TO STUDY THE OUTCOME OF PREGNANCY RELATED ACUTE KIDNEY INJURY IN A TERTIARY CARE CENTRE

Dr Shweta Khopde*, Dr Ashish Vidhate

Assistant Professor, shwetaskhopde@gmail.com

ABSTRACT

AKI is reduction in kidney function, including decreased GFR and kidney failure . Acute renal failure develops rapidly over a few hours or days which may be fatal. It's most common in those who are critically ill and already hospitalised. In Indian states over all 3-7 % cases are contributed by PRAKI (Pregnancy-related acute kidney injury) .

The main objective of the study was to determine the short term maternal outcome, fetal outcome, recovery of pregnancy related Acute Kidney Injury. It will also enlighten the etiological factors and clinical features of pregnancy related Acute Kidney Injury (PRAKI).

Pregnant patients who were not having history of renal disease previously and developed acute renal failure as evident by oliguria (urine output < 400ml/day) or rising azotemia in presence of normal urine output were included in this study. Detailed history, clinical examination, investigation, management and follow up were done according to protocol.

A retrospective study of total 608 AKI pregnant patient was conducted out of which 79 suffered from acute kidney injury. 82.75 % of patient were found from an age group of 20 year -29 year , where as 6.89 % were from age group of less than 20 years and 10.34% were found from age group of more then 29 yrs. Around 86.20% of patient presented in post partum period.

We found HELLP syndrome as the most common etiological factor leading to PRAKI followed by Preeclampsia, Antepartum haemorrhage, sepsis , PIH .

Early diagnosis and effective treatment of pregnancy related complications is the main reason for decline in incidence of PRAKI along with improved healthcare facilities and improved health seeking behavior of people.

Health education along with skilled delivery at the tertiary health care centre hospitals can be the main reason which would help in decreasing the incidence of PRAKI.

INTRODUCTION

Pregnancy-related acute kidney injury (PRAKI) is a major cause of maternal and fetal morbidity and mortality in developing countries. With improvement in antenatal and postnatal care, the incidence of PRAKI in India has steadily declined from 22% in 1960s to 9% in 1980s, and further down to 3–7% in 2000s.[1]

There is a decreasing trend of PRAKI seen in developed countries in last 60 years , from 1 in 3000 in the mid-20th century to 1 in 20,000. [2] However, PRAKI still comprises 25% of referrals to dialysis center in developing countries. [3] The range of incidence in India being from 4.3% to 14.5% in India.

Obstetric AKI/PRAKI has a bimodal occurrence in developing countries with first peak between 8 and 16 weeks of gestation in association with septic abortions while late peak is associated with obstetric complications such as preeclampsia–eclampsia, abruptio placentae, uterine hemorrhage, and puerperal sepsis. [4]

Septic abortion as a cause of PRAKI decreased from 33.3% in 1980-1985 to 6.3% in 1989-1997; however, it still remains one of the most common cause of PRAKI in developing countries. Worldwide, one of the major causes of sepsis leading to PRAKI is illegal abortion. At least 5% of women undergoing illegal abortions become gravely ill.[5] Puerperal sepsis and postpartum hemorrhage are the leading causes of acute tubular necrosis (ATN) in the postpartum period.[6] Renal cortical necrosis, a rare and irreversible cause of AKI, accounts for about 2% of all cases of AKI; and 50-70% of these cases are associated with complications of pregnancy.[7]

A transient decline in glomerular filtration rate with pregnancy-associated complications is not uncommon. It occurs once in 8000 deliveries while PRAKI requiring dialysis occurs in approximately 1 in 20,000 pregnancies.[8]

Septic abortions, poor follow up of patient with pregnancy, limited screening of pregnant patient with hypertensive complications and late referral to specialized treatment centres are responsible for high incidence of obstetric AKI in developing nations.[6]

All the aetiologies that cause AKI in non-pregnant patient can cause AKI in pregnant patient like volume depletion, hemorrhage, sepsis in addition to pregnancy specific aetiologies like HELLP syndrome, acute fatty liver of pregnancy, thrombotic microangiopathy. [6] Also , recent data suggests that the incidence of AKI and PR-AKI is associated with an increased risk of chronic kidney disease (CKD), hypertension and cardiovascular disease. PR-AKI is commonly associated with hypertensive conditions of pregnancy which themselves are associated with increased risks of cardiovascular disease later in life .[9]

As per the geographic regions there is variation in the epidemiological and etiological factors for PRAKI of obstetric origin. Many of such cases are being referred to our tertiary care centre and

mostly they belong to lower to middle socioeconomic class. The prevalence of PRAKI can be reduced by strengthening of peripheral primary and secondary care centres with good infrastructure, equipment's and trained in our country. At the same time, the problem statement under study has to be informed well to treating doctors and other stakeholders. We should study the prevalence on regular intervals in pregnancy so that appropriate health care measures could be taken immediately. The standard of the health care in society can be improved by continuous process of surveillance. Hence, we aimed at evaluation of epidemiology and etiological factors of pregnancy related acute kidney injury.

AIMS & OBJECTIVES

To study the maternal outcome of pregnancy related Acute Kidney Injury , fetal outcome in PRAKI along with recovery of patient (in a tertiary health care centre).

MATERIAL AND METHODS

This retrospective observational study was conducted at a tertiary health care centre over a period of 1 year (February 2019 to February 2020). Patients were enrolled after matching inclusion and exclusion criteria. Ethics committee permission was taken prior to study.

We considered RIFLE criteria for defining Acute Kidney Injury. (Risk, Injury, Failure, Loss of function, and End-stage renal disease (RIFLE) criteria).[10] PRAKI was defined as AKI diagnosed anytime during pregnancy or during postpartum phase (first 6 weeks post-delivery).

By the KDIGO definition, AKI is diagnosed by an absolute increase in sCr, at least 0.3 mg/dL (26.5 μmol/L) within 48 hours or by a 50% increase in sCr from baseline within 7 days, or a urine volume of less than 0.5 mL/kg/h for at least 6 hours

During this study period, total 608 patients were admitted to the hospital with acute renal failure due to various etiology. Out of which, 79 patients were due to renal failure from obstetric origin.

Pregnant patients without any previous renal disease history and who developed acute renal failure as evident by oliguria (urine output < 400ml/day) or azotemia in presence of normal urine output were included in this study. Such 79 patients were observed retrospectively with respect to their history, clinical features, laboratory parameters, precipitating factors for acute renal failure, its complications, maternal and fetal outcome, and renal outcome at 3 months of discharge.

A complete observation of detailed history, clinical examination, investigation, management and follow up was done. In cases where the initial event began outside the hospital , the information was gathered from the patient as well the immediate relative. Details of obstetric, medical, and surgical management including the need for blood transfusion, dialysis, and intensive care were recorded. For hemodialysis, access was obtained either by femoral or right internal jugular vein.
Outcome – Death/ recovery/ renal Recovery

Follow up for 3 months after discharge.

OBSERVATION & RESULTS

During our study period, total 608 cases of acute renal failure were observed at our institute out of which 79 (36.70%) were of obstetric origin. The mean age of patients with obstetric ARF in present study is 26.21 years. Youngest patient was 18 years old and eldest was 36 years old. The maximum incidence of obstetric ARF was found in the age group of 24-29 years (62.06%) and it was least in patients above 35 years (3.44%). Out of these, 6 patients required hemodialysis and 3 patient is requiring long term hemodialysis. Also out of 79 patients maternal mortality was observed in 7 patient.

Table 1 - Distribution of patients with obstetric ARF in different age groups

Age distribution (in years)	No. of patient (n) – 79	Percentage %
18-23	22	27.58
24-29	49	62.06
30-35	5	6.89
>36	3	3.44

In the present study, 41 (51.74%) primigravida patients and 38 (48.27%) patients as multigravida. In our study of 79 patients suffering from obstetric cause of PRAKI , only 8 patients (10.34%) presented in early pregnancy while 35 patients (48.27%) presented in late pregnancy and 35 patients (41.47%) presented in postpartum period.

Out of these 24 (31.03%) where registered ANC cases with ANC visit and 55 (68.96 %) patient presented with no ANC visit. Hospital delivery was conducted in 60 patients (75.86 %) , and 19 (24.13) patient presented with home delivery.

Table-2: Pregnancy status at the time of presentation

Pregnancy status	Number of patients	Percentage
Early Pregnancy (1 and 2 trimester)	8	10.34%
Late pregnancy (3rd trimester)	35	44.8%
Post partum	35	44.8%

In our study, 14 patients (17.24%) presented with oliguric / anuric state, 27 patients presented with fever (34.48%), 25 patients with bleeding PV (31.03 %), 49 (62.03 %) patients presented with CNS alteration including altered level of consciousness and convulsion being 22 (27.58%), 16 (20.68) patients presented with breathlessness, 22 with oedema (27.58%), 27 (34.48 %)patients were hypertensive and 25 (31.03 %) patients were found to be hypotensive.

Table-3 : Symptoms and clinical parameters on presentation

Symptoms	No. of patient	Percentage
Oliguria/Anuria	14	17.24%
Fever	27	34.48%
Bleeding PV	25	31.03%
Altered level of consciousness	49	62.03%
Convulsion	22	27.58%
Breathlessness	16	20.68%
Oedema	22	27.58%
Hypertension (BP > 140/90 mmHg or antihypertensive requirement)	27	34.48%
Hypotension (BP < 90/60 mmHg or vasopressor requirement)	25	31.03%

Amongst the etiological factors , most common was found to be HELLP syndrome in 22 (27.58 %) of patients followed by Preeclampsia / Eclampsia in 19 patients (24.13%) , followed by post abortion sepsis and puerperal sepsis in 11 patients each (13.79%), followed by hemorrhage seen in 13 patients (17.24) and HUS observed in 3 patient only (3.44%).

Table-4: Various etiological factors for ARF of obstetric origin.

Etiological Factor	No. of patient	Percentage%
Post Abortion sepsis	11	13.79%
Hemorrhage (APH)	8	10.34%
Hemorrhage (PPH)	5	6.89%
Preeclampsia/Eclampsia	19	24.13%
Puerperal sepsis	11	13.79%
HELLP	22	27.58%
HUS	3	3.44%

Total of 38 (48.47 %) delivered normally (FTND) and 41 (51.72 %) underwent LSCS. Out of 79 patients maternal mortality was observed in 6 patient (10.34%). In case of fetal outcome 14 death (13.79 %). In case of renal recovery 65 patient underwent complete renal recovery (82.75 %), 5 patient required hemodialysis and had partial recovery (6.89%) and 3 patient was observed

to require long term hemodialysis (3.44 %). We observed that due to improved clinical diagnosis and early availability of tertiary care centre the outcome can be improved. Also recent ANC visits helps the physician identify and treat the risk factors and this would help delay or stop the further progress of disease which helps in improving the maternal outcome.

Table no 5 Comparison of Type of delivery with Maternal Outcome, Fetal outcome and Recovery.

		Type of delivery								Total	P value
		FTND		Induced abortion		LSCS		Ruptured ectopic			
		N	%	N	%	N	%	N	%		
Maternal Outcome	AKI recovered	29	44.40%	5	7.40%	29	44.40%	2	3.70 %	65 (100%)	0.871
	CKD	0	0.00%	0	0.00%	8	100.00 %	0	0.00 %	8 (100%)	
	Death	6	100.00 %	0	0.00%	0	0.00%	0	0.00 %	6 (100%)	
Fetal outcome	Discharged	28	42.90%	0	0.00%	34	52.40%	3	4.80 %	65 (100%)	0.083
	Death	7	50.00%	4	25.00 %	4	25.00%	0	0.00 %	14 (100%)	
Recovery	No	2	36.40%	1	9.10%	3	54.50%	0	0.00 %	6 (100%)	0.708
	Yes	37	50.00%	4	5.60%	28	38.90%	4	5.60 %	73 (100%)	
Total		13	44.80%	2	6.90%	13	44.80%	1	3.40 %	29(100%)	

As seen in the above table there was no significant difference between type of delivery with maternal outcome, fetal outcome and recovery in pregnancy related acute kidney injury.

Table no 6 Comparison of Pregnancy status with Maternal Outcome, Fetal outcome and Recovery

		Pregnancy status						Total	P value
		Early Pregnancy		Late pregnancy		Postpartum			
		Count	%	Count	%	Count	%		
Maternal outcome	AKI recovered	3	11.10 %	12	44.40%	12	44.40%	27 (100%)	0.648
	CKD	0	0.00%	0	0.00%	1	100.00 %	1 (100%)	

	Death	0	0.00%	1	100.00 %	0	0.00%	1 (100%)	
Fetal outcome	Discharge d	1	4.80%	9	42.90%	11	52.40%	21 (100%)	0.189
	Death	2	25.00 %	4	50.00%	2	25.00%	8 (100%)	
Recover y	No	1	9.10%	3	27.30%	7	63.60%	11 (100%)	0.267
	Yes	2	11.10 %	10	55.60%	6	33.30%	18 (100%)	
Total		3	10.30 %	13	44.80%	13	44.80%	29	29(100%)

As seen in the above table there was no significant difference between different pregnancy status with Maternal Outcome, Fetal outcome and Recovery in pregnancy related acute kidney injury.

DISCUSSION

PRAKI is a cause of obstetric complications, and hence the prevention in form of screening should be considered as first line of treatment.[1] The global incidence of pregnancy-related acute kidney injury (AKI) has reduced over recent decades because of improvements in reproductive health care.[11] The incidence of obstetric ARF observed was approximate of 36 %. The incidence of obstetric AKI by various investigators in last decade in India ranging from 3.39 % - 9.82 % and even 22.1 % in a study by Chugh et al.[12] In 1976 , it is evident that incidence of obstetric ARF has declined from 22.1 % in 1976 to 3.3 % to 9.8 in 2015.[11] The reason for the decrease may be attributed to early and successful treatment of complications related to pregnancy, improved health coverage and improved health-care needs.

In this study we observed 79 cases of acute renal failure at our institute, out of which 29 (36.70%) were of obstetric origin. The mean age of patient in present study was 26.21 years which was in accordance with studies from West India by Pahwa *et al*. (26.7 years), Godara *et al*. (26.4 years), Goplani *et al*. (25.6 years).[11,13,14] While it was higher in studies from North India by Krishna *et al*. (28.85%) and Nazar *et al*. (28.94%). [2,15]

PRAKI has declined in INDIA, as medical facilities, better antenatal and postnatal treatment and arrangements for MTP are becoming more and more affordable. In India the PAKI rate in comparison to the developed countries, however, remains high (1-2.8%). [16-18]

Stratta *et al*. quoted that the incidence of obstetrical AKI decreased from 43% (1956-1967) to 0.5% with respect to total AKI cases (1988-1994) and no case of maternal death or irreversible renal damage was observed in the last 7 years. HELLP , Pre-eclampsia, eclampsia, HELLP and The major causes of PRAKI in the developing world appear to be hemolytic uraemic syndrome, and the decrease in PRAKI is largely the result of a substantial reduction in abortions and infections.[19] A study from Casablanca reported that pre-eclampsia and eclampsia accounts for 74.5% cases, sepsis in 11% and hemorrhages for 7.2% PAKI cases.[18] Contrary to the developed countries, postabortal sepsis remains the most common cause of PAKI in India and accounts for about a quarter of all cases in our study. The varying incidence as low as 9.76% to as high as 59.7% of postabortal sepsis causing PAKI has been reported in literature from India.[20,21] Preeclampsia pathogenesis is thought to take place as a result of incomplete cytotrophoblasting of the uterine spiral arteries which leads to ischemic placenta and eventual release of inflammatory, immune, and endothelial functions.[22] Long thought of primarily as a disease of hypertension, it is now well-recognized that preeclampsia is actually a multi-organ syndrome.

Comparison of frequency of pregnancy-associated AKI reported from India in different studies

Table 5 – Incidence of ARF of obstetric origin from different studies in India

Author	Year of study	Region	Incidence of obstetric ARF
Chugh *et al*.[12]	1976	North India	22.10%
Gopalakrishnan *et al*.[23]	2015	South India	7.80%
Krishna *et al*.[2]	2015	Lucknow	3.39%
Nazar *et al.* [15]	2008	Kashmir valley	7.02%
Pahwa *et al*. [13]	2014	Indore	3.59%
Godara *et al*. [14]	2014	West India	9.82%
Goplani *et al.* [11]	2008	West India	9.06%
Present study	2016	West India	9.40%

The high maternal mortality in India is still a great social, economical and medical concern. The maternal mortality of 6.7% in our study is similar to other studies reported from India ranging from 18% to 24%.[11,21] A study from a developed country reported maternal mortality of 9.1% in case of PRAKI, which is almost half of that reported from India. The fetal death of only 5.5% has been

reported in case of PAKI in a study from a developed country. After excluding cases of abortions a fetal mortality of 26.19% was observed in our study, similar to that reported in pregnant women admitted in ICU with renal failure.[24] The major limitation of the study is that it is a retrospective analysis and included only PRAKI patients The study's main strength is to highlights mother and fetus outcomes and common causes and symptoms in PRAKI. In our study, there was no significant difference between type of delivery and different pregnancy status with maternal outcome, fetal outcome and recovery in pregnancy related acute kidney injury.

CONCLUSION

Pregnancy-related causes of AKI such as preeclampsia, acute fatty liver of pregnancy, HELLP (Hemolysis, Elevated Liver function tests, Low Platelets) syndrome, and the thrombotic microangiopathies (thrombotic thrombocytopenic purpura, atypical hemolytic-uremic syndrome [HUS]) exhibit overlapping features and often present as diagnostic dilemmas.[24] More research is sorely needed to develop novel preventive and treatment modalities, especially as pregnancies in women with preexisting comorbidities and risk factors for Pr-AKI are increasing.[25]

HELLP followed by eclampsia / preeclampsia is observed the most common and the most important etiological factors for pregnancy related acute renal failure.[15] PRAKI is associated with maternal and fetal mortality if not treated and diagnosed timely and with the help of recent diagnostic tools and creating awareness we can overcome the poor outcome . Oligoanuria, sepsis and CNS involvement at presentation is associated with greater risk factors seen in PRAKI. Health education, with skilled delivery healthcare personnel , prenatal care, safe and approved abortion services along were the factors that can be worked upon to reduce the epidemiological burden of Pregnancy related acute renal failure . Strengthening of the primary , secondary and tertiary health care centre will contribute to reduce PRAKI and PRARF .

References

1) Mahesh E, Puri S, Varma V, Madhyastha PR, Bande S, Gurudev KC. Pregnancy-related acute kidney injury: An analysis of 165 cases. Indian Journal of Nephrology. 2017 Mar;27(2):113.

2) Krishna A, Singh R, Prasad N, Gupta A, Bhadauria D, Kaul A, Sharma RK, Kapoor D. Maternal, fetal and renal outcomes of pregnancy-associated acute kidney injury requiring dialysis. Indian journal of nephrology. 2015 Mar;25(2):77.

3) Pertuiset N, Ganeval D, Grünfeld JP. Acute renal failure in pregnancy. InThe Kidney in Pregnancy 1986 (pp. 165-184). Springer, Boston, MA.

4) Prakash J, Niwas SS, Parekh A, Pandey LK, Sharatchandra L, Arora P, Mahapatra AK. Acute kidney injury in late pregnancy in developing countries. Renal failure. 2010 Apr 1;32(3):309-13.
5) Prakash J, Tripathi K, Pandey LK, Gadela SR. Renal cortical necrosis in pregnancy-related acute renal failure. Journal of the Indian Medical Association. 1996 Jun 1;94(6):227-9.

6) Fakhouri F, Vercel C, Fre´meaux-Bacchi V. Obstetric Nephrology: AKI and Thrombotic Microangiopathies in Pregnancy Clin J Am Soc Nephrol. 7: 2100–2106.
7) Prakash J, Vohra R, Wani IA, Murthy AS, Srivastva PK, Tripathi K, Pandey LK, Raja R. Decreasing incidence of renal cortical necrosis in patients with acute renal failure in developing countries: a single-centre experience of 22 years from Eastern India. Nephrology Dialysis Transplantation. 2007 Apr 1;22(4):1213-7
8) Selcuk NY, Tonbul HZ, San A, Odabas AR. Changes in frequency and etiology of acute renal failure in pregnancy (1980–1997). Renal failure. 1998 Jan 1;20(3):513-7.
9) Szczepanski J, Griffin A, Novotny S, Wallace K. Acute Kidney Injury in Pregnancies Complicated With Preeclampsia or HELLP Syndrome. Frontiers in Medicine. 2020 Feb 7;7:22.

10) Prasad N, Krishna A. Acute kidney injury: definition controversies and epidemiology. Clinical Queries: Nephrology. 2012 Jan 1;1(1):1-5.

11) Goplani KR, Shah PR, Gera DN, Gumber M, Dabhi M, Feroz A, Kanodia K, Suresh S, Vanikar AV, Trivedi HL. Pregnancy-related acute renal failure: A single-center experience. Indian journal of nephrology. 2008 Jan;18(1):17.

12) Chugh KS, Singhal PC, Kher VK, Gupta VK, Malik GH, Narayan G, Datta BN. Spectrum of acute cortical necrosis in Indian patients. The American journal of the medical sciences. 1983 Jul 1;286(1):10-20.

13) Pahwa N, Bharani R, Kumar R. Post-partum acute kidney injury. Saudi J Kidney Dis Transpl 2014;25:1244-7.

14) Godara SM, Kute VB, Trivedi HL, Vanikar AV, Shah PR, Gumber MR. Clinical profile and outcome of acute kidney injury related to pregnancy in developing countries: a single-center study from India. Saudi J Kidney Dis Transpl. 2014 Jul;25(4):906-11

15) Nazar MS, Shah AR, Wani IA, Reshi R, Banday KA, Bhat MA. Pregnancy related acute kidney injury: A single center experience from the Kashmir Valley. Indian J Nephrol. 2008 Oct; 18(4): 159–161

16) Jayakumar M, Prabahar MR, Fernando EM, Manorajan R, Venkatraman R, Balaraman V. Epidemiologic trend changes in acute renal failure - a tertiary center experience from South India. Ren Fail. 2006;28:405–10.

17) Lufullah A, Gezginc K, Tonbul HZ. Etiology and prognosis in 36 ARF cases related to pregnancy in central Anatolia. Eur J Gen Med. 2005;2:110–3.
18) Hachim K, Badahi K, Benghanem M, Fatihi EM, Zahiri K, Ramdani B, et al. Obstetrical acute renal failure. Experience of the nephrology department, Central University Hospital Ibn Rochd, Casablanca. Nephrologie. 2001;22:29–31.
19) Stratta P, Besso L, Canavese C, Grill A, Todros T, Benedetto C, Hollo S, Segoloni GP. Is pregnancy-related acute renal failure a disappearing clinical entity?. Renal failure. 1996 Jan 1;18(4):575-84.
20) Alsuwaida A. Challenges in diagnosis and treatment of acute kidney injury during pregnancy. Nephro-Urology Monthly. 2012;4(1):340-4.
21) Kilari SK, Chinta RK, Vishnubhotla SK. Pregnancy related acute renal failure. J Obstet Gynecol India. 2006;56:308–10
22) Amaral L, Wallace K, Owens M, Lamarca B. Pathophysiology and current clinical management of preeclampsia. Curr Hypertens Rep. (2017) 19:61.
23) Gopalakrishnan N, Dhanapriya J, Muthukumar P, Sakthirajan R, Dineshkumar T, Thirumurugan s et al Acute kidney injury in pregnancy--a single center experience. Ren Fail. 2015;37(9):1476-80.
24) Naylor DF, Jr, Olson MM. Critical care obstetrics and gynecology. Crit Care Clin. 2003;19:127–49.
25) Jim B, Garovic VD. Acute kidney injury in pregnancy. InSeminars in nephrology 2017 Jul 1 (Vol. 37, No. 4, pp. 378-385). WB Saunders.
26) Rao S, Jim B. Acute kidney injury in pregnancy: the changing landscape for the 21st century. Kidney international reports. 2018 Mar 1;3(2):247-57.