



Factors Associated with Antidepressant Medication Non-adherence

Antidepressan İlaç Uyumçuzluęu ile İliřkili Faktörler

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ABSTRACT

Medication non-adherence is one of the major problems in treating patients with depression. Non-adherence results in an increased risk of relapse and reduced quality of life. The objective of this review was to review and summarize studies that focused on the factors associated with antidepressant medication non-adherence in patients with depression. Literature searches were performed using PubMed/Medline and Google Scholar. The search was limited to articles published in the English language in peer-reviewed journals between January 2000 and December 2019. Studies that analyzed factors of non-compliance in patients with depressive disorders were included in the review.

Patient-related factors such as forgetfulness, comorbidities, and misconceptions about the disease and medication, medication-related factors, polypharmacy, side effects, pill burden and cost, healthcare system-related factors, including physician-patient interactions, sociocultural factors such religious and cultural beliefs and stigma, and logistic factors were found to be the major factors associated with antidepressant non-adherence. Efforts should be made to increase patient adherence to antidepressants by strengthening physician-patient relationships, simplifying medication regimens, and rectifying myths and beliefs held by patients with scientific information and explanations.

Key words: Adherence, antidepressants, depression, associated factors

ÖZ

İlaç uyumsuzluğu depresyon için hastaları tedavi ederken karşılaşılan önemli sorunlardan biridir. Uyumsuzluk relaps riskini artırır ve hayat kalitesini düşürür. Bu derlemenin amacı depresyonu olan hastalarda antidepressan ilaçlara uyumsuzluk ile ilgili çalışmalarını değerlendirmek ve özetlemektir. Literatür araştırması PubMed/Medline ve Google Scholar kullanılarak yapılmıştır. Araştırma Ocak 2000 ile Aralık 2019 arasında İngilizce olarak bağımsız değerlendirme yapan dergilerde yayınlanan makalelerle sınırlandırılmıştır. Depresif bozukluğu olan hastalardaki uyumsuzlukla ilgili faktörler analiz eden çalışmalar derleme kapsamına alınmıştır. Antidepressan uyumsuzluęundaki önemli hasta ile ilgili faktörlerin unutma, komorbidite, hastalık ve ilaç hakkında yanlış bilgisi olma; ilaçla ilgili faktörlerin polifarmasi, yan etkiler, ilaç yükü ve tutarı; saęlık sistemiyle ilgili faktörlerin hekim-hasta ilişkileri ve sosyo-kültürel faktörlerin dini ve kültürel inançlar, ayıplama ve mantıksal faktörler olduęu bulunmuştur.

Antidepressanlara uyumu artırmak için hekim-hasta ilişkilerini güçlendirmek, dozlama rejimlerini basitleştirmek ve bilimsel enformasyon ve açıklamalarla hastalardaki mit ve inançları düzeltmek gibi konularda gayret gösterilmelidir.

Anahtar kelimeler: Uyum, antidepressanlar, depresyon, ilgili faktörler

INTRODUCTION

Depression has become a major public health concern with an increased prevalence and global disease burden due to the associated mental, social, and interpersonal dysfunction.¹ According to the World Health Organization, by 2020, depression will be the second-highest known cause of disability worldwide.² It is characterized by a sad mood, pessimistic thoughts, lowered

interest in day-to-day activities, poor concentration, insomnia or increased sleep, significant weight loss or gain, decreased energy, continuous feelings of guilt and worthlessness, decreased libido, and suicidal thoughts occurring at least once every two weeks.^{1,3} Antidepressant drugs are the most effective and widely used forms of treatment for depression.⁴ Despite the availability of many effective antidepressants, 50% patients do

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not achieve a complete cure of symptoms and even experience recurrence.^{5,6} Therefore, in many patients, depression becomes a chronic disorder and may require lifelong antidepressant treatment. For the desired treatment outcome, adherence to antidepressant medication plays a crucial role, and non-adherence is the key problem associated with antidepressant treatment. Adherence has been defined as “the extent to which a person’s behavior regarding taking medication, following a diet, or executing a lifestyle (change) corresponds with recommendations from a healthcare provider”.⁷ The failure of patients to follow medical advice results in a risk of relapse and reduced quality of life. Many factors, be they patient, medicine, health system, or social and cultural factors, all are associated with patient non-adherence to prescribed antidepressants. Hence, this study was conducted to review and summarize studies focused on the factors associated with antidepressant medication non-adherence in patients with depression.

METHODS

Data sources, literature search, and selection

A comprehensive literature review was conducted using PubMed/Medline and Google Scholar. The search was limited to articles published in the English language in peer-reviewed journals between 2000 and 2019. The keywords used for the article search were depression, depressive patients,

antidepressant, antidepressant adherence, patient compliance, and discontinuation of antidepressants. We also included articles listed in the author’s reference lists and those listed in other systematic reviews. Studies were selected on the basis of relevance. Full articles on those studies that were deemed relevant to our study title were fully reviewed. This study is a narrative review and does not include any statistical analysis (Figure 1).

Study selection

For inclusion in our review, studies must have included adult or elderly patients, irrespective of gender, diagnosed with depression, and prescribed antidepressants by physicians. Literature could be of varying methodologies i.e. observational, prospective, cross-sectional, retrospective, or survey.

Our study outcomes were the factors that caused non-adherence to antidepressants among patients with depressive disorder. Studies that did not meet our criteria were excluded during the review. Studies were discarded if they were clinical trials or reviews.

RESULTS

One hundred fifty-five articles were selected by title/abstract; finally, 21 articles were included. Table 1 shows the main findings of these studies. Two studies were performed in Ethiopia,⁸⁻¹¹ one in Nepal,⁹ one in Malaysia,¹⁰ one in Island,¹²

Data screening and extraction

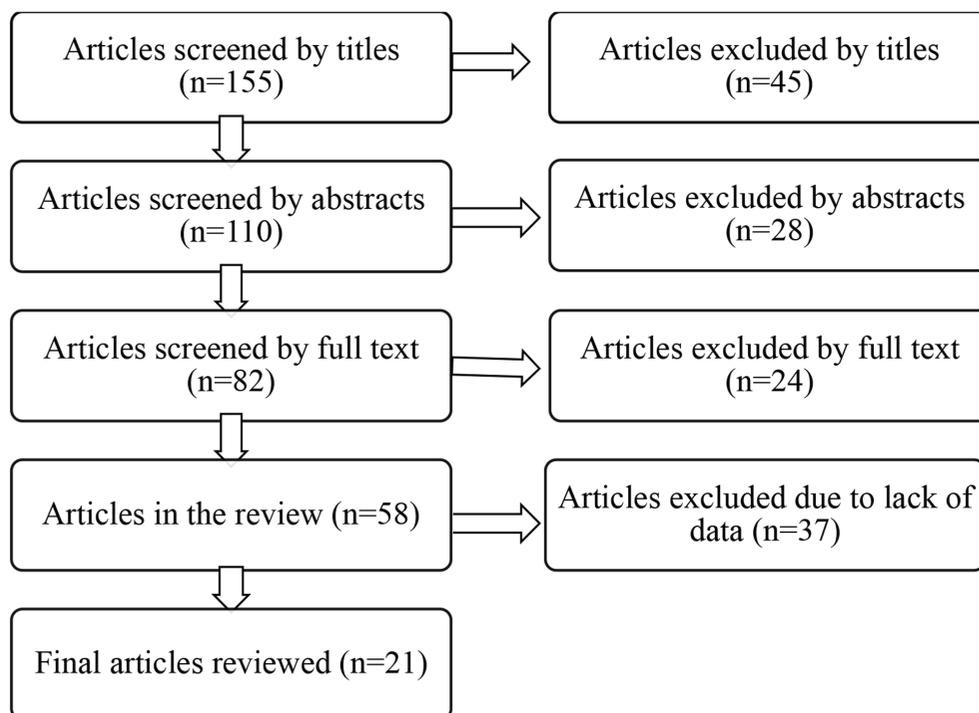


Figure 1. Data screening and extraction

Table 1. Objectives, methods, and major findings of the included studies

Study	Objective	Methodological review	Major findings
Woldekidan et al. ⁸	To determine the patient satisfaction level and factors associated with psychiatric outpatient care	Institution-based cross-sectional study n=250 Age: ≥18 years Structured questionnaires used to collect data	Unsatisfied patients: 69.2% factor associated: Insufficient information on disease condition and drugs from healthcare professionals
Shrestha Manandhar et al. ⁹	To determine the medication adherence pattern and factors associated with non-adherence	Hospital-based prospective study n=60 Age: >18 years Structured questionnaire for demographic details and medication adherence pattern	Only 37% were adherent. Factors in non-adherence: Forgetfulness, occupation of patients, cost of medicine, treatment duration, occurrence of adverse effects, patients' perception toward disease and drug, physician-patient relationship, and availability of medication
Ho et al. ¹⁰	To determine the facilitators and barriers to antidepressant adherence among outpatients with MDD	Qualitative study n=30 Age: ≥18 years Semi-structured and individual in-depth interviews were conducted	Facilitators: perceived health benefits, regular activities, effective patient-provider relationships, and social support networks. Barriers: Incorrect beliefs about disease or medications, forgetfulness, negative attitudes, insufficient knowledge, and comorbidities
Abegaz et al. ¹¹	To determine the level of antidepressant adherence, clinical outcome, and magnitude of ADRs	The hospital-based prospective cross-sectional study n=217 Age: ≥18 years MMAS-8 was used	Low medication adherence was present in 57.1% of patients. Factors affecting adherence: Long-standing depression, distance from the follow-up clinic, and comorbid psychiatric illness
Telinoiu ¹²	To measure adherence to antidepressant medication	Retrospective cohort study n=22,977 Age: 18-75 years Health Plan Employer Data and Information Set, and the proportion of days covered, to measure adherence	Adherent group: Older patients (aged ≥50 years), high economic status, females, patients with more follow-up visits, and patients with comorbid conditions such as diabetes, cardiovascular, respiratory, and mental illness
Lu et al. ¹³	To determine the beliefs associated with antidepressants and associated adherence among older Chinese patients with major depression	Cross-sectional survey n=135 Age: >60 years MMAS, to measure adherence	Factors in non-adherence: Forgetfulness, discontinuing medications when feeling well, concern for long-term effects and addiction, and high-income respondents
Alekhyia et al. ¹⁴	To determine the sociodemographic factors that influence compliance with the treatment of depression	Cross-sectional study n=103 Age: >18 years Questionnaire format (for sociodemographic factors)	Non-adherent group (majority): 21-50 years of age, males, unmarried, low socioeconomic status, and a high level of education
Al Jumah et al. ¹⁵	To determine antidepressant adherence and the factors associated with it	Non-experimental cross-sectional study n=403 Age: 18-60 years Used the MMAS	Factors in low adherence: Specific belief concerns, general harm, overuse beliefs about antidepressant medications and younger age (<40 years). More psychiatrist follow-up visits, effective physician-patient contact, and patient satisfaction increased adherence in patients
Serrano et al. ¹⁶	To determine the adherence level and to analyze the sociodemographic factors and clinical profiles involved in adherence	Longitudinal observational study n=29 Age: ≥18 years Sociodemographic and clinical variables questionnaire, Simplified Medication Adherence Questionnaire, were used	Factors addressing compliance: Awareness of illness, positive attitude toward drugs, and tolerability (in particular regarding the side effects of medication)
Sultana et al. ¹⁷	To determine the rate and predictors of antidepressant treatment discontinuation in depressed older patients	Population-based study n=39,557 Age: ≥65 years A nationwide Italian general practice "Health Search" database was used	Predictors of discontinuation of antidepressants: Polypharmacy, use of other classes of antidepressants other than SSRIs due to intolerance

Table 1. Continued

Study	Objective	Methodological review	Major findings
De las Cuevas et al. ¹⁸	To determine the risk factors for antidepressant non-adherence	Population-based cohort study n=145 Age: ≥18 years The Morisky self-report scale was used to assess adherence	Factors associated with non-adherence: Negative attitude of patients toward their treatment, increased severity of depression, and the presence and severity of side effects
Banerjee and Varma ¹⁹	To determine treatment non-adherence among patients with unipolar depression	Cross-sectional study n=239 Age: 18-60 years The MMAS was used	Non-adherent patients: 66.9% non-adherent group: Women (three times more than men), low socioeconomic status, lack of awareness about diagnosis, and inappropriate intake of medication
Jeon-Slaughter ²⁰	To determine the effect of patients' income on selective SSRI non-adherence	Population-based study n=280 Age: 18-64 years The National Comorbidity Survey-Replication was used	Factors leading to non-adherence: Low income level combined with lack of health insurance, African Americans vs Whites, and major depressive episode comorbidity
Fawzi et al. ²¹	To determine antidepressant adherence in older patients in relation to their beliefs and Knowledge about these medications	Population-based study n=108 Age: >55 years The MARS and a Global Adherence Measure was used	Older patients are more likely to adhere to medication. Potential predictors of adherence: Sociodemographic, medication, and illness variables. Reasons for non-compliance: Insufficient knowledge about the prescribed medication
Park et al. ²²	To determine the factors associated with treatment-seeking in respondents with MDD	Population census n=362 Age: 18-64 years Data used from the Korean Epidemiologic Catchment Area study	Factors affecting treatment-seeking by individuals: Sociocultural factors such as misconception and stigma, severity of depression and comorbid conditions like anxiety, and obsessive-compulsive disorder
Tamburrino et al. ²³	To survey antidepressant adherence among primary care patients so as to better understand the factors associated with non-adherence	Survey n=148 Age: ≥18 years The Medication Adherence scale and the Medical Outcome study were used to measure adherence	The majority were female. Factors on non-adherence: Young age (<40 years), carelessness about taking medications, consciousness of side effects, dissatisfaction with physicians, and patients' demand for a specific antidepressant
Sawada et al. ²⁴	To determine the persistence and compliance with antidepressant drugs	Retrospective study n=367 Age: 16-82 years Medication Possession Rate was used	Persistent and compliant group: Older people, males, and sertraline users
Taj et al. ²⁵	To determine the predictors of non-adherence among psychiatric patients	Questionnaire-based cross-sectional study n=128 Age: ≥18 years A 19-item questionnaire was used	Mean age of patients: 39.49 years. Reasons for non-adherence: Comorbid condition, sedation, high medication cost, forgetfulness, and insufficient patient information
Russell and Kazantzis ²⁶	To determine belief and antidepressant adherence in primary care	Prospective study n=85 Age: 18-65 years The Beliefs about Medication Questionnaire and MARS were used	Reasons for antidepressant adherence: Patients were aware of the need for medication and had fewer symptoms of depression
Yeh et al. ²⁷	To determine the predictors of antidepressant adherence among depressive patients	Cross-sectional study n=181 Age: 23-61 years A self-report questionnaire was used to collect data	Predictors of adherence: Treatment efficacy, severity of depression, mental health professional-patient interaction, awareness of the need to continue medication, social support, and patient income. Negative beliefs and perceptions decrease medication adherence
Ashton et al. ²⁸	To identify the reasons for non-compliance with antidepressant medications	Survey n=344 Age: 18-65 years A 42-question survey was used	Treatment discontinuation: 60% of patients. Reason for non-compliance: Trouble remembering to take the drug, weight gain, inability to have an orgasm, and loss of interest in sex

MDD: Major depressive disorder, ADRs: Adverse drug reactions, SSRI: Selective serotonin reuptake inhibitor, MMAS: Morisky Medication Adherence scale, MARS: Medication Adherence Rating scale

two in China,^{13,27} two in India,^{14,17} one in Saudi Arabia,¹⁵ two in Spain^{16,19}, one in Italy,¹⁸ three in the United States,^{20,23,28} one in the UK,²¹ one in Korea,²² one in Japan,²⁴ one in Pakistan,²⁵ and one in New Zealand.²⁶

DISCUSSION

a. Sociodemographic factors

From this review, it was observed that the majority of patients who were non-adherent to their prescribed antidepressants were younger patients aged <40 years.^{15,21,23} Non-adherence among younger patients could be due to having less experience with depression and associated medications. In contrast, older patients may have more experience with depressive episodes and antidepressants, which makes them more willing to complete their prescribed doses.^{15,23} Additionally, antidepressants are associated with common side effects such as weight gain and impaired sexual function, which may make it troublesome for younger patients to adhere to antidepressant drugs.^{15,21,23,29-31}

Female patients were found to be less adherent to prescribed antidepressants than males.^{19,23,24,32} Women play multiple roles in the family and society, for example, as homemakers, spouses, mothers, professionals, and caregivers, which might cause them difficulty visiting the hospital and making them unable to adhere to their prescribed medications. However, findings contrary to these studies were reported by other works,^{12,14} where males were less adherent to their regimens. This could be because they were not permitted leave from the office, or they may have been concerned about a pay deduction on the particular day they took leave to visit the hospital. Their inability to attend hospital visits on work days might have kept them from adhering to their treatment.^{12,14,19,29,33}

One of the study¹⁴ showed that non-adherence and level of education are inversely proportional. This means that when the level of education increases, adherence decreases, and vice versa. Highly educated people fear side effects and long-term effects of the drugs, which might be due to lack of appropriate information about disease and the drugs prescribed to them and their unwillingness to communicate with their healthcare personnel.^{14,34}

Many studies predicted that people of low socioeconomic status would be less adherent to antidepressants.^{12,14,19,20,27} This could be due to unemployment or an unstable income, inability to afford medications in the long term, and frequent appointments with their physician becoming expensive for them, which leads to premature discontinuation and non-adherence to drug regimens.^{27,35} In contrast, another work¹³ found that patients with a high socioeconomic status were less adherent to antidepressants. This could be because higher-income people generally have a high social status and education level. They might be more concerned about the side effects or potential for dependence on antidepressants, which finally leads to decreased adherence.

b. Patient-related factors

From the literature review, patients often forgetting to take their medications was found to be a common patient-related factor in antidepressant non-adherence.^{9,10,13,25,28,36,37} Inappropriate intake of medication or patient carelessness were other reasons for non-adherence.^{9,19,23}

Patients have incorrect beliefs about the disease itself or prescribed antidepressants.^{10,13,15,22,27} From the findings of our review, a poor understanding of mental illness and medication was found to be the main barrier to depression treatment and hence, to adherence. Even after being diagnosed with depression, many did not consider themselves as having a mental illness. They believed they could easily overcome their mental illness on their own.^{22,38} They also believed that it would be resolved by positive thinking or having a complete rest without taking antidepressants.³ Some people accept depression as a normal part of their aging process, and some even consider it as a result of bad fortune in their lives or a weak personality, rather than a mental illness.^{39,40}

The majority of patients taking antidepressants have misconceptions about them. They believe there is no need to take medication in the absence of any signs or symptoms. They believe they can take less medication or simply discontinue the medication themselves when they feel better.^{10,13,41,42}

The patient's decision to adhere to antidepressants mainly depends on the balance between necessity and concern about the safety and efficacy of the prescribed medication.^{43,44} Therefore, many people believe that long-term use of antidepressants is toxic and may lead to kidney damage. They were also concerned with the potential for addiction and psychological dependence on antidepressants, all of which affect their adherence to treatment.^{10,13,15}

Patients with a positive attitude towards their disease and medication and an awareness of their illness adhere more to their regimens.^{9,10,16,18,19,26,27} They believe they will return to normal functioning if they continue to take their medications. They will communicate regularly with their physicians to enhance their knowledge about their own mental illnesses and medications.¹⁰ All this will help them cope with the response and lead to better health outcomes.⁴⁵

Comorbidity, polypharmacy, and non-adherence are inter-related with each other. Comorbidity increases the number of medications be taken by the patients.^{10,17,25} Patients will feel pill burdens and even an economic burden because they must take different types of medications. The complex dosing schedule and the intention to save money may force patients to discontinue their medication, leading to non-compliance.^{10,20} Comorbidity also leads to logistic problems, as patients must seek medical advice from more than one physician, obtaining appointments and timely medication refills time and again.²⁵

c. Medication-related factors

It is evident from many studies that the majority of patients refuse to continue antidepressants due to the prevalent side effects of the drug prescribed.^{9,11,13,18,25,26,28} Patients mostly prefer

medications that have a lower risk of weight gain, sexual dysfunction, and fatigue.²⁸ Antidepressants are reported to cause many adverse effects such as sedation, restlessness, tremor, dry mouth, decreased libido, weight gain, irregular menstrual cycles, and impotence. These unpleasant effects may impair patient quality of life and self-esteem, resulting in non-adherence to prescribed antidepressants.⁴⁶⁻⁴⁸ In two of the studies,^{17,24} patients prescribed with antidepressants other than selective serotonin reuptake inhibitors (SSRIs) were more likely to be non-adherent. This might be due to the lower side effect profile, low overdose-related cardiotoxicity, better tolerability, and overall favorable risk-benefit ratio attributed to SSRIs.^{11,49-52}

Adherence to treatment is greatly influenced by physician-patient interactions. One of the common reason for non-adherence was the failure of physicians to provide adequate information on patients' illness and medications prescribed.^{9,15,21,25,27} The studies found that the most common patient complaint was the failure of the physician to explain the timing and dosing of the medication completely, along with the benefits of therapy, and the consequence was non-adherence.^{21,25,46,53} Similarly, not trusting the physician and dissatisfaction with the physician and their prescribed medication also led to patients being non-adherent to their treatment.^{10,15,23,54,55}

Due to multiple prescribers, problems communicating with physicians, frequent follow-up, long waiting times in hospitals, repeated medication refills, and unavailability of prescribed medications,¹⁹ many patients choose to discontinue their medications.^{9,10} Patients lose confidence in their physician when there are multiple prescribers, which ultimately affects their medication-taking behavior. Some patients alter/stop their medication without informing their physician, as they find it difficult to communicate with them. To avoid long wait times, patients skip their appointments, leading to an insufficient supply of medication at home.¹⁰

d. Sociocultural factors

Lower adherence to medication depends on the patient's perception of their illness, which may differ according to the religion and culture to which they belong.^{13,56} A study¹⁰ collected the beliefs of people from different religions and cultures. It stated that people from Malaysia believe that mental illness is a social punishment for particular people, or an illness of the soul caused by weakness of the spirit. Similarly, Chinese people believe that mental illness is a symbol of lack of self-worth, which is measured in terms of education and monetary gain that brings honor to the family. Likewise, Indians believe that one gets a mental illness from evildoers.⁵⁷ All of these beliefs create barriers to pursuing and sticking to antidepressant regimens. Some patients want to determine experimentally whether being prayerful will cure their depression, which forces them to stop taking the medication.^{10,13,38}

Depression is still considered a social stigma. Many regard it as a sign of a personal weakness.²⁶ Regular social support and motivation from family members and co-workers help depressive patients get going their antidepressant treatment.^{22,27,58} Due to fear of being stigmatized by society, many patients do not

reveal their mental illness,²² which influences their adherence to medication. Unsupportive family members and co-workers also discourage patients from continuing their medication,¹⁰ which further worsens their mental illness.

e. Logistical factors

Many patients who live far from city areas or hospitals have poor access to healthcare facilities and hence hinder patients from adhering to antidepressants.⁹⁻¹¹

CONCLUSION

From our review, we conclude that patient-related factors such as forgetfulness, comorbidity, and misconception about the disease and medication; medication-related factors such as polypharmacy, side effects, pill burden, and cost; healthcare-system-related factors including the physician-patient interaction; sociocultural factors such as religious and cultural beliefs and stigma; and logistic factors are the major barriers to antidepressant adherence. Hence, efforts should be made to increase patient adherence by strengthening physician-patient relationships. Physicians should emphasize patient education that includes an explanation of the drug, dosage, duration, and timing of administration, possible side effects, adverse effects, lag time before the onset of treatment and relief of symptoms, and consequences of non-adherence. In the case of comorbid conditions, physicians should simplify the medication regimen. Additionally, they should focus on rectifying the myths and beliefs held by patients with scientific information and explanations.

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