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Impact of Text Message Reminders on Drug Adherence in Post-Liver Transplant Patients

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Abstract: Non-adherence among post liver transplant recipients may lead to serious consequences. Hence, there is a dire need to improve medication adherence, particularly among post-liver transplant recipients. Till date, no sufficient data has been published related to our study from Sindh province or even from Pakistan. Therefore, this study will not only help highlight the rate of Medication non-adherence but also implementation of a particular method that could be more helpful to improve the adherence among the study population. The main objective of this study was to determine medication adherence in post-liver transplant recipients before and after text message reminders. A cross sectional study was conducted on 103 post liver transplant patients at Pir Abdul Qadir Shah Institute of Medical Sciences Gambat. BAASIS Scale was used to measure medication adherence among study subjects, after that text messages reminders were given to enrolled patients and adherence was measured again using the same scale to determine the impact of text message reminders on adherence. Among enrolled patients, majority of the study subjects were male, whereas only one participant was transgender. Mostly patients belong to rural areas. Majority of the patients were of matriculation pass, while minorities of the patients were primary pass. Majority of the patients were unemployed, while few had non-government jobs, whereas government job study subjects were in minority. Majority of the patients were of age from 41 to 50, where minority of the patients were aged from 61 to 70. Majority of the patients were prescribed four drugs, whereas no any patient was prescribed only one drug. Majority of the patients were prescribed two immunosuppressant drugs while only few study subjects were prescribed only one immunosuppressant drug. Initially 86% patients were non-adherent to therapy, but after text message reminders, adherence was improved from 24% to 80%. This study concluded that the rate of adherence was improved by giving text message reminders to the patients.

Keywords: adherence, non-adherence, immunosuppressant, liver transplant.

短信提醒对肝移植术后患者药物依从性的影响

摘要：肝移植后接受者的不依从性可能导致严重后果。因此，迫切需要提高药物依从性，尤其是在肝移植后接受者中。到目前为止，还没有足够的数据与我们在信德省甚至巴基斯坦的研究相关。因此，这项研究不仅有助于突出药物不依从率，而且有助于实施一种可能更有利于提高研究人群依从性的特定方法。本研究的主要目的是确定肝移植后接受者在剩余短信前后的药物依从性。在皮尔·阿卜杜勒·卡迪尔·沙阿医学科学研究所赌局对 103 名肝移植后患者进行了一项横断面研究。基础量表用于测量研究对象的服药依从性，之后向登记的患者发出短信提醒，并使用相同的量表再次测量依从性以确定短信提醒对依从性的影响。在登记的患者中，大多数研究对象是男性，而只有一名参与者是变性人。大多数患者来自农村地区。大多数患者为预科及格，少数患者为初等及格。大多数患者没有工作，少数人从事非政府工作，而政府工作研究对象则占少数。大多数患者的年龄在 41 至 50 岁之间，少数患者的年龄在 61 至 70 岁之间。大多数患者开了四种药，而没有任何患者只开了一种药。大多数患者服用了两种免疫抑制药物，而只有少数研究对象仅服用了一种免疫抑制药物。最初 86% 的患者不依从治疗，但在短信提醒后，依从性从 24% 提高到 80%。该研究得出结论，通过向患者发送短信提醒提高了依从率。

关键词：依从性、非依从性、免疫抑制剂、肝移植。

1. Introduction

Non-adherence to post-transplant medications is associated with serious consequences including graft rejection, post-transplant mortality, poor health-related quality of life, and increased healthcare costs. Moreover, medication non-adherence may negatively impact long-term health outcomes. Given that adolescents are at a high risk for non-adherence and associated late graft loss, interventions aimed at promoting medication adherence in this population are urgently needed.

In developing countries such as Pakistan with lesser literacy rate and scarcity of resources, non-adherence among post liver transplant recipients may lead to serious consequences. Hence, there is a dire need to improve medication adherence, particularly among post liver transplant recipients. Till date, no sufficient data has been published related to our study from Sindh province or even from Pakistan. Therefore, this study will not only help highlight the rate of Medication non-adherence but also implementation of a particular method that could be more helpful to improve the adherence among the study population.

Transplantation of the liver due to liver failure provides the chance to patients to live in a pleasant environment and improve their health-related quality of life. The therapeutic objectives of liver transplant only be achieved if the patient becomes adherent to the therapy prescribed by the doctors such as Immunosuppressant drugs and lifestyle as suggested [1, 2]. The endurance of the liver transplant patients in the starting five years after the liver transplant varies from

60%-80%. Survival depends upon the type of illness that leads to liver transplantation, the causative agents, including comorbidities; carelessness in liver-damaging diseases, and fails to manage self-care [2, 3]. The major risk after transplantation, are the organ dysfunction and the graft failure [4]. Therefore, the outcomes of transplant will not be achieved if the patient becomes non-adherent to therapy; on the other hand, the cost will also increase [5, 6].

Non-adherence to therapy in case of post liver transplantation means the patients not taking the immunosuppressant regimen as prescribed by doctors, which will have a negative impact on therapeutic outcomes [7] or non-adherence means errors in taking prescribed dosing and dosage interval. Non-adherence can be determined by the interaction with patients to determine the different factors involved in non-adherence such as healthcare system of the patient, socio-economic condition of the patient, the availability of prescribed medicines, underlying disease, and medical condition of the patient [8]. The patient is said to be adherent if the patient taking 80%-110% medicines according to prescription [9]. In case of liver transplantation non adherence may vary from 2%-67% and the annual average estimated as 35.6%, as a result, graft rejection or failure in transplantation may occur, the cost of treatment may also increase, and morbidity and mortality may also increase [8, 10, 11].

Different tools are used to determine non-adherence, some of them are counting the number of tablets, self-reported questionnaires, reporting of common side effects of immunosuppressive drugs,

determination of serum level of immunosuppressant drugs, and electronic monitoring [8, 9-12]. Out of these methods, the most common, easy, and cost-effective method for assessing the non-adherence in medical practice is self-reporting. Self-reporting method is highly specific because the questionnaire used contains specific questions; it is also used with other tools to obtain the specific information on the patients' medication use behavior [8, 13, 14].

2. Methods/Materials

2.1. Study Settings

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

2.2. Target Population

Adult liver transplant recipients.

2.3. Study Design

Cross-sectional.

2.4. Duration of the Study

6-10 months.

2.5. Sample Size

Sample size was calculated using the Hussey and Hughes model and the Woertman formula.

2.6. Inclusion Criteria

- Post liver transplant recipients after discharge from the hospital and coming for follow-up visits;
- Male, female and transgender, post-liver transplant adult recipients;
- Patients who have used the transplant facility of Pir Abdul Qadir Shah Jeelani Institute of Medical Sciences, Gambat;
- Patients without graft rejection.

2.7. Exclusion Criteria

- Patients admitted after post liver transplant;
- Patients aged above 70;
- Patients with renal failure or on dialysis.

2.8. Measurement of Medication Adherence

The Basel Assessment of Adherence to immunosuppressive medications Scale (BAASIS) was used for measuring Medication Adherence.

2.9. Data Collection Procedure

Liver transplant recipients were enrolled, who were discharged from the Liver Transplant Department, Pir Abdul Qadir Shah Jeelani Institute of Medical Sciences, Gambat, after a successful liver transplant.

The Basel Assessment of Adherence to immunosuppressive medications Scale (BAASIS) was

filled after taking informed consent, on every follow-up visit of the patient after discharge. The same method was applied for all the patients on their visit for prescription refill. For at least 6 visits, each patient was asked to fill the details required.

The patients were reminded to take medication on time by using software through which a predesigned message containing information about the name and dose of drug was sent to enrolled patients, which was followed by patients' response as "OK," which was considered as "Patient has taken his/her medicine. In case of failure to respond, the case was considered non-compliance.

2.10. Data Analysis/Statistical Procedure

The data were analyzed using descriptive statistics.

2.11. Ethical Consideration

All the data were shared with the participants. All the above-mentioned methods have no harmful effects on the patients. Non-adherent participants were counseled that they are at an increased risk of rejection, which can be prevented by taking the medicines on time as prescribed by the doctor and modifications in their lifestyle. This study was approved by the Ethical Review Committee of Ziauddin University Karachi through the Reference Code: 3560321SAPHA.

3. Results

3.1. Demographic Distribution of the Study Subjects

In Table 1, demographic details of the patients are mentioned in which majority of the participants were male, whereas only one participant was transgender, locality wise mostly patients were belongs to rural areas. Education-wise, majority of the patients had matriculation pass, while minority of the patients had primary pass. On the basis of employment, majority of the patients had non-government jobs, whereas government job study subjects were in minority.

Table 1 Demographic details on the study subjects

	Variables	Frequency	Percentage
Gender	Male	70	68
	Female	32	31
	Transgender	01	01
Locality	Rural	73	71
	Urban	30	29
Literacy	Primary	14	14
	Matriculation	29	28
	Intermediate	26	25
	Graduation	19	18
	Un Educated	15	15
Employment	Government Employee	15	14
	Non-Government Employee	37	36
	Un Employed	51	50

3.2. Age-Wise Distribution of the Study Subjects

Table 2 comprises age-wise groups of study subjects, in which majority of the patients were of age from 41 years to 50 years, whereas minority of the patients were of age from 61 years to 70 years.

Table 2 Age-wise distribution

Age in Years	Variable	Frequency	Percentage
	21-30	11	11
	31-40	31	30
	41-50	37	36
	51-60	19	18
	61-70	05	05

3.3. Drug-Wise Distribution of the Participants

In Table 3, patients were divided according to no. of the total drugs and no. of immunosuppressant drugs prescribed to them by the consultants after liver transplantation. Majority of the patients were prescribed four drugs, whereas no patient was prescribed only one drug. According to anti-rejection medicines, majority of the patients were prescribed two immunosuppressant drugs while only few study subjects were prescribed only one immunosuppressant drug.

Table 3 Drug-wise distribution

No. of drugs prescribed?	Variable	Frequency	Percentage
	1	00	00
	2	03	3
	3	23	22
	4	47	46
	5	21	20
	6	09	9
No. of anti-rejection drugs prescribed	1	21	20
	2	48	47
	3	34	33

3.4. Measurement of Non-Adherence in Post-Liver Transplant Recipients before Text Message Reminders

In Table 4, adherence in post-liver transplant recipients was measured using the BAASIS scale before text message reminders to the study participants regarding taking the medicines on time. It was observed that the majority of the patients were non-adherent to therapy; the patients were habitual to miss the doses intentionally and unintentionally and did not take the dose on time as prescribed to them by the doctors.

Table 4 Distribution of adherence according to BAASIS® item before text message reminders

BASIS Item	Variable	Frequency	Percentage
Did you miss any doses, even one, of any of your anti-rejection medications in the past 4 weeks?	Yes	39	36
	No	14	14
(If yes): Could you tell me how often this happened in the past 4 weeks?	Once	9	10
	Twice	15	17
	Three times	23	26
	Four times	20	22
	More than four times	22	25
Did you ever skip two or more doses in a row in the past 4 weeks?	Yes	31	31
	No	28	31
Could you tell me how often this happened in the past 4 weeks?	Once	17	18
	Twice	11	18
	Three times	15	21
	Four times	14	23
	More than four times	06	10
You take your anti-rejection medications at the exact same time as prescribed?	Yes	09	09
	No	54	91
Could you tell me how often this happened in the past 4 weeks?	Once	07	07
	2-3 times	19	20
	Once in a week	27	29
	A couple of times a week	33	35
	Almost every day	08	09
Have you changed the prescribed amount of any of your anti-rejection medications during the past 4 weeks, on your own initiative without your doctor telling you to do that? For example, have you taken more or fewer pills or changed the dose, maybe by cutting a pill in half?	Yes	35	31
	No	20	19
Have you completely stopped taking any of your anti-rejection medications within the past year, on your own initiative without your doctor telling you to do that?	Yes	05	05
	No	98	85
Did your family doctor or a specialist give you any prescriptions for any new medications in the past year? (Maybe high blood pressure medication, cholesterol/lipid lowering drugs?)	Yes	61	59
	No	42	41
Did you fill the prescription at the pharmacy and start taking this new medication?	Yes	49	50
	No	12	20

3.5. Measurement of Non-Adherence in Post-Liver Transplant Recipients after Text Message Reminders

In Table 5, adherence in post-liver transplant recipients was measured using the BAASIS scale after text message reminders to see the impact of reminders for taking the medicines on time as prescribed to them by their consultants after successful liver transplantation. It was observed that due to text message reminders, most study subjects became adherent to therapy prescribed to them, only few patients were non-adherent.

Table 5 Distribution of adherence according to BAASIS® item after text message reminders

BASIS Item	Variable	Frequency	Percentage
1. Did you miss any doses, even one, of any of your anti-rejection medications in the past 4 weeks?	Yes	21	20
	No	82	80
1.1. (If yes): Could you tell me how often this happened in the past 4 weeks?	Once	10	47
	Twice	07	33
	Three times	02	10
	Four times	01	5
	More than four times	01	5
1.2. Did you ever skip two or more doses in a row in the past 4 weeks?	Yes	07	33
	No	14	67
1.3. Could you tell me how often this happened in the past 4 weeks?	Once	03	43
	Twice	02	29
	Three times	01	14
	Four times	01	14
	More than four times	00	00
2. You take your anti-rejection medications at the same time as prescribed?	Yes	75	73
	No	28	27
2.1. Could you tell me how often this happened in the past 4 weeks?	Once	08	29
	2-3 times	13	46
	Once in a week	05	18
	A couple of times a week	02	07
	Almost every day	00	00
3. Have you changed the prescribed amount of any of your anti-rejection medications during the past 4 weeks, on your own initiative without your doctor telling you to do that? For example, have you taken more or fewer pills or changed the dose, maybe by cutting a pill in half?	Yes	11	11
	No	92	91
4. Have you completely stopped taking any of your anti-rejection medications within the past year, on your own initiative without your doctor telling you to do that?	Yes	02	02
	No	101	98
5. Did your family doctor or a specialist give you any prescriptions for any new medications in the past year? (Maybe high blood pressure medication, cholesterol/lipid lowering drugs?)	Yes	67	65
	No	36	35
5.1. Did you fill the prescription at the pharmacy and start taking this new medication?	Yes	52	78
	No	15	22

4. Discussion

The survival of liver transplant patients in the first five years after the liver transplant varies from 60 - 80%. The survival depends upon the type of illness, the causative agents, including comorbidities; carelessness in liver-damaging diseases, and fails to manage self-care. The major risk after transplantation are the organ dysfunction and the graft failure. Therefore, the outcomes of transplant will not be achieved if the patient become non-adherent to therapy on the other hand cost will also increase. Therefore, this study will help determine the percentage of non-adherence and reason for non-adherence among liver transplant recipients. After that, by applying different interventions, the adherence in the patients will be improved, so the patients can be prevented from graft rejection, and the health-related quality of life of patients will also be improved.

Oliveira et al. conducted a cross-sectional epidemiological study for determining non-adherence in liver transplant recipients. It was found that almost all patients were non-adherent to immunosuppressant drugs after liver transplantation. This is similar to the

current study because in the current study, the same scale was used to measure non adherence as well as the majority of the study population was non-adherent to therapy, but after giving the text message reminders, the adherence was improved in the majority of the patients [15].

Maureen Whitsett et al. conducted a review for determining medication non-adherence in liver transplantation. It was found that medication non-adherence was the most common problem for improving the health of liver transplant patients. They found various reasons making the patients non-adherent. Some factors were under control; some factors were uncontrollable. They suggested that a well-designed further study is needed that can examine various interventions and strategies for medication adherence in liver transplant recipients and the challenges faced by patients while taking the medications as prescribed [16]. In the current study, the impact of text message reminders was observed and found excellent results on adherence in post liver transplant recipients.

Nguyen et al. conducted a randomized control trial on patients who were on cardiovascular agents or on oral hypoglycemic agents for 4–12 weeks and declared as non-adherent using a medication adherence questionnaire; the patients were divided into control and intervention groups. It was found that due to intervention on patients, their medication adherence rate was improved compared to the non-intervention group [17]. It is similar to the current study because in the current study, non-adherent patients were targeted. Because of intervention by text message reminders, the non-adherence was improved.

Ganjali et al. conducted a cross-sectional study using the Basel Assessment of Adherence to Immunosuppressive Medications Scale (BAASIS), for determining barriers in medication adherence. It was found that the non-adherence to the immunosuppressant regimen was more than 50% in transplant recipients. The barriers of adherence include concurrent use of immunosuppressants, lack of knowledge about the benefits of immunosuppressants, forgetfulness in taking medicines, confusion about medication taking and quality of life. They concluded that there was a need for interventions either to reduce or to eliminate these barriers and reduce the overall economic burden that incurred on graft rejection [18].

Girgenti et al. conducted a study, to analyze the health-related quality of life and the patient's compliance after liver transplantation, and they retrospectively collected and analyzed the data of 82 liver transplant recipients. It was found that the quality of life of patients who were adherent to their therapy and received good care after transplantation improved compared to non-adherent patients [19].

Khatiban et al. conducted a study, by taking the interview from 82 liver transplant recipients, the team

members were of liver transplant department persons and the family members of recipients for identifying barriers of medication adherence, and they used a purposive sampling method. It was found that there was a need of attention to the barriers that influence medication adherence; therefore, they suggested that collaboration of patient's self-care and planning for achieving therapeutic objectives may be initiated by healthcare providers to increase the health-related quality of life of patients [20].

Jones et al. conducted a study to determine the prevalence of non-adherence in post-liver transplant recipients, their risk factors, and consequences of medications. It was found that in post-liver transplantation, non-adherence to medication was common, resulting in patients suffering from graft rejection and requiring hospitalization. It was found that the most common reasons for non-adherence was the lack of social support, socioeconomic conditions, side effects of medicines, complex therapeutic regimen, poor or lack of counseling, pre transplant substance misuse, depression, communication gap between patients and healthcare providers, poor understanding of patients and low literacy rate. They suggested that different tools may be used to measure the non-adherence and improve the adherence level such as serum drug level, electronic monitoring, text messages, smartphone reminders, easy therapeutic regimens, and pharmacist counseling [21].

5. Conclusion

This study concluded that the rate of adherence among post-liver transplant recipients who availed liver transplant facility at Pir Abdul Qadir Shah Jeelani Institute of Medical Sciences Gambat was very low due to forgetfulness for taking medicines, more than two drugs, frequent dosage intervals, low literacy rate and prolong the duration of therapy. It was observed that study subjects intentionally or unintentionally did not take their medicines on time as prescribed to them by their consultants after post-liver transplantation and follow-up visits. However, when the same patients were reminded through text messages to take the drugs on time, the results were totally different. It was an excellent impact of text message reminders on non-adherent study subject. Initially, the adherence was low up to 20%, but after text message reminders, the adherence was improved up to 80%. Therefore, the study concludes that the rate of adherence among post-liver transplant recipients can be improved if patients are reminded through text messages at the same time, at which they must take the medicine as prescribed to them by the concerned doctor.

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