



## ARAŞTIRMA

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### Medication Nonadherence in Liver Transplant Recipients in Turkey

**Objective:** The purpose of this study was to explore medication nonadherence in the liver transplant recipients after transplantation.

**Material and Methods:** This was a descriptive qualitative study. Data were collected from 21 adult liver transplant recipients in a liver transplantation outpatient clinic from April 2011 till June 2011, when sufficient data accrued. A patient characteristics form and a semi-structured interview were used for data collection. Interviews were recorded, transcribed, analyzed and sorted into themes and subthemes.

**Results:** Three main themes, namely "medication nonadherence", "causes of medication nonadherence" and "expectations from nurses", were formed and each of them had several subthemes. Subthemes for medication nonadherence were "skipping doses", "delaying doses" and "mistaking medication". Subthemes for causes of medication nonadherence were "forgetting", "life-style", "health care system", "insufficient knowledge", "multiple medications use" and "health beliefs". Subthemes for expectations from nurses were "financial guidance", "education" and "showing interest".

**Conclusion:** The liver transplant recipients had medication nonadherence for many reasons and expectations from nurses for prevention of nonadherence. Nurses and other health professionals should be aware of causes of drug nonadherence in the liver transplant recipients after transplantation and should be able to provide them with appropriate counseling and education.

**Key words:** Liver transplantation, medication adherence, nursing, qualitative research.

#### Türkiye’de Karaciğer Transplantasyonu Sonrası Alıcıların İlaç Uyumsuzlukları

**Amaç:** Karaciğer transplantasyonu sonrası alıcıların ilaç uyumsuzluklarını açıklamaktır.

**Gereç ve Yöntem:** Tanımlayıcı, niteliksel bir araştırmadır. Araştırmanın verileri Nisan 2011 ile Haziran 2011 tarihleri arasında karaciğer transplantasyonu polikliniğinde karaciğer nakli yapılan 21 yetişkinden toplanmıştır. Verilerin toplanmasında hasta tanıtıcı bilgi formu ve yarı yapılandırılmış görüşme formu kullanılmıştır. Görüşmeler önce teyp aracılığı ile kaydedilmiş, sonra yazılı hale getirilmiş, analiz edilmiş, ana ve alt temalara ayrılmıştır.

**Bulgular:** Verilerin analizinde ilaç uyumsuzluğu, ilaç uyumsuzluğu nedenleri, hemşirelerden beklentiler olmak üzere üç ana tema ve alt temalar ortaya çıkmıştır. İlaç uyumsuzluğu ana temasının alt temaları "doz atlama", "doz geciktirme", "yanlış ilaç" almaktır. İlaç uyumsuzluğu nedenleri ana temasının alt temaları "unutma", "yaşam biçimi", "sağlık bakım sistemi", "yetersiz bilgi", "çoklu ilaç kullanımı" ve "sağlık inançları"dır. Hemşirelerden beklentiler ana temasının alt temaları "mali danışmanlık", "eğitim", ve "ilgi gösterme"dır.

**Sonuç:** Karaciğer transplantasyonu alıcıları, bir çok nedenden dolayı ilaç uyumsuzluğu yaşamakta ve ilaç uyumsuzluğunun önlenmesinde hemşirelerden beklentileri olduğunu ifade etmişlerdir. Hemşireler ve diğer sağlık profesyonelleri transplantasyonu sonrası ilaç uyumsuzluğu olabileceğinin farkında olmalı, ve ilaç uyumsuzluğunu uygun eğitim ve danışmanlıkla önlemelidir.

**Anahtar Kelimeler:** Karaciğer transplantasyonu, ilaç uyumsuzluğu, hemşirelik, nitel çalışma.

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#### Introduction

At present, liver transplantation (LT) is an effective method for the treatment of end-stage liver disease (1). LT has four important outcomes, i.e. increased life span, improved quality of life, decreased morbidity and increased graft survival rate (2, 3).

Compliance after LT requires taking medication regularly and on time and avoiding high risk habits such as smoking and taking alcohol and sustaining these lifestyle changes (4). Medication-nonadherence is defined as skipping medication at least once a month, two or two and a half hour delay in taking medication and taking wrong medication (5). Nonadherence to immunosuppressives may lead to acute or chronic organ rejection or death (6, 7). Nonadherence after transplantation can be affected by age, gender, education, cultural dimensions of the disease and treatment, race and financial status (8).

Non-complier patients can be divided into three groups, that is, accidental non-compliers, invulnerable non-compliers and decisive non-compliers. Accidental non-compliers experience medication nonadherence due to their forgetting and are recommended making arrangements in a way that daily activities and taking medications do not hinder each other. Invulnerable non-compliers are not aware that forgetting to take medications has an impact on their health. Decisive non-compliers do not feel the need for medications and want to decide about taking medications independently (9).

The rate of medication nonadherence after transplantation ranges from 2% to 73% (4, 6, 10-12). It has been reported that transplant recipients skip doses of their medications or delay taking them for more than two hours (4, 13, 14).

The most frequent factor causing medication nonadherence is forgetting followed by taking more than one medication, advanced ages, insufficient knowledge of immunosuppressive drugs, inability to afford medications due to a low income and beliefs in the need for immunosuppressive drugs (11, 14-20). The male gender, low self-respect, overworking, receiving a live graft, stress, anger, depression, insufficient social support and changes in life style have also been found to be associated with medication nonadherence (13, 19, 21-26). In addition, chronic diseases, necessity to make important changes in behavior imposed by treatment, bitter taste of medications, difficulty in swallowing, insufficient communication with health professionals and inability to involve patients in treatment plans lead to medication nonadherence (6). However, effects of time elapsing after transplantation on medication nonadherence are not clear. Some authors claim that it increases medication nonadherence (13, 17), while others report that it does not affect nonadherence (26).

A qualitative study revealed the following four main themes related to medication nonadherence: reminder methods such as alarms and pillboxes, obtaining medications such as insurance coverage and costs, maintaining routines such as having breakfast, lunch and dinner and problem solving strategies such as skills training and offering information (7). Another qualitative study showed five main themes including fear of transplant failure, loyalty to the transplantation team and donors, health beliefs, forgetting and side effects (27).

Clinical outcomes of medication nonadherence after transplantation are acute organ rejection, graft loss and failure of a graft to fulfill its functions. Financial outcomes of medication nonadherence are hospital, emergency and home care costs and loss of efficiency (28). It has been emphasized in the literature that education has an important role in prevention of medication nonadherence (29). One study revealed that the health professionals from whom patients most frequently wanted to receive education were nurses (20). Education offered to patients improves the quality of their life and helps them to manage their health and disease at the utmost level. Since nurses have a direct and long-lasting communication with patients, they play a more effective role in patients' education than other health professionals (30).

To our knowledge, there have not been any studies on medication nonadherence in liver transplant recipients (LTRs) in Turkey. Therefore, the purpose of this study was to explore medication nonadherence in the LTRs after transplantation in Turkey. It can be anticipated that the results of this study will help nurses understand causes of medication nonadherence among LTRs and know what LTRs expect from them and thus enrich content of education they offer, prevent nonadherence and improve the quality of life in LTRs.

## Materials and Methods

This study was a descriptive qualitative study. The study performed in Liver Transplantation Outpatient Clinic, Dokuz Eylül University. The study started in April 2011 and was completed in June 2011. The interviews continued until a point at which no new information was obtained. A total of 21 adult LTRs were interviewed. In this study, purposive sampling was used (31, 32). The participants who met the following inclusion criteria were recruited: 1) receiving first liver transplant due to acute or chronic liver failure, 2) minimum six months of time elapsing after liver transplantation, 3) being 18 years old or older, 4) speaking Turkish, 5) detection of medication nonadherence 6) ability to receive immunosuppressive medications independently 7) voluntary participation in the study.

The study protocol was approved by the University Non-Invasive Clinical Research Ethical Committee. Written permission to conduct the research was obtained from the Health Directorate of University Hospital. During data collection, patients were informed about the aim and the methods of the research and verbal and written informed consent was obtained from each participant.

Data were collected with a patient characteristics form and a semi-structured interview form. The patient characteristics form included questions about socio-demographic features including age, gender and education, type of donors, etiology of liver transplantation and medications used.

The semi-structured interview form was developed by the researchers and three experts were requested to evaluate the form. In the light of the experts' opinions, the form was revised. The revised version of the form was piloted on three LTRs fulfilling the same criteria as those participating in the study. Data obtained from the pilot study were not included in the analyses. The form included six open-ended questions. Two open-ended questions were about how liver transplant recipients use their medications and how they are affected by the medications. Four open-ended questions were about the problems the recipients experience with the use of their medications, causes of these problems, how their nonadherence with the medications affect their lives and their expectations about their medications from nurses in outpatient and inpatient clinics.

Data were collected by the first author of this article using the in-depth interview technique. In-depth interviews were made in a silent, well-lit and well-air-conditioned room in the liver outpatient clinic and recorded by a voice recorder. Descriptive analytical methods were used to identify medication nonadherence in liver transplant recipients. Interviews were audio taped and transcribed verbatim. The transcripts were read completely and each meaningful unique unit was assigned a code expressing their contents best. The same unit was given the same code throughout the transcriptions. A list of codes was created for each participant. The codes obtained from all the transcriptions were gathered. Similarities and differences between them were examined and the codes associated with each other were integrated and themes were created. The data were summarized and interpreted in accordance with the themes and main themes expressing more general concepts were obtained (33).

Obtained data were analyzed by the two authors of this article separately, findings were compared and two researchers made decisions together to achieve trustworthiness of findings. Both researchers were experienced in offering care for LTRs and conducting a qualitative study. After the two researchers determined themes of the study independently, they compared the themes and decided about them together. The themes on which the researchers agreed were analyzed and confirmed by another researcher (Triangulation) (33). The notes taken by the researchers during the interviews were also used.

To achieve validity and reliability of the study, measures recommended by Lincoln and Guba were used. Lincoln and Guba suggested that the terms internal validity, external validity, internal reliability and external reliability should be replaced by credibility, transferability, dependability and confirmability respectively (34).

*Validity*; To achieve credibility, in-depth interviews and expert examinations were utilized. The researcher did not only record the interviews but also take notes. All the interviews were stopped only when new information

could not be obtained. During evaluation of the research, the researcher questioned both herself and the research process from a critical point of view and determined whether the findings obtained reflected the reality. To achieve transferability, content analysis and purposeful sampling were used, which allowed presentation of data in accordance with emerging concepts and themes without adding comments and by keeping the nature of the data as much as possible (33, 34).

*Reliability*; To achieve dependability, the research was examined by researchers independently. To be able to ensure confirmability, findings were presented clearly. In addition, the notes taken during the interviews, voice recordings, transcriptions and analyses are kept (33, 34).

## Results

The 21 LTRs (6 female, 15 male) interviewed were aged between 32 and 68 years old, with a mean age of 49.61 years (SD, 11.07). Out of 21 LTRs, 47.6% were primary school graduates, 90.5% were married, 47.6% were running their own business, 76.2% were not working after transplantation and 52.4% had an income equal to their expenses. Time elapsing from transplantation was 2-3 years in 52.4% of the recipients, 57.2% of the recipients had a live donor, live donors were first degree relatives in 23.8% of the recipients, 33.4% of the recipients had HBV etiology and 47.6% of the recipients were using other medications and Tacrolimus (Table 1).

As a result of data analyses, three main themes; i.e. medication nonadherence, causes of medication nonadherence and expectations from nurses were obtained.

### **Main Theme 1: Medication nonadherence**

Three subthemes emerged under the main theme of medication nonadherence; namely, skipping doses, delaying doses and misunderstanding medication.

*Skipping doses*: The LTRs reported to skip doses of their medications.

*"When I don't take my medicine in the morning, I just take the dose in the evening." "I haven't taken the doses of my medications in the evening for about one year."*

*Delaying doses*: The recipients noted that they took their medication later than expected.

*"...I am at work at the time when I have to take my medication. When I remember that I haven't taken it, I go home and take it. There is a delay of two hours."*

*Taking wrong medication*: The recipients reported that they mistook their medication with other medications.

*"...There have been times when I take wrong medicine. I mistook a tablet used to treat stomach problems instead of my immunosuppressive medication yesterday"*.

**Table 1.** Demographic and clinical characteristics of the participants (n=21)

Variable	M±SD
<b>Age</b>	49.61±11.07
<b>Gender</b>	<b>n(%)</b>
Female	6 (28.6)
Male	15 (71.4)
<b>Education</b>	
Illiterate	2 (9.5)
Literate	1 (4.8)
Primary school	10 (47.6)
Secondary school	3 (14.3)
High school	4 (19.0)
University and higher levels of education	1 (4.8)
<b>Marital status</b>	49.61±11.07
Married	19 (90.5)
Single	2 (9.5)
<b>Occupation</b>	
Housewife	5 (23.8)
Blue-collars	2 (9.5)
White-collars	-
Having one's own business	10 (47.6)
Retired	3 (14.3)
Other	1 (4.8)
<b>Employment status after transplantation</b>	
Employed	5 (23.8)
Unemployed	16 (76.2)
<b>Income</b>	
Higher than expenditures	-
Equal to expenditures	11 (52.4)
Lower than expenditures	10 (47.6)
<b>Health insurance</b>	
Insurance of Social Security Institution	18 (85.7)
Insurance by a fund for the poor	3 (14.3)
Insurance of a private insurance company	-
<b>Time elapsing from transplantation</b>	
6 months- 1 year	1 (4.8)
2-3 years	11 (52.4)
4 years or over	9 (42.8)
<b>Types of donors</b>	
Live	12 (57.2)
Cadaver	9 (42.8)
<b>Degree of relation in live donors</b>	
First degree relatives	5 (23.8)
Second degree relatives	3 (14.3)
Spouses	3 (14.3)
Stranger	1 (4.8)
<b>Etiology of liver failure</b>	
*HBV	4 (19.0)
HBV+Delta	7 (33.4)
HBV+*HCC	4 (19.0)
*HCV	2 (9.5)
Cryptogenic liver cirrhosis	3 (14.3)
*PSC	1 (4.8)
<b>Medications used after transplantation</b>	
Tacrolimus + *medications (except for immunosuppressives)	10 (47.6)
Tacrolimus + *MMF + medications (except for immunosuppressives)	2 (9.6)
Cyclosporine + medications (except for immunosuppressives)	4 (19.0)
Cyclosporine + MMF + medications (except for immunosuppressives)	1 (4.8)
Cyrolimus / Everolimus + MMF + medications (except for immunosuppressives)	4 (19.0)
<b>Total</b>	21 (100.0)

\*HBV:Hepatitis B virus

\*HCV:Hepatitis C virus

\*HCC: Hepatocellular carcinoma

\*PSC: Primary sclerosing cholangitis

\*MMF: Mikofenolat mofetil

\*Medications except for immunosuppressives: Antiviral and / or antifungal and / or anti-acid and / or antihyperlipidemia and / or antidiabetic and / or antihypertensive medications

## **Main Theme 2: Causes of medication nonadherence**

Six subthemes associated with causes of medication nonadherence emerged; forgetting, life style, health care system, insufficient knowledge, therapy requiring more than one medication and health beliefs.

*Forgetting:* The LTRs admitted that they experienced forgetfulness due to doing housework, work and social life and stress.

*"...I forget to take my medication after breakfast due to fear of being late for work". "...I forget to take my medicine when I get angry". "Since I have a hectic work schedule and since I have to think about many things at a time, I forget to take my medicine".*

*Life style:* The LTRs reported to experience medication nonadherence due to changes in their daily routines led by changes in fulfilling their physiological needs such as not eating and sleeping on a regular basis, skipping meals due to lack of appetite, oversleeping, sleeplessness and tiredness and changes in social life such as living alone, poor time management, coming home late, waking up late in the morning due to not going to work and not having breakfast.

*"I skip doses because I suffer from lack of appetite and that's why I can't take my medicine regularly." "...Since I don't work, I go to bed late and get up late in the morning. For this reason, I can't take my medicine on time." "... I can't think properly due to sleeplessness and tiredness..."*

*Health Care System:* The LTRs commented that they experienced problems due to bureaucracy imposed by the health care system and that these problems caused medication nonadherence.

*"I can't afford to buy some medications and I also have difficulties in obtaining my medications with my health insurance.*

*Insufficient Knowledge:* The LTRs admitted that they experienced medication nonadherence since they did not wonder or did not know what not taking their medications causes, did not know side-effects of their medications, decided not to take their medications by themselves and misunderstood when to take their medications.

*"... I just wondered whether I have complaints or not when I don't take my medication. That's why I stopped taking it". "I think it isn't necessary to take the medication both in the morning and in the evening..."*

*Multiple medications use:* One participant noted that since he had to take more than one medication, he took the wrong medicine. *"...Because I have to take more than one medication, I took another drug instead of the one I was supposed to take".*

*Health beliefs:* The liver transplants did not take their medication when they felt good. They believed that nothing serious happens when they do not take it for a few days. Also, they believed that because long time

elapsed since surgery and they did not find medication important, they experienced medication nonadherence.

*"... Taking my medicine one or two hours after meals does not make any difference". "I don't have any complaints when I don't take my medicine for two or three days ...". " ... It has been two years since transplantation... I feel well. That's why I think nothing bad happens if I don't take my medicine".*

## **Main Theme 3: Expectations from nurses**

Three subthemes related to LTRs' expectations from nurses emerged: financial guidance, education and showing interest.

*Financial guidance:* The LTRs wanted to receive financial guidance from nurses. *"... I need to get information from nurses about financial sources I can use to buy my medications".*

*Education:* The LTRs wanted to receive education to satisfy their needs for knowledge about effects and side-effects of their medication, time of taking their medication and duration of using their medication.

*"... A meeting can be held with patients every two or three months. I want to receive information about doses and modes of medication, conditions likely to appear when the medication is not used, nutrition and return to social life. I would like to know whether return to work will cause any problems or not". "...I wonder whether weight gain is due to medications or not ...".*

*Showing interest:* The LTRs reported that they need to be shown interest.

*The most important need of us is motivation", "I will be glad if nurses show interest."*

## **Discussion**

The liver transplant recipients were found to experience medication nonadherence. In fact, they skipped doses, delayed taking their medication and mistook their medication, which is consistent with the literature (13, 14, 35). In a study by Eberlin et al. (35), liver transplant recipients more frequently failed to take their medication on time in the evening compared to the morning dose. In addition, the recipients missed doses of their medications at weekends in particular (36).

Medication nonadherence described by the patients in this study might have been due to not being offered sufficient information about importance of taking medication and delaying doses and treatment after discharge. In addition, health professionals might not have clearly explained reminders for taking medication and the patients might have experienced difficulties in obtaining their medication due to the deficiencies of the health care system in Turkey. Failure to offer information about medication use at certain intervals during discharge may cause nonadherence.

Causes of medication nonadherence reported by the LTRs were categorized into six subthemes, namely,

forgetting, life style, health care system, insufficient knowledge, multiple medications use and health beliefs. The recipients reported to forget taking their medication due to doing housework, work and social life, not taking their medication with them, being indecisive about whether they took their medication and stress. Forgetfulness which appears among the LTRs can be associated with mood changes due to side effects of immunosuppressives, especially corticosteroids. It can also be explained by the need to think about many things at a time due to hectic life styles. Consistent with the results of this study, it has been reported in the literature that patients' forgetting to take their medication was due to hectic life style, stress, anger, depression, not having a good family life, lack of social support, being divorced, history of substance or alcohol use and pre-transplant nonadherence, having mental health needs, missing clinic appointments and not maintaining medication logs (18, 19, 21-27, 37, 38). Male sex, longer time elapsing from liver transplantation and mood disorder and social support instability before transplantation were predictors of missed-dose nonadherence. Mood disorder and social support instability before transplantation were predictors of altered-dose nonadherence (35). The LTRs living with their partners and having support from their friends and families have been reported to have better medication adherence (19, 24, 26). In addition, this study revealed that patients' inability to understand explanations about their medications made by health professionals, multi-drug use and mood disorders due to side-effects of immunosuppressive medications (especially corticosteroids) cause medication non-adherence.

This study revealed that the LTRs associated their medication nonadherence with not having meals regularly, getting up late and having breakfast late due to not having to go to work, coming home late, skipping meals due to lack of appetite, poor time management, oversleeping, sleeplessness and tiredness. In a qualitative study in Columbia, maintaining routines including having breakfast and other meals was found to be one of the main themes associated with medication adherence (7). Similarly, in the present study, inability to maintain routines was found to be due to changes in social life and insufficient social support. In fact, most of the patients did not go to work after transplantation. For this reason, they did not maintain their daily routines they used to have before surgery, which might have affected medication adherence.

In addition, the patients attributed their medication nonadherence to bureaucratic difficulties in the health care system, multiple medications use, feeling well, the belief that they would not experience any problems, the opinion that not taking the medication is usual and long time elapsing after transplantation. Comparable with the results of this study, it has been shown in the literature that multiple medications use (20), not having a strong belief in the need of medication, feeling well and finding medications unimportant (11, 16, 18, 20), long time elapsing after transplantation (13, 17), are associated with medication nonadherence. Unlike this study, two studies have revealed that time from transplantation

does not have any effects on nonadherence (26). In another study, the rate of medication nonadherence was shown to be higher in 2-5 years after transplantation (37).

A qualitative study in the UK on effects of patients' perceptions on medication adherence showed that health beliefs were one of the main themes associated with medication nonadherence (27). In studies in the USA (15) and Georgia (17), low socio-economic status and difficulties with health insurance have been reported to cause medication nonadherence. In a qualitative study, obtaining medications (insurance payments and costs) was found to be associated with medication adherence (7). In recent years, there have been great changes in the health care system and fierce debates about these changes in Turkey. The new health care system leads to some unfavorable conditions (39). Medication nonadherence associated with the health care system by the patients can be explained by changes in the Turkish health policies and a low number of social workers and financial advisers. Therefore, the patients might have expected nurses to fulfill social workers' and financial advisers' roles, which might have increased work load of nurses and caused nurses' offering insufficient knowledge to patients. Also, it might have been due to lack of a nurse who continuously worked in the liver transplantation outpatient clinic where long-term follow up of patients is performed.

Congruent with the literature, this study revealed that knowledge of medications played an important role in improvement of medication adherence (19). A study from Germany revealed that the most common interventions were training for self-administration of medications and providing booklets containing information about adherence followed by offering printed instructions for medications. The perceived most effective intervention was reported to be training for self-administration of medications (40).

In the present study, the patients' insufficient knowledge can be explained by nurses' insufficient knowledge due to lack of certificate programs for transplantation nursing following baccalaureate nursing education and insufficient training offered to patients before discharge and not offering adequate information about medications and their side-effects and importance of taking medications regularly.

Findings from this study demonstrated that the LTRs had medication nonadherence for many reasons and expectations from nurses for prevention of nonadherence.

Nurses and other health professionals should provide LTRs with information about time, doses and effects of medications in a written way and ask LTRs to reread this information. Education and other services provided for patients should be appropriate for the cultural environment in which patients live and should improve patients' health beliefs, which are considered crucial factors likely to reduce medication nonadherence (7).

Offering certificate programs for transplantation nursing after graduation from university will not only improve nurses' knowledge but also help nurses inform patients effectively. Besides, further studies about medication nonadherence after transplantation and prevention of nonadherence in Turkey are required.

**Limitations:** As this is a qualitative study, the results of the study cannot be generalized to all LTRs. Since

there have not been any other studies on medication nonadherence in Turkey, the results of this study could not be compared with other data.

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