

Study of Adherence Pattern of Antidepressants in Patients with Depression

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ABSTRACT

Background

Depression is one of the leading psychiatric disorders of the world affecting a person's mood, physical health and behavior. It is not permanent and is neither a character flaw nor a lack in discipline for a person to be ashamed of. It is a disorder that is reliably diagnosed and successfully treated. Antidepressants are the standard and the most efficacious approach to treating people with depression. However, adherence to treatment is necessary for achieving effectiveness. The result of non-adherence is severe and may cause therapeutic failure resulting in poor quality of life.

Objective

To determine the medication adherence pattern in patients with depression and assess the factors associated with non-adherence to the prescribed antidepressant therapy.

Method

Patients meeting the inclusion criteria who were diagnosed with depression were taken for the study. Informed consent was taken from the patients or from their relatives in case of their incapability. They were then interviewed using structured questionnaire.

Result

Among the 60 patients included in the study, 78% of them were females. Most of the patients 43% (n=26) were prescribed with atypical antidepressants. Less number (37%) of the patients were adherent to the antidepressant therapy. 68% of the females were non adherent. 82% of housewives were not adherent to therapy. Forgetfulness was the main reason for missing dose in majority (50%) of the non-adherent patients.

Conclusion

Majority of the patients with depression were non-adherent to medication. Forgetfulness was the major reason for missing dose in these patients.

KEY WORDS

Adherence, Antidepressants, Depression, Non-adherence

INTRODUCTION

Depression is one of the leading psychiatric disorders of the world affecting a person's mood, physical health and behavior.¹⁻³ It is believed to be the second most leading cause of disability in the world by 2020.⁴ Depression is common yet serious medical condition characterized by set of complex symptoms including depressed mood, suicidality, psychomotor retardation or agitation, reduced motivation or hopelessness and anhedonia. World Health Organization defines depression as "a common mental disorder, characterized by sadness, loss of interest or pleasure, feelings of guilt or low self-worth, disturbed sleep or appetite, feelings of tiredness, and poor concentration".⁹

Antidepressants are the standard and the most efficacious approach to treating people with moderate to severe depression.^{5,6} These antidepressants are used singularly or in combination with other antidepressants.⁵ To achieve effectiveness in the treatment, it is important to select right medication, deliver it at full therapeutic dose for sufficient treatment duration.⁶ Antidepressants are highly efficacious, however, adherence to treatment is vital for achieving effectiveness. The various factors that influence adherence are nature and duration of therapy, severity and chronicity of health problems, medication adverse effects, drug-drug interactions, comorbid condition, costs of treatment, characteristics of health service facilities, the relation between the physician and patient, patient's characteristics such as socioeconomic factors, patient's perspective about the illness and therapy.^{7,8} In global scenario non-adherence to depression treatment is a common clinical problem.⁷

In developing countries like Nepal limited studies are conducted to measure adherence when adherence is the only way to check the effectiveness of therapy. Our study mainly focuses on patient's adherence to different antidepressants and the factors affecting non-adherence.

METHODS

This was a prospective study conducted in Dhulikhel Hospital, Kathmandu University Hospital, Dhulikhel, Kavre, from June 2015 to October 2015. Ethical clearance was obtained from Institutional Review Committee (IRC), Kathmandu University School of Medical Sciences (IRC approval no. 27/15). All the patients attending the in-patient and out-patient department of psychiatric department above 18 years were included in the study. Only those patients diagnosed with depression and taking antidepressants for at least a month were enrolled in the study. Patients meeting these criteria were explained about the study and their role in it. When consent form was signed by the patients, they were interviewed with structured questionnaire for their demographic details and medication adherence pattern.

Data were entered in Microsoft Office Excel 2007 and

analyzed with Statistical Package for Social Sciences (SPSS) version 16.0. Data expressed as mean \pm standard deviation (SD) with the relevant tables and bar-graphs. The qualitative data was analyzed using Pearson's Chi Square test. P-value < 0.05 was considered statistically significant.

RESULTS

Among sixty depression patients under study, majority 78% (n=47) of them were females. The mean age (SD) was 43.16 years (\pm 14.19). Majority 43.3% (n=26) of the patients belonged to age group 39-58 years followed by 41.7% (n=25) of patients under age group 19-38. In the study, 55% (n=33) were literate. Majority 47% of patients (n=28) were housewives. 95% (n=57) of patients were married and 83% (n=50) of them lived in nuclear family. Majority 43% (n=26) of patients were Brahmin. This was followed by Newar 23% (n=14) and Chhetri 17% (n=10). Majority 92% (n=55) of patients practiced Hinduism followed by three patients practicing Buddhism and two patients practicing Christianity (Table 1).

Table 1. Demographic characteristics and patient's history n=60

Variables	Total (n)	Percentage (%)
Gender		
Male	13	21.7
Female	47	78.3
Age (years)		
19-38	25	41.7
39-58	26	43.3
59-78	9	15
Occupation		
Service	8	13.3
Business	5	8.3
Housewife	28	46.7
Farmer	8	13.3
Students/Unemployed	11	18.3
Marital status		
Married	57	95
Unmarried	3	5
Family type		
Nuclear	50	83.3
Joint	10	16.7
Ethnic group		
Bhramin	26	43.3
Chhetri	10	16.7
Newar	14	23.3
Tamang	4	6.7
Others*	6	10
Literate		
Yes	33	55
No	27	45

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Antidepressant Prescription

Out of sixty patients under study, majority 43% (n=26) of them were prescribed Atypical antidepressants followed by Selective Serotonin Reuptake Inhibitors (SSRIs) in 32% (n=19) of patients and Tri Cyclic Antidepressants (TCAs) in 17% (n=10) of patients. Likewise, Serotonin Nor-epinephrine Reuptake Inhibitor (SNRIs) were prescribed in three patients and combinations of Atypical antidepressants and Selective Serotonin Reuptake Inhibitors (SSRIs) were prescribed in two patients (Fig. 1).

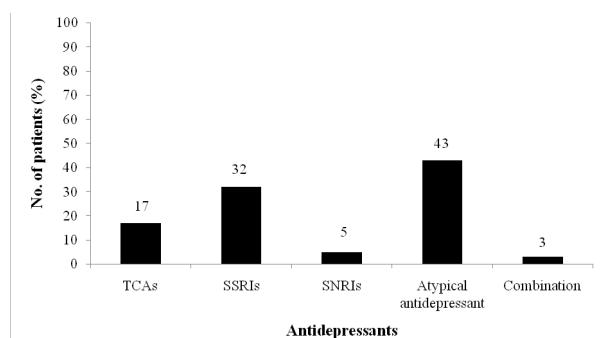


Figure 1. Bar chart showing antidepressant prescription pattern (n=60)

Adherence pattern

Of sixty patients under study, only 37% of them (n=22) were adherent to antidepressant treatment (Figure 2, Table 1). The main reason for patients to miss dose was forgetfulness (50%) (Fig. 3).

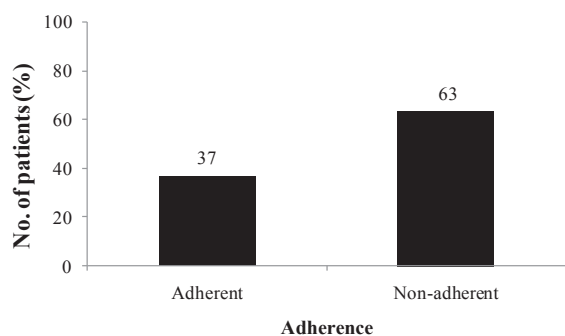


Figure 2. Bar chart showing adherence pattern (n=60)

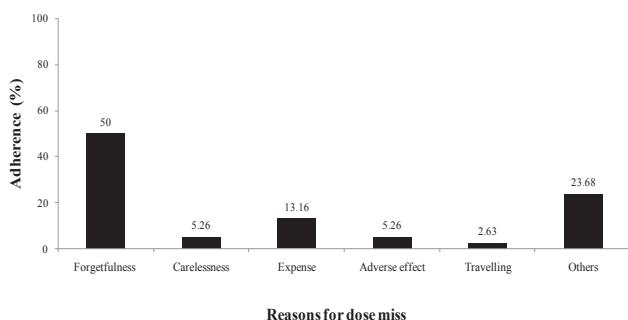


Figure 3. Bar chart showing association between adherence and reasons for missing dose (n=60)

This study revealed that non-adherence was significantly associated with occupation of patients ($p = 0.049$) and cost of medicine ($p = 0.015$). However, there were other factor like treatment duration, occurrence of adverse effects, patient’s perception towards disease, clinician’s factors, and availability of medicine that were not significantly associated, yet were barrier to adherence (Table 2).

DISCUSSION

In our study majority (78%) of patients with depression were females. This was supported by several studies around the world.^{4,9,10} The variation in occurrence of depression among male and female is supposed to be caused due to hormones associated with menstrual cycle and pregnancy affecting mood in female. These hormonal changes in women triggered dysregulation of stress response and made them more vulnerable to depression, especially when exposed to stress.¹¹ Most of the female in this study belonged to reproductive age and had children of their own. However, pregnancy was not the cause of depression. Traditionally, women stayed home to take care of their children after delivery and were exposed to dual responsibility of work and family. This caused more work-related stress that might have led to depression in them.^{12,13} Most of the societies provide less power and status to women, hence, they experience lack of respect, constrained choices and sexual abuse resulting in depression.¹¹

Most of the females in our study were housewives. When interviewed, they reported that loss of dear ones and family problems were the reason for their depression. In study among housewives of Pokhara, depression was caused due to other reasons such as broken families, divorces, husbands not giving adequate time or husbands going to other countries for employment, monotonous lifestyle and lack of entertainment.⁴ Problems with academics (in students) and tedious and repetitive routine (in teachers) added to the cause of depression in patients visiting psychiatric Out Patient Department (OPD) in Dhulikhel Hospital. Most of the depression patients in the present study were young with very few patients above sixty years. This was supported by a study in India where more depression patients were below forty years.⁴ Depression in elderly population was believed to be normal response to aging, physical losses and other life events, thus, were less reported.¹⁴

In the current study, majority of patients were married which was similar to the result of study done in India.⁷ There did not seem to be any influence of marriage on depression but depressions tend to disrupt family stability frequently leading to separation or divorce. Nonetheless, the link between depression and divorce was not explicitly seen in this study. Majority of patients living in nuclear family had depression as supported by a study in India.⁷ Even though there were no literatures supporting family system influencing depression, lack of interaction and

Table 2. Factors affecting adherence in depression patients

Variables	Total(n)	Percentage (%)	Adherent * (n=22) No. (%)	Non-adherent** (n=38) No. (%)	p-value
Treatment characteristics Duration knowledge					
Yes	6	10	1 (17)	5 (83)	0.258
No	54	90	21 (39)	33 (61)	
Adverse effects					
Yes	35	58.3	15 (43)	20 (57)	0.239
No	25	41.7	7 (28)	18 (72)	
Patients factors Disease perception					
Curable	25	41.7	12 (48)	13 (52)	0.302
Incurable	4	6.7	1 (25)	3 (75)	
Managed symptomatically	31	51.7	9 (29)	22 (71)	
Patient's belief					
Yes	58	96.7	22 (38)	36 (62)	0.172
No	2	3.3	0 (0)	2 (100)	
Knowledge of precaution					
Yes	51	85	19 (37)	32 (63)	0.822
No	9	15	3 (33)	5 (67)	
Complicate life					
Yes	15	25	4 (27)	11 (73)	0.353
No	45	75	18 (40)	27 (60)	
Clinician factor Physician's attention					
Yes	57	95	22 (39)	35 (61)	0.092
No	3	5	0 (0)	3 (100)	
Information provided					
Yes	53	88.33	20 (38)	33 (62)	0.631
No	7	11.67	2 (29)	5 (71)	
Patient's satisfaction					
Yes	55	91.67	20 (36)	25 (64)	0.872
No	5	8.33	2 (40)	4 (60)	
Socio-economic factors Cost					
Yes	54	90	22 (41)	32 (59)	0.015
No	6	10	0 (0)	6 (100)	
Availability of medicine					
Yes	41	68.33	16 (39)	25 (61)	0.578
No	19	31.67	6 (32)	13 (68)	
Stock of medicine					
Yes	35	58.33	13 (37)	22 (63)	0.928
No	25	41.67	9 (36)	16 (64)	

* People who had not missed or discontinued medication

** People who had missed or discontinued medication

ignorance from the family members could be the reason for depression in patients living in nuclear family. In this study, majority of patients visiting psychiatric OPD were Brahmin. This was followed by Newar and Chhetri. Similar result was reported in the study done in Manipal Teaching hospital where majority of patients were Brahmins followed by Chhetri, Dalit and Gurung.⁴ This variation in occurrence of depression in different ethnic group was highly influenced by the location of study. Depression was seen more in Brahmin and Newar because our study site was situated

in their locality. More than ninety percent of patients were Hindus followed by few Buddhist and Christians.

In this study most of the patients were prescribed with atypical antidepressants (Mirtazapine) followed by SSRIs (Fluoxetine, Paroxetine, Sertraline, Escitalopram) and TCAs (Imipramine, Amitriptyline). However, SNRIs (Venlafaxin, Duloxetine) and combinations of mirtazapine and fluoxetine were rarely prescribed. This prescription pattern contradicted to the pattern seen in Indian study where SSRIs were prescribed more followed by TCA and SNRI.

Atypical antidepressants were hardly prescribed.¹⁵ Several other studies also reported higher prescription of SSRIs compared to other classes of antidepressant.^{7,16-18} All these findings were different from ours. SSRIs were prescribed more than other antidepressants in many studies because in brain, other antidepressants non-selectively inhibit the reuptake of neurotransmitters serotonin, nor epinephrine and dopamine into presynaptic vesicles thus affect histaminic, cholinergic, adrenergic and postsynaptic serotonin receptors unrelated to depression leading to significant and often intolerable adverse effects.¹⁹

Since SSRIs do not have receptor antagonism, they lack life-threatening adverse effects such as cardiotoxicity and CNS toxicity,²⁰ thus, could be safely used in many patients. However, in our study atypical antidepressant (Mirtazapine) was highly prescribed. As mirtazapine acted as an antagonist at presynaptic α_2 -receptors and at postsynaptic 5-HT₂ and 5-HT₃ receptors, it had fewer adverse effects and greater effectiveness in treating depression, hence, was mostly prescribed by the psychiatrist in this study. Combination of antidepressants was prescribed only when one antidepressant was unable to improve the condition of patients. Nevertheless, they were avoided due to risk of toxicity and drug interaction consequences.

Majority of patients (63%) in our study were non-adherent to the antidepressant therapy. Many studies conducted around the world on adherence to antidepressant therapy have also reported higher non-adherence percent.^{7,21} There seem to be broad range of reasons for non-adherence in patients and the main reason for non-adherence in our study was forgetfulness. Similar to our finding Bulloch & Pattern also found that simply forgetting to take drugs was the major reason for patient non-adherence.²² In contrast, Fortney et al reported that side effect was the reason for antidepressant discontinuation in their study.²³

In our study other reasons like carelessness, travelling without taking medicine, expenses etc. were also responsible for patients to miss dose leading to non-adherence. Earthquake of 2072 B.S. played a significant role in causing non-adherence in patients of our study as they lost their house and their normal lifestyle was disturbed for months. Antidepressants are quite expensive and patients living in villages having economic privation could not afford it all the time. Therefore, expense of the medicine also caused non-adherence in our study. In addition, other studies reported that higher cost of the medication was associated with lower adherence.^{7,24}

The present study revealed that females were more non-adherent to medication than males and among them most were housewives. Banerjee and Verma⁷ in their study also came up with similar findings and reasoned that due to multiple roles of women such as housewife, mother, spouse, professionals and care provider, it was difficult for them to adhere to prescribed medication. In contrast to our finding, more men were reported non-adherent

to antidepressant therapy in Belgium and USA.^{25,26} When interviewed, housewives told us that they had to do all the chores of the house and work in the fields too. By the end of the day, they were too tired to even take their medicine, thus, resulting in poor adherence. In our study, patients enrolled in service and farming reported better adherence rate than patients with other occupation.

The barriers to non-adherence are multifactorial which need to be identified in order to customize interventions to target those problems.²⁷ One of the factors affecting adherence in the present study was drug regimen. Majority of patients in the study were prescribed with only one of the antidepressants. This was similar to the result of a study in Saudi Arabia where most of the patients were prescribed with only one antidepressant.²¹ A study suggested that polypharmacy significantly contributed to non-adherence in patients which might be the reason for avoiding such prescriptions in our study. It is difficult to calculate adherence in individual antidepressant drug when polypharmacy is used.¹⁰ Studies in different places showed that patients were more adherent to SSRIs compared to other classes of antidepressants.²⁸⁻³⁰

The adverse effects experienced by patients after taking antidepressants also caused non-adherence in the patients of our study. Occurrence of adverse effects was seen more in patients prescribed with TCA followed by patients prescribed with SNRI and SSRI. Least occurrence of adverse effect was seen in patients prescribed with atypical antidepressants. In our study, many patients gained weight which resulted in non-adherence. Patients treated with SSRI or SNRI in US showed weight gain as serious adverse effect. Moreover in a study, weight gain was seen in hundred percent of patients prescribed with TCA.³¹ Central nervous system related adverse effects such as drowsiness and sedation were responsible for non-adherence in patients. Since patients had been taking antidepressants for a long period of time, they were tolerant to most of these effects. Dry mouth was reported in few patients in this study. However, our finding contradicted to the finding of a study in Brazil where majority of patient experienced dry mouth after taking antidepressants. Gastrointestinal disturbances such as nausea, abdominal discomforts and constipation were also seen in patients taking antidepressants. Since patients could not tolerate these effects, they missed dose to avoid such effects. None of the patients having these GI disturbances were adherent in the study. Patients should be pre-informed about these adverse effects so that they do not stop taking medicine once they encounter those effects. This information would have increased adherence rate.

Patients in our study agreed that physicians provided them information about disease and medication, yet, adherence rate was not increased. A study has suggested that quality patient-provider relationship and communications have positive effect on adherence.³² However, it could

not result in better adherence as expected in our study. Despite being satisfied with the information shared by their physician, the patients in our study were poorly adherent to antidepressants. Physician provided special attention to majority of patients; spend their time to update with patients' condition, however, this too failed to improve adherence to antidepressant therapy in patients. Physicians can improve adherence simply by providing realistic information about the medication, the time drugs require to show their effect and specific adverse effects that are likely to occur and resolve.³³ In spite of physician playing their role in improving adherence, optimal outcome in adherence was not achieved due to ignorance from patients. Patients also play an important and equal role in improving adherence and there are strong reports supporting certain patient characteristics such as their belief on antidepressant therapy and their perception of disease that affect adherence.^{32,34} In this study, more than half of the patients believed that their disease could only be managed symptomatically by antidepressants. These patients were dependent on antidepressant to elevate their mood, thus, missing dose caused reappearance of depressive symptoms in them. Even those patients who believed their depression could be cured failed to show good adherence. As patients had to take medicine for long period of time, there was higher chance to miss dose which resulted in lower adherence percent than expected in this study.

Majority of patients in our study believed that taking medicine regularly could make them feel better, however, only few among them were adherent to treatment. Very few patients did not believe that taking medicine regularly could make them feel better which was comparable to the findings of previous study.⁷ Some of the patients had their life complicated due to disease management. Even though managing disease did not complicate life in many patients, they tend to miss dose one day or the other due to various reasons in the long run. This hampered adherence to medication. Further, earlier study has also reported that shortage of medicine at medicine shop also one of the cause to miss the dose.⁷ Though, many patients keep stock of medicine at their home, the current study shows that forgetfulness was found to be the major cause of missing the dose leading to poor adherence.

Moreover, this study has highlighted the multi-factorial barriers to non-adherence in antidepressant therapy and strategies targeting those factors need to be developed in order to improve adherence in depression patients. However, due to mono-centered with limited sample size and the use of open ended questionnaires might have effect in the definite result of this study and multi centered studies with large sample size should be able to minimize such variation.

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