

ORIGINAL ARTICLE

Prescribing Pattern of Anti-depressant drugs in Anxiety and Depressive disorder in Kathmandu valley

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ABSTRACT

Introduction: Anxiety and depression embrace a range of mental conditions occurring frequently in primary health care, usually in the form of overt disorders.

Methods: Our study site included three hospitals inside Kathmandu valley. The study was a cross sectional study review of patients attending the outpatients department of the hospital. One hundred and sixty subjects were enrolled in this study and duration of study was six months.

Results: Out of 160 patients, 81 (50.6%) were female and 79 (49.4%) were male with a mean age of 37.75 ± 1.65 . Majority of patients 100 (62.5%) were married. Majority of patient 39 (24.4%) were found to be of bachelor level, which showed prevalence of anxiety and depressive disorder more on educated groups than uneducated groups. Housewives were the highly affected group 40 (25%). Among all the antidepressant drugs prescribed, Escitalopram was highly prescribed with the frequency of 70 (48.3%). Selective serotonin reuptake inhibitors were the most common drug class with frequency 105 (65.6%). Clonazepam was the highly prescribed benzodiazepine in combination with antidepressant. Combination therapy was used in majority of cases 136 (85.0%) and Mono-therapy was used only in 24 (15.0%) cases.

Conclusion: Majority of anxiety and depressive disorder prevalence was observed in Female than in male. In anxiety disorder no mono-therapy was preferred whereas in depressive disorder both combination and mono-therapy was preferred. Combination therapy was preferred over mono-therapy. Most commonly prescribed antidepressant was Escitalopram and highly prescribed drug class was SSRI's. Clonazepam was the highly prescribed benzodiazepine in combination with antidepressant drugs.

Keywords: Anti-depressants, Anxiety Disorder, Depression, Prescribing pattern

INTRODUCTION

Depression (major depressive disorder) is a common and serious medical illness that negatively affects how you feel the way you think and how you act. Depression causes feelings of sadness and/or a loss of interest in activities once enjoyed.¹ It is an illness with more than 300 million people affected worldwide. It can cause the affected person to suffer greatly and function

poorly at work, at school and in the family. At its worst, depression can lead to suicide. Close to 800,000 people die due to suicide every year. Suicide is the second leading cause of death in 15-29-year-olds. The burden of depression and other mental health conditions is on the rise globally.² The term anxiety encompasses feelings of worry, fear and unease. Although it is normal to experience some level of anxiety at times, intense

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or persistent anxiety may be indicative of an anxiety disorder.³

Anxiety and depression embrace a range of mental conditions occurring frequently in primary health care, usually in the form of overt disorders. They are acknowledged as common mental disorders (CMDs) and, in terms of their ubiquity and the burdens they impose, as major disorders of the brain. In the recent Global Burden of Disease Study 2013 (GBD 2013), while mental and substance use disorders collectively accounted for 21.2 % of all years of life lost to disability (YLDs), depression and anxiety were ranked second and ninth highest specific causes of YLDs in both developed and developing countries. The crude prevalence of anxiety was 22.7 % and of depression 11.7 % in Nepal.⁴ Globally, the World Health Organization (WHO) says that almost 300million people have an anxiety disorder (2018).⁵ While depression is the leading cause of disability for both males and females, the burden of depression is 50% higher for females than males. In fact, depression is the leading cause of disease burden for women in both high-income and low- and middle-income countries (WHO, 2008).⁶ There are many risk factors for MDD and anxiety in Nepal, including poverty, illiteracy, a low education level, living in a conflict area, and experiencing disaster. Also, alcoholism and MDD are comorbid among alcohol dependent individuals, the lifetime prevalence of MDD is 45%.⁷

The experience of depression includes some form of sadness, whereas the experience of anxiety is comprised of some type of a fearful or nervous feeling. Anxiety and depression represent mutually exclusive forms of subjective emotional experiences that are qualitatively different; however, they share a number of interrelations, including their tendency to co-occur, having several similar neurological substrates, responding to similar forms of medication, and presenting in similar fashions.⁸

METHODOLOGY

A cross sectional study was conducted at different hospitals of Kathmandu valley (Metro Kathmandu Hospital, Mental Hospital, Kantipur Hospital) for period of six months (December 2018 to May 2019). A total of 159 patients attending the outpatient department were

participated in the study. Structured questionnaire was taken as main study tool.

The study proceeded through data collection, data entry and interpretation. The data was coded by numeric form such as first patient was coded by 1, second by 2 and so on. The socio-demographic characters of patient and drugs prescribed were noted. Data processing steps took place concurrently with the finalization of the checklist and commencement of the study. The data was revised, coded, verified and analysed using Epidata 3.1 and SPSS 16.0. Individual results have been found by calculation from the data collection sheet obtained from sample prescription and suitable statistical calculation was applied.

Sample Size

According to formula,(27)

$$N = z^2 \times p \times (1-p) / d^2$$

Where, N= Samplesize, s=Standardnormal variate=1.96, p= Expected proportion in population=11.7% (4)= 0.11

d= Absolute error= 5% = 0.05

Now,

$$N = (1.96)^2 \times 0.11 \times (1-0.11) / (0.05)^2$$

$$= 3.8416 \times 0.117 \times 0.883 / 0.0025$$

$$= 158.75 \approx 159$$

Therefore, estimated sample was 159.

Ethical Consideration: Approval from the Department of Pharmacy, Kathmandu Multiple college, Metro Kathmandu Hospital, Mental Hospital and Kantipur Hospital was taken for the study. Written consent was taken from patient for the study.

RESULTS

Socio-demographic and behavioural characteristics of patient regarding to their information: A total of 160 patients were selected from a pool of patients. The socio-demographic and behavioural characteristics of patients are presented in Table 1.

Among 160 patients, 81 (50.6%) were female and 79 (49.4%) were male. The mean age was 37.75 ± 1.65

where 24 (15.0%) patients were in the range of age below 20 years, 76 (47.5%) were between 20-40 years, 43 (26.9%) were between 41-60 years and 17 (10.6%) were aged above 60 years. Majority of patients 100 (62.5%) were married followed by 48 (30.0%) unmarried, 4 (2.5%) divorced and 8 (5.0%) widowed.

In case of smoking habit 35 (21.9%) were smokers, 120 (75.0%) were non-smokers and 5 (3.1%) were exceptional cases. Similarly in case of alcohol intake habit 20 (12.5%) took alcohol, 125 (78.1%) didn't take alcohol and 15 (9.4%) were exceptional.

Majority of patient 39 (24.4%) were found to be of bachelor level, 31 (19.4%) were of high school educated, 28 (17.5%) were secondary educated, 26 (16.2%) were basic level educated, 15 (9.4%) could read and write, 15 (9.4%) were illiterate and only 6 (3.8%) were having masters graduation or more. In terms of profession, 40 (25%) patients were housewife, 35 (21.9%) were student, 30 (18.7%) were having self-business, 16 (10.05) were unemployed, 11 (6.8%) were labour, 8 (5.0%) were civil service provider, 5 (3.1%) were health professionals, 5 (3.1%) were engineer and 10 (6.2%) were of other profession.

Table 1. Socio-demographic and behavioural characteristics of patient regarding to their information

S.N.	Variable	Frequency (n=160)	Percentage (100%)
Age range of patient			
1.	<20 years	24	15.0%
2.	20-40 years	76	47.5%
3.	41-60 years	43	26.9%
4.	>60 years	17	10.6%
Gender of patients			
1.	Male	79	49.4%
2.	Female	81	50.6%
Marital Status			
1.	Married	100	62.5%
2.	Unmarried	48	30.0%
3.	Divorced	4	2.5%
4.	Widowed	8	5.0%
Lifestyle			

1.	Smoking:		
	Yes	35	21.9%
	No	120	75.0%
	Exceptional	5	3.1%

2.	Drinking:		
	Yes	20	12.5%
	No	125	78.1%
	Exceptional	15	9.4%

Education			
1.	Illiterate	15	9.4%
2.	Basic Level	26	16.2%
3.	Secondary Level	28	17.5%
4.	Can read and write	15	9.4%
5.	High School	31	19.4%
6.	Bachelor	39	24.4%
7.	Masters and above	6	3.8%

Profession			
1.	Labour	11	6.8%
2.	Health Professional	5	3.1%
3.	Engineer	5	3.1%
4.	Student	35	21.9%
5.	Self-Business	30	18.7%
6.	Civil service	8	5.0%
7.	Unemployed	16	10.0%
8.	Housewife	40	25%
9.	Others	10	6.2%

Regarding the duration of anxiety and depressive disorder prevalence, 66 (41.2%) were suffering since less than 1 year, 75 (46.9%) were suffering from 1-5 years, 14 (8.8%) were suffering from 5-10 years and 5 (3.1%) were suffering since more than 10 years. The duration of disease prevalence is shown in **Table 2**.

Table 2. Duration of disease prevalence

S.N.	Duration	Frequency	Percentage
1	< 1 year	66	41.2%
2	1-5 years	75	46.9%
3	5-10 years	14	8.8%
4	>10 years	5	3.1%

Table 3. Type of disorder where antidepressants were prescribed

S.N.	Type of disorder	Frequency	Percentage
1	Anxiety Disorder	37	23.15%
2	Major Depressive Disorder	34	21.25%
3	Bipolar Disorder	16	10.0%
4	Adjustment Disorder	34	21.25%
5	Mood disorder secondary to illness	18	11.25%
6	Mixed anxiety depression	16	10%
7	Dysthymia	5	3.1%

Among 160 patients enrolled in the study, the predominate diagnosis was Anxiety disorder 37(23.15%) followed by 34(21.25%) Adjustment disorder, 34(21.25%) Major Depressive Disorder, 18(11.25%) Mood disorder secondary to illness, 16(10.0%) Bipolar Disorder, 16(10.0%) Mixed Anxiety Depression and only 5(3.1%) Dysthymia. The frequency of type of disorder is shown in **Table 3**.

Table 4. Prescribed Antidepressants

SN	Drugs	Frequency	Percentage
1	Escitalopram	70	43.8%
2	Sertraline	11	6.9%
3	Fluoxetine	18	11.2%
4	Fluvoxamine	3	1.9%
5	Paroxetine	4	2.5%
6	Duloxetine	9	5.6%
7	Venlafaxine	11	6.9%
8	Amitriptyline	34	21.2%
9	Imipramine	3	1.9%
10	Lithium Salt	3	1.9%
11	Valproic Acid	13	8.1%
12	Mirtazapine	2	1.2%
13	Trazodone	4	2.5%

*Multiple responses

Among all the antidepressant drugs prescribed, Escitalopram was highly prescribed with the frequency of 70 (43.8%), followed by amitriptyline being the second highest drug prescribed with frequency 34

(21.2%), fluoxetine being the third highest with frequency 18 (11.2%) and so on. Mirtazapine was found to be the least prescribed drug with the frequency 2 (1.2%). The antidepressants prescribed and their frequency is shown in table below **Table 4**.

Table 5. Antidepressants drug class

SN	Drug class	Frequency	Percentage
1	SSRI's	105	65.6%
2	SNRI's	19	11.9%
3	Atypical Antidepressants	6	3.8%
4	Tricyclic Antidepressants	37	23.1%
5	Anti-maniac	16	10.0%

Selective serotonin reuptake inhibitors were the most common drug class with frequency 105 (65.6%) followed by Tricyclic antidepressants 37 (23.1%), Serotonin Norepinephrine reuptake inhibitors 19 (11.9%), Anti-maniac agents 16 (10.0%) and Atypical antidepressants 6 (3.8%) which is shown on **Table 5**. The class MAOIs was not prescribed to any patient.

Table 6. Other drugs classes combined with antidepressants

SN	Drug Class	Frequency	Percentage
1	Benzodiazepines	97	60.6%
2	Antipsychotics	53	33.1%
3	Others	21	13.1%

In our study, Benzodiazepines was the highly prescribed drug class given in combination with antidepressants with frequency 97 (60.6%) followed by Antipsychotics 53 (33.1%) and others 21 (13.1%) which is shown in **Table 6**.

Table 7. Benzodiazepines

SN	Drugs	Frequency	Percentage
1	Clonazepam	76	47.5%
2	Lorazepam	16	10.0%
3	Alprazolam	13	8.1%
4	Zolpidem	3	1.9%
5	Chlordiazepoxide	3	1.9%

Among benzodiazepines, Clonazepam was of highest frequency 76 (47.5%) followed by Lorazepam 16

(10.0%), Alprazolam 13 (8.1%), Zolpidem 3 (1.9%) and Chlordiazepoxide 3 (1.9%) shown in **Table 7**.

Table 8. Other drugs except benzodiazepines

SN	Other drugs	Frequency	Percentage
1	Olanzapine	27	16.9%
2	Quetapine	4	2.5%
3	Risperidone	16	10.0%
4	Aripiprazole	6	3.8%
5	Haloperidol	2	1.2%
6	Vitamin B Complex	11	6.9%
7	Methylcobalamin	11	6.9%
8	Pregabalin	1	0.6%

Out of other drugs except benzodiazepines, Olanzapine belonging to class Antipsychotic was found to be highly used with frequency 27 (16.9%). Vitamin B complex and Methylcobalamin were also concomitantly used along with antidepressants with equal frequency 11 (6.9%) each which is shown in **Table 8**.

Table 9. Type of therapy in anxiety and depressive disorder

SN	Type of disorder	Mono-therapy	Combination Therapy
1	Anxiety Disorder	0 (0%)	37 (23.15%)
2	Depressive Disorder	24 (15.0%)	99 (61.85%)

Our study found that all the Anxiety disorder cases were treated with combination therapy 37 (23.15%) and no mono-therapy was in practice. Similarly, in Depressive disorder mono-therapy was practiced in 24 (15.0%) cases and Combination therapy in 99 (61.85%) cases shown in **Table 9**.

Table 10. Mono-therapy and Combination Therapy

SN	Type of therapy	Frequency	Percentage
1	Mono-therapy	24	15.0%
2	Combination Therapy	136	85.0%

The study found that Combination therapy was used in majority of cases 136 (85.0%) and Mono-therapy was used only in 24 (15.0%) cases shown in **Table 10**.

Table 11. Combination Therapy

SN	Combination	Frequency	Percentage
1	SSRI+Benzodiazepines	61	44.85%
2	SSRI+Antipsychotics	10	7.35%
3	SSRI+Tricyclic	10	7.35%
4	SNRI+Benzodiazepines	15	11.02%
5	Tricyclic+Benzodiazepines	7	5.14%
6	SSRI+SNRI	2	1.47%
7	Atypical+Benzodiazepines	3	2.20%
8	Antimaniac+ Benzodiazepines	7	5.14%
9	Tricyclic+Antipsychotics	5	3.67%
10	Others	16	11.76%

Combination of SSRI's and Benzodiazepines was highly used combination with frequency 61 (44.85%) shown in **Table 11**.

Table 12. Mono-therapy

SN	Drugs	Frequency	Percentage
1	Escitalopram	7	29.16%
2	Fluoxetine	6	25%
3	Amitriptyline	5	20.83%
4	Imipramine	3	12.5%
5	Sertraline	2	8.33%
6	Paroxetine	1	4.16%

Escitalopram was the highly prescribed antidepressant in Mono-therapy with frequency 7 (29.16%) shown in **Table 12**.

DISCUSSION

In the present study out of 160 cases 81 (50.6%) were female and 79 (49.4%) were male. This revealed that there is higher prevalence of anxiety and depressive disorder in female than male. This result is in agreement with previous study conducted by Islam, Md. R., & Shafique, A and TeckHweeSoh et al, 2013 who indicated that depression and anxiety disorder are more prevalent in female than in male.¹⁶⁻²¹ A study conducted by Chattar KB et al, 2016 showed that total number of female patients were 176 (61.97%) and males were 108 (38.02%), which also concluded that depression is more prevalent in female than in male.²⁰

In our study it was observed that 62.5% were

married which showed high prevalence of anxiety and depressive disorder in married group than in unmarried, widowed and divorced. Similar result was obtained in a study conducted by E.Avanthi et al, 2013 where it was more commonly seen in married people with (77%) than in unmarried people (23%). In case of education, antidepressants were highly prescribed to literate people than illiterate people, which is similar to the result obtained by E.Avanthi et al, 2013 where 72% were educated and 28% were uneducated.¹⁸ As far as occupation of the patient is concerned, depression and anxiety disorder is most commonly seen in Housewives 25% and secondly seen on Students 21.8%, this was similar to result observed by E.Avanthi et al, 2013 where 44% were housewives and 18% were students.¹⁸

The duration of illness for most of the patients was between 1 to 5 years (46.90%) and others 66(41.2%) were suffering since less than 1 year, 14(8.8%) were suffering from 5-10 years and 5(3.1%) were suffering since more than 10 years. A similar result was obtained on a study where the duration of illness for most of the patients was between 1 to 5 years (52.9%) which was conducted by TeckHweeSoh et al, 2013.¹⁶

In our study it is observed that combination therapy is preferred over mono therapy with 85.0% cases treated with combination therapy. Similar result was observed in a study carried out by E.Avanthi et al, 2013 where combination therapy is preferred over monotherapy with 91% of the cases treated with combination therapy.¹⁸

Most commonly prescribed antidepressant was Escitalopram (43.8%) and highly prescribed drug class was SSRI's (65.6%) which is similar to the result concluded by GianlucaTrifirò et al, 2008 and PradhanSumeet G et al, 2015 in their research.²²⁻²⁴ In our study 57% of benzodiazepines were prescribed in combination with antidepressants, among which Clonazepam had the highest frequency 47.5%. Similar result was obtained by Siddhartha Ghosh and Sugata Roy chaudhury where Clonazepam (76.27%) was highly prescribed.¹⁵

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Declaration of conflicting interests

The authors declare that there is no conflict of interest.

REFERENCES

1. American Psychiatric Association(APA) RP, MD,MPH. Depression: APA; January 2017 [Available from: <https://www.psychiatry.org/patients-families/depression/what-is-depression>].
2. Organization WH. Depression: World Health Organization; 2018 March 22 [Available from: <https://www.who.int/news-room/fact-sheets/detail/depression#>].
3. Leonard J. Everything you need to know about anxiety medications: Medical News Today, MediLexicon, Intl; November 2018 [cited 2019 June]. Available from: <https://www.medicalnewstoday.com/articles/323666.php>.
4. Ajay Risal caKM, Mattias Linde, Timothy J. Steiner, and Are Holen. Anxiety and depression in Nepal: prevalence, comorbidity and associations. 2016 April 14;Vol 16, 2016.
5. Newman T. Anxiety in the West: Is it on the rise? : Medical News Today; September 2018 [Available from: <https://www.medicalnewstoday.com/articles/322877.php>].
6. Marina Marcus MTY, Mark van Ommeren, and Dan Chisholm, Shekhar Saxena DEPRESSION A Global Public Health Concern WHO Department of Mental Health and Substance Abuse 2012 [Available from: https://www.who.int/mental_health/management/depression/who_paper_depression_wfmh_2012.pdf].
7. KECSKES S. Addressing Nepal's Hidden Health Challenge: Depression April 5, 2015 [Available from: <https://yaleglobalhealthreview.com/2015/04/05/addressing-nepals-hidden-health-challenge-depression/>].
8. Staff E. Are Depression and Anxiety Interrelated? May 21, 2019 [Available from: <https://lagunatreatment.com/mood-disorders/depression-and-anxiety/>].
9. Nolan Williams M, & Charles DeBattista,DMH,MD Psychiatric Disorders. In: Maxine A. Papadakis sJM, Michael W. Rabow, editor. CURRENT Medical Diagnosis & Treatment 2017. 56 ed: Cengage Publisher Services; 2017. p. 1050-107.

10. Nordqvist C. All about antidepressants UK: Medical News Today; February 2018 [Available from: <https://www.medicalnewstoday.com/kc/antidepressants-work-248320>].
11. Ncbi. Treatments for depression. Dec 5, 2012.
12. (IQWiG) IfQaEiHC. Depression: How effective are antidepressants? Jan 28, 2015.
13. Schimelpfening N. The 5 Major Classes of Antidepressants: verywellmind; May 08, 2019 [Overview,types, risk factors]. Available from: <https://www.verywellmind.com/what-are-the-major-classes-of-antidepressants-1065086>.
14. Margarita Tartakovsky MS. Depression: New Medications On The Horizon: Psychcentral; 2018 October 8 [Available from: <https://psychcentral.com/lib/depression-new-medications-on-the-horizon/>].
15. Fabre V1 HM. Mechanisms of action of antidepressants: new data from Escitalopram. May 2003.
16. Ghosh S, Roychaudhury S. Prescribing pattern of antidepressant drugs in a tertiary care hospital of eastern India 2014.
17. Teck Hwee Soh LL, Heng Nieng Chan, Yiong Huak Chan. Antidepressant Prescribing Patterns for Depressive and Anxiety Disorders in a Singapore Hospital 2015 March 6.
18. Richard D Howland P, Mary J. Mycek, PhD. Lippincott's Illustrated Reviews: Pharmacology. Third edition ed. Richard A. Harvey P, Pamela C. Champe, PhD, editor: BI Publications Private Limited.
19. E. Avanthi1* HSS, L. Pradeep Kumar2, H. K. Sushma1, C. Y. Sudarshan2, Babbol Raja3. Prescribing pattern of antidepressants in psychiatric unit of a tertiary care hospital. 2014.
20. Abdul Rahman Fata Nahas SASS. Prescribing Patterns of Antidepressants among Depressive Men in Malaysia: A Survey. 2018;10.