Original Article

Adherence and Treatment Satisfaction in Liver Transplant Recipients

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ABSTRACT

Background/Aims: Liver transplantation (LT) is a life-saving intervention for patients with liver failure. LT recipients' adherence to their therapeutic regimen is an essential element for graft survival. According to WHO, the impact of medication non-adherence in solid organ transplantation has shown to cost $15–100 million annually. The aim of the present study was to identify the factors that best predict medication adherence and to explore the relationship between treatment satisfaction and medication adherence in liver transplant recipients. **Patients and Methods:** Adult liver transplant patients at King Abdulaziz Medical City were included in the study. Patients completed the 8-item Morisky Medication Adherence Scale (MMAS-8) and the Treatment Satisfaction Questionnaire for Medication (TSQM 1.4) in addition to several socio-demographic and transplant-related data. **Results:** A total of 154 patients were included in the study and of these 59.7% were adherent. Older age was a significant predictor of adherence ($P < 0.05$). The mean treatment satisfaction score was 91.9 ± 12.7 in Effectiveness, 80.0 ± 25.9 in Side Effects, 83.5 ± 15.7 in Convenience, and 94.6 ± 8.6 in Global Satisfaction. Further analysis indicated that patients in the adherent group had reported significantly higher satisfaction scores than those in the non-adherent group ($P < 0.05$) in all treatment satisfaction domains: Effectiveness (94.4 ± 10.4 vs. 88.6 ± 14.8), Side Effects (83.9 ± 22.0 vs. 74.2 ± 30.1), Convenience (87.0 ± 13.9 vs. 77.2 ± 16.1), and Global Satisfaction (96.9 ± 6.6 vs. 91.2 ± 8.6). **Conclusion:** Older patients and those who were more satisfied with their treatment tend to have better adherence to the prescribed medications. Therefore, increasing patients' satisfaction with their treatment should be an integral element of future care plans designed to improve treatment outcomes in liver transplant recipients.

Key Words: Liver transplantation, medication adherence, treatment satisfaction

Liver transplantation (LT) is a life-saving intervention for patients with liver failure. Diseases such as cirrhosis, hepatitis B (HB), hepatitis C (HC), non-alcoholic fatty liver disease (NAFLD), and hepatocellular carcinoma (HCC) can all lead to liver failure.[1,2]

The prevalence of these conditions in Saudi Arabia is: 1.9% for HB among adults,[3] 1–1.9% for HC,[4] and 7–16.6% for

NAFLD.[5] Furthermore, up to 5.2% of all newly diagnosed cancer cases in Saudi Arabia are HCC.[1] The history of LT operations in Saudi Arabia dates back to the mid-1990s, when LT was performed at Riyadh Armed Forces Hospital, followed in early 1994 by King Fahad Hospital at King Abdulaziz Medical City (KAMC) in the Ministry of National Guard Health Affairs (NGHA).[6] In 2014, there were 198 LT cases, the majority of which received their organs from living donors. Saudi reports indicate that a total of 1596 LT operations were performed in Saudi Arabia between 1990 and 2014.[7]

Adherence to therapy is defined as the extent to which a patient follows the instructions of the health care provider with regard to taking medications and adopting a healthy lifestyle.[8] However, numerous factors have been shown to influence

patients' adherence to prescribed regimens. This includes socioeconomic factors such as gender, age, economic status, educational level, and marital status.[8] Disease and therapy factors have also been shown to affect adherence, including the complexity of the prescribed regimen, as reflected by the number of prescribed medications and the frequency of their administration, perceived side effects of the prescribed medications, duration of therapy, severity of illness, presence of other comorbidities, and possible disease complications.[9-11]

In order to avoid therapy failure and poor treatment outcomes, LT recipients are required to adhere to their prescribed medications, particularly immunosuppressant therapy (IST).[10]

It has been reported that the rate of non-adherence to IST ranges from 15 to 40% in liver transplant patients, which in turn increases the risk of graft rejection or loss.[9] Non-adherence also increases health costs and decreases the quality of life and productivity in liver transplant patients.[11,12] Even a small deviation (as little as 5%) from the prescribed regimen can affect graft survival and worsen outcomes.[10,13] In spite of these consequences, non-adherence to IST is documented due to its numerous side effects such as undue hair growth, increased infection risk, cancer induction susceptibility, and high cost.[2] WHO estimates the cost impact of medication non-adherence in solid organ transplantation to be $15–100 million annually.[14]

Patient's treatment satisfaction is an important tool for making health decisions related to adherence and continuation of treatment.[15] As a part of Patients Reported Outcomes (PROs), treatment satisfaction is largely influenced by the complexity of the prescribed regimen, severity of the disease, duration of treatment, and other factors.[16,17] Recently, treatment satisfaction has been linked to adherence level as an expression of the quality of provided care, as satisfied patients are more likely to adhere better to their medications.[18,19]

The aim of the present study was to explore the predictors of medication adherence and to demonstrate the association between medication adherence and treatment satisfaction in LT recipients.

PATIENTS AND METHODS

Patients and study design
This cross-sectional study was conducted in King Fahad Hospital, KAMC, Riyadh, Saudi Arabia. In this study, 154 patients were selected using the convenience sampling method in the period between January 2013 and January 2014. Data were collected using the validated Arabic version of the 8-item Morisky Medication Adherence Scale (MMAS-8) for measuring the level of adherence and the Treatment

Satisfaction Questionnaire for Medication (TSQM 1.4; Quintiles, Durham, North Carolina, USA) for measuring treatment satisfaction among the study participants. Patients who were residents of Saudi Arabia, aged 16 years or more, and had a liver transplant for at least 1 month prior to the study were included. Of the 160 patients who were approached, a total of 154 patients agreed to participate in the study. A written consent was obtained from all the study participants.

Study instruments
In addition to using MMAS-8 and TSQM 1.4, socio-demographic data including gender, age, level of education, employment, and economic and marital status of the participants were collected for each participant.

The 8-item Morisky medication adherence scale
Medication adherence was assessed using the Arabic version of the validated MMAS-8.[20,21] The MMAS-8 is basically divided into two main sections. The first four items capture the fundamental reasons of medication non-adherence or omission, while the other four items identify and address the circumstances or situations related to adherence behavior. Like the original, the Arabic version of the MMAS-8 is an 8-item questionnaire with seven yes/no questions and one question is answered on a 5-point Likert scale. According to the scoring system of the MMAS-8, a score of 8 denotes high adherence, from 6 to <8 medium adherence, and <6 denotes low adherence. Patients who had low or moderate adherence were classified as non-adherent, while those with a score of 8 on the MMAS-8- were classified as adherent.

Treatment satisfaction questionnaire for medication
TSQM utilizes the three primary dimensions of treatment satisfaction (Effectiveness, Side Effects, Convenience), as well as patient's overall rating of Global Satisfaction to compare the relative importance of various medications used to treat a particular illness. Treatment satisfaction was evaluated using the validated Arabic version of TSQM 1.4, which was generously provided free of charge for academic research by Quintiles Strategic Research Services. The Arabic version of the TSQM 1.4 is a 14-item psychometrically validated instrument comprising four domains: Effectiveness (questions 1–3), Side Effects (questions 4–8), Convenience (questions 9–11), and Global Satisfaction (questions 12–14). TSQM 1.4 domain scores range from 0 to 100, with higher scores indicating higher satisfaction in that domain[22] (scoring manual from Quintiles as a reference).

Statistical analysis
Data were collected and saved into an Excel worksheet and then coded and analyzed using Statistical Package for the Social Sciences (SPSS v. 21; Chicago, IL, USA). Descriptive

statistics were performed to assess the socio-demographic variables and medication use in the study population. Continuous variables were expressed as mean ± SD. Pearson correlation and independent *t*-test were used to examine the association between continuous variables, and Chi-square test was used to identify the associations between categorical variables. Statistical significance was considered at *P* < 0.05.

RESULTS

The characteristics of the study participants are presented in Table 1. Mean age was 57.4 ± 13.1. Most of the participants were males (80.5%), married (88.9%), not employed (74.7%), had lower than a university level of education (64.3%) and low-medium income (76.0%). The mean number of prescribed medications was 9.4 ± 5.2. The prescribed IST was tacrolimus and, rarely, cyclosporin, in addition to mycophenolate mofetil, prednisolone, and in many cases, basiliximab as induction therapy.

According to the MMAS-8, 8.4%, 31.8%, and 59.7% of the 154 participants reported low (4.9 ± 0.3), moderate (6.7 ± 0.4), and high (8.0 ± 0.0) levels of medication adherence, respectively, as shown in Figure 1. For the purpose of the present analysis, the LT recipients were divided into two groups: The non-adherent group which included those with low and medium adherence (40.3%) and the adherent group which included those with a high level of adherence (59.7%).

Of the 154 participants, 81.8% had a deceased donor transplant. Results indicated no significant difference (*P* > 0.05) between those who had a family member or friend donor versus a deceased donor in terms of medication adherence [Table 1].

Pearson correlation showed a significant association between age and adherence scores (*r* = 0.213, *P* < 0.05), i.e. medication adherence was higher in older patients. The rest of the results revealed no other significant associations between adherence and socio-demographics and clinical factors [Table 1].

As shown in Figure 2, the mean satisfaction scores were: For Effectiveness = 91.9 ± 12.7, Side Effects = 80.0 ± 25.9, Convenience = 83.5 ± 15.7, and for Global Satisfaction = 94.6 ± 8.6. Further analysis of the association between medication adherence and treatment satisfaction demonstrated that patients in the adherent group reported significantly higher satisfaction scores (*P* < 0.05) when compared with patients in the non-adherent group with regard to Effectiveness (94.4 ± 10.4 vs. 88.6 ± 14.8), Side Effects (83.9 ± 22.0 vs. 74.2 ± 30.1), Convenience (87.0 ± 13.9 vs. 77.2 ± 16.1), and Global Satisfaction (96.9 ± 6.6 vs. 91.2 ± 8.6), as shown in Table 2 and Figure 3.

## Table 1: Single predictor analysis of medication adherence (*N*=154)

Variables	Total n (%)	Adherent n (%) 92 (59.7)	Non-adherent n (%) 62 (40.3)
Age*			
Mean±SD	57.4±13.1	59.1±11.2	54.6±15.2
Gender			
Male	124 (80.5)	77 (83.7)	47 (75.8)
Female	30 (19.5)	15 (16.3)	15 (24.2)
Level of education			
Illiterate	36 (20.1)	23 (63.9)	13 (36.1)
High school or below	63 (29.9)	38 (60.3)	25 (39.7)
University or above	55 (35.7)	31 (56.4)	24 (43.6)
Employment status			
Yes	39 (25.3)	21 (53.8)	18 (29.1)
No	115 (74.7)	71 (61.7)	44 (70.9)
Economic status (in Riyals)			
Low (≤5000)	69 (44.8)	47 (68.1)	22 (31.9)
Medium (5001-1000)	48 (31.2)	26 (54.2)	22 (45.8)
High (>10000)	37 (24.0)	19 (51.4)	18 (48.6)
Marital status			
Married	137 (88.9)	84 (91.3)	53 (85.5)
Others	17 (11.1)	8 (8.69)	9 (14.5)
Medication administration			
Self	135 (87.7)	81 (60.0)	54 (87.1)
Care giver	19 (12.3)	11 (57.9)	8 (12.9)
Graft function			
Good	149 (96.8)	89 (96.7)	60 (96.8)
LFT	5 (3.2)	3 (3.3)	2 (3.2)
Any other diseases			
Yes	140 (90.8)	82 (89.1)	58 (41.4)
No	14 (9.1)	10 (10.9)	4 (28.6)
Number of medications			
Mean±SD	9.4±5.2	9.0±4.9	10.0±5.6
Donor			
Living related donor	28 (18.2)	18 (19.6%)	10 (16.1%)
Deceased donor	126 (81.8)	74 (80.4%)	52 (83.9%)

*Significant at 0.05. SD: Standard deviation; LFT: Liver function test

DISCUSSION

Limited data is available in the literature regarding the assessment of variables affecting medication adherence, treatment satisfaction, and the relationship between them among liver transplant recipients. Non-adherence has been identified as a barrier to optimal outcomes in patients with different diseases. Therefore, assessing the level of adherence is a critical step in developing interventions to improve medication adherence and health outcomes in patients with various diseases.[23]
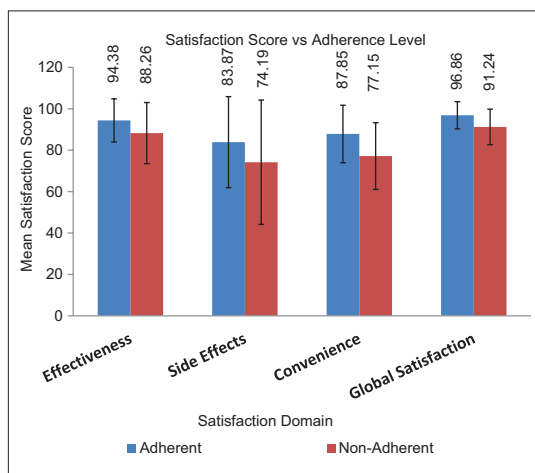
Adherence in the present study was assessed using an Arabic version of MMAS-8, as it is the most commonly used method
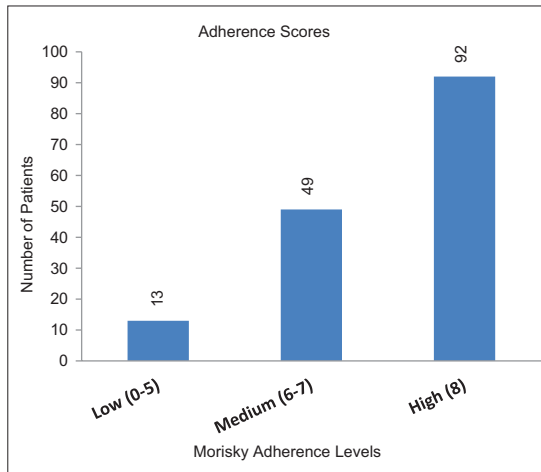
Figure 1: Distribution of the study participants according to their level of adherence
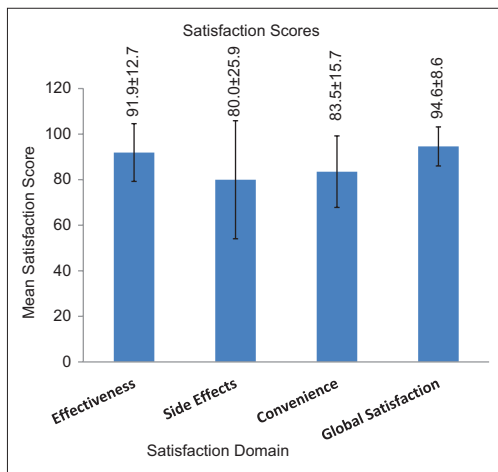
Figure 2: Mean satisfaction scores in treatment satisfaction domains

Figure 3: Mean treatment satisfaction scores based on whether the patient is adherent or non-adherent

Table 2: Treatment satisfaction stratified according to the levels of adherence

Variable	Overall satisfaction score	Adherent (*n*=92) Mean±SD	Non-adherent (*n*=62) Mean±SD
Effectiveness*	91.9±12.68	94.4±10.4	88.3±14.8
Side effects*	80.0±25.9	83.9±22.0	74.2±30.1
Convenience*	83.5±15.7	87.9±13.9	77.15±16.1
Global satisfaction*	94.6±8.6	96.9±6.6	91.2±8.6

*Significant at 0.05. SD: Standard deviation

self-reported Morisky scale in liver transplant recipients. The MMAS-8 is relatively inexpensive, simple, and can be conducted rapidly in any clinical setting, when compared with other methods of adherence assessment. Although this method of assessment might overestimate adherence as it is prone to bias due to social desirability in the answers given by patients, it has been shown to be as effective as other indirect measures, including pill count and refill rates.[25] Furthermore, MMAS-8 has been validated and found to be reliable and widely used in several medication adherence studies as a "gold standard" against which new adherence measurement instruments are tested.[26-31]

It is crucial to identify patients whose prescribed medication experiences may increase the risk of poor medication adherence. One way to achieve this goal is to assess patients' level of satisfaction with the prescribed treatment. Treatment satisfaction in the present study was assessed using TSQM 1.4. Again, the TSQM 1.4 has been found to be validated and reliable in several studies that assessed treatment satisfaction in patients with different disease states.[15,32]

The results of this study indicated that 59.7% of the liver transplant recipients were adherent to their medications. This finding is consistent with the findings from another study on adherence among liver transplant recipients in the US but using a different method of adherence assessment, where the adherence rate was reported to be 61.8%.[33] In general, the rate of medication adherence among adult liver transplant patients ranges from 60% to 85%. The variety of methods used to measure adherence along with the different definitions of the term "non-adherence" may have contributed to the wide range of reported adherence rates in liver transplant recipients.[9]

It is commonly believed that elderly patients report lower adherence to therapy because of their declining cognitive function.[34] However, this was not found to be the case in this study. Current data show that older age was significantly associated with higher medication adherence, which is consistent with many previous reports.[32,35-37] Our finding might be justified by the fact that older patients are more likely to have disease progression and to develop

to assess adherence.[24] To the best of our knowledge, the current study is the first to assess medication adherence using

130

Volume 22, Number 2
Jumada Al Thani 1437H
March 2016

The Saudi Journal of
Gastroenterology

disease complications, which in turn may lead to increased awareness of the severity of their illnesses and realization of the importance of medication adherence.[23] Furthermore, we speculate that the close relationship between family members in the Middle East region including Saudi Arabia helped older participants in this study receive good support from the family members and caregivers, which may have contributed to their improved adherence behavior. Earlier research demonstrated the positive impact of family support on adherence to prescribed therapy.[12,34]

With regard to treatment satisfaction, liver transplant recipients demonstrated high treatment satisfaction, particularly in the Global Satisfaction and Effectiveness domains followed by Convenience and Side Effects domains. Nevertheless, all satisfaction domains had significant association with medication adherence. In other words, adherent patients tended to report significantly higher treatment satisfaction in all domains compared to non-adherent patients. Comparing the results of our study with other published data in different diseases substantiates our findings. A study conducted on epileptic patients that used both MMAS-8 and the TSQM 1.4 scales indicated that patients with high level of adherence showed significantly higher satisfaction in the Effectiveness and Convenience domains, but not in the Side Effects or Global Satisfaction domains, when compared with patients with low or medium level of adherence.[32] Another study conducted on patients with hypertension reported a significant difference in mean scores in the Effectiveness, Convenience, and Global Satisfaction domains, but not in the Side Effects domain among patients with different levels of adherence.[15] This variation in findings can be attributed to the different disease states assessed in each study, in addition to the different environments in which other studies were conducted. Nevertheless, patients with a high adherence rate in the indicated studies tended to have higher scores in the four satisfaction domains when compared with those with a low or medium adherence rate, which is consistent with the findings of the present study. Other studies that used different instruments to assess treatment satisfaction reported significant association between medication adherence and overall treatment satisfaction in patients with different disease states.[38-41]

Although the mechanism through which medication adherence is associated with treatment satisfaction is unknown, lower treatment satisfaction appears to be associated with lower psychosocial well-being which can adversely influence patients' ability to manage their health problems.[21,22] Kennard et al.[42] stated that psychological distress due to low self-esteem, social adjustment problems, and behavioral difficulties were reported in medically non-adherent liver transplant recipients. It was found that

in other disease populations, e.g. patients with hypertension, treatment satisfaction was linked to patients' beliefs, their perceived level of competence, knowledge and attitudes toward disease treatment, and their overall attitude toward life, which are known to be precursors to medication adherence.[15] These conclusions should be applicable in this current work.

Study limitations

The major limitation of this study is its cross-sectional design, which precludes identification of causal relationships. Another possible limitation is that the study participants were selected by convenience sampling, which may undermine the generalizability of the findings. Furthermore, questions 2 and 3 in the efficacy domain in the TSMQ 1.4 do not apply to immunosuppressive therapy, as they do not treat symptoms but prevent rejection. Finally, social desirability associated with the methods used to assess medication adherence and treatment satisfaction could have influenced the findings of this study.

CONCLUSION

The current study revealed that liver transplant recipients who are older and have higher treatment satisfaction are more likely to adhere to their medication regimens. Therefore, increasing patient satisfaction by improving the perceptions about treatment effectiveness and possible side effects, along with selection of the most convenient treatment should be considered an integral part of future care plans intended for achieving optimal treatment outcomes. Further research is warranted to understand the real mechanisms through which treatment satisfaction is associated with medication adherence and to identify appropriate and targeted interventions in an effort to improve treatment satisfaction in liver transplant recipients.

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132

Volume 22, Number 2
Jumada Al Thani 1437H
March 2016

The Saudi Journal of
Gastroenterology