cases [14,18,24] aligning with our study's findings. Preeclampsia, characterized by new-onset hypertension and proteinuria after 20 weeks of gestation, involves hemodynamic disturbances leading to renal ischemic injury due to decreased renal plasma flow, glomerular filtration rate, and vasoconstriction of renal vessels [39].

Our study also found that sepsis and post-partum haemorrhage were significant factors that contributed to the development of PRAKI. A study conducted in Canada similarly indicated that postpartum hemorrhage was the most common risk factor for PRAKI [40]. Postpartum haemorrhage can result in hypovolemia, causing inadequate perfusion to renal areas and subsequently reducing the glomerular filtration rate. Prolonged hypovolemia leads to ischemic injury in parts or the entirety of the kidneys [41]. In line with our findings, other studies have reported sepsis contributing to 30–60% of PRAKI cases [24]. The elevated incidence of puerperal sepsis underscores the necessity for enhanced quality in antenatal and perinatal care.

The study's limitations include potential sampling bias due to purposive sampling, hindering generalization to the entire population. The small sample size (180 participants) restricts the study's representativeness for the entire country. Despite these constraints, the study benefits from the availability of clinical data, a reasonable follow-up duration with minimal patient attrition, and a comparison with a control group.

V. Conclusion

Pregnancy-Related Acute Kidney Injury (PRAKI) remains prevalent in Bangladesh, significantly contributing to maternal and perinatal complications. Key risk factors include pregnancy-induced hypertension, sepsis, post-partum haemorrhage, and advanced maternal age. This study finding are crucial for preventing and managing AKI risks during pregnancy, enhancing outcomes for pregnant mothers with AKI. Obstetricians in Bangladesh can benefit from this information for improved PRAKI case management. Proposed actions include heightened awareness of PRAKI, initiating kidney function tests and hypertension monitoring at pregnancy onset, accurate and prompt diagnosis, and a community-based study with a larger sample size.

Declarations

Ethics approval and consent to participate: The study was approved by the Ethical Review Committee of American International University - Bangladesh (AIUB). Informed written consent was obtained from all eligible participant who agreed to participate. The authors declare no human subjects were harmed and the procedures followed were in accordance with the ethical standards and regulations established by the Helsinki Declaration of the World Medical Association.

Consent for publication: Not applicable

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