Role of renal replacement therapy in pregnancy related acute kidney injury and its outcome

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ABSTRACT

Background: Pregnancy-related acute kidney injury (PRAKI) has bimodal distribution. The rates of maternal mortality and perinatal mortality in patients with PRAKI have increased. The aim of this study was to evaluate magnitude of PRAKI in North Indian women and to assess morbidity, mortality, and outcomes in patients who received renal replacement therapy.

Materials and Methods: This prospective observational study was carried out in the Department of Obstetrics and Gynaecology, in collaboration with nephrology. A total of 150 women suffering from PRAKI were recruited and total 98 obstetrics AKI, requiring renal replacement therapy, classified as per KDIGO guidelines 2012 were enrolled for dialysis. Six patients were lost to follow up before final analysis. Haemodialysis was carried out by B. Brawn machine. Results: Approximately 82% cases of PRAKI diagnosed in postpartum period. Mean cycles of dialysis was 9.06 ± 7.75 approximately half of the females required 1–5 cycles of dialysis. Higher percentages of maternal deaths were observed within 1–5 cycles of dialysis. Women received dialysis after 72 h showed increased chances of partial recovery. After 3 months of follow-up, rate of complete recovery was significantly higher in Stage I (100%) and Stage II (84.6%) PRAKI while rate of partial recovery and deaths were significantly higher in Stage III PRAKI (37.3%). Stage of AKI, baseline K+ levels, treatment modality, duration of ICU stay and use of Vasopressure showed significant association with adverse outcome.

Conclusion: Higher percentages of deaths were observed in those who referred late and delay in initiation of dialysis and it was observed within 1–5 cycles of dialysis.

Keywords: Haemodialysis, intensive care, pregnancy related acute kidney injury, recovery, renal replacement therapy

Introduction

A term renal replacement therapy (RRT) is referred to modalities of treatment used to replace the waste filtering function of a normal kidney.[1] Dialysis is one of the most commonly used RRT in present era. Acute kidney injury (AKI) is characterized by sudden decline in glomerular filtration rate leading to decreased excretion of nitrogenous waste products such as urea, creatinine and uremic products.[2]

In India, pregnancy-related AKI requiring dialysis has decreased from 15% to 10% in 1992 to 2002, with a concurrent decrease in maternal mortality from 20% to 6.4% in 2002.[3] This marked decline of PRAKI, because of reduction in sepsis and improved management of postpartum haemorrhage and placental abruption. Sepsis was mainly associated with abortion and childbirth,[3,4] PRAKI has a bimodal distribution.[3‑8] The first observed peak is between the 7th and 16th week of gestation, while the second peak is noted between the 34th and 36th week of gestation.[5‑8] Hyperemesis gravidarum and septic abortion in first trimester and other causes in third trimester mainly causing...
AKI in pregnancy. Hypothesis of this study is early initiation of RRT or haemodialysis in pregnancy related AKI will affect the renal recovery and survival of women. This study is relevant for the general physician on the basis of this hypothesis.

This study included the women suffering from PRAKI defined on the basis of KDIGO guideline 2012.[9] In this study serum creatinine level of 0.8 mg/dL or >72 micromole has been taken as lower reference limit, because this level is considered normal in pregnancy and an indicator of normal renal function. Various studies reported increase in maternal mortality (30%) and perinatal mortality (60%) in patients with PRAKI mainly when dialysis is required.[10] Thus there is a need for further evaluation of AKI in pregnancy to improve obstetric outcomes as well as practices. Hence this study was planned to evaluate role of RRT in obstetric AKI in North Indian women.

The aim of this study was to evaluate the magnitude of PRAKI in North Indian women and to assess morbidity, mortality and outcomes in patients who received RRT.

Material and Methods

This prospective observational study was carried out in the Department of Obstetrics and Gynaecology, in collaboration with Nephrology unit, Department of Medicine, and Trauma ventilator unit, King George’s Medical University, Lucknow, Uttar Pradesh, India, from June 2019 to October 2020. After informed consent and ethical clearance from institutional ethics committee (96th ECM II B- Theis/P68), 150 women suffering with pregnancy related acute renal failure were recruited and total 98 obstetrics AKI, classified as per KDIGO guidelines 2012 requiring RRT were enrolled for dialysis. Six patients were lost to follow up before final outcome analysis. All patients were followed up to next 3 months for final outcome in terms of partial recovery, complete recovery.

Haemodialysis was done in those women who were suffering with PRAKI and full filling criteria for dialysis. Dialysis was carried out by B. Brawn machine. Bicarbonate dialysis was done at the blood flow rate of 250–300 mL/min, duration of dialysis 4 hours/day for 3 days/week, rate of filtration depends upon volume overload. Serum creatinine (measured by Jaffe method) and urine output was measured after each haemodialysis and at every 24 h.

After taking informed consent and ethical clearance from institutional ethic committee, patients were enrolled for the study. Information was gathered from the patients through structured questionnaire consisting of patient age, complete postal address, registration number, contact number, religion, symptoms and signs. For each patient a detailed history and thorough physical examination including obstetric and pelvic examination was carried out. Specific investigations including automated blood count, random blood sugar, serum electrolyte, blood urea, serum creatinine, coagulation profile, ABG, LFT and renal ultrasonography were done prior to enrolment. Other investigations including blood culture, high vaginal swab culture sensitivity and urine routine, microscopy, culture sensitivity were done.

Haemodialysis was performed in those who were fulfilling the criteria, by B. Brawn machine with Bicarbonate dialysis at the blood flow rate of 250-300 mL/minute, duration of dialysis 4 h/day for 3 days/week, rate of filtration depends upon volume overload. Serum creatinine (measured by Jaffe method) and urine output was measured after 6 h of each haemodialysis in Group A and after every 24 h in group A, B, and C.

Indications for dialysis

Serum creatinine increase ≥3 fold from baseline or serum creatinine >4 mg/dL (353.6 µmol/L) or urine output <0.3 mL/kg/hr for >24 h or Anuria more than 12 h, commenced RRT irrespective of stage. Other indication are:

- Refractory hyperkalaemia >7 mmol/L (normal value 3.5 to 5.0 mmol/l)
- Intractable fluid overload
- Acidosis producing circulatory compromise
- Overt uraemia manifesting as encephalopathy, pericarditis, or uremic bleeding
- Oliguria with Added- urine output <0.5ml/kg/h for 6 hrs
- Acidaemia (pH <7.0)

Statistical analysis

Data were collected in term of fix variable such as age, gender, race, place socioeconomic status and in term of continuous variable such as blood urea, serum creatinine, input, output and improvement in clinical symptoms and sign. Continuous variable were measured after 6 h of each haemodialysis and after 24 h per day for 7 days in each group. Simple t-test and chi square test was used for quantitative and qualitative analysis and analysis of variance was used to estimate the improvement in parameter.

Results

After comparison between different stages of PRAKI, significant differences were observed about parity (p = 0.042) and ANC registration (p = 0.009) [Table I].

Total 82% (n = 123) cases of PRAKI were diagnosed in postpartum period. Remaining 18% (n = 27) cases of PRAKI were diagnosed in antenatal period, out of these 13.3%, (n = 20) in third trimester, 2% (n = 3) in second trimester and 2.7% (n = 4) in first trimester and post-abortion group.

Percentages of multiparous women (53.0%) were higher in Stage III AKI as compared to Stage I and II AKI (33.3% vs. 15.4%). None of the women were registered at our centre. Out of registered women from outside, total 16 patients of AKI stage I and II enrolled in this study. Majority, 62% (n = 10) of these were referred from PHC/CHC. While percentages of Stage III AKI (30.6%) were significantly higher among those women who
were referred from district hospitals. 88% women referred within 1-3 days of development of AKI [Table 1].

Only 1 woman (0.7%) of Stage III AKI died in ICU after admission within 24 hours of stay. All women of Stage I and Stage II AKI and 53.7% of Stage III AKI required ICU stay of 1-5 days. 45.5% of women with Stage III AKI required ICU stay of >5 days. In this study, duration of ICU stay was significantly associated with Stages of PRAKI (p = 0.013). [Table 2]

Overall ventilator support required in 18% (n = 27) of cases and out of these 15.7% (n = 21) were from stage III AKI. Requirement of ventilator support and stages of AKI has significant association (p value 0.034)

Use of Vasopressure was maximum in Stage I (66.7%) followed by Stage II (30.8%) and minimum in Stage III AKI (18.7%), though the number was less but these patients were very sick, required early management and ICU care [Table 2].

Dialysis was carried out in 98 patients out of 150 patients whenever indicated on priority basis after admission. Mean cycles of dialysis was 9.06 ± 7.75. Approximately half of the females required 1-5 cycles of dialysis (48.0%), >10 cycles of dialysis were required in 31.6% women. Majority of women underwent dialysis after >72 hours of referral (64.3%). Only 14.3% received dialysis within 24 hours, 6.1% within 48 hours and 15.3% were received dialysis within 72 hours. [Table 3]

Though the number of dialysis and time for initiation of dialysis from duration of referral not significantly associated with outcome in terms of recovery or mortality, higher percentages of deaths were observed within 1-5 cycles of dialysis (46.5%). Increase chances of partial recovery was observed when women received dialysis after 72 hours (55.7%). [Table 4]

After 3 months of follow up, rate of complete recovery was significantly higher in Stage I (100%) and Stage II (84.6%) AKI while rate of partial recovery and deaths were significantly

### Table 1: Stage wise comparison of Obstetric profile

|                      | Stage I (n=3) | Stage II (n=13) | Stage III (n=134) | Total (n=150) |
|----------------------|--------------|-----------------|-------------------|--------------|
|                      | No. | %    | No.  | %     | No.  | %     | No.  | %     |
| Gravida              |     |      |      |       |      |       |      |       |
| G1                   | 0   | 0.0  | 5    | 38.5  | 18   | 13.4  | 23   | 15.3  |
| G2                   | 1   | 33.3 | 3    | 23.1  | 37   | 27.6  | 41   | 27.3  |
| G3+                  | 2   | 66.7 | 5    | 38.5  | 79   | 59.0  | 86   | 57.3  |
| χ²=6.355 (df=4); P=0.174 |
| Parity               |      |      |      |       |      |       |      |       |
| Nullipara            | 0   | 0.0  | 5    | 38.5  | 19   | 14.2  | 24   | 16.0  |
| Primipara            | 2   | 66.7 | 6    | 46.2  | 44   | 32.8  | 52   | 34.7  |
| Multipara            | 1   | 33.3 | 2    | 15.4  | 71   | 53.0  | 74   | 49.3  |
| χ²=9.922 (df=4); P=0.042 |
| ANC Registration outside (Booked) |      |      |      |       |      |       |      |       |
| PHC/CHC              | 2   | 66.7 | 8    | 61.5  | 21   | 15.7  | 31   | 20.7  |
| District hospitals   | 0   | 0.0  | 3    | 23.1  | 41   | 30.6  | 44   | 29.3  |
| Multispecialty.      | 0   | 0.0  | 0    | 0.0   | 4    | 3.0   | 4    | 2.7   |
| Other**              | 1   | 33.3 | 1    | 7.7   | 47   | 35.1  | 49   | 32.7  |
| Unbooked             | 0   | 0.0  | 1    | 7.7   | 21   | 15.7  | 22   | 14.7  |
| χ²=20.485 (df=8); P=0.009 |
| No. of ANC Visits    |      |      |      |       |      |       |      |       |
| No visit             | 0   | 0.0  | 2    | 15.4  | 18   | 13.4  | 20   | 13.3  |
| 1-3                  | 1   | 33.3 | 3    | 23.1  | 54   | 40.3  | 58   | 38.7  |
| 4-6                  | 1   | 33.3 | 6    | 46.2  | 51   | 38.1  | 58   | 38.7  |
| ≥7                   | 1   | 33.3 | 2    | 15.4  | 11   | 8.2   | 14   | 9.3   |
| χ²=4.140 (df=6); P=0.658 |
| Period of pregnancy  |      |      |      |       |      |       |      |       |
| 1st Trimester        | 0   | 0.0  | 0    | 0.0   | 4    | 3.0   | 4    | 2.7   |
| 2nd Trimester        | 0   | 0.0  | 0    | 0.0   | 3    | 2.2   | 3    | 2.0   |
| 3rd Trimester        | 0   | 0.0  | 5    | 38.5  | 15   | 11.2  | 20   | 13.3  |
| Post-partum          | 3   | 100.0| 8    | 61.5  | 112  | 83.6  | 123  | 82.0  |
| χ²=8.675 (df=6); P=0.193 |
| Day of referral to the hospital |      |      |      |       |      |       |      |       |
| 1-3                  | 3   | 100.0| 12   | 92.3  | 117  | 87.3  | 132  | 88.0  |
| 4-6                  | 0   | 0.0  | 0    | 0.0   | 11   | 8.2   | 11   | 7.3   |
| >6                   | 0   | 0.0  | 1    | 7.7   | 6    | 4.5   | 7    | 4.7   |
| χ²=1.802 (df=4); P=0.772 |

ANC: Antenatal care; PHC: Primary Health Center; CHC: Community Health Center
higher in Stage III AKI (37.3%). \( \chi^2 = 32.986 \) (df = 8); \( P < 0.001 \) [Figure 1]

After multivariate analysis it was found that, stage of AKI, baseline K + levels, treatment modality, duration of ICU stay and use of Vasopressure only had significant association with adverse outcome in patients of PRAKI. [Table 5] [Figure 2]

### Discussion

Most of the patients in our study were multipara (49.3%) and in stage III AKI 53.0% were multipara, other authors reported PRAKI more common in multipara 62%,11 61.1%,12 and 79.6%13 respectively, while two studies reported PRAKI more common in primipara (52%).14,15

In present study, majority of women (82%) developed AKI in postpartum period and 15.3% women developed AKI during pregnancy. Only 2.7% women reported AKI in post-abortion period. Another author reported, occurrence of AKI, in post-partum period (68%) and 32% during pregnancy.13

In our study 83.6% post-partum AKI were of stage III while another studies reported 52% and 60% postpartum stage III AKI.11,14 Other studies reported more frequent occurrence in third trimester (61%)17 and (86%).18

Majority (52%) of women has not received antenatal check-up and only 48% were registered at some other centre and had inadequate visits or visited in last trimester of pregnancy. One study reported 67.7% unbooked patients with inadequate antenatal supervision.12

In present study, total hospital deliveries were 94%, six were home deliveries and out of these two were assisted by untrained personnel. These findings are similar to other studies.16,19 One study has reported 100% institutional delivery.15

In present study, majority of patients referred from PHC/CHC (30.6% vs 0.0%) were of stage 1 and stage 2 AKI and (23.1%) stage 3 AKI, were referred from District hospital. Other authors concluded, late referral from PHC was one of the reason of poor pregnancy outcome in their study.10,12 One study reported that out of 40 patients with sepsis AKI, 34 (85%) were referred from primary care centres (PHC).19

It was observed that females who were referred directly from PHC/CHC on the basis of suspicion had lesser degree of
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Table 4: Association of outcome with number of dialysis and difference in time of initiation of dialysis (in Group A n=92 only)

|                | CR (n=8) | PR (n=43) | CKD (n=5) | Expiry (n=36) |
|----------------|----------|-----------|-----------|---------------|
|                | No.  %   | No.  %    | No.  %    | No.  %        |
| No. of dialysis|          |           |           |               |
| 1-5            | 5 11.6   | 16 37.2   | 2 4.7     | 20 46.5       |
| 6-10           | 2 11.1   | 12 66.7   | 0 0.0     | 4 22.2        |
| >10            | 1 3.2    | 15 48.4   | 3 9.7     | 12 38.7       |

χ²=7.964 (df=6); P=0.241

Time for initiation of dialysis from referral

|                | CR (n=8) | PR (n=43) | CKD (n=5) | Expiry (n=36) |
|----------------|----------|-----------|-----------|---------------|
|                | No.  %   | No.  %    | No.  %    | No.  %        |
| Within 24 h    |          |           |           |               |
| Within 48 h    | 2 15.4   | 3 23.1    | 1 7.7     | 7 53.8        |
| Within 72 h    | 0 0.0    | 1 20.0    | 0 0.0     | 4 80.0        |
| >72 h          | 2 15.4   | 5 38.5    | 0 0.0     | 6 46.2        |

χ²=10.916 (df=6); P=0.282

Table 5: Multivariate analysis for Adverse Outcome (Expired + CKD)

|                | B       | S.E.    | Wald   | Df   | Sig. | Exp (B) 95.0% C.I. for EXP (B) |
|----------------|---------|---------|--------|------|------|-----------------------------|
|                |         |         |        |      |      | Lower  | Upper  |
| Stage of AKI   | 4.282   | 2.123   | 4.069  | 1    | 0.044 | 72.387 | 1.129  | 4640.36 |
| HTN disorders of pregnancy | 0.850   | 0.669   | 1.614  | 1    | 0.204 | 2.340  | 0.630  | 8.688   |
| Edema          | -0.055  | 0.713   | 0.006  | 1    | 0.939 | 0.947  | 0.234  | 3.828   |
| Haemoglobin    | -0.143  | 0.100   | 2.040  | 1    | 0.153 | 0.866  | 0.712  | 1.055   |
| S. urea        | 0.005   | 0.005   | 1.030  | 1    | 0.310 | 1.005  | 0.995  | 1.014   |
| S. creatinine  | 0.057   | 0.124   | 0.210  | 1    | 0.647 | 1.059  | 0.830  | 1.350   |
| K              | 0.516   | 0.261   | 3.903  | 1    | 0.048 | 1.676  | 1.004  | 2.796   |
| INR            | 0.679   | 0.445   | 2.327  | 1    | 0.127 | 1.972  | 0.824  | 4.719   |
| Treatment mode | 1.430   | 0.481   | 8.821  | 1    | 0.003 | 4.177  | 1.626  | 10.729  |
| ICU Stay       | 2.182   | 0.578   | 14.272 | 1    | <0.001| 8.866  | 2.858  | 27.307  |
| Requirement of Vasopressures | -2.084  | 0.642   | 10.546 | 1    | 0.001 | 0.124  | 0.035  | 0.438   |
| Constant       | -20.001 | 6.988   | 8.191  | 1    | 0.004 | 0.000  |        |         |

HTN - Hypertension; S - Serum; K - Potassium; INR - International Normalize ratio; ICU - Intensive care unit; CKD - chronic kidney disease

Figure 2: Survival analysis of Stage II and amp; III PRAKI at follow up after 3 month

Survival Functions

Stage of AKI acc to EDG0
1 - censored
2 - censored
3 - censored

Stages of PRAKI had significant association with duration of ICU stay (p value 0.013). 45.5% of stage III AKI required ICU stay more than five days. Other authors reported median ICU stay of 8 days and 5.6 days.[14,16] As the stage of AKI increases duration of ICU stay also increases.

Ventilatory support and Vasopressure were required in 18% and 20.1%, while other reported requirement of ventilator support in 29.7% and Vasopressure in 21.6%.[19]

In present study most of the patients of stage 1 and 2 AKI were suffering from hypertensive disorder of pregnancy; recovered early with good outcome and required ventilator support, vasopressure for shorter duration.

Complete Recovery was higher with use of Vasopressure and development of CKD was only 2.6% because vasopressure in patients of shock increase the renal perfusion and thus prevent further progression of kidney injury. While another author
reported time to death was shorter in patients with higher stage of AKI. Use of vasopressure and haemodialysis therapy were independently associated with maternal mortality.[21]

Need of ICU care was found to be more in stage I and stage II AKI, because they were very sick at admission and received prompt resuscitative measures and intensive care management. Thus, their level of kidney injury would be less and early recovery sets in, instead of progression of injury.

Duration of ICU stay of patient and its association with final maternal renal outcome was found statistically significant (p < 0.001). With the increase in duration of ICU stay (>5 days) mortality increases (44.8%) and complete recovery decreases (3.4%), those who had more than 5 days of ICU stay showed more partial recovery as compared to complete recovery.

Rate of mortality was exclusively higher among mothers who expired within 24 hours of ICU admission before receiving dialysis because they were hemodynamically unstable. While another study reported early or late initiation of RRT does not make difference in maternal mortality or morbidity but significantly better foetal outcome with early RRT.[22] Similarly, in our study, no significant association between number of dialysis and maternal renal outcome, but dialysis has a definite role in overall improved outcome. Comparison of various risk factors with types of recovery and adverse outcome. Proportion of patient with higher stage of AKI (OR = 72.387), increased baseline potassium levels (OR = 1.67), treatment modality (OR = 4.177), duration of ICU stay (OR = 8.866), and use of vasopressure (OR = 0.124), were significantly associated with adverse outcomes. On stage wise comparison at 3 months of follow up (P < 0.001), rate of Complete recovery was significantly higher in stage 1 AKI (100%) and stage 2 AKI (84.6%). Number of deaths were significantly higher in stage 3 AKI (37.3%).

Approximately half of the females required 1 to 5 cycles of dialysis (48%), >10 dialysis were required in 31.6% females. Other authors reported mean number of dialysis 8 ± 1, 6 ± 5 and 5.1 ± 4.2 respectively.[13,15,19] Since the number of patients is very small, so interpretation about timing of dialysis could not be made out. But early initiation of dialysis has proven role in complete recovery of AKI.[5,24]

Overall complete recovery (n = 41) 28.5%, contrary to that, much higher recovery rate was reported by various authors 86%, 75%, 89.4%,[13,14,28] Lower complete recovery rate in present study could be because of delayed arrival to tertiary care centre and involvement of multi-organ at the time of admission. After 3 months of follow up, 27.3% cases recovered completely, 31.3% recovered partially, 3.39% progressed to CKD, 34% cases expired and 4.0% were loss to follow-up.

This study good for general physician because results of this study showed prolonged ICU stay, increases the chances of secondary infection, like VAP (ventilator associated pneumonia), Urosepsis (catheter related) and increase mortality and incomplete recovery.

**Conclusions**

In present study 82% women developed AKI in postpartum period, thus careful monitoring and evaluation of renal function in postpartum period is very important in high risk pregnancy. Women who were referred directly without delay showed good outcome. As per our study increase chances of partial recovery was observed when women received dialysis after 72 hours. Because more delay in initiation of RRT more will be renal insult. With the advancement stage of AKI, increase in duration of ICU stay, increase in infection associated with bad outcomes in terms of increase maternal mortality, poor renal outcome. Complete recovery was higher with use of vasopressure and prompt resuscitative measures and intensive care management.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient (s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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**Conflicts of interest**

There are no conflicts of interest.

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