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Evaluation of Random Blood Sugar (RBS) Levels In Renal Transplant Patients On Tacrolimus Therapy: A Prospective Study

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ABSTRACT

Tacrolimus, an immunosuppressive drug used post organ transplant to mitigate rejection risk, often induces significant blood glucose fluctuations, contributing to posttransplanthyperglycemia and diabetes. This study aimed to assess RBS levels pre and post transplantation (days 1 and 90) and tacrolimus levels in diabetic patients. Renal transplant recipients (n=93, age >18 years) were included, excluding hemolyzed samples, pregnancy, and immunocompromised conditions. Statistical analysis (SPSS v20) revealed a significant increase in mean RBS levels from baseline (128.55±35.92 mg/dl) to day 1 (200.66±68.84 mg/dl) and a modest rise at day 90 (132.11±50.84 mg/dl). Among diabetic patients (14%), tacrolimus trough levels were significantly higher on day 1 (8.89 ng/ml) compared to nondiabetics (5.75 ng/ml), with sustained elevation seen at day 90 (8.4 ng/ml vs. 7.53 ng/ml). These findings underscore the association between tacrolimus levels and diabetes risk post transplantation.

Keywords: Tacrolimus, Immunosuppressive, Hyperglycemia, Diabetes, Renal transplant, RBS levels, Tacrolimus trough level, SPSS v20, Nephrotoxicity, Morbidity, new onset of diabetesmellitus (NODM), as posttransplant diabetes mellitus (PTDM).

INTRODUCTION

Renal transplantation is a critical intervention for patients suffering from end stage renal disease (ESRD)[1]. It improves the quality of life and extends the lifespan of patients who would otherwise rely on dialysis. Tacrolimus, a cornerstone immunosuppressant drug, is widely used in renal transplantation to prevent organ rejection[2]. However, tacrolimus therapy

is associated with several side effects, including nephrotoxicity, neurotoxicity, and metabolic disturbances such as posttransplant diabetes mellitus (PTDM).

PTDM is characterized by hyperglycemia[3] that arisespost transplantation due to immunosuppressive drugs like tacrolimus, preexisting glucose intolerance, obesity, and the use of corticosteroids[4]. PTDM can lead to increased cardiovascular morbidity and mortality, as well as a higher risk of graft loss. Tacrolimus has been shown to interfere with insulin secretion and action, contributing to the development of hyperglycemia and PTDM. Given the critical role of tacrolimus in transplantation and its potential to cause significant metabolic side effects, it is imperative to monitor blood glucose levels in patients receiving this medication closely[5].

This studyaims to evaluate the random blood sugar (RBS) levels in renal transplant patients on tacrolimus therapy. By understanding the correlation between tacrolimus levels and RBS, we can better manage and mitigate the risks associated with PTDM, ultimately improving patient outcomes posttransplant.

OBJECTIVE

The primary objective of this study is to assess the impact of tacrolimus therapy on RBS levels in renal transplant patients. The study aims to determine if there is a significant correlation between tacrolimus trough levels and RBS levels at various postoperative intervals.

REVIEW OF LITERATURE

Previous studies have highlighted the importance of therapeutic drug monitoring (TDM) in managing tacrolimus therapy. Tacrolimus is known for its efficacy in preventing acute rejection but poses a risk for posttransplant diabetes mellitus (PTDM). Research by Kasiske et al. (2003) and others indicates that higher tacrolimus exposure correlates with an increased risk of PTDM[6].

MATERIALS AND METHODS

The study included renal transplant recipients aged 18 years and older, excluding samples affected by hemolysis, pregnancy, or immunocompromised conditions. RBS levels were measured in 93 subjects both pretransplant and posttransplant (on days 1 and 90). Statistical analysis was conducted using SPSS version 20.

STUDY DESIGN

Prospective, longitudinal and single centric study was conducted at institute of kidney diseases and research centre, Ahmedabad. Study is approved by institutional ethical committee (IKDRC-ITS).

RESULTS

Demographic and Clinical Characteristics

The study cohort consisted of 93 renal transplant patients with a significant gender disparity: 69.9% were male and 30.1% were female. The mean age of the patients was 37 years, with an age range spanning from 18 to 65 years.

RBS Levels and Tacrolimus Trough Levels

A significant positive correlation was found between tacrolimus trough levels and random blood sugar (RBS) levels at multiple postoperative intervals, specifically on days 1and 90. Among the 93 patients, 13 (14%) were identified as diabetic. On day 1, the mean tacrolimus trough level for diabetic patients was significantly higher at 8.89 ng/ml compared to 5.75 ng/ml in nondiabetic patients. By day 90, the mean tacrolimus trough level for diabetic patients remained elevated at 8.4 ng/ml, while nondiabetic patients had a mean level of 7.53 ng/ml. (Table 1)

Group	Day 1	Day 30	Day 60	Day 90
NonDiabetics	5.75 ± 2.95	7.70 ± 3.45	8.31 ± 4.25	7.53 ± 3.93
Diabetics	8.89 ± 5.57	9.48 ± 5.61	10.30 ± 4.81	8.42 ± 4.42

Table 1: Comparison of Mean Tacrolimus Trough Levels Among Non-Diabetics and Diabetics

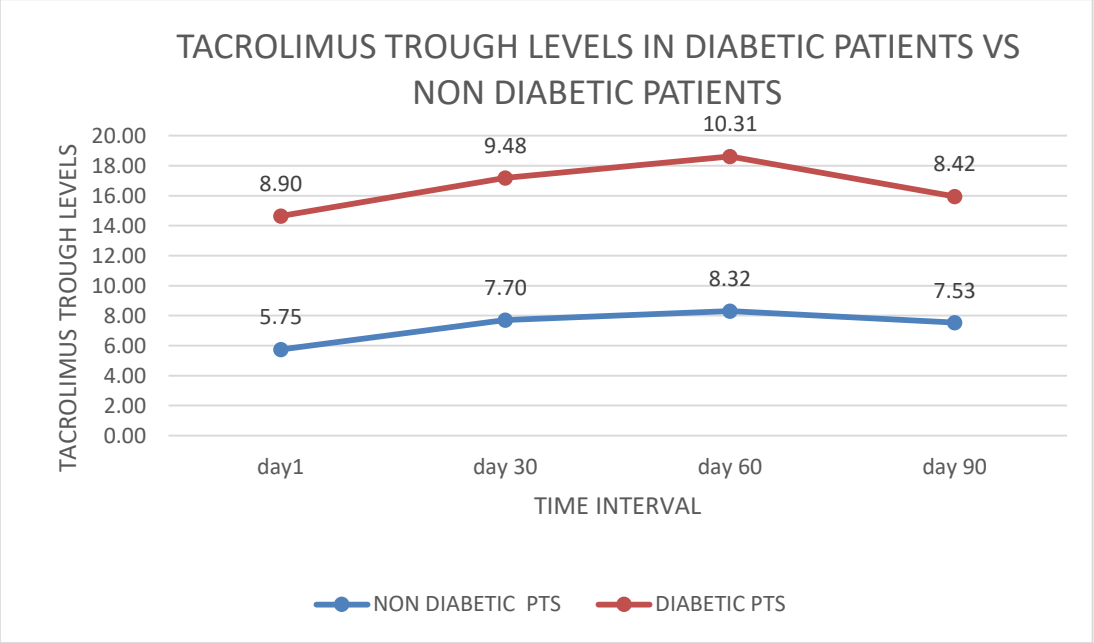

Figure 1:Tacrolimus Trough Levels in Diabetic Patients Vs Non-Diabetic Patients

Diabetic patients consistently have higher mean tacrolimus levels compared to nondiabetic patients at all time points. Both groups show an increase in levels by Day 60, with a slight decrease by Day 90.

Mean RBS levels of study population:

Significant increase inMean RBS levels over time. On day 1 posttransplant, the mean RBS level increased by 72 mg/dl from the baseline, reaching 200.66±68.84 mg/dl, compared to the baseline level of 128.55±35.92 mg/dl. By day 90, the mean RBS levels saw a smaller increase of 4 mg/dl from the baseline, reaching 132.11±50.84 mg/dl.

Observations

RBS Levels in Pre-Existing Diabetic Patients:

There is a significant increase in RBS levels from baseline to Day1. After 90 days, RBS levels decrease but remain slightly higher than the baseline, indicating the need for adjustment in dose of hypoglycemic drugs.(Table 2.)

RBS (mg/dl)	Mean ± SD
Baseline	187 ± 55.31
Day 1	289.23 ± 81
After 90 days	194.69 ± 49.11

Table 2: Mean RBS Levels of Pre-existing Diabetic Patients

RBS Levels in New Onset Diabetic Patients:

There is a notable increase in RBS levels from baseline to Day 1 and further increase after 90 days, indicating the development of new onset diabetes posttransplant.(Table 3).

RBS (mg/dl)	Mean ± SD
Baseline	122 ± 14.84
Day 1	227.5 ± 61
After 90 days	267 ± 31

Table 3: Mean RBS Levels in New Onset Diabetic Patients

Changes in RBS Levels:

Preexisting diabetic patients show a substantial change in RBS levels on Day 1 when compared to baseline with minimal change by 90 days. (Table 4)

Change in RBS from Baseline (mg/dl)	Mean ± SD
Day 1	101.81 ± 76
After 90 days	7.30 ± 71.32

Table 4: Mean Change in RBS Levels of Pre-Existing Diabetic Patients from Baseline.

Change in RBS from Baseline (mg/dl)	Mean ± SD
Day 1	67.27 ± 50
After 90 days	2.95 ± 45.1

Table 5: Mean Change in RBS Levels of Nondiabetic Patients from Baseline

Nondiabetic patients also show an increase in RBS levels on Day 1, but it is less pronounced compared to diabetic patients. By 90 days, the change in RBS levels is minimal, indicating effective management. (Table 5)

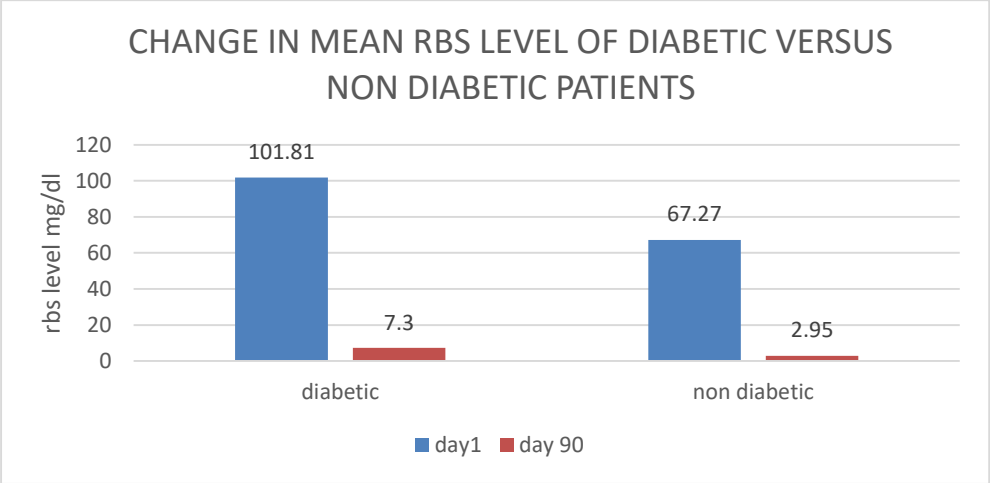

Figure 2: Changemean RBS Levels in Diabetic vs. Non-Diabetic Patients

DISCUSSION

The study cohort showed a notable gender disparity, with a higher percentage of male patients (69.9%) compared to female patients (30.1%). This aligns with existing literature suggesting a higher incidence of renal transplantation among males. The age distribution of the patients, with a mean age of 37 years, reflects the typical demographic of renal transplant recipients and which indicate notable younger population in this study.

Correlation BetweenTacrolimus Levels and RBS:

The significant correlation between higher tacrolimus levels and increased RBS levels, particularly in the early postoperative period, underscores the need for careful monitoring and management. The findings align with previous studies indicating the diabetogenic potential of tacrolimus.

Diabetic vs. Nondiabetic Patients:

In study population 14% were Diabetic patients and they exhibited significantly higher tacrolimus trough levels compared to nondiabetic patients, both at day 1 and day 90 posttransplant. This suggests a potential interaction between preexisting diabetes and tacrolimus metabolism, warranting individualized dosing and vigilant monitoring. (Table 1&Figure1)

Mean RBS Levels:

Significant increase in mean RBS level immediately after post-transplant on day 1, small increase at day 90 possibly dueto post-surgical stress and medication. This suggests fluctuation in RBS levels unlikely for long time but effective treatment required to control random blood sugar levels to reduce renal transplant complications.

New Onset Diabetes:

We found 4 patients who were non diabetic before renal transplant developed new onset of diabetesafter 90 days of tacrolimus therapy. These patients showpersistent increased RBS levels throughout this study period possibly due to immunosuppressive therapy with tacrolimus in particular along with other medications.

Recommendations for Clinical Practice:

Given the findings, it is recommended to implement routine monitoring of RBS levels in all renal transplant patients, with particular attention to those on tacrolimus therapy. Adjustments in immunosuppressive regimens and proactive management of hyperglycemia can help mitigate the risk of PTDM and improve patient outcomes[7&8].

CONCLUSION

This study highlights the significant impact of tacrolimus therapy on RBS levels in renal transplant patients. The data demonstrate a clear correlation between higher tacrolimus levels and increased RBS levels, particularly in the early postoperative period. Diabetic patients exhibited significantly higher tacrolimus trough levels compared to nondiabetics, emphasizing the need for individualized dosing and vigilant monitoring. By optimizing tacrolimus therapy and implementing proactive measures to manage hyperglycemia, clinicians can improve patient outcomes and reduce the incidence of PTDM in renal transplant recipients.

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DISCLOSURES

The Authors do not have any relevant conflicts of interest to disclose.

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