Medication adherence among patients in a chronic disease clinic

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ABSTRACT

الأهداف: تقييم الدافع والمعرفة المرتبطين بنية الالتزام بتناول الأدوية، بالإضافة إلى تحديد مسبباتها لدى مرضى العيادات الخارجية.

الطريقة: أُجريت هذه الدراسة المقطعية بين المرضى الذين يراجعون عيادة الأمراض المزمنة، قسم طب الأسرة والمجتمع، مدينة الأمير سلطان الطبية العسكرية، الرياض، المملكة العربية السعودية وذلك خلال الفترة من يونيو إلى سبتمبر 2010م. لقد تم تقييم نية الالتزام باستخدام مقياس موروسكى المعدل. وتم تحديد مسببات انخفاض الدافع والمعرفة المرتبطين بنية الالتزام بتناول الأدوية باستخدام نماذج الانحدار اللوجستي.

النتائج: لقد قمنا بإجراء المقابلات مع ما مجموعه 347 من المرضى خلال فترة الدراسة. وكانت غالبية المرضى (75.5%) يعانون من مرضين أو أكثر من الأمراض المزمنة، و يتناولون في المتوسط 6.3±2.3 دواء، و6.5 ± 2.9 حبة دواء في كل وصفة. وكان معدل الالتزام المنخفض (4.6%) والمتغير (37.2%) والمرتفع (58.2%). ولقد وجدنا باستخدام الانحدار اللوسجتي المتعدد المتغيرات أن صغر السن ووجود الربو يرتبطان بشكل كبير من الناحية الإحصائية مع انخفاض الدافع، بينما يرتبط كون المريض ذكراً، وعازباً، ولا يعاني من ارتفاع ضغط الدم مع انخفاض المعرفة. كما كانت العزوبية من العوامل المستقلة المرتبطة بالنية المنخفضة للالتزام.

خاتمة: لقد وجدنا أن أكثر من 40% من المرضى الذين يعانون من أمراض مزمنة متعددة، وارتفاع معدل الأمية لديهم نية منخفضة أو متغيرة للالتزام بتناول الأدوية الموصوفة. وقد يساعد تحديد العوامل المرتبطة بذلك بين هذه المجموعة في توفير برامج تدخلية خاصة بكل مجموعة.

Objectives: To assess motivation and knowledge domains of medication adherence intention, and to determine their predictors in an ambulatory setting.

Methods: We conducted a cross-sectional survey study among patients attending a chronic disease clinic at the Family and Community Medicine Department, Prince Sultan Military Medical City, Riyadh, Kingdom of Saudi Arabia between June and September 2010. Adherence intention was assessed using Modified Morisky Scale. Predictors of low motivation and/or knowledge were determined using logistic regression models.

Results: A total of 347 patients were interviewed during the study duration. Most patients (75.5%) had 2 or more chronic diseases with an average of 6.3 ± 2.3 medications, and 6.5 ± 2.9 pills per prescription. The frequency of adherence intention was low (4.6%), variable (37.2%), and high (58.2%). In multivariate logistic regression analysis, younger age and having asthma were significantly associated with low motivation, while male gender, single status, and not having hypertension were significantly associated with low knowledge. Single status was the only independent predictor of low adherence intention.

Conclusion: In a population with multiple chronic diseases and high illiteracy rate, more than 40% had low/variable intention to adhere to prescribed medications. Identifying predictors of this group may help in providing group-specific interventional programs.

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Chronic diseases (CD) are conditions that are persistent (usually more than 3 months), or long-lasting in nature. They tend to be progressive, and may cause mortality and disability. The World Health Organization (WHO) estimated that CDs such as heart disease, stroke, cancer, diabetes, and chronic respiratory diseases are responsible for almost 60% of deaths worldwide. Moreover, the associated mortality are projected to increase by 15%.[1] The Center for Disease Control (CDC) estimated that 25% of Americans with CD suffer from some sort of disability.[2] In the Kingdom of Saudi Arabia (KSA), it was estimated that CDs are responsible for 65,766 deaths (67% of all deaths) in 2004, with cardiovascular diseases including hypertension (37%), cancer (11%), and diabetes (5%) as the main contributors.[3] Chronic diseases rarely resolve spontaneously, and are generally not cured by medication. However, lifetime regular medications are required in many CDs to control symptoms and reduce complication. Many patients with chronic illnesses do not adhere to their long-term therapies. Non-adherence to the prescribed medications among patients suffering from CDs is a worldwide problem of striking magnitude.[4] The WHO estimated that only 50% of patients with chronic illnesses in developed countries adhere to their long-term therapies.[4] The magnitude of the problem in developing countries is even higher. Poor adherence is associated with a wide range of adverse outcomes including higher mortality, and increased hospitalization.[5,6] Moreover, poor adherence results in poor quality of life and increased healthcare costs.[7,8] Many strategies have been described to improve adherence. The key elements in these strategies included patient education and behavioral changes, or both.[9,10] However, no single intervention strategy has been shown to be effective across all patients' conditions, and settings.[11] Therefore, interventions strategies need to be tailored to particular patient groups.[12,13] Assessment of the patients' adherence intentions is critical for the development and implementation of any adherence improvement plans.[12] Self-reported questionnaire to assess the patient's knowledge and motivation to adhere to prescribed medications was used by Morisky and colleagues from mid-1980s.[14] The adherence guidelines of the Case Management Society of America used a modified version of the original Morisky scale.[15] Data regarding medication adherence and its barriers are largely lacking in KSA. Limited and old data showed that almost half of the patients do not adhere to their long term therapies.[16] The KSA is experiencing increased prevalence of CDs concurrent with major socioeconomic developments over the last 2 or 3 decades.[17] The aim of this study was to assess motivation and knowledge domains of medication adherence intention, and to determine their predictors among Saudi patients with CDs using the Modified Morisky Scale (MMS).

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Methods.

Population. This study was carried out among patients attending the CD clinic at the Family and Community Medicine Department, Prince Sultan Military Medical City (PSMMC), Riyadh, Kingdom of Saudi Arabia between June and September 2010. The PSMMC is an approximately 936-bed tertiary care facility that provides healthcare services to approximately 1.3 million Saudi military personnel and their families. The care provided ranged from primary and preventive to tertiary care. The CD clinic is serving approximately 120 CD patients daily.

Eligibility. Male and female adult patients above the age of 18 years with one or more CDs attending the CD clinic at PSMMC during the study period were eligible for the study. Diseases covered included hypertension, diabetes, dyslipidemia, asthma, thyroid disorders, rheumatoid disease, osteoarthritis, and complex chronic disorders. The response rate was 82%, and approximately 5% were excluded. The exclusion criteria included those with diseases that may affect their ability to answer the study questionnaire. These diseases included cognitive impairment, dementia, psychiatric disorders, hearing impairment, and vision impairment. Verification of eligibility was carried out by self-reported and medical records data.

Study design. We conducted a cross-sectional survey study for 3-months duration. Pharmacy students from the pharmacy department interviewed the patients attending the CD clinic using a structured data collection form. The form was pre-tested in Al-Wazarat primary health care center through a pilot study of 30 patients to check for the understandability and language clarity of questions, and all valid comments were taken into consideration in the main survey.

Predictors' data collection. The questionnaire covered the patient's socio-demographic information (age, gender, marital status, and educational level), medical history (the number and type of CDs under treatment),

and medication history (number of medications, and number of pills per prescription).

Outcome data collection. The intention to adhere to prescribed medication was assessed using MMS. The scale consists of 6 questions to assess the motivation and knowledge domains of adherence.[15] Different versions of the scale were shown to be a valid tool of medication adherence.[14,18,19] Questions 1, 2, and 6, which measure forgetfulness and carelessness, are considered to be indicative of motivation (or lack thereof), and consequently impact the motivation aspects of adherence intention. Questions 3, 4, and 5, which measure if patients stop medications and understand the long-term benefits of continued therapy, were considered to be indicative of knowledge (or lack thereof), and consequently impact the knowledge aspects of adherence intention. All questions on the MMS are answered on a "yes" or "no" scale. The MMS scale is used to assign the evaluated patients to a certain quadrant of adherence intention. Those who had both low motivation and knowledge on MMS scale were assigned low adherence intention. Those who had both high motivation and knowledge were assigned high adherence intention. Those who had only low motivation or low knowledge were assigned variable adherence intention.

Study ethics. The study design was approved by the research committee in PSMMC. Patients were enrolled into the study only after obtaining their informed consent, following full explanation of the study design and objectives. Patients' sensitive information were protected during data collection and analysis. All collected data were kept confidential and only for the above stated study purposes.

Statistical methods and sample size. Assuming adherence prevalence of 50%, and equal motivation and knowledge domains of adherence intention, it was estimated that 344 patients will be required to detect 15% difference of a given characteristic (for example, higher education) between each of adherence domains and non-adherence with 80% power, and 95% level of confidence. The frequency of each of the 4 quadrants of adherence intention was estimated. Symmetric association between motivation and knowledge groups (low versus high) was assessed using Gamma statistics. To study the effect on adherence domains of patient's socio-demographic information, medical history, and medication history, we ran univariate (with one variable at a time), and multivariate (with all variables together) logistic regression models with low motivation, knowledge, or adherence as an outcome. Variables selection in multivariate models was carried out using backward stepwise selection. All *p*-values were 2-tailed. A $p<0.05$ was considered significant. The Statistical Package for Social Sciences version 17 (SPSS Inc, Chicago, IL, USA) was used for all statistical analyses.

Results. A total of 347 patients were interviewed during the study duration. Patients' characteristics were shown in **Table 1**. The mean age was 55.2 ± 13.0 years. Those who were ≥45 years represented 78.4%. The patients were 50.7% females, and most were married (95.1%). Most patients were illiterate (54.2%) and only few (6.6%) had university education. A total of 75.5% had 2 or more CDs. Patients were receiving on average of 6.3 ± 2.3 medications per prescription, and 6.5 ± 2.9 pills per prescription. The most common diseases

Table 1 - Demographic, clinical, and prescription characteristics of patients (N=347) attending the chronic disease clinic of Prince Sultan Military Medical City, Riyadh, Kingdom of Saudi Arabia.

Characteristics	Mean ± SD n (%)
Age, years	
Mean ± SD	55.2 ± 13.0
<45	75 (21.6)
45-60	146 (42.1)
>60	126 (36.3)
Gender	
Male	171 (49.3)
Female	176 (50.7)
Educational level	
Illiterate	188 (54.2)
School education	136 (39.2)
University education	23 (6.6)
Marital status	
Single	17 (4.9)
Married	330 (95.1)
Comorbid diseases	
Hypertension	241 (69.5)
Diabetes	282 (81.3)
Dyslipidemia	113 (32.6)
Asthma	52 (15.0)
Thyroid disorders	43 (12.4)
Number of comorbid diseases	
Mean ± SD	2. 1± 0.9
One disease	85 (24.5)
2 diseases	151 (43.5)
3 or more diseases	111 (32.0)
Medications per prescription	
Mean ± SD	6.3 ± 2.3
<median (<6)	178 (51.3)
≥median (≥6)	169 (48.7)
Pills per prescription	
Mean ± SD	6.5 ± 2.9
<median (<7)	171 (49.3)
≥median (≥7)	176 (50.7)

SD - standard deviation

Table 2 - Univariate predictors of low motivation and/or knowledge among patients attending the chronic disease clinic of Prince Sultan Military Medical City, Riyadh, Kingdom of Saudi Arabia.

Variables	Low motivation		Low knowledge		Low/variable adherence	
	Odds ratio (95% CI)	*P*-value	Odds ratio (95% CI)	*P*-value	Odds ratio (95% CI)	*P*-value
Age (10 years increase)	0.73 (0.58-0.91)	0.005	0.94 (0.79-1.13)	0.526	0.88 (0.74-1.04)	0.120
Male gender	0.99 (0.57-1.74)	0.983	2.17 (1.35-3.49)	0.001	1.65 (1.07-2.54)	0.022
Marriage	0.35 (0.12-0.99)	0.048	0.27 (0.10-0.73)	0.010	0.37 (0.13-1.03)	0.058
School education	1.48 (0.83-2.64)	0.183	1.17 (0.72-1.90)	0.528	1.36 (0.87-2.13)	0.178
University education	0.86 (0.24-3.08)	0.813	1.39 (0.56-3.48)	0.476	1.01 (0.42-2.46)	0.978
Comorbid diseases (2)	0.53 (0.27-1.04)	0.064	0.51 (0.29-0.89)	0.018	0.48 (0.28-0.82)	0.008
Comorbid diseases (≥3)	0.63 (0.31-1.28)	0.201	0.40 (0.21-0.73)	0.003	0.42 (0.23-0.75)	0.003
Hypertension	0.45 (0.25-0.80)	0.006	0.54 (0.33-0.87)	0.012	0.47 (0.29-0.74)	0.001
Diabetes	0.69 (0.35-1.35)	0.282	0.84 (0.47-1.51)	0.568	0.74 (0.43-1.28)	0.285
Dyslipidemia	0.81 (0.44-1.50)	0.500	0.67 (0.40-1.11)	0.119	0.67 (0.42-1.07)	0.094
Asthma	2.60 (1.33-5.10)	0.005	0.87 (0.45-1.68)	0.672	1.35 (0.75-2.44)	0.320
Thyroid disorders	1.34 (0.61-2.98)	0.465	0.51 (0.23-1.14)	0.102	0.72 (0.37-1.40)	0.328
Medications per prescription ≥median (6)	0.74 (0.42-1.29)	0.287	0.77 (0.48-1.23)	0.271	0.80 (0.52-1.23)	0.315
Pills per prescription ≥ median (7)	0.85 (0.49-1.50)	0.582	0.86 (0.54-1.36)	0.519	0.81 (0.53-1.24)	0.323

CI - confidence interval

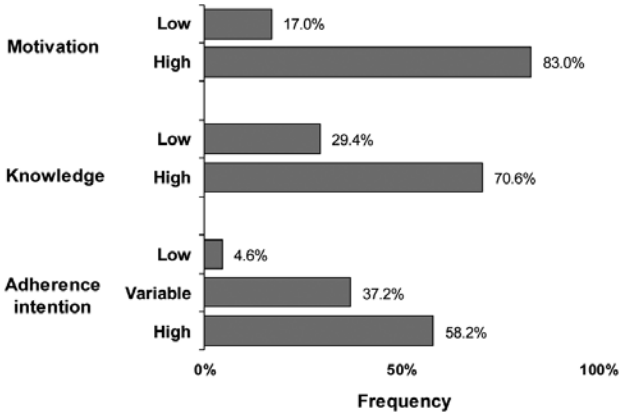

Figure 1 - Distribution of individual questions of adherence domains among patients attending the chronic disease clinic of Prince Sultan Military Medical City, Riyadh, Kingdom of Saudi Arabia.

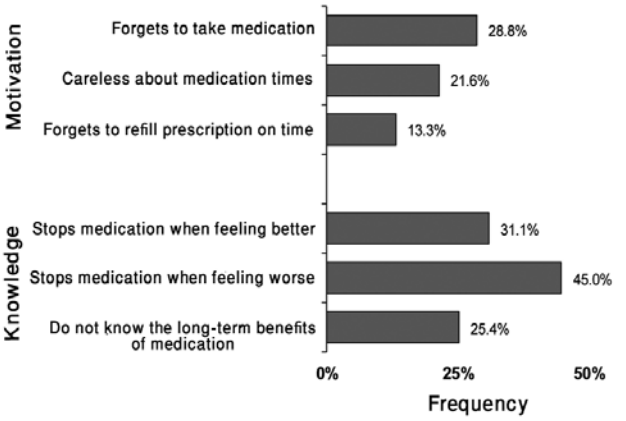

Figure 2 - Distribution of individual questions of Modified Morisky Scale among patients attending the chronic disease clinic of Prince Sultan Military Medical City, Riyadh, Kingdom of Saudi Arabia.

encountered were diabetes (81.3%), hypertension (69.5%), dyslipidemia (32.6%), asthma (15%), and thyroid disorders (12.4%). **Figure 1** showed that the frequency of low motivation was 17.0% (59/347). Those who ever forgot to take their medication were 28.8% (**Figure 2**). There are those who were careless regarding the times of taking their medication (21.6%). Those who sometimes forgot to refill their prescribed medication on time was 13.3%. The frequency of low knowledge was 29.4% (102/347). When feeling better, 31.1% sometimes stopped taking their medication, while 45% sometimes stopped taking their medication if they feel worse. A total of 25.4% did not know the long-term benefits of taking their medication as told by their doctors or pharmacists. There was no symmetric association between motivation and knowledge score groups (Gamma statistics: -0.07, p=0.668). Out of 347, 16 (4.6%) had low, 129 (37.2%) had variable, and 202 (58.2%) had high adherence intention (**Figure 1**). In univariate logistic regression analysis, younger age, single status, having single disease, not having hypertension, and having asthma were significantly associated with low motivation, while male gender, single status, having single disease, and not having hypertension were significantly associated with low knowledge, as well as low/variable adherence (**Table**

Table 3 - Multivariate predictors of low motivation and/or knowledge among patients attending the chronic disease clinic of Prince Sultan Military Medical City, Riyadh, Kingdom of Saudi Arabia.

Variables	Odds ratio (95% CI)	*P*-value
Low motivation		
Age (10 years increase)	0.76 (0.61-0.95)	0.018
Asthma	2.23 (1.12-4.46)	0.023
Low knowledge		
Male gender	2.03 (1.25-3.28)	0.004
Marriage	0.28 (0.09-0.90)	0.032*
Hypertension	0.60 (0.36-0.98)	0.043
Low/variable adherence		
Male gender	1.51 (0.97-2.34)	0.068
Hypertension	0.50 (0.31-0.80)	0.004
Low adherence		
Marriage	0.08 (0.03-0.28)	<0.001

*Using forced analysis otherwise using backward stepwise selection. Removal testing is based on the probability of the likelihood-ratio statistic based on conditional parameter estimates.
CI - confidence interval

2). On the other hand age, educational level, number of medications per prescription, and number of pills per prescription were not significantly associated with adherence intention (**Table 2**). In multivariate logistic regression analysis younger age and having asthma were significantly associated with low motivation, while male gender, single status, and not having hypertension were significantly associated with low knowledge (**Table 3**). Single status was the only independent predictor of low adherence intention.

Discussion. In this study, we report more than 40% low/variable intention of adherence to prescribed medications among Saudi population with multiple CDs and high illiteracy rate. There is a great variability of estimating poor adherence among patients with CDs. Many review reports showed that at least half of patients with CDs do not adhere to their long-term therapies.[4,20] However, much lower rates were also reported.[21] Such variability is partly due to different diseases studied, methodology used, and population covered.[22] Unfortunately, data estimating such rates among patients with CD in KSA are largely lacking. The only local study we were able to retrieve was relatively old, and showed 47% compliance to anti-hypertension medications.[16]

Reviewing the studies examining adherence to chronic treatment published between 1998 and 2007 showed that most of these studies failed to use state-of-the-art methods to measure adherence.[22] We assessed the intention of adherence to prescribed medication using MMS, which is more efficient than the original 4-questions Morisky Scale in assessing patients with long-term continuation of therapy. Although the original Morisky Scale had demonstrated the ability to predict medication poor adherence,[14,23] it was not designed to explain persistence on long-term therapy, which is a significant factor in the long-term management of CDs.[15] Moreover, the lack of the threshold score, or individual question that yielded high sensitivity and positive predictive values necessitates the addition of more questions to improve the scale consistency and predictability. Data describing predictors of non-adherence to treatment of multiple CD is scarce,[24] and largely limited to a single disease.[25-27] Hypertension in the current study was a predictor of high adherence. Adherence to anti-hypertension medication was reported to be between 50% and 70%.[25,28] Lowry et al[25] found that approximately one-third of their hypertension patients were non-adherent to medication, and non-adherence was largely related to medication adverse effects. Moreover, more than three-fourths of this observed non-adherence was unintentional, and was related to low educational level.[25] Patients with asthma in the current study were associated with low motivation. Similarly, several studies reported low adherence to anti-asthmatic medications.[29,30] Moreover, low adherence to prescribed medications was an important factor for treatment failure in these patients.[31] Higher number of chronic diseases in the current study was associated with high adherence in univariate but not multivariate analysis. This univariate finding is difficult to interpret, and was opposite to what was reported elsewhere.[24] For example, a retrospective analysis of huge national pharmacy claims of 6 chronic conditions showed that higher comorbidity score was associated with lower adherence to medications.[24] Although several studies linked medication knowledge to adherence,[28,32] a prospective study among new Medicare enrollees with multiple chronic diseases failed to link education level, nor health literacy to refill adherence. Education level in the current study was not associated with adherence. This finding should be understood in the context that most of our patients were illiterate. Cognitive impairment is frequent among patients with chronic disease,[33] and affect self-reported adherence.[34] Although we excluded those with dementia or psychiatric disorders, we can not exclude the possibility of contribution of psychological problem on the study results.

Several types of interventions are effective in improving medication adherence in chronic medical conditions, but few significantly affected clinical outcomes.[35] Incorporating a behavioral or social support components to education interventions may

increase potential efficacy of the intervention strategy.[9] Physician-patient mutual collaboration is essential to maximize patient satisfaction and adherence.[11] For example, understanding patient's beliefs, attitudes, subjective norms, cultural context, social supports, and emotional health challenges is crucial to the patient's adherence. Identifying predictors of poor adherence the study subjects may help to provide group-specific interventional programs. The Case Management Society of America for improving patient adherence to medication therapies published detailed guidelines for interaction based on patient placement in any given adherence intention quadrant. For example, those with low motivation and/or knowledge may require motivational interviewing, and multiple layers of education for the patients and their family members. On the other hand, those with high motivation and knowledge may only require open-ended discussions, and continued knowledge and motivation reinforcement/support. Clinical pharmacist as being involved now gradually in the ambulatory care of CD patients can play a key role to assess medication adherence, medication understanding, and whether medication non/low adherence is contributing to medication-related problems, or failure to achieve desirable outcomes.

In the current study, we utilized MMS to assess poor adherence, which is convenient to use in a busy CD clinic. The distribution of comorbidity among our patients enabled us to calculate poor adherence rates to polypharmacy typically seen at the CD clinic. However, we acknowledge some limitations of the study. First, non-adherent subjects may have been less likely to participate in study with the possibility of diluting the actual rates. The fact that we used patients' self-reported answers in the absence of family members may result in recall bias, especially with the older age of our patients. However, this should have minimal effect on the study results as we excluded those with dementia. Due to the variability of comorbidity among our patients, the results of this study should be generalized only to Saudi patients attending the CD clinic.

In conclusion, we are reporting a high rate of non-adherence to prescribed medications among Saudi population with multiple CDs. Identifying barriers of such non-adherence may help providing group-specific interventional programs. The results showed that young age, single status, and male gender were especially vulnerable to non-adherence and probably need to be targeted. Suggested strategies to improve patient adherence may include: sending patient-specific reminders (for example, telephone calls) to cover medication use, dose, and side effects; submitting empty medication bottles before getting new ones; running individual rather than group coaching sessions; incorporating both the caregiver and the patient in formulating the treatment plan; and including family in the healthcare decision to best manage the disease.

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