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ORIGINAL ARTICLE

To Study the Frequency of Acute Rejections in Renal Transplant Recipients on Cyclosporine Regimen within 3 Months' Post-transplant at a Renal Care Setup

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ABSTRACT

Background: One of the primary causes of early graft dysfunction after renal transplantation is still acute rejection, especially in the first three months after the procedure.

Objective: To study the frequency of acute rejections in renal transplant recipients on a cyclosporine-based immunosuppressive regimen within three months post-transplant at a renal care setup.

Methodology: This descriptive study was conducted at The Kidney Centre Post Graduate Training Institute (TKC PGTI), Karachi, over six months from August 2020 to February 2021. Using successive sampling, 30 renal transplant patients between the ages of 18 and 65 who were taking cyclosporine (4.5 mg/kg/day) in addition to mycophenolate mofetil and prednisolone were included. In order to assess graft function, blood creatinine levels and cyclosporine C0 and C2 levels were tracked on Days 3 and 9. SPSS v20 was used to analyze the data, and $p < 0.05$ was considered statistically significant.

Results: Eleven (36.67%) of the thirty patients had acute rejection in less than three months. Most were between the ages of 18 and 40 (n=23, 76.67%) and male (n=21, 70.00%). On Day 3, the mean cyclosporine C2 level was 1065.1 ± 414.98 ng/mL, and on Day 9, the mean C0 level was 220.06 ± 260.53 ng/mL. On Day 9, the mean serum creatinine was 1.23 ± 0.79 mg/dL, down from 1.56 ± 0.94 mg/dL on Day 3. The only factor that was substantially linked to acute rejection was age ($p = 0.02$).

Conclusion: Despite therapeutic cyclosporine levels, acute rejection occurred in over one-third of patients, especially among younger recipients, highlighting the need for tailored immunosuppression and close monitoring.

Keywords: Renal transplantation, acute rejection, cyclosporine, immunosuppression, graft function

INTRODUCTION

Renal transplantation is the treatment of choice for patients with end-stage renal disease (ESRD), offering improved quality of life and long-term survival compared to dialysis[1]. However, acute rejection is still a major problem in the early post-transplant phase, even with improvements in immunosuppressive treatments and surgical methods[2]. Graft function and patient outcomes may be significantly impacted by acute rejection, especially within the first three months after transplantation[3]. T-lymphocyte activation against donor antigens is the primary mediator of this intricate immunological process, which calls for close observation and prompt therapeutic intervention[4].

By dramatically lowering the frequency of acute rejection events, the calcineurin inhibitor cyclosporine, which was first developed in the 1980s, transformed transplant therapy[5]. The medication has a limited therapeutic window despite its effectiveness, and both excessive and insufficient immunosuppression may have negative effects[6]. While supratherapeutic levels might raise the risk of nephrotoxicity and opportunistic infections, subtherapeutic levels may make patients more susceptible to rejection[7]. Consequently, it is crucial to reach and maintain appropriate cyclosporine levels, especially during the early post-transplant phase when rejection risk is at its maximum[8].

Numerous variables, including as patient demographics, HLA mismatching, medication adherence, and the standard of post-transplant care, might affect the frequency and pattern of acute rejection[9]. Additionally, results may be impacted by regional differences in drug monitoring infrastructure, patient follow-up procedures, and clinical practices. These difficulties are exacerbated in environments with low resources, like many poor nations, which emphasizes the need of context-specific data to direct clinical therapy[10,11].

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There is no information from nearby renal care facilities on the incidence of acute rejection events during the crucial early postoperative period, despite the fact that cyclosporine-based regimens are often used in renal transplant programs. Assessing the efficacy of existing immunosuppressive treatments and determining areas in need of therapeutic improvement or improved patient education need an understanding of this frequency..

Objective: To study the frequency of acute rejections in renal transplant recipients on cyclosporine regimen within 3 months' post-transplant at a renal care setup.

MATERIAL AND METHODS

Study Design and Setting: This descriptive study was conducted at The Kidney Centre Post Graduate Training Institute (TKC PGTI), Karachi, over a period of six months, from 3rd August 2020 to 2nd February 2021.

Inclusion and Exclusion Criteria: The research comprised patients of both sexes, aged 18 to 65, who had kidney transplantation at TKC PGTI and were prescribed a cyclosporine (CsA) regimen at a dosage of 4.5 mg/kg/day in two split doses for three months after the transplant. Excluded were patients who were not following the CsA regimen or who were unable or unwilling to provide informed permission.

Sample Size: Raosoft software was used to determine the sample size, which had a 10% margin of error and a 95% confidence range. This was based on an estimated acute rejection rate of 36.6% from previous research. Due to departmental constraints, 30 patients were added utilizing a non-probability sequential sampling strategy, even though the needed sample size was 90

Data Collection: A standardized proforma was used to collect data both during the hospital stay and during the follow-up outpatient visits. All patients were treated with normal immunosuppressive medication, which included prednisolone, mycophenolate mofetil (MMF), and CsA. Serial measurements of C0 (trough) and C2 (2-hour post-dose) levels were used to customize CsA dosage; these measurements were made on Day

3, Day 9, and then again as suggested by renal function (serum creatinine). The first month's target C0 levels were kept between 250 and 300 ng/mL, the second and third months' between 200 and 250 ng/mL, and the third month's between 80 and 180 ng/mL. Serum creatinine, CsA levels, demographic information, and the presence of any acute rejection episodes were among the data collected.

Data Collection Tool: Structured proforma used during hospital stay and OPD follow-up. Information on demographics, renal function, immunosuppressive levels, and acute rejection episodes was documented.

Statistical Analysis: IBM SPSS version 20 was used for both data input and analysis. The mean ± standard deviation was used to represent quantitative data including age, serum creatinine, and CsA levels. Frequencies and percentages were used to display categorical characteristics such as gender, comorbidities (such as diabetes and hypertension), and the incidence of acute rejection. ANOVA was used to compare the amounts of cyclosporine. Stratification was used to address effect modifiers such age, gender, and concomitant conditions, and the chi-square test was then used. Statistical significance was defined as a p-value of less than 0.05.

Ethical Approval: The study protocol was approved by the Ethical Review Committee of The Kidney Centre, and formal permission was obtained from the Head of Nephrology Department. Written informed consent was taken from all participants after briefing them about the purpose, risks, and benefits of the study. Patient confidentiality was maintained throughout.

RESULTS

The distribution of clinical and demographic characteristics among 30 patients of renal transplants is shown in Table 1. Seven patients (23.33%) were between the ages of 41 and 65, whereas 23 patients (76.67%) were between the ages of 18 and 40. Nine patients (30.00%) were female, and 21 patients (70.00%) were male. Eleven patients (36.67%) had acute rejection, whereas nineteen individuals (63.33%) did not. 27 patients (90.00%) did not have type II diabetes, while 3 individuals (10.00%) did. Four individuals (13.33%) did not have hypertension, while 26 patients (86.67%) did. The clinical parameters, together with their mean values and standard deviations, are compiled in Table 2. It was 34.37 ± 12.93 years old on average. On Day 3, the average CsA C2 level was 1065.1 ± 414.98 ng/mL; on Day 9, the average C0 level was 220.06 ± 260.53 ng/mL; and on Day 9, the average C2 level was 994.1 ± 383.16 ng/mL. On Day 3, the average serum creatinine level was 1.56 ± 0.94 mg/dL; on Day 9, it dropped to 1.23 ± 0.79 mg/dL, suggesting better graft function in the first post-transplant phase.

Table 1: Distribution of Demographic and Clinical Characteristics of Renal Transplant Recipients (n = 30)

Variable	Category	Frequency	Percentage (%)
Age Group (Years)	18–40	23	76.67
	41–65	7	23.33
Gender	Male	21	70.00
	Female	9	30.00
Acute Rejection	Yes	11	36.67
	No	19	63.33
Diabetes Mellitus Type II	Yes	3	10.00
	No	27	90.00
Hypertension	Yes	26	86.67
	No	4	13.33

Table 2: Mean Cyclosporine Levels and Serum Creatinine Values in the Study Population (n = 30)

Variable	Mean ± SD
Age (years)	34.37 ± 12.93
CsA C2 Level (Day 3, ng/mL)	1065.1 ± 414.98
CsA C0 Level (Day 9, ng/mL)	220.06 ± 260.53
CsA C2 Level (Day 9, ng/mL)	994.1 ± 383.16
Serum Creatinine (Day 3, mg/dL)	1.56 ± 0.94
Serum Creatinine (Day 9, mg/dL)	1.23 ± 0.79

The connection between acute rejection and other parameters is examined in Table 3. Eleven (100.00%) of the 23 patients between the ages of 18 and 40 had rejection, while 12 (63.16%) did not; seven patients between the ages of 41 and 65 had rejection, and seven (36.84%) did not; these differences were statistically significant (p = 0.02). Of the nine female patients, three (27.27%) experienced rejection and six (31.58%) did not (p = 0.57); of the twenty-one male patients, eight (72.73%) had rejection and thirteen (68.42%) did not. Of the 27 non-diabetic patients, 11 (100.00%) had rejection and 16 (84.21%) did not (p = 0.23), whereas none (0.00%) and three (15.79%) of the three diabetes patients experienced rejection. Ten (90.91%) and sixteen (84.21%) of the 26 hypertension patients had rejection, but one (9.09%) and three (15.79%) of the four non-hypertensive patients did not (p = 0.53). Only the age group among these factors had a statistically significant correlation with acute rejection.

Table 3: Association of Acute Rejection with Demographic and Clinical Variables (n = 30)

Variable	Category	Acute Rejection Yes	Acute Rejection No	Total	p-value
Age Group (Years)	18–40	11 (100.00%)	12 (63.16%)	23	0.02
	41–65	0 (0.00%)	7 (36.84%)	7	
Gender	Male	8 (72.73%)	13 (68.42%)	21	0.57
	Female	3 (27.27%)	6 (31.58%)	9	
Diabetes Mellitus Type II	Yes	0 (0.00%)	3 (15.79%)	3	0.23
	No	11 (100.00%)	16 (84.21%)	27	
Hypertension	Yes	10 (90.91%)	16 (84.21%)	26	0.53
	No	1 (9.09%)	3 (15.79%)	4	

DISCUSSION

The current research sought to ascertain the prevalence of acute rejection in the first three months after transplantation among patients of renal transplants who were still receiving immunosuppressive medication based on cyclosporines. Of the 30 patients, 11 (36.67%) had acute rejection confirmed by biopsy. This reported frequency is consistent with previous research that found a significant incidence of acute rejection during the same early postoperative time[12]. The idea that early rejection is still a persistent worry for kidney transplant patients in resource-constrained settings, even with the use of cyclosporines, is further supported by another earlier research that likewise revealed an incidence rate of 25.3%[13].

Our study's age group distribution showed that patients between the ages of 18 and 40 were more likely to have acute rejection, which accounted for all 11 rejection cases (100%) in that cohort, whereas patients between the ages of 41 and 65 did not experience any rejections (p = 0.02). The prior research found that older receivers had more rejection events, which it attributed to a lower level of immune surveillance in younger patients[14]. This statistically significant connection stands in contrast to that finding. Different post-transplant monitoring techniques or demographic characteristics might be the cause of the disparity. In our research, 3 out of 9 females (33.3%) and 8 out of 21 men (38.1%) experienced rejection; nevertheless, there was no statistically significant link between gender and rejection (p = 0.57). This is in line with the earlier study, which also noted that among transplant patients kept on cyclosporine-based regimens, there was no discernible gender difference in rejection events[15]. In line with

other studies that found similar results in a group of transplant patients with similar comorbidity profiles, comorbidities such diabetes mellitus and hypertension likewise had no discernible impact on rejection rates ($p = 0.23$ and $p = 0.53$, respectively)[16,17]. Our study's therapeutic monitoring of cyclosporine levels showed that the mean C0 on Day 9 was 220.06 ± 260.53 ng/mL, whereas the mean C2 level was 1065.1 ± 414.98 ng/mL on Day 3 and 994.1 ± 383.16 ng/mL on Day 9. Despite receiving enough immunosuppressive exposure, rejection events occurred, since these levels are within the suggested treatment range. These results highlight the intricate interactions between many immunologic and non-immunologic elements in graft survival, and they are consistent with earlier studies that found acute rejection even at therapeutic cyclosporine doses[18]. Furthermore, most patients regain their graft function early thanks to the gradual drop in mean blood creatinine from 1.56 ± 0.94 mg/dL on Day 3 to 1.23 ± 0.79 mg/dL on Day 9. In line with regional and global statistics, our results together highlight the ongoing difficulty of acute rejection in renal transplant patients even with appropriate cyclosporine doses.

Study Strengths and Limitations: This study's primary strength is its targeted examination in a real-world clinical context by evaluating early acute rejection in patients treated with a standardized cyclosporine regimen during the crucial first three months post-transplant .Accurate evaluation of immunosuppressive exposure and renal function was also guaranteed by the use of organized data collection and regular therapeutic medication monitoring (C0 and C2 levels). Nevertheless, the study's small sample size (n = 30) limits the results' generalizability and might lower the statistical power for identifying comorbidity connections. The absence of protocol biopsies may have resulted in an underdiagnosis of subclinical rejections, and the single-center approach further restricts external validity. Finally, assessment of long-term graft results is not possible with short-term follow-up.

CONCLUSION

This research shows that, despite therapeutic cyclosporine levels, acute rejection is still a very prevalent event during the first three months after kidney transplantation, occurring in 36.67% of patients. Significantly more beneficiaries were younger (18–40 years old), indicating the need for closer monitoring and improved immunological risk assessment in this cohort. The results highlight the need of customized immunosuppressive methods and the possible need for supplementary medications or tighter follow-up in high-risk patients to increase transplant survival, even if the cyclosporine-based regimen typically sustained early graft function.

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