

**O IMPACTO DA ADESÃO À MEDICAÇÃO NA QUALIDADE DE VIDA RELACIONADA À SAÚDE DE PACIENTES DIABÉTICOS NO REINO DA ARÁBIA SAUDITA: CONCLUSÕES DE UM ESTUDO TRANSVERSAL****THE IMPACT OF MEDICATION ADHERENCE ON HEALTH-RELATED QUALITY OF LIFE OF DIABETIC PATIENTS IN THE KINGDOM OF SAUDI ARABIA: FINDINGS FROM A CROSS-SECTIONAL STUDY****أثر التقيد بالأدوية على الجودة الصحية ذات الصلة بحياة مرضى السكري في المملكة العربية السعودية: نتائج من دراسة متقاطعة**ALSHAYBAN, Dhfer<sup>1</sup>; JOSEPH, Royes<sup>1\*</sup><sup>1</sup> Department of Pharmacy Practice, College of Clinical Pharmacy, Imam Abdulrahman Bin Faisal University, Dammam, Saudi Arabia.

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**RESUMO**

O diabetes é uma doença crônica comum que é considerada um dos problemas de saúde que mais crescem no mundo. A adesão aos medicamentos pode ser um fator importante na redução dessas complicações e na melhoria da qualidade de vida. O objetivo desta pesquisa foi avaliar o impacto da adesão ao tratamento na qualidade de vida relacionada à saúde em pacientes com diabetes tipo 2. Um estudo transversal multicêntrico foi realizado com 368 pacientes com diabetes. A Escala Geral de Adesão à Medicação foi utilizada para avaliar o nível de adesão e o EuroQol-5D para avaliar a qualidade de vida. Os resultados mostram que 19%, 21% e 23% dos pacientes mantiveram baixa adesão à medicação devido ao comportamento intencional ou não intencional do paciente devido a doenças adicionais ou sobrecarga de pílulas e devido a restrições financeiras, respectivamente. No geral, 43% (n = 162) participantes mantiveram alta adesão à medicação e 37% (n = 138) mantiveram baixa adesão à medicação para medicamentos antidiabéticos. Quase um terço (31%) dos pacientes com alta adesão geral apresentou um estado de saúde perfeito em comparação com 4% entre os pacientes com baixa adesão. Além disso, a menor proporção (21%) de pacientes com alta adesão geral apresentou um estado de saúde perfeito em comparação com a dos pacientes com baixa adesão (34%). Além da adesão geral, a associação foi estatisticamente significativa para os domínios relacionados à não adesão devido ao comportamento intencional ou não intencional do paciente (valor de  $p < 0,001$ ) e não adesão devido a doenças adicionais ou sobrecarga de comprimidos (valor de  $p < 0,001$ ) após levar em consideração as características sociodemográficas e clínicas. Em conclusão, os resultados sugerem que os formuladores de políticas devem estabelecer uma intervenção para melhorar a adesão ao tratamento diabético e, assim, melhorar a qualidade de vida dos pacientes diabéticos tipo 2.

**Palavras-chave:** *Diabete, Adesão, qualidade de vida relacionada à saúde***ABSTRACT**

Diabetes is a common chronic disease that is considered as one of the fastest-growing health problems in the world. Adherence to medications could be an important factor in reducing these complications and improving the quality of life. The purpose of this research was to assess the impact of treatment adherence on health-related quality of life in patients with type 2 diabetes. A multicenter cross-sectional study was carried out among 368 diabetes patients. General Medication Adherence Scale was used to assess the adherence level and EuroQol-5D to assess the quality of life. The results show that 19%, 21%, and 23% of patients had maintained low medication adherence due to patient's intentional or unintentional behavior due to additional diseases or pills burden and due to financial constraints, respectively. Overall, 43% (n=162) participants had maintained high medication adherence, and 37% (n=138) had maintained low medication adherence to antidiabetic drugs. Nearly one-third (31%) of patients with high overall adherence had perfect health state in comparison with 4% among patients with low adherence. Further, the lower proportion (21%) of patients with high overall adherence had

perfect health state in comparison with that among patients with low adherence (34%). In addition to the overall adherence, the association was statistically significant for the domains related to non-adherence due to the patient's intentional or unintentional behavior ( $p$ -value $<0.001$ ) and non-adherence due to additional diseases or pills burden ( $p$ -value $<0.001$ ) after taking into account of socio-demographic and clinical characteristics. In conclusion, the findings suggest that the policymakers should establish an intervention to improve adherence to diabetic treatment, and thus improve the quality of life for the type 2 diabetic patients.

**Keywords:** *Diabetes, Adherence, Health-related quality of life*

## الخلاصة

داء السكري هو مرض مزمن شائع يعتبر من أسرع المشاكل الصحية نمواً في العالم. يمكن أن يكون الالتزام بالأدوية عاملاً مهماً في الحد من هذه المضاعفات وتحسين جودة الحياة. كان الغرض من هذا البحث هو تقييم أثر الالتزام بالعلاج على نوعية الحياة المتعلقة بالصحة لدى مرضى السكري من النوع 2. أجريت لتقييم EuroQoL-5D دراسة مستعرضة متعددة المراكز بين 368 من مرضى السكري. تم استخدام مقياس الالتزام بالأدوية العامة لتقييم مستوى الالتزام وجودة الحياة. أظهرت النتائج أن 19% و 21% و 23% من المرضى قد حافظوا على التزام منخفض بالأدوية بسبب سلوك المريض المتعمد أو غير المتعمد بسبب أمراض إضافية أو عبء حبوب ويسبب القيود المالية، على التوالي. بشكل عام، حافظ 43% (ن = 162) مشاركاً على التزام عالٍ بالأدوية، و 37% (ن = 138) حافظوا على انخفاض التزام الأدوية بالأدوية المضادة لمرض السكر. ما يقرب من ثلث (31%) من المرضى الذين لديهم التزام عام مرتفع لديهم حالة صحية مثالية بالمقارنة مع 4% بين المرضى الذين يعانون من انخفاض الالتزام. علاوة على ذلك، كانت النسبة الأقل (21%) من المرضى الذين لديهم التزام عام عالٍ بحالة صحية مثالية مقارنةً بالمرضى من ذوي الالتزام المنخفض (34%). بالإضافة إلى الالتزام العام، كان الارتباط مهماً إحصائياً للنطاقات المتعلقة بعدم الالتزام بسبب سلوك المريض المتعمد أو غير المقصود (القيمة الاحتمالية  $>0.001$ ) وعدم الالتزام بسبب أمراض إضافية أو عبء حبوب (قيمة بعد مراعاة الخصائص الاجتماعية والديمغرافية والسريية. في الختام، تشير النتائج إلى أنه يجب على واضعي السياسات إنشاء تدخل لتحسين ( $p < 0.001$ ) الالتزام بعلاج مرض السكري، وبالتالي تحسين نوعية الحياة لمرضى السكري من النوع

الكلمات المفتاحية: داء السكري، الالتزام، جودة الحياة المتعلقة بالصحة

## 1. INTRODUCTION

Diabetes mellitus (DM) is a common metabolic disease that is considered as one of the fastest-growing health problems in the world. It results from a complex inheritance-environment interaction together with other risk factors such as lifestyle as lack of exercise, unhealthy diet, obesity, and overweight (Naeem, 2015; Daya, Bayat and Raal, 2016). It has both short and long-term complications such as hypoglycemia and hyperglycemia and cardiovascular diseases. Diabetic patients are prone to suffer from depression. These complications and comorbidities are responsible for significant societal and economic burden, and they have a negative impact on health-related quality of life (HRQoL) (Al-Ghamdi *et al.*, 2018).

Saudi Arabia ranks second-highest in the Middle East and is seventh in the world for the rate of diabetes. It is reported that 7 million of the population have been diagnosed with diabetes, and the number of prediabetes population has reached 3 million (Robert *et al.*, 2016). It has been shown that patients with type 2 DM (T2DM) experienced significantly decreased HRQoL compared with those without diabetes, and their HRQoL further decreases with disease development and complications (Holmes *et al.*, 2000; Koopmanschap and CODE-2 Advisory Board, 2002; Wexler *et al.*, 2006; Grandy and Fox, 2008). Our previous publication on HRQoL of

T2DM patients in the Eastern Province, Saudi Arabia, reported that only one-fifth of the patients were in perfect health state, and more than a quarter were in poor health state (Alshayban and Joseph, 2019).

Improving medication adherence to diabetes medications have the potential to significantly reduce the complications of diabetes and reduce the risk of hospitalization and ER visits, and thus improves HRQoL of the patients (Polonsky and Henry, 2016; Ahmed, Abugalambo and Almethen, 2017; Farhat *et al.*, 2019). Although both adherence to diabetic treatment and HRQoL are important factors for the treatment success of therapeutic interventions (Heng *et al.*, 2015; Daya, Bayat and Raal, 2016), the association between them has rarely been studied in diabetes. A previous study, from the Makkah region of Saudi Arabia, had been reported that a positive association between medication adherence and quality of life among patients with diabetes and hypertension (Khayyat *et al.*, 2019). Since the previous study was focused on patients with multiple chronic conditions and with limited to small sample size, a large-scale study that focuses on T2DM patients is warranted. If a positive relationship is found, more attention can be directed on reinforcing adherence to therapy to improve HRQoL for diabetic patients in Saudi Arabia. Therefore, this study aimed to assess treatment adherence and its association with the quality of life in patients with type 2 diabetes.

## 2. MATERIALS AND METHODS

### 2.1. Study setting and subjects

The study setting and methodology were detailed elsewhere (Alshayban and Joseph, 2019). A multicenter cross-sectional study was carried out from November 2017—April 2018. Patients were selected from outpatient clinics of King Fahad Hospital of the University, Khobar, and Family and Community Medicine Centre, Dammam. Hospital records indicate that both hospitals serve patients from several urban and rural areas within the Eastern Province. Patients aged 18 years or older and had T2DM for a minimum of one year were considered. Patients with other chronic/serious illness or pregnancy were excluded. The study was designed to target 385 diabetes patients based on sample size calculation. Ethical approval was obtained from the Institutional Review Board at Imam Abdulrahman Bin Faisal University (IRB-2019-05-391).

### 2.2. Data Collection

Patients at the waiting lounge of the hospitals were approached and explained the purpose of the study, and informed consent was obtained if they agreed to participate in the study. The questionnaire was administrated in the Arabic language, which is the national language of Saudi Arabia. The questionnaire did not request any information that could identify individual participants during or after data collection.

The study questionnaire had three sections. In the first section, patients' demographic and clinical characteristics were requested. The variables included sex, age in years, education qualification, family income, random blood glucose level, presence of diabetes-related conditions, and type and number of antidiabetic medications used. In the second section, as detailed elsewhere (Alshayban and Joseph, 2019), the HRQoL of participants was assessed using the EQ-5D-5L (Herdman *et al.*, 2011), and the EQ-5D index (Devlin *et al.*, 2018) was derived. Using the EQ-5D-5L, health status was assessed in terms of mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Patients were classified as with perfect health state if no problem in domains of EQ-5D, slight/moderate health state if problems in one or more domains but not worse than moderate health in any domains, or severe/unable health state if a health status with problems worse than moderate health in some domains (Alshayban and Joseph, 2019).

In the final section, adherence to antidiabetic drugs was measured using the General Medication Adherence Scale (GMAS) (Naqvi *et al.*, 2018). The questionnaire was validated with good reliability and high sensitivity and specificity among Saudi patients with chronic diseases (Naqvi *et al.*, 2019). The questionnaire consists of a total of eleven questions under three-domains. The domains are 1) non-adherence due to patient behavior (unintentional and intentional), 2) non-adherence due to additional disease and pill burden, and 3) non-adherence due to financial constraints. All questions in the GMAS were answered on a 4-point scale (0-3; from always to never) with a higher score indicating a higher medication adherence. The domain-specific score is calculated by summing the scores of relevant individual items. The summative scores may range 0-15, 0-12, and 0-6 for the first, second, and third domains, respectively. A score of greater than or equal to 13, 11, and 6 is regarded as high adherence in first, second, and third domains, respectively. A score of less than or equal to 10, 8, and 4 is regarded as low adherence in first, second, and third domains, respectively. In addition, a score between high and low adherence is referred to as moderate adherence to medications. Overall, medication adherence is calculated by summing scores for all the 11 items in the questionnaire, and it may range from 0 to 33. An overall score of 30—33, 27—29, and less than 27 is regarded as high, good, and low overall medication adherence, respectively.

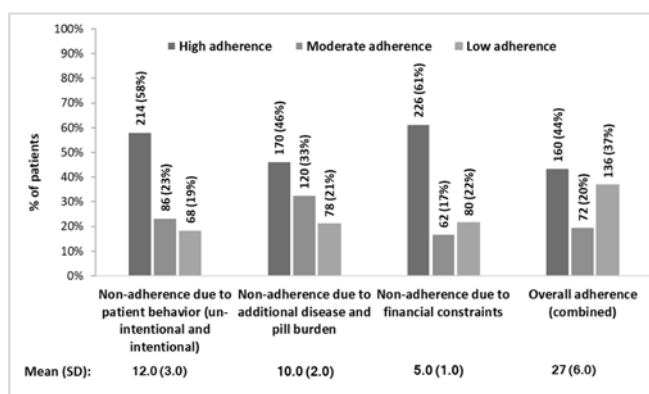
### 2.3. Statistical analysis

Data management and analyses were carried out using SPSS Statistics 24.0. Data were summarized as frequency (percentage) and mean (standard deviation) for categorical and continuous variables, respectively. The association of the level of medication adherence on HRQoL was assessed using 1) chi-square test where outcome variable was HRQoL with three levels, 2) multiple logistic regression where outcome variable was a binary variable indicating 'perfect health' or 'not', and 3) multiple linear regression where the dependent variable, EQ-5D index, was transformed using a cubic function to achieve normally distributed residuals. Regression estimates were adjusted for demographic information and clinical characteristics. A p-value of less than 0.05 was considered statistically significant

## 3. RESULTS AND DISCUSSIONS

The study was completed by 378 patients;

however, 10 participants were excluded due to incomplete data. The socio-demographic and clinical characteristics of participants were presented in a previous publication (Alshayban and Joseph, 2019). The participants involved an equal proportion of male and female patients; more than two-thirds were older than 50 years. Among the participants, nearly half of them (n=178) had a random glucose level 200 mg/dl or higher; three-fourth (n=286) had complications related to diabetes; more than half (n=224) were on oral antidiabetic medications only; and two-third (n=253) were on multiple antidiabetic medications.



**Figure 1.** Level of adherence to antidiabetic drugs (measured using GMAS)

The level of medication adherence is summarized in Figure 1. The results show that 19%, 21%, and 22% of patients had maintained low medication adherence due to patient's intentional or unintentional behavior, due to additional diseases or pills burden, and due to financial constraints, respectively. Overall, 44% (n=160) participants had maintained high medication adherence, and 37% (n=136) had maintained low medication adherence to antidiabetic drugs. The mean (standard deviation) overall GMAS score was 27.3 (5.6) on a 0–33 scale.

Table 1 presents the association of level of medication adherence on the level of HRQoL. The results show that the proportion of patients with the perfect health was higher among the high adherence patients, and the proportion of patients with the severe/extreme health was higher among the low adherence patients in comparison with contrary groups. The results were statistically significant for the domains related to non-adherence due to the patient's intentional or unintentional behavior (p-value<0.001) and non-adherence due to additional diseases or pills burden (p-value<0.001). Overall, 31% of patients with high overall medication adherence reported

as having perfect health against the proportion among patients with moderate overall adherence (28%) and with low overall adherence (4%). Further, a lower proportion (21%) of patients with high overall adherence had perfect health state in comparison with that among patients with low adherence (34%).

**Table 1.** Overall health-related quality of life by the level of medication adherence

Adherence level	Overall health status: n (%)		
	Perfect health	Slight-Moderate	Severe-Extreme
	76 (20.6)	190 (51.6)	102 (27.7)
Non-adherence due to patient behavior (unintentional and intentional)**			
HA (13-15)	66 (30.8)	94 (43.9)	54 (25.2)
MA (11-12)	6 (7)	52 (60.5)	28 (32.6)
LA (<12)	4 (5.9)	44 (64.7)	20 (29.4)
Non-adherence due to additional disease and pill burden**			
HA (11-12)	52 (30.6)	78 (45.9)	40 (23.5)
MA (9-10)	18 (15)	66 (55)	36 (30)
LA (<9)	6 (7.7)	46 (59)	26 (33.3)
Non-adherence due to financial constraints <sup>NS</sup>			
HA (6)	54 (23.9)	116 (51.3)	56 (24.8)
MA (5)	10 (16.1)	30 (48.4)	22 (35.5)
LA (<5)	12 (15)	44 (55)	24 (30)
Overall adherence (Cumulative)**			
HA (30-33)	50 (31.3)	76 (47.5)	34 (21.3)
MA (25-29)	20 (27.8)	30 (41.7)	22 (30.6)
LA (<25)	6 (4.4)	84 (61.8)	46 (33.8)

HA – High Adherence; MA-Moderate Adherence; LA-Low Adherence. \*\*p-value<0.001; <sup>NS</sup> – not statistically significant

Table 2 presents the adjusted odds ratio and its 95% confidence interval from a multiple logistic regression on an outcome variable indicating 'perfect health' or 'not'. The adjusted odds ratios for the first domain (non-adherence due to patient's intentional or unintentional behavior) indicates that the odds of having perfect health state among patients with moderate medication adherence and among patients with a low adherence were 86% and 91%, respectively, lower than that among patients with high medication adherence (p-value<0.05). Similarly, the adjusted odds ratio for the second domain (non-adherence due to additional disease or pills burden) indicates that the odds of having perfect health state among patients with low medication adherence was 87% lower than that among patients with high medication adherence (p-value<0.05). Overall, the odds of having perfect health state among patients with low medication adherence was 91% lower than those among patients with high medication adherence (p-value<0.05).

**Table 2.** Adjusted odds ratio for perfect health status and its 95% confidence interval

Adherence level	Odds ratio <sup>#</sup> (95% CI)	p-value
Non-adherence due to patient behavior (unintentional and intentional)		
HA (13-15)	1.0	
MA (11-12)	0.14 (0.05-0.45)	0.001
LA (<12)	0.09 (0.03-0.33)	<0.001
Non-adherence due to additional disease and pill burden		
HA (11-12)	1.0	
MA (9-10)	0.45 (0.21-1.01)	0.051
LA (<9)	0.13 (0.05-0.39)	<0.001
Non-adherence due to financial constraints		
HA (6)	1.0	
MA (5)	0.76 (0.27-2.18)	0.614
LA (<5)	0.52 (0.23-1.21)	0.13
Overall adherence (Cumulative)		
HA (30-33)	1.0	
MA (27-29)	0.91 (0.4-2.07)	0.815
LA (<27)	0.09 (0.03-0.27)	<0.001

HA – High Adherence; MA-Moderate Adherence; LA-Low Adherence. <sup>#</sup>Adjusted for gender, education status, monthly income, no. of comorbidities, type of antidiabetic medication, and random blood glucose level.

**Table 3.** Results of multiple linear regression model for the cubic function of EQ-5D index

	Regression Coefficient (95% CI)	p-value
Non-adherence due to patient behavior (unintentional and intentional)	0.024 (0.014, 0.033)	<0.001
Non-adherence due to additional disease and pill burden	0.021 (0.010, 0.033)	<0.001
Non-adherence due to financial constraints	0.010 (-0.008, 0.030)	0.268
Overall adherence (Cumulative)	0.011 (0.006, 0.016)	<0.001

<sup>#</sup>Adjusted for age, gender, education status, monthly income, no. of comorbidities, type of antidiabetic medication, and random blood glucose level.

Table 3 presents the results of a multiple linear regression, where the cubic function of the EQ-5D index was the outcome variable. The cubic transformation was carried out to achieve the normality assumption. The adjusted regression coefficients with a 95% confidence interval are reported. The estimates were consistent with the results of the logistic model. It suggests that lower adherence due to patient's intentional or

unintentional behavior, low adherence due to due to additional disease or pills burden, and low overall medication adherence were prone to have a lower EQ-5D index. In specific, for a unit increase in overall adherence score, there was an increase of 0.011 units in the cubic function of the EQ-5D index (p-value<0.001).

#### 4. CONCLUSIONS

To the best of our knowledge, the present study was among the few studies conducted to assess the relationship between both the adherence and the quality of life in Saudi Arabia. The survey gathered responses from a considerable number of patients with almost an equal number of male and female participants. The main finding of this study revealed that there is an association between medication adherence and quality of life among patients with diabetes even after taken into account socio-demographic characteristics. That is, subjects with low medication adherence to treatment may have a lower quality of life compared to those with high medication adherence. These findings are consistent with a previous study that was conducted in primary care clinics in Makkah, Saudi Arabia, that found a strong association between medication adherence and quality of life for participants with chronic diseases (Khayyat *et al.*, 2019).

Not surprisingly, the findings showed a low level of medication adherence among participants due to patient behavior and/or due to additional disease and pill burden. These findings are consistent with the previous studies that documented the same results among Saudi patients with diabetes and/or hypertension (Khayyat *et al.*, 2017, 2019). Furthermore, the results revealed that non-adherence to diabetic medications due to financial constraints was not statistically significant, and this might be because Saudi patients have free access to medications and health care services. These findings conflicted with the findings from previous studies (Adisa and Fakeye, 2014; Polonsky and Henry, 2016; Rezaei *et al.*, 2019), which found that the financial barrier was seen among a significant proportion of patients and might have contributed to low adherence.

Overall, a strong positive correlation between adherence to medication and health-related quality of life was observed. The study considered possible confounding factors age, gender, education status, monthly income, no. of comorbidities, type of antidiabetic medication, and

random blood glucose level (Alshayban and Joseph, 2019) and accounted in the analysis using multiple regression modeling. Importantly, it was found that patients who had a high adherence based on behavior-related non-adherence were mostly in perfect health as compared to those with moderate and low adherence who had a compromised quality of life irrespective of their socio-demographic and clinical characteristics. The findings were supported by a previous cohort study that found side effects and forgetfulness as the most common reasons for non-adherence (Krack *et al.*, 2018).

In a German study involving cardiovascular patients, adherence was significantly associated with HRQoL (Krack *et al.*, 2018). Quality of life tended to drop with decreasing adherence to medications. Further, the adjusted odds ratio for perfect health status indicated that patients with low adherence had less than 20% probability of achieving a perfect health status. Furthermore, with a unit increase in adherence score, there was a significant increase in quality of life score. In a study in Lebanon, it was observed that an increase in QoL would translate into an increase in adherence (Farhat *et al.*, 2019).

Besides, patients who demonstrated high adherence in the face of comorbidities and high pill burden were mostly in perfect health ( $p < 0.001$ ). There was no significant association between financial issues and health status ( $p > 0.05$ ). The finding was likely as Saudi patients do not pay out-of-pocket for the health care service. Hence, economic issues are not a determinant of adherence and may not affect the quality of life (AlQarni *et al.*, 2019).

Despite the fact this present study was among the few studies that explore the association between adherence and quality of life for diabetic patients in Saudi Arabia, it has some limitations. Selection bias is frequently linked to convenient sampling. Therefore, since the hospitals were selected based on our convenient accessibility, the generalization of our findings may be limited. Remarkably, some disease characteristics were not included in our analyses (e.g., HbA1c and duration of illness) due to the fact that most of the patients were not exactly able to remember them.

The study found that adherence was directly associated with HRQoL among diabetes patients in Saudi Arabia. The adherence to antidiabetic medications could be improved if patients are counseled regarding the importance of adherence and its repercussions. This could translate into a better quality of life. Finally, the

study might contribute to the growing body of evidence regarding treatment adherence and its impact on the quality of life, and it might provide important information to Saudi decision-makers to develop an effective intervention that can help in improving both adherence and quality of life for diabetic patients in Saudi Arabia.

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