DOI: https://doi.org/10.53350/pjmhs2115113417

ORIGINAL ARTICLE

Pregnancy-Related Acute Kidney Injury, Dialysis Versus Conservative Management in the Nephrology Ward

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ABSTRACT

Aim: To determine the overall frequency of patients suffering from P-AKI in the third trimester requiring dialysis as compared to conservative management.

Study Design: Prospective study

Place and Duration: Nephrology department of Fatima Jinnah Medical University/Sir Ganga Ram Hospital, Lahore from 3rd June 2017 to 31st December 2017.

Methodology: 106 pregnant women having age 15 to 45 years with AKI during the third trimester or postpartum period (42 days of delivery) who were hemodynamically stable and shifted to the Nephrology department without any surgical intervention or ICU requirements were included in the study. For the diagnosis of AKI, KDIGO guidelines were utilized. After taking informed consent from patients, current clinical data, baseline S. Cr before pregnancy, and current renal function tests were recorded. Clinical progress was monitored, and patients were treated as per SOPs of the department. Records of conservative management and dialysis were made. Patients were followed up from the day of admission to the date of discharge.

Results: The mean age of the patients was 27 ± 4.169 years. Almost 70% (n=74) of the patients had age 15-29 years, while 30 % (n=32) of patients had age 30-45 years. The mean creatinine of the patients was 4.76 ± 3.55 mg/dl. The frequency of patients requiring dialysis was 23.6% (n=25) and 76.4% patients (n=81) were treated conservatively. Patients who received conservative management, 55 patients (67.9%) had full recovery of renal functions, 25(30.9%) had mildly raised serum creatinine (1.3 to 2mg/dl), and only 1.2% had S. Cr of more than 3mg/dl. 14(56%) were off hemodialysis while 11(44%) were needed regular hemodialysis. Of those who were off hemodialysis, 6(24%) had complete recovery, 5(20%) had mildly raised serum creatinine and 1(4%) had moderate derangement of S.Cr. Of those patients who were discharged on dialysis 13(52%) had severely deranged serum creatinine.

Conclusion: It is concluded that conservative treatment is effective for renal recovery with short hospital stay. Sepsis is leading cause of P-AKI in third trimester. HD is required only in 23.6% of P-AKI patients in Nephrology ward.

Keywords: Pregnancy, Acute Kidney Injury, Conservative Management, Dialysis

INTRODUCTION

Changes in renal hemodynamics start at beginning of pregnancy. Glomerular filtration rate (GFR) and renal plasma flow rise to 40% above normal in the first trimester and begins to fall in the third trimester and reaching normal state at end of pregnancy usually 6-8 weeks after delivery.[1] Clinically we can check these changes from fall in serum creatinine (S.Cr) value to 0.4mg/dl. Overall blood volume increases up to 1.2 liters to provide nutritional support to mother and fetus.[2] If there is an abrupt or gradual decline in blood volume it will lead to decrease renal blood flow resulting in acute kidney injury (AKI). In the first trimester leading cause of AKI is hyperemesis gravidarum.[3] However in the third trimester multiple pathological factors like hypertension, thrombotic microangiopathies, severe sepsis, uterine hemorrhages, fatty infiltration of the liver, and autoimmune disorders lead to AKI.[4] In developing countries pregnancy-related AKI (P-AKI) incidence is almost 5 to 20% which has declined significantly from 20 to 40% recorded in the 1960 era. This improvement is due to the availability of better antenatal and postnatal health facilities but still, developing countries are far behind in health care as shown by the incidence of less than 1% of P-AKI cases in developed countries.[5] Among causes of P-AKI three causes account for almost 90% of cases i.e. sepsis, pre-eclampsia, and antepartum/post-partum hemorrhages leading to Ischemic acute tubular necrosis.[6,4]

Clinical diagnosis of AKI depends upon the rise of serum creatinine more than 0.3 mg/dl and reduced urine output of <0.5 ml/kg/h for 6–12 h from baseline value occurring within a week. If kidney disease is irreversible and persists for more than 3 months, then the clinical diagnosis of chronic kidney disease (CKD) is labeled.[7] However, labeling of kidney disease that occurs between one week to 3 months is still a matter of discussion, and recently term acute kidney disease (AKD) has been introduced for such disorders.[8] Traditionally RIFLE criteria and AKIN criteria are utilized for diagnosis of AKI; To avoid confusion and differences between these two classification systems, Kidney Disease Improving Global Outcomes (KDIGO) proposed a unified classification system of AKI.[9] In pregnancy use of these classifications of AKI is questionable however in absence of a defined P-AKI diagnostic system, KDIGO AKI classification is currently been used worldwide.[10]

Treatment of P-AKI is almost the same as treatment of AKI in the general population. Management revolves around four basic steps; 1) resorting to adequate volume status and normalization of electrolyte abnormalities, 2) Avoidance of nephrotoxic agents, 3) Treat the cause of AKI, and finally, 4) Dialysis when indicated.[11] For dialysis hemodialysis (HD) is the only option as peritoneal dialysis is not recommended due to the gravid uterus. Intermittent HD is the preferred choice for patients who are hemodynamically stable and continuous renal replacement therapy is reserved in ICU settings where patients are hypotensive and respiratory distressed.[12] Intermittent HD is started early in P-AKI when GFR falls below 20ml/min.[13] Intractable fluid overload with oliguria, severe symptomatic hyperkalemia, severe metabolic acidosis, uremic pericarditis, and uremic encephalopathy are indications for initiation of HD.[14] Outcome of P-AKI patients is variable in different parts of the world depending upon awareness of disease process among patients and availability of health care facilities. A recent study from India reported 36.1% of P-AKI patients underwent HD and 63.8% were improved with conservative management, 91.6% of patients showed improvement in renal functions while 8.3% of patients remained dialysis-dependent.[15] In Pakistan study conducted in a teaching hospital of Abbottabad mentioned almost similar data, where 31% P-AKI cases reported in the first trimester and 33% in the third trimester, full renal recovery was observed in 78.4%, AKI leading to CKD in 17%, HD was done in 30% and mortality was 4%.[16]

This study was designed to determine the overall frequency of patients suffering from P-AKI in the third trimester requiring dialysis as compared to conservative management who were treated in the Nephrology department.

MATERIALS & METHODS

A prospective study was conducted at the Nephrology department of Fatima Jinnah Medical University/Sir Ganga Ram Hospital, Lahore from 3rd June 2017 to 31st December 2017 after taking permission from the institutional ethical review board vide letter no. 03-Nephrology/IERB dated 15-04-2017. Using the non-probability purposive sampling technique, 106 patients were enrolled. The sample size was calculated using the WHO calculator with a 95% confidence level, 5% margin of error, and taking an expected percentage of 33% of PR-AKI in the third trimester.[16] All pregnant women having age 15 to 45 years with AKI during the third trimester or postpartum period (42 days of delivery) who were hemodynamically stable and shifted to the Nephrology department without any surgical intervention or ICU requirements were included in the study. For the diagnosis of AKI, KDIGO guidelines were utilized.[9] Patients with pre-existing renal disease or renal insufficiency, (S. Cr more than 1.3mg/dl before pregnancy) were excluded from the study. Those patients who were admitted to ICU due to multiple comorbidities were also excluded from the study. After taking informed consent from patients, current clinical data, baseline S. Cr before pregnancy, and current renal function tests were recorded. Clinical progress was monitored, and patients were treated as per SOPs of the department. Records of conservative management and dialysis were made. Patients were followed up from the day of admission to the date of discharge. The data was entered and analyzed through SPSS v23.0. Frequencies and percentages were used for describing and summarizing qualitative variables like the stage of AKI, conservative treatment, and HD. Quantitative variables like age and serum creatinine were described by Mean ±S.D. Data was stratified for age, stages of AKI, hospital stay in weeks, causes of AKI, discharge status and S. Cr at discharge (S.Cr values, 1.2 mg/dl or less = Normal, 1.3 to 2mg/dl= mild, 2.1 to 3mg/dl=moderate, more than 3= severe). Post-stratification, the Chi-Square test was used for statistical correlation. A p-value ≤0.05 was considered significant.

RESULTS

A total of 106 patients fulfilling the criteria were enrolled in the study. The mean age of the patients was 27 ± 4.169 years. Almost 70% (n=74) of the patients had age 15-29 years, while 30 % (n=32) of patients had age 30-45 years. The mean creatinine of the patients was 4.76 ± 3.55 mg/dl. The frequency of stages of AKI in patients with P-AKI was, 22.6% (n=24) with stage 1 AKI, 34% (n=36) with stage 2 AKI, and 43.4% (n=46) with stage 3 AKI. Regarding hospital stay of patients, mean duration was 12.2 ±8.3 days, 34 (32.1%) remained in hospital for 1 week, 46 (43.4%) for 2 weeks, 9(8.5%) for 3 weeks, 8(7.5%) for 4 weeks and 9(8.5%) remained admitted in hospital for >4 weeks. The frequency of patients requiring dialysis was 23.6% (n=25) and 76.4% patients (n=81) were treated conservatively.

Among patients who responded to conservative management, 62(76.5%) were 15-29 years old while the remaining 19(23.5%) were 30 to 45 years old. Most of these conservative treated patients remained in hospital for 2 weeks (n=77, 95.1%) while 4.9% remained admitted longer than 3 weeks. More than half of patients (58%) were suffering from sepsis, pre-eclampsia and eclampsia accounted for 35.8%, while the remaining 4.9% had Ischemic ATN secondary to antepartum or postpartum hemorrhage, and only 1.2% had HELLP syndrome as the cause of AKI. At the time of discharge 55 patients (67.9%) had full recovery of renal functions, 25(30.9%) had mildly raised serum creatinine (1.3 to 2mg/dl), and only 1.2% had S. Cr of more than 3mg/dl.

Among patients who underwent hemodialysis, mean age was 29±4 days, 12(48%) were 15-29 years old while 13(52%) remaining were 30 to 45 years old. These dialyzed patients remained in hospital, 3(12%) for 2 weeks, 6(24%) for 3 weeks, 7(28%) for 4 weeks, and 9(36%) for more than 4 weeks. Most of these patients (96%, n=24) developed AKI secondary to sepsis. None of these patients had pre-eclampsia, eclampsia, and HELLP syndrome as the cause of P-AKI. Only one patient (4%) had Ischemic ATN secondary to antepartum or postpartum hemorrhage. At the time of discharge 14(56%) were off hemodialysis while 11(44%) were needed regular hemodialysis. Of those who were off hemodialysis, 6(24%) had complete recovery, 5(20%) had mildly raised serum creatinine and 1(4%) had moderate derangement of S.Cr. Of those patients who were discharged on dialysis 13(52%) had severely deranged serum creatinine and mean age of these patients was 30.4±4.7 years.

Table 1: Demographic and statistical data are shown in table.

		Conservative treatment	Hemodialysis during admission	
	Total no. (%)	no. (%)	no. (%)	p value
	106 (100%)	81 (76.4%)	25 (23.6%)	
Age (years)	27.1 ±4.1	26.3±4	29±4	
15-29	74 (69.8%)	62(76.5%)	12(48%)	0.002
30-45	32(31.1%)	19(23.5%)	13(52%)	0.002
Stages Of AKI				
AKI-1	24 (22.6%)	24(29.6%)	0(0%)	0.002
AKI-2	36 (34%)	36(44.4%)	0(0%)	<0.001
AKI-3	46 (43.4%)	21(25.9%)	25(100%)	<0.001
Hospital Stay	12.2 ±8.3 days	8.5±3.4 days	24.4±8 days	<0.001
1 week	34 (32.1%)	34(42%)	0(0%)	
2 weeks	46 (43.4%)	43(53.1%)	3(12%)	
3 weeks	9 (8.5%)	3(3.7%)	6(24%)	
4 weeks	8(7.5%)	1(1.2%)	7(28%)	
>4 weeks	9(8.5%)	0(0%)	9(36%)	
Causes of AKI				
Sepsis	71 (67%)	47(58%)	24(96%)	<0.001
Pre/eclampsia	29 (27.4%)	29(35.8%)	0(0%)	<0.001
APH/PPH/ischemic	5(4.7%)	4(4.9%)	1(4%)	0.84
HELLP	1(0.9%)	1(1.2%)	0(0%)	0.57
Discharge Status				<0.001
Conservative	95(89.6%)	81(100%)	14(56%)	
On Hemodialysis	11(10.4%)	0(0%)	11(44%)	
Serum Creatinine at discharge				
normal	61 (57.5%)	55(67.9%)	6(24%)	<0.001
Mild	30 (28.3%)	25(30.9%)	5(20%)	0.29
Moderate	1 (0.9%)	0(0%)	1(4%)	0.16
Severe	14(13.2%)	1(1.2%)	13(52%)	<0.001

As Sepsis was biggest cause of P-AKI (67%), in this group, mean S.Cr was 5.9±3.7 mg/dl, length of hospital stay was 14.3±9.2 days, 66.2% (n=47) patient were in age group 15-29 years, 33.8 % (n=24) were 30-45 years old, 11.3% (n=8) developed stage-1 AKI, 26.8% (n=19) stage-2 AKI, 59.2% (n=42) stage-3 AKI, 66.2% (n=47) responded to conservative treatment, 33.8% (n=24) underwent HD, 43.7% (n=31) were discharged with normal creatinine, 35.2% (n=25) discharged with mildly raised creatinine, 1.4% (n=1) discharged with moderately raised creatinine, 19.7% (n=14) were having severely raised creatinine at time of discharge, 15.5% (n=11) patient were discharged on HD whereas 84.5% (n=24) were discharged on conservative management.

When correlation was checked between conservatively treated and HD patients among different age groups, young patients between age 15 to 29 years recovered with conservative treatment (p-value 0.002) while patients having age 30 to 45 years needed dialysis (p-value 0.002). Patients with Stage 1 and 2 of AKI responded with conservative management (p-value 0.002 and <0.001) while a strong correlation was present with AKI stage 3 and hemodialysis (p-value <0.001). Long hospital stay duration had a strong correlation with hemodialysis (p-value <0.001). Septic patients needed dialysis more as compared to other causes (p-value <0.001) while patients with pre-eclampsia and eclampsia responded to conservative treatment (p-value <0.001). No statically significant difference was found among patients with

antepartum/postpartum hemorrhage and HELLP syndrome between conservative managed and dialyzed groups (p-value 0.84,0.57 respectively). Patients who were on conservative treatment had normal S. Cr at the time of discharge (p-value <0.001) while the dialyzed group had severely deranged S. Cr at the time of discharge (p-value <0.001). No statically significant difference was found among patients with mild to moderately deranged S. Cr at discharge (p-value 0.29 and 0.16 respectively) between conservative treatment and HD groups.

DISCUSSION

All over the world, hospitalization and AKI have strong correlation with almost 22% of AKI cases reported during hospital stay.[17]On other hand 80% of global AKI cases occurs in developing countries.[18] In tertiary care hospitals of developing countries substantial amount of consultation requests (25%) have been sent to nephrology department for deranged renal function tests and decreased urine out from gynecology department especially for pregnant patients.[3] In developing countries incidence of AKI among pregnant females is 9 to 25% as compared to 1 to 2.8% in developed world.[19] In China incidence of 7.3% is reported in 2019.[20] From African continent, 6.6 cases of P-AKI out of 1000 pregnancies have been recorded in Morocco.[21]

Age of patient at time of pregnancy is linked to development of AKI. In our study mean age of P-AKI is 27.1 ±4.1 years, similar finding has been observed in other parts of Pakistan where mean age of 29±5.4 years has been documented.[22] A study from India where mean age among P-AKI patients is 25 years whereas in Morocco mean age is 29±6.3 years.[23,21] In our research, mean age of patients treated conservatively is 26.3±4 years, patient of P-AKI requiring HD mean age is higher with 29±4 years whereas those patients requiring HD at discharge mean age is even higher (30.4±4.7 years). In developing countries, poor antenatal care and increased maternal age are related to P-AKI and mortality.[24]

In our study 22.6% developed AKI stage-1, 34% stage-2 and 43.4% AKI stage-3; in contrast a study from another hospital in Lahore reported 10% patients at stage-1, 10% at stage-2 and 80% at stage-3 of AKI.[25] This discrepancy is probably due to late referral of patients to nephrology department which is not only seen in our country but prevalent in other parts of world as well.[26]

It is well known fact that patients with AKI have longer hospital stay days and increased cost of hospitalization.[27] In our study mean hospital stay is 12.2 ±8.3 days. If patients are promptly diagnosed and cause of AKI is treated as early as possible then chances of full recovery of renal functions are high. This fact is reflected in our study where AKI stage-1 patients have shortest hospital stay with 66.7% patients discharged within a week, while 20.2% stayed for 2 weeks and only 4.2% stayed in hospital for 3 weeks. HD is usually reserved for patients with AKI stage 3 with overt symptoms of uremia. Double lumen catheterization is required for dialysis and AKI may take one and half month for conversion of oliguric phase to diuretic phase and full recovery. If renal functions remain deranged for more than 90 days then irreversible damage to kidney is evident and clinical diagnosis of CKD is made.[28] Likewise in our study longest hospital stay is observed in stage-3 AKI patients where 53.4% stayed in hospital for 3 or more weeks. Those patients who needed HD mean hospital stay is 24.4±8 days while conservatively managed group has shorter hospital stay of 8.5±3.4 days. Those patients who didn't show recovery of renal function and needed HD at time of discharge, then mean hospital stay of 28.8±8.1 days is observed. To our knowledge local data is sparse regarding P-AKI and hospital stay duration. Recently study from China showed average value of 11 days of hospitalization among P-AKI patients.[29]

Regarding cause of P-AKI situation varies from countries to countries depending upon health care facilities. Preeclampsia and eclampsia (PE&E) are biggest causes of P-AKI in Uruguay, South Africa, China and Turkey with 47%, 48%, 21.2% and 75% respectively.[21,30] Preeclampsia and eclampsia accounts for 12 to 16.6% in Pakistan and in 15 to 30.5% in India.[31,22] In our study PE&E occurred in 27.4% cases and all patients recovered with conservative treatment, whereas sepsis is leading cause of P-AKI found in 67% cases. This figure is even higher from previous Pakistani and Indian studies where reported percentages are 9.9-11.4% and 47- 50% respectively.[4,32] This high figure of sepsis is probably due to referral of large number of " Dai " handling cases from villages to tertiary care hospitals. Dai's are traditional non-professional ladies who help in home deliveries and attempts unsafe methods of abortions. This custom is still widely practiced in urban population of Pakistan.

HD is required in AKI stage-3 in selective cases especially if patients are oliguric. In our study 23.6% patients required HD and 76.4% responded to conservative management, this is quite opposite to previous Pakistani studied where almost 70 to 75% patients required HD.[22] Studies have proved that early intervention by Nephrology team at AKI stage1 and stage 2 will give better outcome regarding renal recovery.[33] In our hospital strict policy of early referral to nephrology department is practiced where even slight derangement in serum creatinine and decreased urine out put is usually reported to Nephrology department and early shifting of patient to Nephrology ward is mandatory. In our study 89.6% patient had renal recovery only 10.4% patients needed HD at time of discharge whereas in previous local studies reported renal recovery is 51 to 87.4%.[22] Indian study reported 52.6% complete renal recovery and 47.3% partial and nil recovery.[34]

CONCLUSION

Early referral of patient to nephrology team can enhance renal recovery with conservative treatment with short hospital stay. Sepsis is leading cause of P-AKI in third trimester. HD is required only in 23.6% of P-AKI patients in Nephrology ward.

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