Research Article

EVALUATION OF RISK FACTORS AND CLINICAL OUTCOMES OF ACUTE RESPIRATORY FAILURE FROM POST RENAL TRANSPLANT RECIPIENTS: A FIVE-YEAR DATA OF A SINGLE CENTER

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ABSTRACT

Acute Respiratory Failure (ARF) requiring Intensive Care Unit (ICU) admission is a common complication following renal transplant and is a diagnostic and therapeutic challenge. This study aimed to evaluate etiological factors and clinical outcomes of ARF following a renal transplant. This was a retrospective observational study. Data was recruited from last five –years' records of Renal Transplant Unit of Dow University of Health Sciences, Karachi, Pakistan. Patients who developed ARF after renal transplantation whether requiring hospitalization (both in ICU or in ward) were included and their severity, etiologic diagnosis, and clinical outcomes were evaluated. During past five years (June 2017 till June 2023) a total of 450 kidney allografts were done and 35 patients (7.8%) developed ARF. Out of which 15 patients were shifted to the ICU. Mortality of female patients was higher as compared to males (26.1% versus 20.4%). Hypertension was found to be the most common comorbidity whereas glomerulonephritis was the most common cause of End Stage Renal Disease (ESRD).

Acute rejection was observed in 20.89% (n = 94) of recipients. Bacterial pneumonia was the most common cause of ARF, one patient needed on mechanical ventilation whereas two patients were dialysis dependent survivors. ARF following renal transplant is associated with higher mortality and loss of graft function because of compromised immunity. Anti-bacterial prophylaxis and early intensive management appears to help in improving the outcome while integrating the graft function.

Key Words: Acute Respiratory Failure, Acute Respiratory Distress Syndrome, Intensive Care Unit, Renal transplant.

INTRODUCTION

Kidney transplant accounts for around two-third of total organ transplants in various hospitals across the globe. Practically, kidney transplantation has significantly improved life quality and survival of end-stage kidney patients relatively at lower cost than routine dialysis (1). Furthermore, advancement in drug management, immunosuppressive drugs and understanding of immune modulation have decreased rate of acute rejection episodes (2). In addition, these advances have brought dramatic betterment in long-term results. Beyond these facts, renal transplant recipients possess long-term historical background of chronic kidney damage and routine dialysis in addition to other serious comorbidities such as diabetes and cardiovascular disease related with immune deficiencies (3). This combination of health dilemmas consequently leads to several complications including lung diseases (4). Renal transplant recipients are particularly at higher risk for acute respiratory failure (ARF) during anti-lymphocyte globulin therapy or graft failure for rejection. Renal transplant recipients that are often recommended to ICU admissions due to ARF, suffer from high graft loss in addition to high

probability of mortality. Nonetheless, ARF drastically influences short as well as long-term consequences including the requirement for intensive care unit (ICU) sometimes among Renal Transplant Recipients (RTR) with ARF (5).

The epidemiological aspects of ARF in renal transplant recipients are crucially affected by various regional attributes. Several studies reveal that almost one-half of renal transplant recipients account for ARF (6). Nevertheless, 22.5% of kidney patients die generally within 90 days after transplantation, but most of the survivors are left with obsolete grafts. All complications relevant to pulmonary manifestations after kidney transplantation approximately range between 3-17% (1, 4).

Certain research findings certify that within one month of renal post-transplant duration, cardiogenic pulmonary edema is diagnosed in almost half of the patients (7). On the contrary, pulmonary toxicity related to drugs and opportunistic fungal contamination is clinically present with symptoms and need hospitalization within six months of renal post-transplant duration (8). Fungal and bacterial infections are the leading causes of mortality in patients with ARF after renal transplantation (9, 10). Some studies suggest major factors of ARF in kidney transplant candidates and suggest certain recommendations to control mortality rate in various hospitals in addition to provision of sufficient care and adequate treatment (11-13). However, current data in terms of respiratory complications that are prevalent in renal transplant recipients of developing countries is scarce and need more research and analysis. Therefore, this study was designed to evaluate outcomes of post renal transplant recipients in terms of management, survival and deaths related to ARF.

METHODS

This cross-sectional study was conducted at Renal Transplant Unit of Dow University Hospital, Dow University of Health Sciences, Karachi, Pakistan. This study involved patients who developed ARF post renal transplant anytime within three months' period. However, patients who developed ARF after this duration, or blood borne infections leading to septicemia, rejection or any other post renal transplant complication were not included in this study. Five-year data was obtained from the hospital record of the patients who underwent renal transplant and developed ARF afterwards including both who shifted to Intensive Care Unit (ICU) or not during the period from 1st January 2017 to 30th December 2022. All adult recipients (≥ 18 years old) of kidney transplant were screened for ARF while they were staying after surgery and their follow-up visits during the specified period. Parameters used to diagnose ARF were respiratory rate ≥ 30 breaths per minute, severe dyspnea or oxygen saturation less than 92% or arterial pressure of oxygen less than 60mmHg at room temperature without any mechanical support. Fiberoptic bronchoscopy was done to visually examine the airways of lungs. Life sustaining treatments were given on the discretion of attending physician that included non-invasive or invasive mechanical ventilation, renal replacement therapy, or vasopressors alone or in combination depending on the physical state of the patients. Decision for non-invasive and endothelial mechanical ventilation was also based on the evaluation of attending physician. The decision for non-invasive or invasive mechanical ventilation, renal replacement therapy, vasopressors were also determined by the attending physicians. The study was approved by the local medical ethics committee of Dow University of Health Sciences (IRB-2952/DUHS/EXEMPTION/2023/142) and was carried out as per the principles outlined in the Declaration of Helsinki. Confidentiality of data was maintained throughout the course of study.

Statistical analysis

Statistical analysis was done using Statistical Package for Social Sciences (SPSS) version 21.0. Frequency (n) and percentage (%) of patients were measured and chi-square test ($\chi 2$) was applied to

compare statistical difference of the categorical variables among post renal transplant patients who were hospital survivors and hospital non-survivors keeping the level of probability(p) 5% at 95% Confidence Interval (CI) and a significant p-value <0.05.

RESULTS

In this retrospective cross-sectional study, 450 kidney allografts were done in five years' period at Renal Transplant Unit of Dow University of Health Sciences. Out of 450 patients 274 (60.89) were males and 176 (39.1%) were females. A total of 35 patients (7.8%) developed ARF. Among patients who developed ARF 15 were shifted to ICU. The outcome of 450 renal transplant recipients' in terms of mortality and survival is mentioned in flow chart in figure 1.

The baseline characteristics, demographics and clinical features of the study population are summarised in Table 1. The mean age of the population is 67.8 ± 1.83 years. Of the 450 subjects, males were 60.89% (n = 274), the mortality of female subjects is 26.1% (n = 46 out of 176) as compared to males 20.43% (n = 56 out of 274).

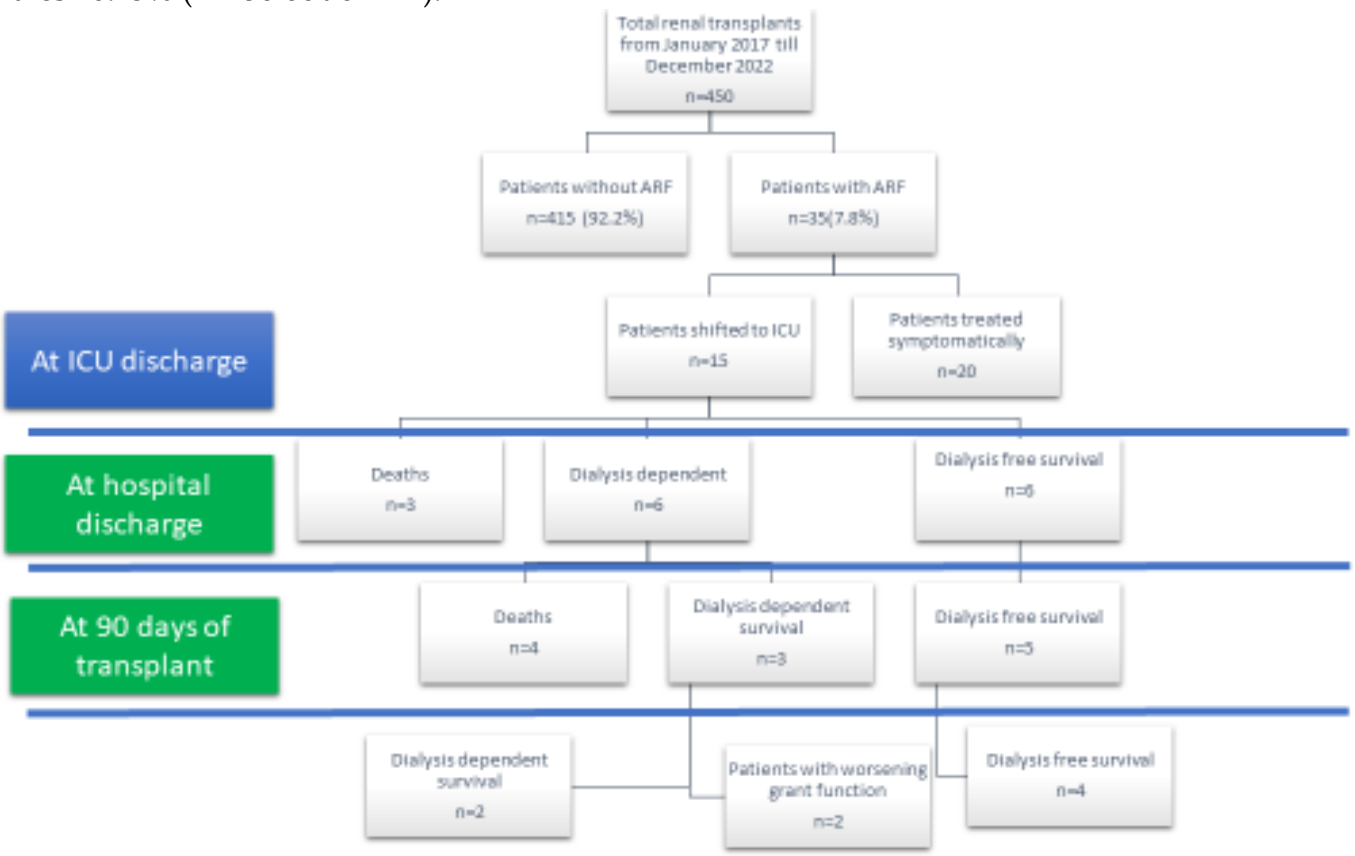

Figure 1. Summary of the patients underwent renal transplant and developed acute respiratory failure

Hypertension was found to be the most common comorbidity 82.67% (n = 372) whereas glomerulonephritis was the most common cause of ESRD 26.44% (n = 119) followed by nephroangiosclerosis 11.56% (n = 52). Acute rejection was observed in 20.89% (n = 94) of recipients whereas Cytomegalovirus (CMV) sero positivity was seen in 19.33% (n = 87) of subjects. Table 2 demonstrates characteristics of pulmonary involvement, severity and mechanical support for the patients admitted in ICU as per the cause of ARF.

Table 1. Summary of characteristics of patients underwent renal transplant and developed acute respiratory failure

S.no	Baseline characteristics		All patients N = 450 (%)	Hospital survivors N = 348 (%)	Hospital deaths N = 102 (%)
1.	Gender	Male	274 (60.89)	218 (62.64)	56 (54.9)
		Female	176 (39.11)	130 (37.36)	46 (45.1)
2.	Age (in years)	25-39	11 (2.22)	10 (2.87)	1 (1.0)
		40-49	23 (5.11)	21 (6.03)	2 (2.0)
		50-59	97 (21.56)	83 (23.85)	14 (13.7)
		60-69	177 (39.33)	123 (35.3)	54 (52.9)
		70 and above	142 (31.56)	111 (31.90)	31 (30.4)
3.	Comorbidities	Hypertension	372 (82.67)	316 (90.80)	56 (54.9)
		Heart failure	210 (46.67)	99 (28.45)	67 (65.9)
		Diabetes mellitus	124 (27.56)	67 (19.25)	57 (55.9)
4.	Causes leading to renal failure	Glomerulonephritis	119 (26.44)	93 (26.72)	24 (23.6)
		Nephroangiosclerosis	52 (11.56)	46 (13.22)	11 (10.8)
		Polycystic kidney disease	51 (11.33)	31 (8.91)	16 (15.7)
		Uropathy	29 (6.44)	27 (7.76)	6 (5.9)
		Diabetes mellitus	72 (16)	67 (19.25)	22 (21.7)
		Other undetermined causes	127 (28.22)	104 (29.89)	23 (22.6)
5.	Characteristics of transplant	First kidney allograft	294 (65.33)	219 (62.93)	75 (73.5)
		Kidney retransplanation	156 (34.67)	129 (37.07)	27 (26.5)
6.	Immuno suppressive agent	Cyclosporin	247 (54.89)	126 (36.21)	36 (35.3)
		Tacrolimus	162 (36)	57 (16.38)	38 (37.3)
		Mycophenolate mofetil	322 (71.56)	234 (67.24)	59 (57.9)
		Sirolimus	57 (12.67)	8 (2.30)	9 (8.8)
		Azathioprine	55 (12.22)	39 (11.21)	14 (13.7)
		Steroids	389 (86.44)	302 (86.78)	74 (72.6)
7.	Acute rejection		94 (20.89)	74 (21.26)	20 (19.6)
8.	Opportunistic infections	Cytomegalovirus disease, *n* (%)	87 (19.33)	66 (19.0)	23 (22.6)
		BK virus	43 (9.5)	27 (7.76)	16 (15.7)

DISCUSSION

The study presents the outcomes of post renal transplant patients in terms of survival and mortality. We have found that 22.67% of mortality post renal transplant out which 3.33% were secondary to ARF from a single centre.

These findings are in line with previously reported study where the rate was 2.9% (14). ARF is one of the serious problems in renal transplant recipients, mainly due to cardiogenic pulmonary edema and secondarily to lung injury in addition to bacterial pneumonia and COVID-19. It is because the study showed the data of last five years, out of which two years were affected by COVID-19 pandemic. Although, none of the study participant have ever suffered from COVID-19 during the study period and that could be considered as one of the main reasons of lower morbidity and mortality of

patients who developed ARF. Nevertheless, early diagnosis of pneumonia in renal transplant recipients reduces administration of excessive immunosuppressive drugs, but the use of glucocorticoids, antibiotics and antiviral agents is still made frequent (15-16).

Table 2. Characteristics of lung infiltration of patients admitted in Intensive care unit as per the cause of Acute Respiratory Failure

S. no.	Cause of ARF		Number of cases N (%)	Average duration since the onset of symptoms (in days)	Presence of ARDS at admission*	Lung infiltration**	Shock at admission***	Mechanical ventilation	Renal replacement therapy	Vasopressors administration
1.	Bacterial infection	Bacterial Pneumonia	6	2	5	4	4	3	3	3
		Extrapulmonary ARDS	2	1	2	1	2	1	1	2
2.	Cardiogenic pulmonary edema		2	1	3	4	1	2	1	1
3.	Opportunistic fungal infection	*Pneumocystis* pneumonia	2	7	2	3	-	1	1	1
		Invasive aspergillosis or Candidemia	1	8	1	1	-	-	-	-
		Viral pneumonia	1	5	1	1	-	-	-	-
4.	Drug-related pulmonary toxicity		1	7	1	1	-	-	-	-
	All patients		15	4	15	15	7	7	6	7

ARF= Acute Respiratory Failure, ARDS= Acute Respiratory Distress Syndrome. *diagosis of ARDS which depends on the ratio of partial pressure of arterial oxygen to fraction of inspired oxygen i.e. $PaO_2/FiO_2 \geq 200$, ** presence of lung infiltration in more than three quadrants on Chest X-ray.

Acute Respiratory Distress Syndrome (ARDS) accompanied by high level of creatinine in severe cases also leads to higher rates of deaths in renal transplant recipients (11, 17-19). Strategic measures of prevention, early diagnosis, appropriate treatment of respiratory disorders, sufficient nutrition to improve immune system are required to reduce incidence rate of ARDS (20, 21). Besides this, substantial use of invasive mechanical ventilation and adequate chemoprophylaxis is recommended to minimize the drastic consequences of ARF. This endorsement is highly crucial in decreasing death rates among pneumonia patients who have already gone through renal transplantation because of chronic kidney disease and low immunity (22-25).

The study was conducted from a single center for five years and a consecutive series of patients was recruited where the same treatment protocols were followed, thus this is considered as strength of

the study. However, retrospective nature of the study is considered as a limitation. With the evaluation of our data we agree with the current literature about the timely remedial measures to be taken to improve outcomes among post-renal transplant patients sustainable to develop such complications.

CONCLUSION

The study revealed that ARF accounts for 7.8% of total kidney transplantation, out of which 15 patients needed ICU management. A large number of graft recipients suffered to death or become dialysis dependent. In short, we can conclude that the outcome of post kidney transplant recipients who developed ARF depends on the underlying cause, comorbidity and the time taken to seek medical advice. The study suggests the addition of antibacterial and antifungal prophylactic drugs to reduce to incidences of ARF which would eventually help in better outcome.

Conflict of interest:
Authors declare no conflict of interest
Funding source:
The study did not receive any external funding
Ethical Approval:
The study was approved by the local medical ethics committee of Dow University of Health Sciences (IRB-2952/DUHS/EXEMPTION/2023/142) and was carried out as per the principles outlined in the Declaration of Helsinki. Confidentiality of data was maintained throughout the course of study.

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