

EVALUATION OF NON-ADHERENCE TO IMMUNOSUPPRESSANT DRUGS THROUGH TACROLIMUS TEST AMONG POST LIVER TRANSPLANT RECIPIENTS AT PIR ABDUL QADIR SHAH JEELANI INSTITUTE OF MEDICAL SCIENCES GAMBAT. SINDH. PAKISTAN

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DOI: <https://doi.org/>

Received	Accepted	Published
27 November, 2024	11 June, 2025	25 June, 2025

ABSTRACT

Medicinal Non-adherence after the hepatic transplant is correlated with harmful side effects including graft rejection (it develops when the immune system invades the donated organ and starts damaging or destroying the transplanted liver/organ) and graft loss (removal of graft, re-transplantation or expire of the recipients).

Objectives: To determine the Non-adherence to Immunosuppressant Drugs in Post Liver Transplant Recipients.

Methodology: A Cross sectional study was performed on Liver Transplant recipients who have been discharged from Liver Transplant Department, Pir Abdul Qadir Shah Jeelani Institute of Medical Sciences, Gambat, after successful liver transplant. Tacrolimus test of enrolled patients was performed during follow up visits to check the serum concentration of immunosuppressant drug.

Results: In this study patients were divided into different age groups, 13% belongs to 23-30 years of age, 16% were of 31-40 years, 21% were 41-50 years, 46% were of 51-60 years and 4% were of 61-70 years of age. Gender wise 59% were male, 41% were females. 64% were belongs to rural areas where as 36% belongs to urban areas. Literacy wise 68% study subjects were undergraduates, 27% were graduates and 5% patients were uneducated. Employment wise 26% patients were having government job, 55% were have private job and 19% were unemployed. 25% participants were transplanted in less than 1 year, 19% were have 1-2 years, 38% were have 2-3 years and 18% were have transplanted more than 3 years. 7% patients were prescribed 1-3 drugs, 40% were prescribed 3-5 drugs, 43% were prescribed 5-7 drugs and 10% participants were prescribed more than 7 drugs. Among total drugs 90% patients were prescribed 2 immunosuppressant drugs and 10% patients were prescribed 3 immunosuppressant drugs. Among all patients 32% patients were taking drugs on time where as 68% were not taking drugs on time. Serum Tacrolimus test results of 33% patients was in normal range while 67% patients were below normal range.

Conclusion: The study concluded that the rate of Non-adherence to immunosuppressant drugs in post liver transplant recipient was very high.

Keywords: Adherence, Non-Adherence, Immunosuppressant, Liver Transplant.

INTRODUCTION

Medicinal non-adherence after the hepatic transplant is correlated with harmful side effects including graft rejection (it develops when the immune system

invades the donated organ and starts damaging or destroying the transplanted liver/organ) and graft loss (removal of graft, re-transplantation or expire of the

recipients). Over the previous many decades, modernization and advancement in the surgical methods and techniques along with immunosuppressed medications had yielded to ameliorate existence in vital organs transplantation [1,2].

Furthermore, efficacy with maximum IS generally, obstructed via exceedingly complicated poly-pharmacy medicines that acquire rigorous adherence over the long period [22]. This problem is remarkably important due to 50.1% of late acute rejection & 15.2% misappropriation of adolescent is allocated to IS non-pharmacological [1,3]. Approximately, 25 to 30.1% of vital organs transplanted patients might be non-adherence to IS medicinal therapy throughout the period. In accordance to the Dew et al., in 2007, lack of education, non-white people, insufficient social support, low-level of self-divulged health were noticed as a correlated factor for non-adherence [4,5, 23].

Albeit, an incidence and probability for non-adherence in transplanted patients had been demonstrated formerly, rest of the studies carried out on the small sample size, retrospective research, limited calculations, and different definitions of non-adherence. In addition, the large sample size study and nature of the medication-associated issues amongst LT patients are less commonly familiar [6,7]. A comprehensive research regarding the medication-related problems and assessment of the dosage attachment and effects on pharmacological results of LT patients are acquiring for the betterment of the recipients' condition [8]. Additionally, education related to medicines and their indications as well as contraindications, appropriate dosage form are the factors that can influence post-transplant self-care. Ethnically (non-white people) and sociodemographic are considered to be more effective in LT recipients and impact on: poly-pharmacy, dosage regimen, and frequently changes in medication therapy [9]. Non-adherence (skipped dosage regimen) showed low prevalence rate in Liver transplant recipients, the claiming about accuracy noticing non-adherence & recommendations require for evaluation of other characteristics of medicinal-related outcome to estimate peoples' capability accurately controlled multi-drugs administration [10,11]

An explanation from 2009 survey of Non-adherence in transplantation was at peak considerable tasks about appropriately adherence to organs transplanted patients [12,21]. There are some problems associated with non-adherence in transplantation including

sociodemographic, clinical, and psychologically risk factors leading to medication misunderstanding and also lower income people, transplantation within a year, large number of medicines, and lack of education were indirectly correlated with lack of treatment awareness [13,20]. Transplanted patients receiving huge amount of medicines while those recipients are lack of knowledge were more conceivably non-adherent, which is calculated via tacrolimus trough scale [14,19]. Tacrolimus is an immunosuppressive medication that suppresses the immune system and aids in preventing organ rejection by preventing T-lymphocyte activation [15,16]. People who have had an organ transplant are prescribed it to be taken orally or intravenously. Tacrolimus blood levels are monitored to keep them within a therapeutic range [17]. Organ rejection happens when the concentration is low, while poisoning symptoms appear when the concentration is too high [18].

Normal range for tacrolimus test is 05-15ng/ml.

Methodology

Study Setting

Patients were recruited from Liver Transplant Department, who were discharged after Liver Transplantation from Pir Abdul Qadir Shah Jeelani Institute of Medical Sciences, Gambat.

Target Population

Adult Liver Transplant Recipients

Study Design

Cross sectional

Duration of Study

8 months

Sample Size

450

Inclusion Criteria

Post liver transplant recipients after discharge from hospital and coming for follow up visits.

Both male and female post liver transplant adult recipients. Patients who have utilized transplant facility of Pir Abdul Qadir Shah Jeelani Institute of Medical Sciences, Gambat. Patients who have not gone to graft rejection.

Exclusion Criteria

Patients admitted after post liver transplant. Patients with age above 70. Patients with renal failure or on dialysis.

Measurement of Medication Adherence

Tacrolimus test was used for measuring Medication Adherence.

Data Collection Procedure

Liver transplant recipients were enrolled, who have been discharged from Liver Transplant Department, Pir Abdul Qadir Shah Jeelani Institute of Medical Sciences, Gambat, after successful liver transplant. Clinical examinations were done by consultant Hepatologist (Liver Transplant Specialist) for all patients. Serum Tacrolimus test of enrolled patients was performed during follow up visits to check the serum concentration of immunosuppressant drug.

Data Analysis/Statistical Procedure

The data was analyzed by using descriptive statistics.

Ethical Consideration

All the data was shared with the participants. All the methods mentioned above have no harmful effects on the patients.

Results

Demographic Characteristics of Participants

In this study, the age of the participants was in the range of 20 years to 70 years. 59% of the patients were male while only 41% participants were females. 64% of the patients belonged to rural areas while 36% belonged to urban areas. Among the participants, 68% were undergraduates, 27% were graduates and 05% were post-graduates. As per employment status, 55% were having private job, 26% were having job in public sector organizations and 19% were jobless.

Table 1: Demographic Characteristics

Age in years	20-30	61(13.0%)
	31-40	73(16.0%)
	41-50	93(21.0%)
	51-60	207(46.0%)
	61-70	16(4.0%)
	Total	450 (100.0%)
Gender	Male	267(59.0%)
	Female	183(41.0%)
	Total	450 (100.0%)
Locality	Rural	289(64.0%)
	Urban	161(36.0%)
	Total	450 (100.0%)
Literacy	Undergraduate	307(68.0%)
	Graduate	119(27.0%)
	Post graduate	24(5.0%)
	Total	450(100.0%)
Employment	Government Job	115(26.0%)
	Private Job	249(55.0%)
	Jobless	86(19.0%)
	Total	450(100.0%)

Liver Transplantation Duration in Years

Out of total study participants 25% of the patients were have less than 01 year of liver transplantation

time, while 19% have 1-2 years, 38% patients have 2-3 years while only 18% have more than 03 years of liver transplant time.

Table 2: Liver transplantation time in years

Liver transplantation time in years	Less than 1 year	112(25.0%)
	1-2 year	87(19.0%)
	2-3 years	172(38.0%)
	More than 3 years	79(18.0%)

	Total	450(100.0%)
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Total Drugs Prescribed

Out of 450 patients, 43% of the patients were prescribed 5-7 drugs, while only 7% patients were prescribed 1-3 drug.

Table 3: Total drugs prescribed

Total drugs prescribed	1-3	31(7.0%)
	3-5	178(40.0%)
	5-7	196(43.0%)
	More than 7	45(10.0%)
	Total	450(100.0%)

Number of Immunosuppressant Drugs Prescribed

Out of total patients 90% of the patients were prescribed 02 immunosuppressant drugs while only 10% patients were prescribed 03 immunosuppressant drugs.

Table 4: Immunosuppressant drugs prescribed

No: of immunosuppressant drugs prescribed	2	407(90.0%)
	3	43(10.0%)
	Total	450(100.0%)

Dose Administration History

Out of total study participants only 32% patients take the drugs on time as prescribed to them after

liver transplantation while 68% patients don't take the medicines on time as prescribed to them.

Table 5: Dose administration

Are you taking drug on time	Yes	145(32.0%)
	No	305(68.0%)
	Total	450(100.0%)

Measurement of Adherence

After performing tacrolimus test on study subjects, serum drug concentration of 33% patients were normal means they were adherent while serum drug

concentration of 67% patients becomes lower than the normal ranges which indicates that they were non-adherent to their therapy.

Table 6: Measurement of Adherence through Tacrolimus test

Tacrolimus Test	Normal Range	149(33.0%)
	Below Normal Range	301(67.0%)
	Total	450(100.0%)

Discussion

Medicinal non-adherence after the hepatic transplant is correlated with harmful side effects including graft rejection (it develops when the immune system invades the donated organ and starts damaging or destroying the transplanted liver/organ) and graft loss (removal of graft, re-transplantation or expire of the recipients). Over the previous many decades, modernization and advancement in the surgical methods and techniques along with immune-suppressant medications had yielded to ameliorate existence in vital organs transplantation. Furthermore, efficacy with maximum IS generally, obstructed via exceedingly complicated poly-pharmacy medicines that acquire rigorous adherence over the long period. This problem is remarkably important due to 50.1% of late acute rejection & 15.2% misappropriation of

adolescent is allocated to IS non-pharmacological. Approximately, 25 to 30.1% of vital organs transplanted patients might be non-adherence to IS medicinal therapy throughout the period. In accordance to the Dew et al., in 2007, lack of education, non-white people, insufficient social support, low-level of self-divulged health were noticed as a correlated factor for non-adherence.

Liu et al; conducted a randomized control trial to measure the adherence in which the majority of the participants were male, whereas employment wise 20% patients were unemployed as similar with this study where gender wise Out of 450 enrolled patients 59% were male while 41% patients were females, Job wise 26% patients have government job, 55% have private job & 19% were unemployed [10]. **Jain et al;** conducted study on adult liver transplant recipients

to determine the Medication Adherence among them in which they selected the age group i.e 20-70 years , the majority of the patients were male, the reported patients were have total number of drugs 3-7 and adherence of the enrolled patients was measured through questionnaire similar with this study where the same age group was selected, majority of the patients were males as compared to females, Out of 450 patients 31% patients were prescribed 01-03 drugs, 40% were prescribed 03-05 drugs, 43% were prescribed 05-07 drugs and 10% were prescribed more than 07 drugs and the adherence of the patients was also measured through Tcrolimus test which is direct method and more authentic method. **XIA, et al;** There was an across-sectional survey. Immunosuppressant Medicine beliefs were measured using a self-created questionnaire that was inspired by the health belief model. Drug adherence was evaluated using the Basel Assessment of Adherence to Immunosuppressive Medications Scale [13]. In current study same belief was measured through on reported patients to measure the drug adherence. It was found that the majority of the reported patients were non-adherent to immunosuppressant drugs.

Conclusion

This study concluded that the majority of enrolled study subjects were male and belongs to rural areas. Majority of the patients were prescribed 5-7 drugs among them majority were prescribed 2 immunosuppressant drugs. The rate of Non-adherence to immunosuppressant drugs among enrolled post liver transplant recipients was very high.

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