

Review

Adherence to medication among chronic patients in Middle Eastern countries: review of studies

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الالتزام بالعلاج الدوائي بين المرضى المزمنين في بلدان الشرق الأوسط: مراجعة للدراسات

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الخلاصة: استعرض هذا البحث الدراسات التي تقصّت مستوى الالتزام بالعلاج الدوائي بين المرضى المصابين بحالات مزمنة في بلدان الشرق الأوسط. وقد أسفر البحث المستفيض في البحوث المنشورة عن العثور على 19 دراسة ذات صلة بالموضوع، وهي بحوث ركّزت على مقدار ومُنبيئات عدم الالتزام بالعلاج الدوائي في مختلف الحالات، بما في ذلك فرط ضغط الدم، والداء الرئوي المُسدّ المزمن، والربو، والسكري، والاكْتئاب، والفصام، والصرع. وتراوحت المعدلات التقديرية لعدم الالتزام بالعلاج الدوائي من 1.4% إلى 88%. وتؤكد هذه الدراسة على الوجود الفعلي لمشكلة عدم الالتزام بين المرضى المصابين بالأمراض المزمنة، وتنحى مدى إدراكنا للأسباب والمتغيرات التي تؤثر على التزام المرضى بعلاجهم الدوائي في بلدان الشرق الأوسط. إلا أن هذه الدراسات قد استخدمت قطاعاً عريضاً من الأساليب غير المحدودة أحياناً، مما يدل على وجود حاجة لمزيد من العمل لتحديد انتشار وأسباب عدم التزام المرضى بالعلاج الدوائي في بلدان الشرق الأوسط حتى يمكن التوصية بأفضل التدخلات لتحسين مستوى هذا الالتزام.

ABSTRACT This paper reviewed studies that have investigated adherence to medication among patients with chronic conditions in Middle Eastern countries. A comprehensive literature search yielded 19 relevant studies. These focused on the extent and predictors of nonadherence to medication across different conditions, including hypertension, chronic obstructive pulmonary disease, asthma, diabetes, depression, schizophrenia and epilepsy. Estimated rates of nonadherence to medication ranged from 1.4% to 88%. This review confirms the existence of nonadherence as a problem among patients with chronic diseases and examines our understanding about the reasons and variables affecting patients' adherence to their medication in the Middle Eastern countries. However, the studies employed a wide range of methods, sometimes with limitations. Further work to determine the prevalence and causes of patients' nonadherence to medication in Middle Eastern countries is needed in order to recommend the best interventions to improve adherence.

Observance thérapeutique chez les patients atteints d'affections chroniques dans les pays du Moyen-Orient : analyse de plusieurs études

RÉSUMÉ Le présent article a analysé des études ayant pour objet de recherche l'observance thérapeutique chez les patients atteints d'affections chroniques dans les pays du Moyen-Orient. Une recherche exhaustive de la littérature a permis de sélectionner 19 articles pertinents. Ces derniers étaient axés sur l'étendue de la non-observance thérapeutique et les facteurs prédictifs en la matière, par types de pathologies telles que l'hypertension, la bronchopneumopathie chronique obstructive, l'asthme, le diabète, la dépression, la schizophrénie et l'épilepsie. Les taux estimés de non-observance thérapeutique allaient de 1,4 % à 88 %. La présente analyse confirme l'existence d'un problème de non-observance chez les patients atteints d'affections chroniques et présente nos conclusions sur les raisons et variables influant sur l'observance thérapeutique des patients dans les pays du Moyen-Orient. Toutefois, les études analysées ont utilisé un large éventail de méthodes, et présentaient parfois des limites. Une recherche plus approfondie pour déterminer la prévalence et les causes de la non-observance des patients dans les pays du Moyen-Orient est nécessaire pour être en mesure de recommander les interventions les plus efficaces afin d'améliorer l'observance.

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Introduction

Adherence is defined by the World Health Organization (WHO) as “the extent to which a person’s behaviour—taking medication, following a diet, and/or executing lifestyle changes—corresponds with agreed recommendations from a health care provider” [1]. Nonadherence remains a major problem in patient care, despite the large number of research studies that have been conducted in this area in recent decades. Patients’ poor adherence to their medication is a complex problem for health care services, especially in the care of chronic illness, for which the correct, effective treatment is essential for a patient’s quality of life and survival rate. Failure to take the appropriate drug regimen as recommended may lead to poor therapeutic outcomes, wasted health care resources and inappropriate changes to treatment by prescribers.

A report by the WHO estimated that the average rate of adherence to medication is around 50% among patients suffering from chronic diseases in developed countries, and this is assumed to be lower in developing countries where there is limited access to health care and medicines [1]. Although there might be similarities in the rate and reasons for nonadherence in the Middle East compared with the rest of the world, there may also be important differences. This is because reasons for nonadherence are complex. They are affected by operational factors in the health care system (including access to medicines), by relationships between health care professionals and patients, by cultural perceptions about the use of medication and by patients’ beliefs.

The aim of this paper was to review the relevant research into adherence to medication regimens among patients with chronic conditions in the Middle East region. The objectives were to establish the extent to which adherence to medication regimens has been studied in this region of the world, and review

evidence regarding adherence rates, the reasons for nonadherence and the variables found to influence adherence/nonadherence behaviours.

Search strategy

A systematic search of studies related to medication adherence in chronic diseases in the Middle East region was performed using the following databases: EMBASE, MEDLINE, PSYCHINFO, CINAHL, PubMed, International Pharmaceutical Abstracts and the Web of Knowledge. The search terms were: (adherence or compliance AND therapeutic alliance or nonadherence to medication or therapy refusal AND Middle East or United Arab Emirates or Saudi Arabia or Kuwait or Bahrain or Qatar or Oman or Jordan or Egypt), with or without the combination of the keywords: (treatment or regimen). A further search with the Google search engine was carried out to identify all health care and clinical journals in Middle East countries. All journals were searched for relevant papers and the citations of relevant papers were hand searched for further articles.

All the studies were analysed for their findings and the quality of the research. In this review, the definition or classification (level) of adherence, study setting, population and sampling, methods of data collection and measurement of adherence were taken into account.

Results

A total of 19 studies were identified from all regions of Middle East (Table 1): Egypt (4 studies), Sudan (1), Libyan Arab Jamahiriya (1), Saudi Arabia (6), Kuwait (3), United Arab Emirates (1), Palestine (1), Turkey (1) and Pakistan (1). Of the studies 17 were conducted among adult populations and 2 among children [2,3].

The studies focused on different disease and illness groups, including hypertension [4–10], diabetes [11–14], mental illness [15–17], asthma [3,18], epilepsy [2,19] and chronic obstructive pulmonary disease [20]. They were conducted in primary health care centres, outpatient clinics and diabetes centres.

The sample sizes ranged from 104 to 1000, with a median of 278 patients.

Measures employed for data collection on adherence to medication

Adherence to medication was measured using self-reports, pill counts and outcome measures. Almost all of the studies (17 of 19) used patients’ self-reporting either alone [2–7,11,12,14,17,18,20] or combined with other methods, especially pill counts [8,9,13,15,16]. In one study of epileptic patients pill counts only were used [19] and in another study of hypertensive patients pill counts were combined with blood pressure measurements [10].

In 12 studies self-reports were obtained using structured questionnaires [2–6,9,11,12,14,17,18,20]. Two studies [4,5] used a previously validated measure: the Morisky medication adherence scale [21]. However, in 1 of these studies [4] details were not provided on the translation or cross-cultural validity of the tool. In another 2 studies, the authors reported that they had adapted a questionnaire from earlier relevant published studies [18] or from a medical textbook [6], but details of this adaptation process were not provided.

In 7 studies, respondents were directly asked about their adherence to medication, e.g. the total number of tablets they had been prescribed per week and how many pills they took and missed in the last 3, 5 and 7 days [4] or previous month [7] or whether they had taken their medication as directed by the physician [13,15,16,19]

or whether they were taking their drugs regularly or not [8].

In 4 studies, questionnaires were administered by the patient's physician [3,11–13].

Definition or classification (level) of adherence/nonadherence

Different definitions of adherence or nonadherence were employed; 14 studies provided information on these definitions.

In 6 studies patients were considered to be adherent if they reported taking $\geq 80\%$ of their doses as prescribed [4,5,8,10,15,16]. In a further study the cutoff used was 75% [14]. In another study, adherent patients were those who used their medication correctly (knowledge about at least 2 of their bronchodilator medication doses and correct inhalation technique) and regularly (every day) [20]. In 1 study the doctors made a judgement about patients' compliance based on their answers to questions, the details of which were unspecified in the paper [3].

Conversely, nonadherence was defined variously as: missing a total of 1 day of doses/week [2], or $< 90\%$ of their pills [7], or 4 doses per month [13] or a total of 3 days' doses/month [19]. One study did not report actual values but instead defined nonadherence as "failure to take medications as prescribed for a period greater than a week" [17].

Adherence/nonadherence rates

Overall, the estimated rates of nonadherence to medication in these Middle East countries ranged from 1.4% and 88% in the different studies. Studies in which questionnaires were completed by the patient's physicians tended to report low nonadherence rates compared with the other studies [3,11,13,15]. In one study in which data on adherence were collected both by patients' self-reports and by physicians, the physicians overestimated the level of their patients'

adherence to medication; physicians estimated the nonadherence rate as 29%, whereas patients' self-reports gave an estimate of 48% [5].

Within the same illness group, 7 studies among hypertensive patients reported medication nonadherence rates between 23% and 49.5% and 4 studies among diabetic patients reported nonadherence rates between 1.4% and 27.1%. However, 2 studies conducted with patients with depression reported nonadherence rates of 24% to 30% in one study [16] and 88% in another [15].

Reasons for nonadherence

A wide range of reasons were given by patients for nonadherence to medications. These included: forgetfulness [2,7,10,15,18,19], drug side-effects [7,10,15,17,19], wanting a "drug holiday" [7], concerns about drug dependency [15,17], feeling well [7,10,15,18], medication was not helping them feel better [15,18], irregularity of follow-up [9], lack of health education [10], shortage of drugs [10,19], unawareness of the chronicity of the disease [20], busy parents [2], not having been told to continue the treatment [19], disbelief about the value and need for adherence [19], social stigma [17], complexity of the treatment regimen [17], inability to see their usual doctor [15], only using the medication as needed [18], feeling better (with bronchodilators) [18], inability to afford the drugs [8] and feeling lazy [18].

Discussion

The results of this review indicate that, as elsewhere in the world, there is a problem of nonadherence to medication among patients with chronic conditions in a number of Middle Eastern countries. However, caution must be taken before drawing a conclusion about the rate of nonadherence due to the wide discrepancy in the estimates

of nonadherence rates between these studies, which varied from 1.4% to 88%. This variation could be due to the different disease conditions studied, different patient populations, differences in the definitions of adherence/nonadherence to medications used or to differences in the methods employed. All methods of measurement have their advantages and limitations and therefore there is no "gold standard" for the assessment of adherence.

The nonadherence rate was higher among hypertensive patients than those with diabetes, which could be due to the nature of hypertension disease (asymptomatic) or to different perceptions of the seriousness of the condition. Also findings from a small number of studies must be viewed with caution. This is supported by the international literature, as WHO reports [1] that estimates of the extent to which patients adhere to pharmacotherapy for hypertension vary from 50%–70%, compared with an estimated 36%–93% adherence to hypoglycaemic agents [22].

The 4 studies where interview-based questionnaires were administered by physicians reported lower nonadherence rates compared with other studies, ranging from 1.4% to 27.1% [3,11–13]. This could be as a result of patients exaggerating their degree of medication adherence to their treating physician for fear that admitting poor adherence would affect the quality of care they would receive or to gain their physician's approval.

Many variables were suggested to affect patients' adherence to their medication (Table 1), but there were some contradictory results. For example, in 2 studies nonadherence was shown to be higher in younger patients [9,17] and in 1 study it was higher in older age groups [10].

The reasons reported by patients for nonadherence to their medication varied across the studies but the 2 most frequently reported reasons were

Table 1 Studies of adherence/nonadherence to chronic medication in Middle Eastern countries

Study/setting/ country	Sample	Definition of patients' adherence/ nonadherence	Methods/ measures	Study findings and conclusions
Al-Faris et al. 2002 [2] Outpatient clinics, Saudi Arabia	147 children with epilepsy	Noncompliant: missed a total of 1 day doses/week	Cross-sectional study Adherence to medication measured by patients' self-report using detailed questionnaire	14% of patients noncompliant with medication Variable linked to noncompliance: type of seizures Variables <i>not</i> linked to noncompliance: age; nationality; sex; family size; area of residence; frequency of medication; side-effects of medication
Bassili et al. 1998 [3] Outpatient clinics, Egypt	250 children with bronchial asthma	Compliant, poorly compliant or noncompliant (physicians' judgement)	Cross-sectional study Adherence to management measured using questionnaire filled by physicians	2.8% of patients poorly compliant or noncompliant with symptomatic management during acute attacks.38.4% poorly compliant or noncompliant with prophylactic management
Hashmi et al. 2007 [4] Outpatient clinics, Pakistan	438 patients with hypertension	Adherent: took ³ 80% of doses as prescribed	Cross-sectional study Adherence to medication measured by 2 self-report methods: total number of tablets prescribed/ week and how many pills taken and missed; Morisky scale [21]	23% of patients noncompliant with medication. Variables linked to noncompliance: increasing age; better awareness; higher number of pills prescribed. Variables <i>not</i> linked nonadherence: depression.
Fahey et al. 2006 [5] 2 primary health care (PHC) centres, UAE	203 patients with hypertension	Noncompliant: took < 80% of doses correctly	Cross-sectional study Adherence to medication measured by: 7-item questionnaire modified from Morisky scale [21] to determine patients' adherence; and 10-item questionnaire to elicit physician's estimate of patients' adherence	Nonadherence: patients' self-report) 48%; physicians' estimate 29% Nonadherence (patients' report): negatively correlated with: achieving target blood pressure; and positively correlated with physician's evaluation of seriousness of disease Nonadherence (physicians' estimate): negatively correlated with treatment effectiveness: patients' knowledge, communication quality; seriousness of condition
Baune et al. 2004 [6] Outpatient and PHC clinics, Palestine	336 patients: case group of 112 with acute stroke and hypertension and control group of 224 with hypertension only	No clear classification	Case-control study. Adherence to medication measured using questionnaire	25% of case patients noncompliant 4.5% of control patients noncompliant
Youssef and Moubarak, 2002 [7] PHC centres, Egypt	316 patients with hypertension	Fully compliant: no doses missed Partially compliant: took ³ 90% of doses Noncompliant: took < 90% of doses	Cross-sectional study Adherence to medication measured by patients' self-report using questionnaire	22.2% of patients partially compliant and 25.9% noncompliant Variables linked to noncompliance: education level; complications related to hypertension; side-effects; smoking; restriction of dietary salt and fat; knowledge about nature of disease; associated complications and ideal management plan; perception of benefits of adherence to treatment; blood pressure control; susceptibility to unfavourable events related to hypertension Variables <i>not</i> linked to noncompliance: patients' demographic characteristics; duration of the original illness; presence of coexisting health problems; number of hypertensive drugs; frequency of dose; patients' perception of danger of original disease; compliance to ideal exercise and ideal body weight

Table 1 Studies of adherence/nonadherence to chronic medication in Middle Eastern countries (continued)

Study/setting/ country	Sample	Definition of patients' adherence/ nonadherence	Methods/measures	Study findings and conclusions
Elzubier et al. 2000 [8] Outpatient clinic, Sudan.	198 patients with hypertension.	Noncompliant: took < 80% of pills.	Cross-sectional study. Adherence to medication measured by: patients' self-report of whether taking medication regularly or not; pill counts; and verified by blood pressure measurement.	49.5% of patients noncompliant (40% with the pill count method). Variables linked to noncompliance: inability to buy drugs; asymptomatic nature of hypertension; complications of hypertension; blood pressure level. Variables <i>not</i> linked to noncompliance: lack of belief in drugs; side-effects from drugs; number of drugs taken; dosage regimen.
Al-Sowielem and Elzubier, 1998 [9] 4 PHC centres, Saudi Arabia.	190 patients with hypertension.	No clear definition of adherence.	Cross-sectional study. Adherence to medication measured by: patients' self-report using a questionnaire; and verified by therapeutic outcome (diastolic blood pressure > 90 mmHg).	25.3% of patients noncompliant based on self-report and 65.8% based on therapeutic outcome (diastolic blood pressure). Variables linked to noncompliance: irregular follow-up; younger age; better educated. Variables <i>not</i> linked to noncompliance: sex; nationality; difficulty with compliance; presence of other diseases; continuity of care with same physician; preference of place of care; number of drugs taken for hypertension; mode of diagnosis of hypertension.
Khalil and Elzubier, 1997 [10] 5 PHC centres and 2 outpatient clinics, Saudi Arabia.	347 patients with hypertension.	Pill count (average of 2 visits 3 weeks apart). Noncompliant: took < 80% of medications, based on the average.	Cross-sectional study. Adherence to medication measured by: pill count; and verified by blood pressure measurement.	47% of patients noncompliant. Variables linked to noncompliance: age; sex (female); nationality (Saudi Arabian nationals had higher noncompliance); duration of disease; presence of complications; follow-up in PHC rather than hospital; side- effects; duration of treatment; number of drugs; education about disease offered by health care provider; illness-associated symptoms.
Roaeid & Kablan, 2007 [11] Diabetes centre, Libyan Arab Jamahirriya.	805 patients with diabetes (type 1 and 2).	No clear definition or classification.	Cross-sectional study. Adherence to treatment measured by patients' self-report through interviews and questionnaire filled by physicians.	27.1% of patients not taking treatment regularly.
El-Shazly et al. 2000 [12] 14 outpatient clinics and diabetic centres, Egypt.	1000 patients with diabetes (type 1 and 2).	No clear definition or classification.	Cross-sectional study. Adherence to medication measured using questionnaire filled by physicians.	11.4% of patients noncompliant (15.1% in non-health insured patients and 5.7% in health insured patients). Variable linked to noncompliance: not having health insurance.
Khattab et al. 1999 [13] PHC centre, Saudi Arabia.	294 patients with diabetes (type 1 and 2).	Compliance: good - took medications as prescribed; fair - missed 1-3 doses/month; poor - missed 4 doses/month	Cross-sectional study Adherence to medication measured by: self-report questionnaire filled by physicians (diabetic follow-up card); and pill count	1.4% of patients had poor compliance, 14% fair compliance and 84.2% good compliance. Variables <i>not</i> linked to noncompliance: sociodemographic characteristics of patients; care characteristics; and disease characteristics.

Table 1 Studies of adherence/nonadherence to chronic medication in Middle Eastern countries (continued)

Study/setting/ country	Sample	Definition of patients' adherence/nonadherence	Methods/measures	Study findings and conclusions
Kamel et al. 1999 [14] Diabetic clinic, Egypt	300 patients with diabetes (type 1 and 2)	Poor compliance: took < 50%. Satisfactory compliance: took 50%-75%. Very good compliance: took > 75% of medications	Cross-sectional study Adherence to medication measured by patients' self-report using a questionnaire	1.7% of patients had poor, 20% satisfactory and 78.3% very good compliance Variables <i>not</i> linked to noncompliance: use of insulin injections, medication names and medication types.
Al-Saffar et al. 2005 [15] Outpatient clinic, Kuwait	278 patients with depression	Noncompliant: took < 80% of expected pill count <i>and</i> self-reported failure to take medication as prescribed	Educational interventional study Adherence to medication measured at 2 months and 5 months by patients' self-report and tablet count	88% of patients nonadherent in the control group at both follow-ups. Variables <i>not</i> linked to noncompliance: concern that therapy would impose restrictions on patients' lifestyle or have an adverse affect on their work; patients' belief that their physicians really understood the nature of their problem; and side-effects of medications.
Al-Saffar et al. 2003 [16] Outpatient clinic, Kuwait	176 patients with depression	Good compliance: divergence from prescribed treatment time. Noncompliance: self-reported failure to take medication as directed	Cross-sectional study Adherence to medication measured by: patients' self-report; and prescription refill adherence	30% of patients noncompliant (via pill counts) and 24% (via self-report) Variables linked to noncompliance: underlying intention to take medications; little or no confidence that symptoms were amenable to medical intervention; views about whether depression was more of a psychological than a medical problem; female sex; belief that depression was a disease best treated by medication; concern about the addictive nature of therapy; and uncertainty whether or not physicians can do anything to help Variables <i>not</i> linked to noncompliance: patients' characteristics and side-effects of medication
Fido and Hussein, 1998 [17] Outpatient clinic, Kuwait	120 patients with psychiatric problems	Nonadherent: failure to take medication as prescribed for > 1 week	Cross-sectional study Adherence to medication measured by patients', caretakers' or relatives' self-report using questionnaire (checklist)	55% of patients prematurely discontinued medication Variables linked to non-compliance: male sex; previous multiple hospital admission; diagnosis of schizophrenia and mania; age; being single; and educational level
Al-Jahdali et al. 2007 [18] Outpatient clinic, Saudi Arabia	334 patients with asthma	No clear definition or classification	Cross-sectional study Adherence to inhaled corticosteroids measured by patients' self-report through structured questionnaire interviews	38% of patients noncompliant Variables linked to noncompliance: education; negative perception of the role of inhaled corticosteroids in management of bronchial asthma; and negative perception regarding inhaled corticosteroids safety e.g. leading to addiction Variables <i>not</i> linked to noncompliance: duration and severity of asthma

Table 1 Studies of adherence/nonadherence to chronic medication in Middle Eastern countries (concluded)

Study/setting/ country	Sample	Definition of adherence/ nonadherence	Methods/measures	Study findings and conclusions
Jabbar and Al-Shammari, 1993 [19] Outpatient clinic, Saudi Arabia.	104 patients with epilepsy	Noncompliant: missed a total of 3 day's doses/ month	Cross-sectional study Adherence to medication measured by pill count	30.8% of patients noncompliant Variables linked to noncompliance: educational level; and adverse effects of disease on patients' academic performance Variables <i>not</i> linked to noncompliance: sex; marital status; age; family history of disease; duration of disease; type of the epilepsy; level of control; and therapeutic regimen
Gulbay et al. 2006 [20] Outpatient clinic, Turkey	140 adults with chronic obstructive pulmonary disease	Used medication "correctly": patients who had correct knowledge on ≥ 2 of their bronchodilator doses & who used convenient inhalation technique Used medication "regularly": patients who said they took medication every day. Adherent: used medication correctly and regularly	Cross-sectional study Adherence to medication measured by patients' self-report using questionnaire	10%–20% of patients did not use medication correctly and regularly Risk of poor adherence by increased 44.4 fold with: lower educational level; female sex; unawareness of chronicity of disease; and being uninformed

forgetfulness (6 studies) and drug side-effects (5 studies). The reasons reported by patients in the Middle East are similar to those reported in the international literature. However, some common reasons reported by the international literature were not reported by these patients, such as patient satisfaction and/or lack of trust in health care providers and lack of social support. The reason for this could be that patients in the Middle East may be more afraid to complain about their doctors in order to avoid problems that might compromise their treatment. These studies were not designed to explore barriers to medication adherence (intentional/nonintentional) and beliefs about the perceived value of medication and concerns regarding side-effects. There is a need for a more qualitative approach to explore how factors such as the context of the health care system, access to medication and beliefs affect nonadherence to medication for patients with chronic illness in the Middle East.

Limitation of the review

The literature search found only 1 article through databases searches and the rest were found by hand searching. Therefore some relevant papers in this field could have been missed. Although most of the journals in the Middle East publish in English language, studies published in other languages may have been missed papers as only English language papers were included in the search.

Conclusions

This review confirms the existence of nonadherence to medication as a problem among patients with chronic diseases in the Middle East. However, there was great variation in the reported rates of nonadherence, probably due to differences in the definitions of adherence/nonadherence used as well as other differences in the study methods. Some barriers and predictors of nonadherence among patients in this region were identified. However, these 19 studies did not enable meaningful conclusions regarding level of adherence to be drawn. The review findings highlight the need to expand this area of research in the region and to improve the quality of such research. Therefore, there is a need for further research on the rate of nonadherence and barriers to patients' adherence to their medications in order to identify the type of interventions that may be needed for improving adherence.

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