

Review Article

Pregnancy Induced Acute Kidney Injury (AKI) and Its Consequences: An Updated Review!

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Introduction

Acute kidney injury (AKI) is a heterogeneous syndrome in pregnant women and is caused by multiple etiology. AKI that occurs during pregnancy or in post-partum period remains a life-threatening obstetric complication. This pathological obstetrics status induces significant maternal and fetal morbidity and mortality. Although pregnancy related acute kidney injury PR-AKI has decreased dramatically over the last three decades in developing countries; the data from developed countries are more nuanced. While occurrence of pregnancy related acute kidney injury PR-AKI declined in developed countries in only 1–3% due to utilization of better antenatal care (ANC) and rare cases of septic abortion, though rarely.¹⁻³ However, high rate (4.2–15 %) was reported from developing countries mainly due to limited inaccessibility of ANC & emergency Obs healthcare facilities.⁵⁻⁷

Overall Occurrences of AKI -AKI

In recent years, there is a significant decline in the incidence of patient requiring dialysis which is fewer than 1 in 20,000 pregnancies.² **PR-AKI** mainly occurs due to obstetrical complications, principally more like- septic abortion, abruptio placentae, uterine hemorrhage, intrauterine fetal death (IUD), and puerperal sepsis, notably, these obstetric complications may occur even in women with previous healthy kidneys.

Current state of PR-AKI

With the gradual improvement in ante- and post-natal care, incidence of **PR-AKI** has steadily been declined from 22% in 1960s to 9% in 1980 in India, yet went down further to 3–7% in 2000.^{8,9} However, the levels continue to remain higher in developing countries than the levels seen in developed countries (1 in 20,000 pregnancies), sepsis and hemorrhage account for >50% of cases of Pregnancy related AKI **PR-AKI**⁵ in contrast, chronic hypertension, renal disease and preeclampsia and eclampsia are important causes in developed countries.⁶ Incidence of **PR-AKI** has decreased in the developed countries to only 1-2.8% due to better antenatal care and rare cases of septic abortion in these countries.^{2,3} Thus, the afore-mentioned literature evidences that **PR-AKI** is not that easy to bring down neither its prevalence nor the incidence which remains truer for Bangladesh like in other lower SES country. That is what has been tried to describe in this updated review.

Diagnostic criteria of AKI in pregnant women PR-AKI

A creatinine level of ≥ 1 mg/dl or a rapid rise (by definition in 48 h) of 0.3 mg/dl above baseline should be investigated for evidence of AKI. This information is important because serum creatinine and blood urea nitrogen of 1.0 mg/dl and 13 mg/dl, respectively, would

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be considered normal in a nonpregnant individual but reflect renal impairment in a pregnant woman. Besides the diagnosis of **PR-AKI** is based on increase in serum creatinine.¹

Following criteria can be considered for diagnosis of AKI in pregnant women: -

1. Sudden increase in serum creatinine ≥ 1 mg/dl,
2. Oliguria/anuria, and
3. Require dialysis¹⁰

The definitions can range from an increase in the serum creatinine to the need for dialysis. This is further confounded by the physiologic decrease in serum creatinine seen in pregnancy. The frequently cited **RIFLE** (Risk, Injury, Failure, Loss and End stage)¹¹ and the **AKIN** (Acute Kidney Injury Network) criteria¹² for the non-pregnant population have not been well validated in pregnancy. More recent obstetric studies, however, have begun to use these classifications. For example: having a high RIFLE class predicted higher mortality in obstetric patients in an intensive care unit.¹³ Investigators from the Mayo Clinic, using the **AKIN** criteria, discovered that most of the patients belonged to the AKIN stage 1 category, with only transient increases in serum creatinine.¹⁴ In addition, these women with AKI tend to have comorbid conditions such as hypertension, diabetes or chronic kidney disease, and pregnancy-related complications such as, preeclampsia/**HELLP** (Hemolysis, Elevated Liver function tests, Low Platelets), hemorrhage or infections. Investigators will be better able to assess whether they can be used to risk-stratify obstetric patients as more studies utilize these criteria.

Pregnancy Outcomes in PR-AKI

Between 1998 and 2009 in the United States death rate during delivery hospitalizations was 17.4% and 31.5% amongst post-partum hospitalizations in women with AKI of any etiology.¹⁵ Hypertensive disorders of pregnancy are an important contributor to the burden of AKI in pregnancy, preeclampsia and **HELLP** syndrome particularly.¹⁶ Along with maternal complications **PR-AKI** also has a significant impact on fetal morbidity and mortality. Mortality rate is estimated to be 23.5–38% among babies born to women with **PR-AKI**.¹⁷ Obstetric complications are a significant contributor to renal injury during pregnancy. **PR-AKI** is attributed to rare obstetric complications, such as atypical hemolytic uremic syndrome, thrombotic thrombocytopenic purpura and acute fatty liver of pregnancy.¹⁶

Lack of antenatal care (57%) & history of traditional birth attendants TBA (Dai) assisted home delivery as compared to 6 (14%) cases with adequate antenatal care was observed in an observational and prospective hospital-based study at a tertiary care hospital in Hyderabad for one year conducted.¹⁷ Clinical spectrum of pregnancy related ARF showed APH in 6 (14%) cases, PPH in 9 (24%) cases, septic abortion and puerperal sepsis and DIC in 13 (31%) cases, IUD in 6 (14%) and preeclampsia / Eclampsia in 5 (12%) cases. 30 patients (71%) received hemodialysis where 12 (29%) did not require dialysis. Commonest clinical diagnosis was ATN in 23 cases (55%) with complete recovery. Acute bilateral renal cortical necrosis was seen in 9 (21%) cases and 2 (5%) patients had patchy cortical necrosis. Overall morbidity was 19% and mortality 26%.²²

Golani et al. 2008 conducted a study to evaluate the contributing factors and to assess the frequency of cortical necrosis.¹⁸ In this prospective study, the incidence of pregnancy-related ARF was 9.06%. Puerperal sepsis was the most common etiological factor in 61.42% of the patients. Preeclampsia accounted for 28.57% of ARF. Two-thirds of patients recovered with dialysis and supportive care. The incidence of biopsy proven renal cortical necrosis was 14.8%. The incidence of renal cortical necrosis was 28.57% in the early pregnancy group and 10.71% in the late pregnancy group. Approximately 20% cases occurred due to post-aborted complications in early pregnancy and 80% following complications in late pregnancy. Post-aborted sepsis was the most common precipitating event for renal cortical necrosis. Maternal mortality was 18.57%. Sepsis accounted for a majority of deaths (61.53%).¹⁸

Long-Term Consequences of PR-AKI

Though AKI was considered as a reversible syndrome previously, recent studies shows that AKI may increase risk of developing CKD resulting in kidney damage or requiring dialysis even after delivery.^{16,19} A meta-analysis on **PR-AKI** reported that 2.4% of women with AKI during pregnancy progressed to ESRD and needed long-term dialysis.²⁰ A study showed that 21.2% patients with **HELLP** syndrome and AKI for up to 1 year of postpartum required dialysis. Women with **HELLP** syndrome are more prone to need dialysis and remain hypertensive in the post-partum period.^{21,22} Generally, 82.7-89.4% of the patients recovers completely however long-term data regarding dialysis in women with a history of AKI in pregnancy is insufficient. Absolute risk of ESRD after preeclampsia is low, however, preeclampsia in one or

more pregnancies is a risk factor for development of long-term renal dysfunction.¹⁵ According to some studies several years (7.2 ± 5.2 year) following a pregnancy complicated with aHUS 53% of patients had progressed to ESRD²³ whereas poor renal outcome in patients with pregnancy associated aHUS were reported in other studies where 21–36% of patients either developed CKD received a renal allograft, were on dialysis or developed ESRD.²⁴

Reports on similar study on PR-AKI

18 cases of pregnancy-related acute renal failure (PR-ARF), 9% of the total number of ARF were observed where mean age of the women was 32 years (22–40 years) in a study conducted between 1982 and 1992 by Alexopoulos et al. 1993.²⁴ 61% of the cases were due to uterine hemorrhage and preeclampsia/eclampsia which causes ARF significantly. Patchy renal cortical necrosis was suspected in 2 cases whereas signs of disseminated intravascular coagulation (DIC) or microangiopathic hemolytic anemia were present in 6 (33%) and 9 (50%) cases, respectively. Ten women required hemodialysis; and 6 of them, additional plasma exchange sessions. Five patients (28%) died during the acute phase of the illness, mainly due to brain damage, hepatic failure, and sepsis. Among the survivors, a complete (61.5%) or partial recovery (23.1%) was usually seen, but irreversible renal failure was recorded in 2 cases with postpartum hemolytic uremic syndrome (HUS).²⁴

Acute renal failure occurred in 53.3% cases in early part of their pregnancy, whereas in 46.7% cases in later of the pregnancy.²⁵ Fifty three percent patients had not received any antenatal visit, and had home delivery, 33.4% patients had delivered in hospitals but without antenatal care and 13.3% patients received antenatal care and delivered in the hospitals. Anuria was observed in 38.3% cases, remaining 61.7% cases presented with oliguria. Septicemia was present in 41.7%, hypertensive disorder of pregnancy in 33.3%, hemorrhage in 13.3%, abortion in 8.3%, hemolysis elevated liver enzymes low platelets count (HELLP) syndrome in 1.67% and disseminated intravascular coagulation in 1.67%. 61.7% patients were not dialyzed, 55% recovered normal renal function with conservative treatment. Complete recovery was observed in 75% patients, 8.4% patients developed irreversible renal failure. Maternal mortality was nine 15% and fetal loss was 41.7%.²⁵

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India from January 2009 to January 2011.²⁶ The age range was 19–38 years (mean 26 ± 3.8). The first trimester, second trimester and puerperal groups comprised of 8%, 50% and 42% respectively.

Hemorrhage was the etiology for AKI in 30%, APH in 20% and PPH in 10% patients. 22% patients had lower segment caesarian section (LSCS) while 78% patients had normal vaginal delivery. In 40% patients, puerperal sepsis was the etiological factor, while pre-Eclampsia, Eclampsia and HELLP syndrome accounted for 36% patients. 4% patients had disseminated intravascular coagulation on presentation while 2% patient was diagnosed with hemolytic uremic syndrome. Maternal mortality was 12%. Of the 88% surviving patients, 42% had complete recovery of renal function, 16% patients had partial and 30% patients required dialysis on a long-term basis.²⁶

Reports on Similar Studied research conducted in other institutions/ our country

An observational study on- "Association of Acute Kidney Injury in Complicated Pregnancy and its Outcome after 28 weeks of Pregnancy" is in progress which is carried out by "Ad-din women's Medical College and Hospital" under supervision of Ad-din research unit (ARU).

In Mymensingh Medical College Hospital (MMCH) from April 2011 to March 2012, only one prospective case control study was done on- Outcome of Pregnancy Related Acute Kidney Injury Observed in a Tertiary Care Hospital. Another prospective observational study was done to observe the status of ARF in pregnancy in Nephrology Department of Dhaka Medical College during 2007.

Conclusive Remarks

Pregnancy induced AKI is a deadly situation which significantly causes both maternal and fetal mortality. Even though the rate is deteriorating in the developed countries, still common in developing countries like Bangladesh (21.6%). Maternal outcome of Pregnancy related acute kidney injury is not acceptable in Bangladesh due to limited data availability on the occurrence, demography, etiology and outcome of **PR-AKI** of Bangladeshi population in complicated pregnancy. Around 21.7% pregnancy induced AKI patients usually died while 6.7% did not recover at the time of hospital discharge. So, we can conclude **PR-AKI** as a critical situation associating with the worst prognosis. More studies should intend to find out the

occurrence, characteristics such as demographic characteristics, clinical parameters, etiology and outcome of **PR-AKI** in different clinical settings in a tertiary care hospital of Bangladesh. Such study results will help to plan better prevention of **PR-AKI** to reduce the burden of unwanted maternal and fetal death.

Bottomline

Pregnancy related AKI (**PR-AKI**) stands a critical clinical condition towards fatal prognosis, unless intervened. Since, AKI remains a reversible condition it can be well prevented utilizing in-time proper therapeutic interference, appropriate counselling and regular apposite follow up for a prescribed time frame.

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