Research Article

Self-Reported Antidepressant Drug Side Effects, Medication Adherence, and Its Associated Factors among Patients Diagnosed with Depression at the Psychiatric Hospital of Nepal

Nirmal Raj Marasine,1 Sabina Sankhi,1 Rajendra Lamichhane,2 Nabin Raj Marasini,3 and Nim Bahadur Dangi1

1Pharmaceutical Sciences Program, School of Health and Allied Sciences, Pokhara University, Pokhara-30, Kaski, Nepal
2Department of Public Health, Asian College for Advance Studies, Purbanchal University, Lalitpur, Nepal
3Department of Public Health, La Grande International College, Kaski, Nepal

Correspondence should be addressed to Nirmal Raj Marasine; nirmalmarasine@gmail.com

Received 6 July 2020; Revised 19 September 2020; Accepted 5 October 2020; Published 20 October 2020

Objective. The present study is aimed at evaluating the side effects of antidepressant drugs, medication adherence (MA), and associated factors among patients diagnosed with depression at a psychiatric hospital in western Nepal. Methods. A prospective cross-sectional study was conducted among 174 patients visiting the outpatient clinic of a psychiatric hospital. The antidepressant side effect checklist (ASEC) was used to classify the reported antidepressant drug side effects into mild, moderate, and severe types. The Naranjo adverse drug reaction (ADR) probability scale was employed to assess the ADRs, and the Morisky Green Levine Adherence (MGLA) score was employed to determine the rate of medication adherence. Descriptive statistics and bivariate analysis were used, and a P value < 0.05 was taken as statistically significant in the multivariate analysis. Results. The patients were mostly female (55.74%), with a median (IQR) age of 32 (20) years. Approximately 74.13% of the patients experienced antidepressant side effects, where insomnia (17.05%) and anxiety (17.05%) were the most common. More than half of the patients (52.29%) had a low level of adherence. Females were 1.01 times more likely to be nonadherent to their antidepressant medications compared to males, adjusted odds ratio (AOR): 1.001 (0.31-1.63). Similarly, illiterate patients tended to be more nonadherent compared to literates, AOR: 1.342 (0.93-2.82), and unemployed individuals were 1.5 times more likely to be nonadherent to their medications compared to employed individuals, AOR: 1.46 (1.16-4.13). Likewise, patients with severe side effects were more prone to develop nonadherence than those with moderate side effects, AOR: 1.173 (0.42-3.25). A significant association was found between the Naranjo score and medication adherence. Conclusions. This study suggests that antidepressant drug side effects were more prevalent and medication adherence was extremely poor among depressive patients in psychiatric hospitals. Factors such as gender, occupation, education, side effects, and ADRs attributed to poor medication adherence in patients.

1. Introduction

Depression, a common chronic psychiatric illness, interferes with physical and mental performance as well as the social life of the individual. More than 264 million people worldwide suffer from depression [1]. The World Health Organization (WHO) estimated that by year 2020, it would become the second-highest known cause of worldwide disability [2], and by 2030, it would possibly become the most significant factor contributing to the global burden of disease [3]. Nepal has a high prevalence of depression with the second-highest rate of “disability-adjusted life years” in the
world [4]. In Nepal, 1 in every 3 people suffers from mental illness, and more than 90 percent of the population in need of mental health services has no access to treatment [4]. The first epidemiological field survey conducted in the Kathmandu valley by the government of Nepal in 1984 estimated the prevalence of mental illness to be approximately 14% [5].

Antidepressant medication is often considered to be the best treatment option for depression [6]. American Psychiatric Association (APA) guidelines (2010) has endorsed selective serotonin reuptake inhibitors (SSRIs), serotonin and noradrenaline reuptake inhibitors (SNRIs), and selective serotonin-noradrenaline reuptake inhibitors (SSNRIs) as first-line medication owing to their similar efficacy and lower overdose-related toxicity when compared to tricyclic antidepressants and monoamine oxidase inhibitors [7].

However, other factors, such as adverse effect profiles, cost, safety profile, history of prior medication treatment, and patient preference, are important in the initial selection of antidepressants and should be considered by healthcare professionals [7, 8]. In a study from the United States, it was reported that the patients with bothersome side effects are more likely to nonadhere to their antidepressant medications [9]. This affects the efficacy of antidepressant medications [10]. Moreover, antidepressant drug side effects are the significant determinants of antidepressant-associated nonadherence, which is predicted to be considerably high among depressive people [11]. The determination of drug-associated side effects will guide the development of policies for the effective management of severe and probable types of side effects, and medication adherence will contribute to the assessment of the effectiveness of interventions for better therapeutic outcomes. Therefore, this study is aimed at evaluating the antidepressant drug side effects, medication adherence (MA), and associated factors among patients diagnosed with depression at a psychiatric hospital in western Nepal.

2. Methods

2.1. Study Setting. A prospective cross-sectional study was conducted between August and October 2019, among patients visiting the outpatient department of B.G. Hospital. B.G. Hospital is a 25-bedded psychiatric hospital that provides both inpatient and outpatient services. It is the only psychiatric hospital in Kaski district, located in Pokhara-12, Kaski, Nepal. Easy accessibility makes it one of the busiest hospitals in Pokhara.

2.2. Sample Selection Criteria. All patients aged ≥18 years, diagnosed with depression, and under antidepressant medication for at least 1 month before the commencement of the study were included in the study. Pregnant or lactating mothers; those with a history of psychotic, bipolar disorder, or drug abuse; those with cognitive impairment; and those unable to communicate and understand the Nepali language were excluded from the study. To discard the patients with dementia, an upper age limit of 65 years was selected.

2.3. Sample Size. The calculated sample size for this study was 174. It was calculated based on the study conducted at two universities in Nepal in 2016 [12]. As per the study, the prevalence of depression was 11.7%. Setting the worst acceptable level at 5.0% and a confidence interval at 95.0%, a sample size of 158 was obtained using Epi Info 6. 10% of 158, i.e., 16, was added to make up for errors. Therefore, a total of 174 patients were enrolled in the study.

2.4. Study Variables. Antidepressant drug side effects and levels of medication adherence were our dependent variables. Likewise, sociodemographic characteristics of the patient, such as age, gender, education, occupation, and marital status, were the independent variables.

2.5. Data Collection Tools and Technique. Data were collected prospectively from the patients and their prescriptions by communicating with psychiatrists. Information on demographics (age, gender, education, marital status, religion, occupation, and residence) and antidepressants prescribed were collected. The antidepressant side effect checklist (ASEC), which was developed by the Royal College of the Psychiatrist, was employed to classify the reported side effects into mild, moderate, and severe types, as it consist of list of all the side effects associated with antidepressant drugs [13]. The Naranjo adverse drug reaction (ADR) probability scale, with 10 items, was employed to assess the antidepressants-associated ADRs. As per the scale, a score of >9 indicated definite ADR, 5-8 indicated probable ADR, 1-4 indicated possible ADR, and 0 indicated doubtful ADR [14]. Similarly, the Morisky Green Levine Adherence (MGLA) score was employed to determine the rate of medication adherence.

### Table 1: Sociodemographic characteristics of patients (n = 174)

| Characteristics | Category       | n (%) |
|-----------------|----------------|-------|
| Gender          | Female         | 97 (55.74) |
|                 | Male           | 77 (44.25) |
| Education       | Literate       | 124 (71.26) |
|                 | Illiterate     | 50 (28.73) |
| Marital status  | Married        | 120 (69.0) |
|                 | Single         | 54 (31.0) |
|                 | Hinduism       | 146 (83.9) |
|                 | Buddhism       | 12 (6.9) |
| Religion        | Christianity   | 6 (3.4) |
|                 | Muslim         | 10 (5.7) |
|                 | Business       | 24 (13.8) |
|                 | Employment     | 57 (32.8) |
| Occupation      | Farmer         | 21 (12.06) |
|                 | Housewife      | 64 (36.78) |
|                 | Others         | 8 (4.59)  |
| Residence       | Urban          | 133 (76.43) |
|                 | Rural          | 41 (23.56) |

| Age             | 18 to 65       | 32 (20) |

1Median (IQR) instead of n (%).
The majority of patients (146; 83.9%) were Hinduism in religion. The study patients were predominantly married (120; 69%) and literate (124; 71.26%). Most of the patients were housewives (64; 36.78%) and resided in urban areas (133; 76.26%), as depicted in Table 1.

Out of 174 patients, 150 (86.20%) were on monotherapy. Of these, SSRIs were prescribed in 101 (58.04%) patients, SNRIs in 24 (13.79%), TCAs in 17 (9.77%), and atypical antidepressants in 8 (4.59%) patients, respectively. The most frequently prescribed antidepressant was fluoxetine (40; 22.98%), as shown in Table 2. Antidepressants prescribed as a combination therapy are depicted in Table 3.

Of approximately 129 (74.13%) patients encountered with antidepressant drug side effects, the most common were insomnia and anxiety (22; 17.05%), followed by dry mouth (14; 10.85%) and weight gain (13; 10.07%), respectively. Tachycardia was rarely reported (1; 0.77%) by the patients. Patients reported antidepressant drug side effects are illustrated in Figure 1.

Based on ASEC, the majority of the reported side effects were moderate (98; 56.32%), followed by severe (22; 12.64%) and mild (9; 5.17%), respectively. Based on the Naranjo score, approximately 83.72% of ADRs were probable, and 16.27% were possible, as shown in Table 4.

Based on the scoring of MGLA, more than half of the patients (91; 52.29%) were found to have a low level of medication adherence, which are listed in Table 6. Females

### Table 2: Antidepressants prescribed as monotherapy (n = 174).

| Class of drugs                              | n (%)  | Individual drugs, n (%)         |
|---------------------------------------------|--------|---------------------------------|
| Selective serotonin reuptake inhibitor (SSRIs) | 101 (58.04) | Fluoxetine (40; 22.98) |
| Serotonin and noradrenaline reuptake inhibitors (SNRIs) | 24 (13.79) | Sertraline (24; 13.79) |
| Tricyclic antidepressants                   | 17 (9.77) | Duloxetine (15; 8.62) |
| Atypical antidepressants                   | 8 (4.59)  | Venlafaxine (9; 5.17) |

### Table 3: Antidepressants prescribed as a combination therapy (n = 174).

| Drugs                      | n (%)  |
|----------------------------|--------|
| Fluoxetine+buproprion      | 8 (4.59) |
| Sertraline+mirtazapine     | 9 (5.17) |
| Sertraline+amitriptyline   | 4 (2.29) |
| Fluoxetine+amitriptyline   | 3 (1.72) |
were 1.01 times more likely to be nonadherent to their antidepressant medications compared to males, adjusted odds ratio (AOR): 1.001 (0.31-1.63). Similarly, illiterate patients tended to be more nonadherent compared to literates, AOR: 1.342 (0.93-2.82), and unemployed individuals were 1.5 times more likely to be nonadherent to their medications compared to employed individuals, AOR: 1.46 (1.16-4.13). Likewise, patients with severe side effects were more prone to develop nonadherence than those with moderate side effects, AOR: 1.173 (0.42-3.25). A significant association was found between the Naranjo score and medication adherence.

4. Discussion

This study evaluated the antidepressant drug side effects, medication adherence, and associated factors among depressive patients visiting the outpatient clinic in a psychiatric hospital in Nepal for three months among 174 patients. The majority of the patients were female, with a median (IQR) age of 32 (20) years. This study revealed that the antidepressant drug side effects were more prevalent and that the level of medication adherence was extremely poor among depressive patients. Although the findings represented a small number of patients, monotherapy was predominant in most of the patients, where SSRIs (fluoxetine, escitalopram, and sertraline) were the most frequently prescribed antidepressants, followed by SNRIs (duloxetine, venlafaxine) and TCA (amitriptyline), respectively. These findings were similar to several studies conducted globally. A study from Malaysia reported that SSRIs were the most frequently prescribed antidepressants whose prescriptions increased rapidly in the last decade [16]. Similar findings were also reported from the Europe [17]. A study from the United States revealed the increased prescription of SSRIs from 54.8% to 66.9% and declined prescription of TCAs from 35% to 11.1% between 1996 and 2005 [18]. The reason behind the frequent use of SSRIs compared to TCAs might be fewer side effects and better tolerability offered by SSRIs than the latter [19]. In contrast, amitriptyline (28.1%) followed by fluoxetine (27.2%) were the most often prescribed antidepressants as monotherapy in a study from Malaysia [11].

This study found that side effects are most common in depressive patients, as above 70% of the patients experienced antidepressant drug side effects. This finding was comparably higher than that of an Indian study (26.87%) [20] and lower than that of an Ethiopian study (85.7%) [10]. A total of 15 side effect types were identified in this study, where general ones such as insomnia, anxiety, dry mouth, and weight gain were more common among the study population. This finding was in contrast to that of a study conducted in India, wherein dry mouth was the most common, closely followed by nausea and tremor [21]. All side effects should be given equal attention, as a good number of them were moderate and probable as per the ASEC and Naranjo scales. Most of the reported side effects were not associated with discontinuation of antidepressants. However, some side effects might be strong predictors of antidepressant discontinuation. For example, sexual dysfunction, although relatively uncommon, could lead to nonadherence and poor improvement in mental condition, which can eventually increase suicidal ideation in patients [22]. As these side effects are treatable, specific attention is needed to enable collaborative decision-making.
and maximize the chance of an individual receiving effective medication with a minimal burden of adverse effects [23].

The study showed that the majority of patients with depression had a low level of adherence (52.29%) towards antidepressant medications. This finding showed consistency with two other studies conducted in Ethiopia and Saudi Arabia, both of which ascertained lower adherence to antidepressant medications, i.e., 52.29% and 57.1%, respectively [10, 24]. In this study, females were found more likely to be non-adherent than males with AOR: 1.001 (0.31-1.63). In Nepal, women play multiple roles in the family and society, such as homemakers, spouses, mothers, professionals, and caregivers, which might cause them difficulty in making time for hospital visits, making them nonadherent to their prescribed medications. A similar study from Canada also reported on men with better compliance with their antidepressant medication than women [25]. However, a finding opposite to this study was reported from the USA and Belgium, wherein men were found more likely to discontinue their treatment even without consent from their physicians [26, 27]. This study showed unemployment, the reason for medication nonadherence. This is because such patients cannot afford medicines for the long term, and frequent appointments with their physicians become expensive for them. Medication adherence was found to be significantly associated with the probability and severity of antidepressant drug adverse effects/side effects at a “P” value of 0.05. This contradicts the finding of the Ethiopian study [10]. In this study, illiterate patients were observed to be more nonadherent than literate patients. This might be due to illiterate patients being afraid of the drug side effects owing to their limited knowledge about diseases and drugs, in addition to their unwillingness to discuss the same with medical professionals. Similar findings regarding poor compliance among less-educated patients were reported in a study from Spain [28].

5. Limitation and Strength of the Study

There are some limitations to this study. It was limited to a single center in western Nepal, which along with its small sample size shrinks the power of the study to determine the factors associated with antidepressants adherence. A self-reported medication adherence tool was used, which might be associated with subjective bias. Hence, other experimental methods, such as pill count and mechanical device recording, could strengthen the findings on medication adherence. Additionally, patients who were unable to speak and understand the Nepali language were discarded, which might be associated with language bias. However, the findings of this study are expected to have a good impact on the education of psychopharmacology.

6. Conclusions

This study revealed that in depressive patients, self-reported antidepressant drugs side effects were highly prevalent, and anxiety, insomnia, dry mouth, and weight gain were more frequent. Medication adherence was extremely poor in a psychiatric hospital. This was attributed to factors such as gender, occupation, education, side effects, and ADRs. Psychiatrists should carry out adherence-enhancing interventions for their patients. Education and assurance of patients about side effects associated with medications will enhance their adherence to antidepressants and hence improves the therapeutic outcomes.

Data Availability

The raw data used to support the findings of this study are made available from the corresponding author upon reasonable request.
Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors’ Contributions

NiRM developed the proposal, collected and analyzed the data, and drafted the manuscript. NiRM, SS, and NBD analyzed the data and contributed to manuscript development. Project supervision was done by NBD. SS, RL, and NaRM participated in reviewing the proposal, guided data collection and analysis, and critically revised the manuscript. All authors read and approved the final manuscript.

Acknowledgments

The authors are equally thankful to the doctors, nurses, and all other staffs of B.G. Hospital for their help during data collection and to the patients along with their relatives for their warm support and coordination throughout this study. The authors also acknowledge the School of Health and Allied Sciences, Pokhara University, for the necessary guidance and support.

Supplementary Materials

The supplementary file contains the data collection sheet. (Supplementary Materials)

References

[1] World Health Organization (WHO), “Mental Health: world mental health day 2017,” June 16, 2020 https://www.who.int/mental_health/world-mental-health-day/2017/en/.

[2] World Health Organization, The World Health Report 2001: Mental health: new understanding, new hope, World Health Organization, 2001, June 16, 2020 https://www.who.int/whr/2001/chapter2/en/index4.html.

[3] World Health Organization, The global burden of disease 2004 update, WHO, 2008, June 16, 2020 https://www.who.int/healthinfo/global_burden_disease/2004_report_update/en/.

[4] “Mental Health in Nepal: what do evidence say?,” June 16, 2020 https://www.herd.org.np.

[5] S. K. Regmi, A. Pokharel, S. P. Ojha, S. N. Pradhan, and G. Chapagain, “Nepal mental health country profile,” International Review of Psychiatry, vol. 16, no. 1-2, pp. 142–149, 2009.

[6] C. Armstrong, “APA releases guideline on treatment of patients with major depressive disorder,” American Family Physician, vol. 83, pp. 1219–1227, 2011.

[7] A. J. Gelenberg, M. P. Freeman, J. C. Markowitz, J. F. Rosenbaum, M. E. Thase, M. H. Trivedi et al. et al., “American Psychiatric Association practice guidelines for the treatment of patients with major depressive disorder,” The American Journal of Psychiatry, vol. 167, pp. 9–118, 2010.

[8] A. Qaseem, V. Snow, T. D. Denberg, M. A. Forcica, D. K. Owens, and for the Clinical Efficacy Assessment Subcommit-tee of the American College of Physicians, “Using second-generation antidepressants to treat depressive disorders: a clinical practice guideline from the American college of physicians,” Annals of Internal Medicine, vol. 149, pp. 725–733, 2008.

[9] M. B. Tamburrino, R. W. Nagel, M. K. Chahal, and D. J. Lynch, “Antidepressant medication adherence: a study of primary care patients,” The Primary Care Companion to The Journal of Clinical Psychiatry, vol. 11, no. 5, pp. 205–211, 2009.

[10] T. M. Abegaz, L. M. Sori, and H. N. Toleha, “Self-reported adverse drug reactions, medication adherence, and clinical outcomes among major depressive disorder patients in Ethiopia: a prospective hospital based study,” Psychiatry Journal, vol. 2017, Article ID 5812817, 8 pages, 2017.

[11] S. C. Ho, S. A. Jacob, and B. TangsiSureus, “Barriers and facilitators of adherence to antidepressants among outpatients with major depressive disorder: a qualitative study,” PLoS One, vol. 12, no. 6, p. e0179290, 2017.

[12] D. Kunwar, A. Risal, and S. Koirala, “Study of depression, anxiety and stress among the medical students in two medical colleges of Nepal,” Kathmandu University Medical Journal, vol. 53, no. 1, pp. 22–26, 2016.

[13] R. Uher, A. Farmer, N. Henigsberg et al., “Adverse reactions to antidepressants,” British Journal of Psychiatry, vol. 195, no. 3, pp. 202–210, 2009.

[14] C. A. Naranjo, U. Busto, E. M. Sellers et al., “A method for estimating the probability of adverse drug reactions,” Clinical Pharmacology & Therapeutics, vol. 30, no. 2, pp. 239–245, 1981.

[15] D. E. Morisky, L. W. Green, and D. M. Levine, “Concurrent and predictive validity of a self-reported measure of medication adherence,” Medical Care, vol. 24, no. 1, pp. 67–74, 1986.

[16] A. R. F. Nahas and S. A. S. Sulaiman, “Prescribing patterns of antidepressants among depressive men in Malaysia: a survey,” Journal of Young Pharmacists, vol. 10, no. 1, pp. 98–101, 2018.

[17] M. Bauer, B. U. Monz, A. L. Montejo et al., “The FINDER study, national patterns in antidepressant medication treatment,” Archives of General Psychiatry, vol. 66, no. 8, pp. 848–856, 2009.

[18] M. Olsson and S. C. Marcus, “National patterns in antidepressant medication treatment,” Journal of Clinical Psychiatry, 2001, vol. 66, no. 8, pp. 27–35, 2001.

[19] J. M. Ferguson, “SSRI antidepressant medications: adverse effects and tolerability,” The Primary Care Companion to The Journal of Clinical Psychiatry, vol. 3, no. 1, pp. 22–27, 2001.

[20] S. Mishra, T. R. Swain, and M. Mohanty, “Adverse drug reaction monitoring of antidepressants in the psychiatry outpatients department of a tertiary care teaching hospital,” Journal of Clinical and Diagnostic Research, vol. 7, no. 6, pp. 1131–1134, 2013.

[21] S. Mukherjee, S. Sen, S. S. Chatterjee, N. Era, M. Ghosal, and S. K. Tripathi, “Adverse drug reaction monitoring of antidepressants in the psychiatry out patient department at a tertiary care teaching hospital in India: a cross-sectional observational study,” European Journal of Psychology and Educational Studies, vol. 2, no. 1, pp. 14–19, 2015.

[22] P. S. Masand and S. Gupta, “Long-term side effects of newer-generation antidepressants: SSRIS, venlafaxine, nefazodone, bupropion, and mirtazapine,” Annals of Clinical Psychiatry, vol. 14, no. 3, pp. 175–182, 2002.

[23] T. J. Hudson, J. C. Fortney, J. M. Pyne, L. Lu, and D. Mittal, “Reduction of patient-reported antidepressant side effects, by type of collaborative care,” Psychiatric Services, vol. 66, no. 3, pp. 272–278, 2015.

[24] K. Al Jumah, M. A. Hassali, D. Al Qhatani, and K. El Tahir, “Factors associated with adherence to medication among...
depressed patients from Saudi Arabia: a cross-sectional study,” *Neuropsychiatric Disease and Treatment*, vol. 10, pp. 2031–2037, 2014.

[25] T. A. Burra, E. Chen, R. S. McIntyre, S. L. Grace, E. R. Blackmore, and D. E. Stewart, “Predictors of self-reported antidepressant adherence,” *Behavioral Medicine*, vol. 32, no. 4, pp. 127–134, 2007.

[26] J. W. Goethe, S. B. Woolley, A. A. Cardoni, B. A. Woznicki, and D. A. Piez, “Selective serotonin reuptake inhibitor discontinuation,” *Journal of Clinical Psychopharmacology*, vol. 27, no. 5, pp. 451–458, 2007.

[27] K. Demyttenaere, “Compliance during treatment with antidepressants,” *Journal of Affective Disorders*, vol. 43, no. 1, pp. 27–39, 1997.

[28] M. J. Martin-Vazquez, M. Garcia-Toro, F. Campoamor et al., “Use and results of antidepressant treatment: patients' perception,” *Current Drug Therapy*, vol. 6, no. 4, pp. 271–277, 2011.