Original Research Article

The study of clinico-pathological correlation and treatment outcome in acute allograft rejection in the immediate post renal transplant period

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ABSTRACT

Background: The kidney Tx is the treatment of choice for patients with ESRD. However, episodes of AR have a negative impact on short- and long-term graft survival. In spite of immunosuppressive medications, CNI, MMF and steroid, the AR remains a crucial problem for Tx. This analysis was performed to evaluate the changing profile of early AR (during first week of transplant) and its repercussions on graft survival.

Methods: This study was an observational cohort study and included 50 renal transplant patients irrespective of age, sex and race who developed bx proven AR within first week of transplant. Three groups were made according to histopathology: ACR, AMR and mixed rejection group. The patients were followed for 6 months thereafter.

Results: AR within a week of renal Tx were less symptomatic except decrease in UO. ACR was more common (72%) than AMR and mixed rejections. AMR and Mixed group required more therapeutic modalities than ACR. More patients required HD during AR in AMR and mixed rejection group than ACR. The mean s.cr at 6 months was 1.3,1.5 and 1.6 in ACR, AMR and mixed group respectively. There were more incidences of BK viremia, CMV infection UTI and rejection fronts follow up in AMR and mixed group than ACR group.

Conclusions: Acute rejections within a week are less symptomatic and ACR occurred more frequently than AMR and mixed rejection There were more incidences of BKV, CMV and UTI for 6 months follow up in AMR and Mixed rejection group.

Keywords: Acute rejection, Immunosuppression, Kidney transplant

INTRODUCTION

The number of patients with end-stage renal disease (ESRD) has increased dramatically over the past decade.[1] The treatments available for ESRD are hemodialysis (HD), peritoneal dialysis (PD) and kidney transplantation. The kidney transplant is more desirable because it has been found to be associated with greater longevity, better quality of life and economic benefits resulting from successful transplantation for the patients.[2] So the kidney transplant (Tx) is the treatment of choice for patients with ESRD.

However, episodes of acute rejection (AR) have a negative impact on short- and long-term graft survival. Although acute rejection can occur at any time after transplantation, it is most commonly occurring within the first 6 months. The incidence of acute rejection continues to decrease with the development of newer immunosuppression drugs.[3] In spite of immunosuppressive medications, such as calcineurin

inhibitors (CNIs), mycophenolate mofetil and steroid, the AR remains a crucial problem for Tx.[4]

An acute rejection episode is characterized by a decline in kidney function that is caused by an immune reaction against the allograft. With routine monitoring of plasma creatinine and immunosuppressive drug levels, symptoms and signs of acute rejection which are rarely pronounced, but low-grade fever, oliguria, and graft pain or tenderness may occur. Definitive diagnosis of acute rejection requires biopsy. Acute rejection involves cellular (Acute Cell mediated rejection, ACR) or humoral immune mechanisms (Acute antibody mediated rejection, AMR). Acute AMR may occur alone or with ACR. The modified -Banff classification is a widely used schema for classifying the rejection.[5]

Although acute rejection is frequently reversed, retrospective studies shows that it is strongly associated with the development of chronic rejection and poorer allograft survival. Poorer allograft outcome also correlates with the severity of rejection, the number of rejection episodes, and with resistance to steroid therapy. So, reducing the incidence of acute rejection is the major goal in kidney transplantation.[6-10]

Uncomplicated ACR is generally treated with a short course of high dose steroids. Steroid resistant ACR is usually treated with depleting antibodies, rabbit anti thymocyte globulin (r-ATG).[11] While optimal treatment of AMR is yet unknown5. Strategies that have been used to treat AMR include combinations of plasma exchange, IV immunoglobulins, pulse steroids, anti-CD-20 monoclonal antibody 9 rituximab) and bortezomib, to suppress donor specific antibodies.[11-13]

Infection affects all kidney transplant recipients, in one form or another. Immunosuppressive drugs used to prevent and treat allograft rejection predispose the transplant recipient to a wide variety of bacterial, viral, fungal, and parasitic infections.[14] The goal of this study is to determine the clinical and histo-pathological features of acute rejection in immediate post-renal transplant period and their correlation with treatment outcome, further graft function and complications.

METHODS

This study was an observational cohort study and included all renal transplant patients irrespective of age, sex and race who developed acute rejection within first week of transplant, admitted at Indraprastha Apollo Hospital, New Delhi between 1st June 2014 to 31st Dec 2015. As there is no same kind of study has been done before, this study can be considered as a pilot study.

Inclusion criteria

- Post renal transplant patients who develop AR within first week of transplant, both serum creatinine and

biopsy criteria of AR should be fulfilled and patients willing to participate.

Exclusion criteria

- Patient who develop AR diagnosed clinically, but not biopsied.

Patients having renal transplant were observed for one week post renal transplant. The patients were investigated for renal function test daily as per package of Renal Tx at Indraprastha Apollo hospital. Patients found to develop acute rejection as defined by serum creatinine level (increase by 20% from the baseline) and allograft biopsy (fulfilling Pathologic features that met Banff 2007 update criteria for AMR., ACR and mixed rejection), informed about the study and participants giving consent were included in the study. Antibody against donor HLA (DSA) was not done because of unavailability.

Their clinical presentation, histo-pathological manifestations and treatment given were analyzed. All patients were followed for 6 months to monitor graft function and Incidence of CMV, BK viremia, urinary tract infection, CNI toxicity and acute rejection.

Duplex ultrasonography was done in all patients after transplant. Resistive index greater than 0.90 based on the main renal artery flow pattern was considered as high and significant value. Acute CNI toxicity was diagnosed when graft dysfunction was associated with high CNI levels, other features of CNI toxicity and graft dysfunction improved after reduction the dose.

Induction and maintenance immunosuppression

ATG was considered as induction immunosuppression in patients who were in pre sensitized category e.g. second transplant, biologically unrelated donor (husband), multiparous women, history of multiple blood transfusions. However, all patients were given choice for induction with IL-2R blocker (basiliximab) and given to those who agreed. The main constraint to use induction in all patients was financial. Calcineurin inhibitors, mycophenolate mofetil and steroids were given as maintenance immunosuppression.

Renal allograft pathology and C4d

One core needle biopsy core was obtained from each renal allograft for morphologic studies. This core was fixed in formalin.

Hematoxylin and eosin, periodic acid Schiff, and Masson trichrome stains were routinely used. C4d staining was performed by immunohistochemistry on paraffin sections using a rabbit polyclonal Antibody specific for human C4d. C4d staining in PTCs was considered to be positive if seen in >10% areas of PTCs, excluding scarred or necrotic areas.

Statistical analysis

Descriptive data were expressed as the range (minimum, maximum), mean± standard deviation for quantitative variable and frequency (%) for qualitative variable. The statistical significance of quantitative variable across the three groups was determined by applying non-parametric Kruskal-Wallis test since most of the quantitative variable does not follow normal distribution. Chi square test or Fisher exact test was applied for assessing the significance of categorical variable across the three groups. The level of statistical significance was taken p value ≤0.05. Analysis of data carried out using the SPSS 16.0 software.

RESULTS

This Prospective observational study enrolled 50 eligible patients who underwent kidney transplant at Indraprastha Apollo hospital, New Delhi. Kidney transplant patients who developed biopsy proven acute rejection within 7 days of Kidney transplant. Patients were followed for 6 months and monitored for kidney function, development of either infection; BK Viremia, CMV, UTI or calcineurin inhibitor toxicity or rejection.

Three groups were made according to biopsy findings (Banff classification 2007 update.) Acute cellular rejection, acute antibody mediated rejection and mixed. Amongst a total of 50 patients 36 patients (72%) were male and 14 patients (28%) were female. Out of total cases majority of the patients were in the age group of 31-40 (40%) and then in 41-50 (22%). The mean age in group I (ACR group) was 39.92±10.59, in group II (AMR group) was 37.90 ±14.11, in group III (mixed group) was 33.75±7.58. All three groups were comparable (p value-0.423). 12 (24%) cases were having diabetic nephropathy, 5 (10%) were having hypertensive nephrosclerosis. In most of the patients in others category (64%), the primary disease was not known and clinically they were diagnosed as chronic glomerulonephritis (CGN) or chronic tubulointerstitial nephritis (CIN). All three groups were comparable in terms of basic renal disease (p value -0.794). HLA typing was not done in all transplant cases. It was done where the donor was the first degree relative of recipient. Out of 13 cases, 4 cases had 2 and 9 cases had 3 HLA mismatch. induction immunosuppression was used in 10 cases. Basiliximab was used in 9 while ATG was given to one patient as an induction agent. 44 (88%) were given (Tacrolimus+ MMF+ Prednisolone) and remaining 6 cases (12%) were given (cyclosporine+ MMF +prednisolone). All 6 cases who received cyclosporine were in group I (ACR) (p value-0.266). Cyclosporine was given to patients those treated for either tuberculosis or hepatitis C and Hepatitis B (Table 1).

Table 1: Baseline characteristic of study patients in all three groups.

Variable	ACR group I (% within group)	AMR group II) (% within group II)	Mixed (group III) (% within group III)	P - value
Number of cases	36 (72%)	10 (20%)	4 (8%)	1.37
Age (years)	39.92±10.59	37.90±14.11	33.75±7.58	0.423
Male N (%)	27 (75%)	6 (60%)	3 (75%)	0.64
Female N (%)	9 (25%)	4 (40%)	1 (25%)	---
Pre-sensitization				
Blood transfusion N (%)	13 (36.1%)	5(50%)	2 (50%)	0.667
Pregnancy	4 (44.44%)	1(25%)	1 (25%)	0.394
Previous transplant	Nil	Nil	Nil	
Native kidney disease				
Diabetic nephropathy	10 (27%)	2 (20%)	0 (0%)	
Ischemic nephropathy	4 (11.1%)	1 (10%)	0 (0%)	
ADPKD	1 (28%)	0	0	
Others	21 (58.3%)	7(70%)	4 (100.0%)	
Donor characteristics				
First degree relation	10 (27.8%)	3 (30%)	0	0.461
Mean age	43.17±10.28	40.80±12.56	51.50±7.00	2.46
Laparoscopic donor nephrectomy N (%)	18 (50%)	5 (50%)	3 (75%)	0.631
Immunosuppression				
Induction-Basiliximab N (%)	8 (22.2%)	1 (10%)	0 (0.0%)	0.226
ATG n (%)	0 (0.0%)	1 (10%)	0 (0.0%)	
Maintenance- TAC+ MMF+ steroid	30 (83.3%)	10 (100%)	4 (100%)	
CYC + MMF +steroid	6 (16.7%)	Nil	Nil	

Table 2: Different biopsy findings in all patients according the Banff classification (2007 update).

Biopsy findings	Frequency	Percent	Valid percent (in individual group)
Borderline	14	28	38.8
ACR-1A	8	16	22.2
ACR-1B	5	10	13.8
ACR-2A	7	14	19.4
ACR-2B	1	2	2.7
ACR-3	1	2	2.7
AMR-1	6	12	60
AMR-2	3	6	30
AMR-3	1	2	10
Mixed	4	8	100
Total	50	100	

Table 3: Different treatment modalities used across the three groups.

		Treatment given				
		Pulse steroids	ATG	IvIg	TPE	Bortezomib
Group	Group I (ACR) count	36	13	1	0	0
	N=36% within group	100%	36.1%	2.7%	0.0%	0.0%
	Group II (AMR) count	10	8	5	8	1
	N=10 % within group	100%	80%	50%	80%	10%
	Group III (mixed) count	4	4	1	3	1
	N=4 % within group	100%	100%	25%	75%	25%
Total	N=50 count	50	25	7	11	2

Day of onset of rejection and clinical features

There were 66.7% cases in group I had onset of rejection after 3 days while 80% and 75% cases had onset of rejection within 3 days in group II and III (p value-0.016). 12 (24%) patients had fever during acute rejection. Subgroup analysis revealed 22.2%, 30.0% and 25% cases had fever in group I, II, III respectively (p value 0.877). 8 cases (16%) had graft tenderness. Subgroup analysis revealed 13.9%, 20%, 25% cases had graft tenderness during acute rejection (p value-0.787) and 46 cases (92%) had significant fall in urine volume. Subgroup analysis revealed 88.9%, 100% and 100% cases had fall in urine volume in each group I, II, III respectively (p value-0.429).

There were 10 cases (20%) had fall in hemoglobin level of >1 gm% during acute rejection. On subgroup analysis this was 16, 20%, 50% in group I, II, III respectively (p value-0.287). 10 cases (20%) had fall in albumin level >0.3gm%. On subgroup analysis this was 16.7%, 20%, 50% in group I, II, III respectively. (P value-0.287).

RI values were high in 31 cases (62%). RI value was high in 58.3%, 70%, 75% cases in group I, II, III respectively (p value-0.682). CNI level at the time of acute rejection was low in 23 cases (46%), normal in 16 cases (32%) and high in 11 cases (22%) (p value-0.817). 7 cases (14%) cases required hemodialysis during acute rejection.

Subgroup analysis revealed that hemodialysis was done in 2.8%, 40%, and 50% of cases in group I, II, III respectively (p value-0.001). 36 (72%) had acute cellular rejection, 10 cases (20%) had acute antibody mediated rejection and 4 cases (8%) had mixed rejection. Subgroup analysis revealed that 14 cases (38.88%) had borderline rejection in group I. 6 cases (60%) had grade I AMR in group II (Table 2).

Treatment

Pulse steroid, ATG, IvIG, therapeutic plasma exchange (TPE), Bortezomib was used as a treatment modality in different groups. While rituximab was not given to any of the patients. Subgroup analysis revealed that all 50 patients received pulse steroids. ATG were given in 36.11%, 80%, 100% cases in each group I, II, III respectively. IvIG were given in one patient in group I, while 50% and 25% cases of group II and III respectively. Plasma exchange was done in 80% and 75% cases of group II and III respectively. Bortezomib given to one patient in each group II and III (Table 3).

Treatment outcome

There were no patients in controlled category across the three groups. Out of 50 cases 50% had complete reversal and 48% had partial reversal after 10 days of acute rejection following treatment (Figure 1).
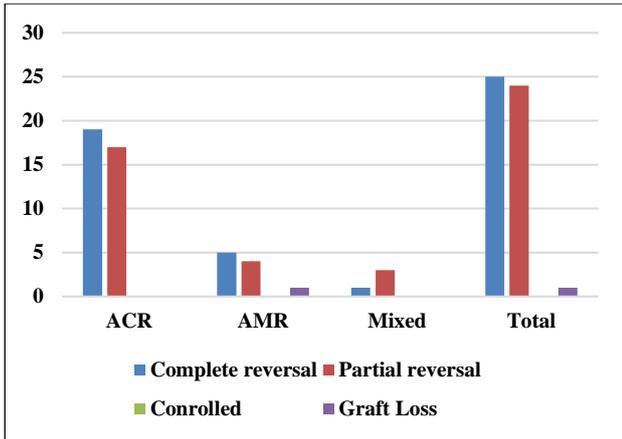
Figure 1: Treatment outcome in different groups of graft rejection.

Mean serum creatinine during follow up of 6 months

Out of 50 cases 1 had graft loss which was in AMR (group II) and 2 patients in ACR (group I) were lost to follow up. So, the following mean serum creatinine values were calculated out of 47 cases. The mean serum

creatinine levels were 1.147, 1.250, and 1.2 after 3 months in groups I, II, III respectively (p value-0.473). The mean serum creatinine levels were 1.318,1.516, and 1.675 after 6 months in groups I, II, III respectively (p value-0.463) (Figure 2).
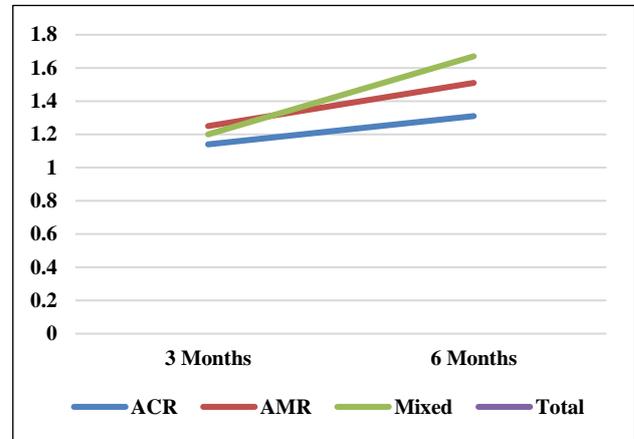

Figure 2: Mean serum creatinine at 3 and 6 months in all three groups.

Table 4: Complications which were seen for 6 months follow up across the three groups.

		BKV	CMV	UTI	CNI toxicity	Rejection
Group	Group I (ACR) count	4	4	9	4	4
	N=34% Within group	11.76%	11.76%	26.47%	11.6%	11.76%
	Group II (AMR) count	2	2	5	1	2
	N=9% within group	22.2%	22.2%	55.5%	11.1%	22.2%
	Group III count (mixed)	2	1	3	0	1
	N=4% within group	50.0%	25.0%	75.0%	0.0%	25.0%
Total	Group count	8	7	17	5	7
	N=48% within	16.6%	14.5%	35.4%	10.4%	14.5%

Incidences of complications during follow up of 6 months

The 47 patients (3 were lost to follow up including one of graft loss) were followed for 6 months and monitored for BK viremia, CMV infection, UTI, CNI toxicity and rejection. BK viremia was detected in 11.76%, 22.22% and 50% cases across the three groups I, II, III respectively (p value-0.324). CMV infection was detected in 11.76%, 22.22% and 25% cases across the three groups I, II, III respectively (p value-0.822) UTI was detected in 26.47%, 55.55% and 75%cases across the three groups I, II, III respectively (p value-0.190).CNI toxicity was detected in 11.6%, 11.11% and 0.0% cases across the three groups I, II, III respectively. Rejection was seen in 11.76%, 22.22% and 25% cases across the three groups I, II, III respectively (p value-0.822) (Table 4). Although incidence BK viremia, CMV infection, urinary tract infection and rejection were more in group II

and III. But p value was not significant, as the number of patients were less.

DISCUSSION

This analysis was performed to evaluate the changing profile of early acute rejection (AR) (during first week of transplant) on kidney transplant recipients and its repercussions on graft survival. As described in other reports AR rates have progressively decrease, probably due to evolution of better immunosuppressive regimens, especially after tacrolimus and MMF introduction. [14,15]

All patients in present study had signs of graft dysfunction, such as decrease in urine volume and elevated serum creatinine. Most patients did not develop fever and graft tenderness across the three groups. 75 to 80% of patients in AMR and mixed rejection group had onset of rejection within 3 days while 67% patients in

ACR developed after 3 days, which was statistically significant. 80% patients did not have fall in hemoglobin (>1 gm %) and albumin (>0.3gm %) during AR.

Chung YC et al, compared cyclosporin-A treated renal allograft recipients to that of patients treated with conventional azathioprine and steroid therapy.[16] Compared to conventional therapy, the classical systemic manifestations of rejection, such as malaise, lethargy, apathy, general weakness, vague discomfort, increase in body weight, swelling of graft with tenderness, were all milder and less frequent in the cyclosporin-A-treated group. Similar findings were observed in present study.

In a study of fifty-six kidney allograft recipients with C4d positive AR done by Q Sun, Z-H Liu et al, reported fever in 71.4% of Very early rejection (VER) group (within 14 days of transplant).[17] Urine volume <1 litre a day was reported in 96.4% of VER cases. The range of onset of rejection was 9.7±7.1 days. The difference of incidence of fever might be because only C4d positive cases were taken in the study, while>70 percent of cases in present study had acute cellular rejection.14 days was taken as cut off point to be included in the VER group in which infection rates are usually high. They reported fall in hemoglobin (>1 gm%) in 7.1% and fall in albumin (>0.3gm%) in 10.7% cases in VER group of C4d positive AR, while it was significant in late onset of rejections. 62% of patients had high RI values on graft ultrasound Doppler during acute rejection which was comparable in all three groups. In the study done by Perrella RR et al. the sensitivity of the test was 43%, with a 67% of specificity.[18] They conclude that duplex Doppler sonography alone is inadequate to evaluate acute rejection in renal transplants.

In present study 46% patients had low CNI trough level (TAC<7 and CYC<150 ng/ml) during acute rejection. Subgroup analysis was comparable statistically. Out 0f 50 patients, 36 patients had ACR (including 14 cases of borderline rejection), 10 patients had AMR and 4 patients had mixed rejection. Out of 50 cases 28% had borderline, 16% IA, 10% IB, 14% IIA, 2% IIB, 2% III, 12% AMR-I, 6% AMR-II, 2% AMR-III and 8% had mixed rejection.

RL Heilman et al, studied 457 transplant recipients treated with rapid steroid withdrawal, out of which 46 (10%) experienced subclinical rejection and 36 (7.8%) had clinical rejection.[19] The Banff grade of rejection was higher in clinical rejection group. Out of 36 cases of clinical rejection 11% had borderline, 31% IA,31% 1B, 11% IIA, and 14% had AMR. The mean Tacrolimus trough level during acute rejection was 8.8±3.4 during clinical rejection. So, the CNI level does not correlate with the onset of AR.

Present study revealed 40-50% of patients in AMR and mixed rejection group required hemodialysis while it was done in only 2.8% cases in acute cellular rejection group. This was statistically significant. Q Sun et al, reported that 75% of patients with C4d positive AR required dialysis within 2 weeks of the onset of AR.[17]

All 50 patients were given pulse steroids. ATG were given in 36.11%, 80%, 100% cases in each group I, II, III respectively. IvIG were given in one patient in group I. while 50% and 25% cases of group II and III respectively, received IvIG. Plasma exchange was done in 80% and 75% cases of group II and III respectively. Bortezomib given to one patient in each group II and III. In the study done by RL Heilman et al, out of 36 cases of clinical rejection 72% received pulse steroid, 2.77% r-ATG, 17% therapeutic plasma exchange and rituximab. IvIG and bortezomib were not used in this group.[19]

Out of 50 cases one patient had graft loss that had AMR. Remaining patients were either recovered to normal range of creatinine or recovered partially after getting treatment. Mean serum creatinine at 6 months was 1.319, 1.516 and 1.675 in group I, II and III respectively. Although this was comparable across all three groups statistically. A study done by Sijpkens YW et al, Doxiadis II et al, concluded that late acute rejection episodes (ARE) has a detrimental impact on long-term graft survival and is associated with MHC class I incompatibility, whereas early ARE is correlated with HLA-DR mismatches and has a better prognosis.[20] Opelz et al, demonstrated that AR followed by partial loss of graft function exerts a more detrimental effect on long term outcome than rejection with total recovery.[21] The mean serum creatinine was comparable in present study, might be because we have taken cases that developed acute rejection within 7 days only and due to better evolution of immunosuppression and anti -rejection therapy. The study of C4d positive acute rejection cases performed by Q Sun et al, Z-H Liu et al, found that most cases of very early rejection, that was occurrence of rejection within 14 days of transplant ,were reversed with Tacrolimus and mycophenolate mofetil treatment, with or without immunoadsorption and with a 1 year graft survival rate of 96.4%.[17] Which is comparable to present study, 6-month graft survival was 98% in present study.

Although graft function was comparable in all three groups during follow up, however percentage of patients who had infections (BKV, CMV, UTI) and Rejection during follow up in AMR and mixed rejection groups were more in comparison to ACR group. Out of 50 cases 16.66% developed BK viremia, 14.58% CMV infection, 35.41% UTI, 10.4% CNI Toxicity and 14.58% rejection for 6 months follow up. Subgroup analysis revealed BK viremia in (11.76%, 22.22%, 50%), CMV infection (11.76%, 22.22%, 25%), UTI (26.47%, 55.55%, 75%), CNI toxicity (11.6%, 11.11%, 0.0%), rejection (11.76%, 22.22%, 25%) in group I, II, III respectively. Although this comparison was statistically insignificant across the three groups, probably due to small sample size. Patients who developed AR during follow up in present study, most of them were associated with infections or non-compliance with drugs the same was observed by Q Sun

et al31 in their study on patients with C4d positive rejections. 14.58% of total and up to 20% of patients in mixed rejection group developed CMV infection in present study despite of giving CMV prophylaxis to patients with D+ and R- status and whoever received ATG. Sagedal S et al, Nordal K et al, noted the incidence of CMV infections in first transplant was 68% in D+R- and D±R+ serostatus groups, whereas the incidence of CMV disease was higher in D±R-(56%) than in D±R (20%, P<0.001).[22] Khourya JA et al, Storch GA et al, conclude that more patients in pre-emptive group (59%) than in the prophylaxis group (29%) developed CMV DNAemia.[23] Both strategies were effective in preventing symptomatic CMV. A retrospective study of 1625 patients of renal transplant recipients done by Vinod PB, RK Sharma et al24 found that CMV infection was common with 25.9% and BKV was there in 0.67% cases. Present study suggest that up to 20% of patients who were treated for rejection developed CMV infection despite using prophylaxis in D+ and R- serostatus and in those who were treated with ATG, So CMV prophylaxis should be given to all patients except D-/R- serostatus and whoever treated with ATG as KDIGO guideline suggests.

The study done by Khourya JA et al, Storch et al, also documented more CMV DNAemia in pre-emptive group than in the prophylaxis group while overall costs were similar for either monitoring or drug.[23] But side effects of drugs will remain a matter of concern. 16.66% patients had BK viremia in present study. Hirsch HH et al, Knowles W et al, reported out of 78 patients, 23 patients had decoy-cell shedding a median of 16 weeks after transplantation, 10 patients had BKV viremia at a median of 23 weeks, and 5 had BKV nephropathy at a median of 28 weeks.[25] Kaplan-Meier estimates of the probability of decoy-cell shedding, viremia, and nephropathy were 30%, 13% and 8% respectively. Antirejection treatment, particularly with corticosteroids, was associated with BKV replication and nephropathy. Sachdeva MS et al, Nada R et al, Jha V et al, Skuja V et al, retrospectively screened for BK polyoma virus in 414 renal allograft biopsy specimens from 321 transplant recipients presenting with allograft dysfunction.[26] 9.3% were positive for BK polyoma virus, suggesting a high incidence of this infection in Indian transplant recipients. BK virus infection coexisted with acute rejection in a majority of patients. So, the regular screening for BKV is required after transplant.

In present study, 35.41% of total patients had urinary tract infection, which was more in AMR and mixed rejection group than ACR. Dilip M Babu, NK Hase et al, conducted retrospective analysis of 200 renal transplant recipients the incidence of UTI during the first 3 months was 20% (equivalent for both men and women) and at 1 year was 60% for women and 47% of men.[27] Significant risk factors for post renal transplant UTI were advanced age, female gender, use of cyclosporine ,MMF and azathioprine, post operation duration of per urethral

catheterization and D-J stent. UTI was the most common infection out of three we have monitored in our study. This study suggests that acute rejections within a week of renal transplant were less symptomatic while significant urine output fall during acute rejection occurred in almost all cases. We found acute cellular rejection (ACR) more commonly than acute antibody mediated rejection (AMR) and mixed rejections. Patients with AMR and Mixed rejection required more therapeutic modalities than ACR. More patients required dialysis during AR in AMR and mixed rejection group than ACR. The mean serum creatinine at 6 months was 1.319, 1.516 and 1.675 in ACR, AMR and mixed rejection group respectively. Although this was comparable across the three groups statistically (p value=0.463). However, there were more incidences of BK viremia, CMV infection, urinary tract infection and rejection for 6 months follow up in AMR and mixed rejection group than ACR group; which was statistically comparable across the three groups, probably because of small sample size.

Limitations of this study were to the limitation of present study is relatively small sample size. Hence results did not reach statistical significance, was an observational study. Different treatment modalities were not randomized, HLA typing could not be done in all patients because of financial constraints, the patients were not studied for long term follow up.

CONCLUSION

This study suggests that acute rejections that occur within a week of renal transplant were less symptomatic in terms of fever, graft tenderness. Significant urine output fall during acute rejection occurred in almost all cases. More than ¾ cases of AMR and mixed rejection occurred within 3 days and 2/3 cases of ACR occurred after 3 days of transplant.

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