Analysis of psychotropic medications prescriptions in Turkey

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Abstract- In psychiatry, where definitive and clear diagnosis has been and still a major problem and where polypharmacy is common, off-label prescribing is particularly common. This study also informs the extent to which family physicians and non-psychiatrists are prescribing psychotropic medications. We used data from the 2014 IMS Health Turkey Medical Index (TMI). The survey in TMI data base is conducted each quarter in a sample of 705 medical doctors, which is projected to a universe of 62 562 physicians. The TMI is a nationally representative survey of an office-based panel of physicians to examine the diagnoses for which medications are being recommended. Descriptive analysis has been conducted with TMI data. Descriptive analysis has been conducted with TMI data about the consumption of psychotropic medications. Although there are limitations of the study, it is the first time an analysis conducted to understand the usage of psychotropic medications from a survey data in Turkey. Psychotropic medications are one of the most common and costly classes of prescription drugs in the substantial extent of prescription written by family physicians is of great concern, also. In order to improve quality and safety of health care services provided to patients and to ensure rational use of health care resources, it is essential to know the reasons why psychotropic medications are prescribed to patients.

Keywords: psychotropic medications, psychiatry, Turkey

1.Introduction

In psychiatry, where definitive and clear diagnosis has been and still a major problem and where polypharmacy is common, off-label prescribing is particularly common (Kharadi et al., 2015). Off-label drug use has become widely entrenched in clinical practice and continues to be predominant treatment options for certain clinical conditions. For example, tricyclic antidepressants do not have FDA approval as a treatment for neuropathic pain, yet this class of drugs is considered a first-line treatment option (Dworkin et al., 2010).

In Turkey, health services are financed through a social security scheme covering the majority of the population, the General Health Insurance Scheme, and services are provided both by public and private sector facilities. Most of antidepressants and antipsychotics can be prescribed by all physicians on the basis of a report issued by psychiatrists and neurologists. There is also a current guideline on the off-label use of all drugs. Turkish Pharmaceuticals and Medical Devices Agency (TITCK) limits and controls how the medications are prescribed by physicians once the medications are available on the market. Marketing license does not signify the best use of medicine in unlicensed indication so another list published by TITCK is "the off-label medication list which can be used without any additional approval" (T.C. Sağlık Bakanlığı) for example use of antidepressant amitriptyline in the case of panic disorder. Clinicians can prescribe off-label or unlicensed drugs with approval if it is not on the list. The presence of such a list raises the potential for medication errors, off-label use and concerns about the quality of prescribing. Because of the lack of monitoring, concerns remain about whether the prescription practice is concordant with evidence-based medicine and clinical guidelines. So regular monitoring of prescribing patterns is an important tool for rational use of drugs.

Off-label drug use is concerning because of the high rates of metabolic and extrapyramidal side effects and inadequate monitoring of these complications (Pringsheim & Gardner, 2014). This concern has primarily involved the limited safety and efficacy research for the diagnoses for which psychotropic medications are being prescribed without approval and the presence of comorbidity, or multiple co-occuring psychiatric diagnoses (Gulla et al., 2016).

To some extent, off-label drug uses provide a pathway for clinical innovation. Since identifying the off-label uses can provide a clue to the stakeholders including healthcare providers, patients, and medication manufacturers to further the investigation on drug efficacy and safety, it raises the demand for a systematic way to detect off-label uses.

In this study, we sought to determine the extent to which antidepressants, anxiolytics, antipsychotics and hypnotic-sedative medications were prescribed for psychiatric and non-psychiatric diagnoses. This study also informs the extent to which family physicians and non-psychiatrists are prescribing psychotropic medications. The large role of family physicians in psychotropic drug prescribing is important

for easy access to treatment. However, there are growing concerns about the quality of treatments (Brijnath et al., 2017).

2.Materials & Methods:

The nature of this study was based on analysis of data from physician participants within office-based medical practices. We used data from the 2014 IMS Health Turkey Medical Index (TMI). The TMI is a nationally representative survey of an office-based panel of physicians to examine the diagnoses for which medications are being recommended.

TMI uses a two-stage, stratified and randomly drawn sampling methodology. In the first stage, physicians were sampled. During the second stage, a start day for each physician is assigned to report data for seven consecutive workdays per quarter. This survey is conducted each quarter in a sample of 705 medical doctors, which is projected to a universe of 62 562 physicians. 705 physicians constitute a representative sample, both geographically and by specialty, with weighting adjustments made to determine national drug recommendations each year. The sample includes 15 primary specialties involved in direct office-based care. Geographic area is defined by the five Turkey geographic regions of West, Northwest, Southeast, Northeast and Mid.

The survey collects information through the use of a confidential log book in which physicians record information for each drug mention (i.e. each drug recommended or issued to a patient) and related diagnoses over a specified period. The term 'drug mention' is used for data obtained from TMI database as not all prescriptions given to patients are dispensed and because physicians may link a single mention to multiple diagnoses.

Diagnoses in each record of a drug therapy within TMI are grouped using the International Classification of Diseases 10th Revision (ICD-10) (WHO, 2010). Diagnoses, coded using ICD-10-CM, were grouped into psychiatric and non-psychiatric categories. Psychiatric diagnoses were defined at those of ICD-10-CM codes F00-F99.

The current study focused on drug mentions of the four main categories of psychotropic medications, defined according to the World Health Organization categories and comprised the following subgroups of the Anatomic Therapeutic Chemical (ATC) classification system: antidepressants (NO6A), anxiolytics (N05B), antipsychotics (N05A) and hypnotics and sedatives (N05C).

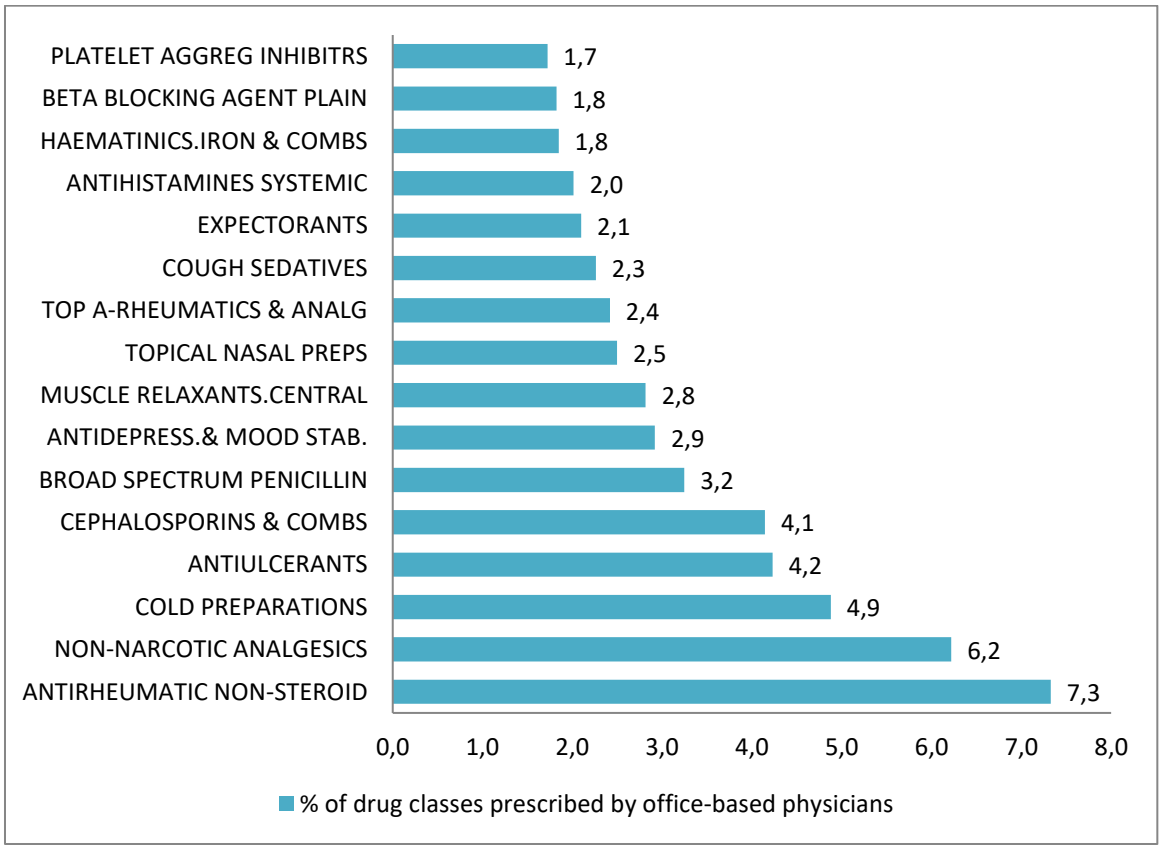
Based on the physician-reported diagnostic codes associated with each psychotropic medication treatment visit, we searched the summary of that product characteristic. Medication reporting reflects the physicians's best knowledge of new or continuing medications. The TMI does not capture information on patient adherence or unreported self-medication. It is not known whether the recommendation resulted in a prescription being dispensed, there is not necessarily a direct correlation between the number of prescriptions dispensed and the frequency with which drug is recommended. We present annual data as the aggregate of the quarterly surveys conducted within each year.

For the TMI estimates, 95.5% confidence intervals were calculated using tables of relative standard errors that accounted for the complex TMI sampling design. The data were extracted by staff at IMS Health Turkey and provided to the investigators in the form of an Excel spreadsheet. Statistical methods were not employed for two reasons. First, the goals of the study were descriptive. Second, the data points represented treatment recommendations rather than individual people, violating the statistical assumption of independence. The reported indications were simply tabulated and graphed for each psychotropic medication groups in each year. The diagnoses provided during data collection were coded using ICD-10-CM codes by IMS staff. However, these were parsed into four categories by the principal investigator: depressive disorders, anxiety disorders, other psychiatric disorders and non-psychiatric disorders.

3.Results & Discussions:

The TMI reported an estimated 878 million total drug mentions for the year 2014. With approximately 25 million drug mentions, antidepressants were the most commonly prescribed of the four drug classes examined. It was followed by antipsychotics and anxiolytics with 6 million and 2.8 million respectively. The antidepressant medications identified in this sample accounted for approximately 2.9% of all estimated prescription drug use in 2014 and antidepressants were ranked seventh in the most prescribed groups of medication in Turkey. (Figure 1).

Figure 1: Frequency of use of drug classes as a percentage of total drug recommendations in Turkey (2014).



Serotonin-Noradrenaline Reuptake Inhibitors (SSRIs) dominated the prescription trends representing 66% of the total antidepressant prescriptions. Only 3 SSRIs (escitalopram, sertraline and paroxetine) comprised 52.4% of total antidepressant prescriptions. Of the total number of antidepressant drug mentions, 93.7% were prescribed for psychiatric conditions. The most common (48.2%) were depression, followed by anxiety disorders (33.5%). Antidepressants were also used for a variety of other psychiatric conditions including obsessive-compulsive disorder (2.4%), bipolar disorder (2%), behavioral and emotional disorders with onset usually occurring in childhood and adolescence (1.8%), somatoform disorders (1,7%) and others. Approximately 6.3% of antidepressant prescriptions were prescribed for a variety of non-psychiatric diagnoses. About 1.6% was prescribed for sleep disorders (including insomnia). Especially trazodone was frequently (6.2%) prescribed for sleep disorders. Another 1% was prescribed for headaches (including migraine), and 0.8% for 'other soft tissue disorders' (e.g. fibromyalgia). Duloxetine was more commonly used for fibromyalgia (3.8%) (Table 1 & 2).

Table 1: National estimates of antidepressants prescribed by office-based physicians by patient diagnosis categories[a]

Drug	Patient diagnosis[b]	Number of drug mentions (000)	% of all antidepressant mentions
Antidepressants (NO6A)	**Total**	**25 654**	
	PSYCHIATRIC	24 037	93,7
	Major Depressive disorder	12 371	48,2
	Anxiety disorders	8 594	33,5
	Obsessive-compulsive disorder	621	2,4
	Bipolar disorder	532	2
	Disorders with onset usually occurring in childhood/adolescence	465	1,8
	Somatoform disorders	429	1,7
	NON-PSYCHIATRIC	1 616	6,3
	Sleep disorders	419	1,6
	Headaches; including migraine	252	1
	Soft tissue disorders (e.g. fibromyalgia)	209	0,8
	Sexual dysfunction	133	0,5
	Unknown and unspecified causes of mobidity	307	1,2

[a]. From the 2014 Turkey Medical Index, a survey of nationally representative office-based physicians that captures each mention of a psychiatric medication and the diagnosis for which it is recommended.
[b]. Diagnoses categories are based on International Classification of Diseases 10th Revision (ICD-10)

Table 2: National estimates of duloxetine prescribed by office-based physicians by patient diagnosis categories[a]

Drug	Patient diagnosis[b]	% of all duloxetine mentions
Duloxetine	**Total**	**100**
	PSYCHIATRIC	**84,9**
	Major depressive disorder	53
	Anxiety disorders	21,9
	Somatoform disorders	5
	Bipolar disorders	2,2
	Obsessive-compulsive disorder	1
	Schizophrenia or other psychotic disorders	0,6
	Disorders with onset usually occurring in childhood/adolescence	0,2
	Mental and behavioural disorders due to psychoactive substance use	0,1
	NON-PSYCHIATRIC	**15,1**
	Other soft tissue disorders; e.g. fibromyalgia	7,4
	Headache; including migraine	2,1
	Diabetes mellitus	0,7
	Diseases of esophagus, stomach and duodenum	0,7
	Unknown and unspecified causes of morbidity	1,3

[a]. From the 2014 Turkey Medical Index, a survey of nationally representative office-based physicians that captures each mention of a psychiatric medication and the diagnosis for which it is recommended.
[b]. Diagnoses categories are based on International Classification of Diseases 10th Revision (ICD-10)

Hydroxyzine and alprazolam were the 2 anxiolytic medications most commonly prescribed in 2014. Of the total number of anxiolytic drug mentions, 24.6% were prescribed for psychiatric conditions. The most common psychiatric diagnoses were

anxiety disorders (comprising 15.8% of all drug mentions), followed by major depressive disorder (4.2%). Almost 75% of anxiolytic drug mentions were for non-psychiatric conditions. This situation is substantially the result of hydroxyzine prescriptions. Hydroxyzine was more commonly prescribed for non-psychiatric conditions than for psychiatric conditions. In particular, 19.3% of hydroxyzine mentions were for 'diseases of the skin and subcutaneous tissue' (e.g. urticarial, dermatitis). Another 6.8% of hydroxyzine were prescribed for sleep disorders (including insomnia), and 8.1% for allergic reactions. About 3.5% were for 'unspecified illness' and about 3.3% were for 'diseases of the respiratory system' (e.g. acute upper respiratory infections and diseases of upper respiratory tract) and 1.4% were for varicella (Table 3).

Table 3: National estimates of anxiolytics prescribed by office-based physicians by patient diagnosis categories[a]

Drug	Patient diagnosis[b]	Number of drug mentions (000)	% of all anxiolytics mentions
Anxiolytics (N05C)	**Total**	**2 794**	
	PSYCHIATRIC	**689**	**24,7**
	Anxiety disorders	441	15,8
	Major depressive disorder	117	4,2
	Schizophrenia	26	0,9
	NON-PSYCHIATRIC	**2 104**	**75,3**
	Dermatitis		5,3
	Sleep disorders	127	4,5
	Urticaria - Erythema		4,2
	Adverse effects		4,2
	Unpsecified illness		2

[a]. From the 2014 Turkey Medical Index, a survey of nationally representative office-based physicians that captures each mention of a psychiatric medication and the diagnosis for which it is recommended.

[b]. Diagnoses categories are based on International Classification of Diseases 10th Revision (ICD-10)

Quetiapine, olanzapine and risperidone were the 3 antipsychotic medications most commonly prescribed by physicians in 2014. Of the total number of antipsychotic drug mentions, 94.1% were prescribed for psychiatric conditions. The most common diagnoses, comprising 43.2% of all drug mentions, were mood disorders such as major depression (25.2%) and bipolar disorder (15%). The second most common psychiatric diagnosis was schizophrenia or other psychotic disorders, comprising 30.6% of drug mentions. Approximately 9.2% of drug mentions were for anxiety disorders. Obsessive compulsive disorder was the diagnosis

indicated on 3.4% of all drug mentions. About 1% of antipsychotic prescriptions were for dementia. 'Behavioral and emotional disorders with onset usually occurring in childhood and adolescence' (e.g. attention-deficit hyperactivity disorders) comprised 1.8% of antipsychotic drug mentions. Alzheimer was indicated on 2.8% of antipsychotic drug mentions. Of the total number of the most commonly prescribed antipsychotic medication – quetiapine – mentions, 9.6% were prescribed for non-psychiatric conditions. About 5% of quetiapine mentions were for Alzheimer (Table 4 & 5).

Table 4: National estimates of antipsychotics prescribed by office-based physicians by patient diagnosis categories[a]

Drug	Patient diagnosis[b]	Number of drug mentions (000)	% of all antidepressant mentions
Antipsychotics	**Total**	**6 273**	
	PSYCHIATRIC	**5 903**	**94,1**
	Schizophrenia or other psychotic disorders	1 645	30,6
	Major depressive disorder	1 580	25,2
	Bipolar disorder	938	15
	Anxiety disorders	576	9,2
	Obsessive-compulsive disorder	215	3,4
	Disorders with onset usually occuring in childhood/ adolescense (e.g. attention-deficit hyperactivity disorders)	116	1,8
	Dementia	64	1
	NON-PSYCHIATRIC	**370**	**6,1**
	Alzheimer's disease	175	2,8

[a]. From the 2014 Turkey Medical Index, a survey of nationally representative office-based physicians that captures each mention of a psychiatric medication and the diagnosis for which it is recommended.

[b]. Diagnoses categories are based on International Classification of Diseases 10th Revision (ICD-10)

Table 5: National estimates of quetiapine prescribed by office-based physicians by patient diagnosis categories[a]

Drug	Patient diagnosis[b]	Number of drug mentions (000)	% of all quetiapine mentions
Quetiapine	**Total**	**2 113**	**100**
	PSYCHIATRIC	**1 908**	**90,3**
	Major depressive disorder	663	31,3
	Schizophrenia or other psychotic disorders	425	20,1
	Bipolar disorders	364	17,2
	Anxiety disorders	206	9,7
	Dementia	43	2
	Obsessive-compulsive disorders	28	1,3
	Mental and behavioural disordes due to psychoactive substance use	26	1,2
	Disorders with onset usually occurring in childhood/adolescence	20	0,9
	Personal disorders	14	0,7
	Behavioural syndromes; including eating and sleep disorders and sexual disfunction	6	0,3
	Mental retardation	5	0,2
	NON-PSYCHIATRIC	**204**	**9,6**
	Alzheimer's disease	105	5
	Insomnia		2
	Epilepsy		0,4
	Parkinson's disease		0,3
	Migraine		0,1
	Asthma		0,1
	Unknown and unspecified causes of morbidity		0,6

[a]. From the 2014 Turkey Medical Index, a survey of nationally representative office-based physicians that captures each mention of a psychiatric medication and the diagnosis for which it is recommended.

[b]. Diagnoses categories are based on International Classification of Diseases 10th Revision (ICD-10)

Doxylamine, passiflora incarnata and zopiclone were the 3 hypnotic and sedative medications most commonly prescribed by physicians in 2014. The top 3 diagnoses, accounting for 65.6% of hypnotics and sedatives recommendations, were anxiety disorders (32.4%), sleep disorders (23.8%) and major depressive disorder (9.4%). About 2.1% of hypnotic and sedative medication prescriptions were for dermatitis and urticaria. 'Unspecified illnesses' comprised 3.3% of hypnotic-sedative drug mentions (Table 6).

Table 6: National estimates of hypnotic-sedatives prescribed by office-based physicians by patient diagnosis categories[a]

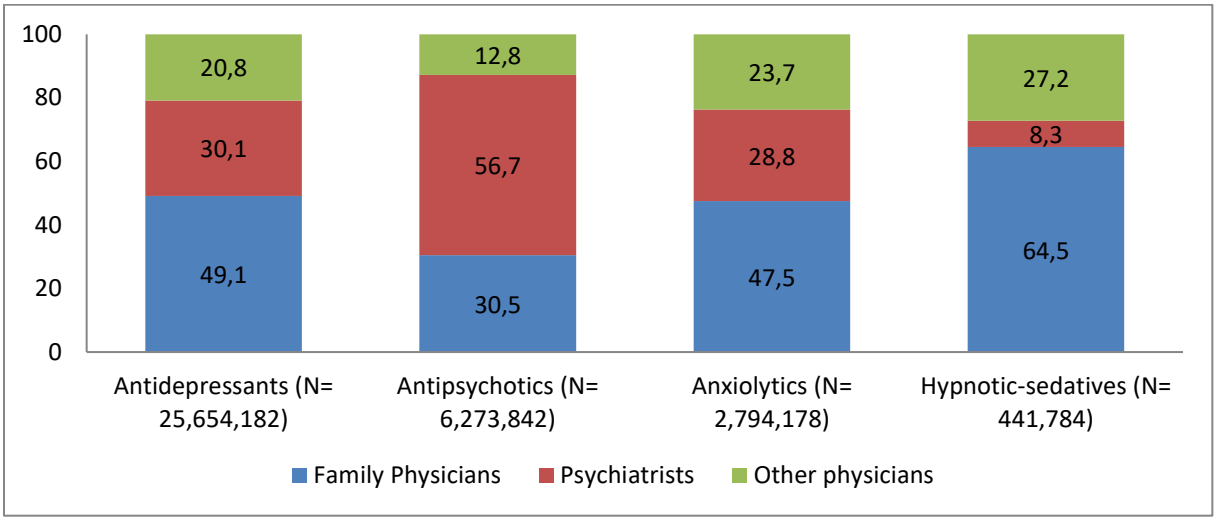
Drug	Patient diagnosis[b]	Number of drug mentions (000)	% of all antidepressant mentions
Hypnotics-Sedatives (N05B)	**Total**	**441**	
	PSYCHIATRIC	**237**	**53,8**
	Anxiety disorders	143	32,4
	Major depressive disorder	41	9,4
	Behavioral syndromes associated with physiological disturbances and physical factors	4,6	1
	Disorders with onset usually occurring in childhood/adolescence	3,2	0,7
	NON-PSYCHIATRIC	**204**	**46,2**
	Sleep disorders	105	23,8
	Dermatitis + Urticaria	9,4	2,1
	Unknown and unspecified causes of morbidity	14	3,3

[a]. From the 2014 Turkey Medical Index, a survey of nationally representative office-based physicians that captures each mention of a psychiatric medication and the diagnosis for which it is recommended.
[b]. Diagnoses categories are based on International Classification of Diseases 10th Revision (ICD-10)

Of the 25 million prescriptions for antidepressants, 49.1% were written by family physicians, 30.1% by psychiatrists, and 20.8% by other physicians. Family physicians wrote prescriptions for 30.5% of the antipsychotropic medications in the sample, 64.5% of the hypnotics and sedatives and 47.5% of the anxiolytics. Psychiatrists wrote prescriptions for 56.7% of the antipsychotropic medications, 8.3%

of the hypnotics and sedatives and 28.8% of the anxiolytics. (Figure 2)

Figure 2: Percentage of Turkey psychotropic prescriptions written in 2014, by the type of prescriber



The study has some limitation as including data based on survey, not a real world data. Depending on the lack of legislation, it is not possible to retrieve real world data from Turkey`s health system. It is needed to conduct a registry system which may not possible to cover the cost for an academic study. Another limitation is the available data timeline as the dataset retrieved from IMS` 2014 data base which is only available free to use for academic studies.

There is a need to raise awareness of off-label prescribing problem among psychiatricians so as to improve the prescribing of drugs. Off-label use of psychotropic medications can have significant consequences. For example, as TMI data has shown, in 2014, 2% of antidepressant drug mentions or 532 thousand antidepressant drug mentions were prescribed for bipolar depression. Initiating treatment with an antidepressant alone in patients, who are at risk for bipolar disorder, may precipitate an acute switch into mixed/manic episode and induction of mixed episodes, as well as rapid cycling (Muneer, 2016). So prior to initiating treatment, patients with bipolar disorder should be screened with their detailed psychiatric history. To ensure appropriate intervention, the clinician must evaluate and monitor patients with bipolar disorder for the presence and the development of comorbid psychiatric and medical conditions (Ranga & Krishnan, 2005). Bipolar disorder is a lifelong illness, ultimately, best treated by a mental health specialist. In Turkey, a large number of psychiatric prescriptions have been being written by nonspecialist physicians. As the overall care of the patient rests with the family physician, it is highly important that they have enough knowledge of the

potentially adverse effects of the psychotropic medications and they should be aware that bipolar disorder has several associated physical and neuropsychiatric comorbidities.

Sleep disturbances has many potential aetiologies including some that are primary and some that are secondary to other psychiatric and/or non-psychiatric disorders. As many as 90% of patients with depression will have sleep quality complaints (Tsuno, Besset & Ritchie, 2005). About two thirds of patients undergoing a major depressive episode will experience insomnia, with about 40% of patients complaining of other sleep disturbances (Hamilton, 1989; Perlis et al., 1997). This analysis found that of 25 million recommendations, 1.6 % were for sleep disorders, consistent with a study conducted in Canada, of 1.2 million recommendations for amitriptyline, 9% were for sleep disorders (Patten, Esposito & Carter, 2007). Similarly Azermai et al (2011) found that the overall prevalence of psychotropic drug use among Belgian nursing home residents was 79% and antidepressants were prescribed in 40% of which 1/3 was indicated for insomnia. It is important for clinicians to carefully evaluate sleep symptoms in patients with depression. Although sleep disturbances are typical features of depression, such symptoms sometimes appear prior to an episode of depression. The bidirectional associations between sleep disturbance (especially insomnia) and depression increase the difficulty of differentiating cause-and-effect relationships between them (Franzen & Buysse, 2008).

One of the controversial usages of antipsychotic medications is for the treatment of dementia. TMI data revealed that in 2014, 2% of quetiapine drug mentions were prescribed for dementia, and 5% were for Alzheimer. In recent years, there are valid concerns around the practice of off-label prescribing of both conventional and atypical antipsychotics in elderly patients affected with dementia and the possible risks for stroke and sudden death (Gill et al., 2007). According to the U.S. Food and Drug Administration, pneumonia is one of the most frequently reported causes of death in elderly patients with dementia who are treated with antipsychotic drugs (Gareri et al., 2014; Steinberg & Lyketsos, 2012).

The development of diabetes mellitus (DM) was one of the serious and chronic adverse effects among psychotropic drug-induced adverse events in the general population (Bhuvaneswar et al., 2009). Many studies has established that use of antipsychotics increases the risk of new onset DM in patients with schizophrenia and bipolar disorder (Campayo et al., 2010; Guo et al., 2006). A study conducted in Republic of Kore indicated that antipsychotics used in patients with Alzheimer's disease might increase the development of DM (Chang et al., 2015). Elderly patients with Alzheimer's disease should hence be monitored for the risk of DM while receiving antipsychotics in clinical practice.

With the increasing use of psychotropic medications in patients with Alzheimer to influence cognitive performance, safety of these medications has become a matter of concern. Some trials

indicated that quetiapine and olanzapine are responsible for greater cognitive decline (Vigen et al., 2011). Elderly patients with Alzheimer should hence monitored while receiving antipsychotics. The use of psychotropic medications in the elderly is especially of vital importance because of the potential for polypharmacy and greater medical comorbidity.

While this study does not include data on the age of those treated, it reveals that 1,8 % of both antidepressant and antipsychotic drug mentions were for 'behavioral and emotional disorders with onset usually occurring in childhood and adolescents' (e.g. attention-deficit hyperactivity disorders). Thereupon the increasing concern that the use of antidepressant medications may include suicidal thinking and behavior in children and adolescents, the FDA adopted a 'black box' label warning (FDA) indicating antidepressants may increase the risk of suicidal thinking and behavior in some children and adolescents with MDD. Some studies show that prescribers respond to black box warnings and risk associated with prescribing medications to particular populations, for particular conditions, or both (Friedman, 2014; Larkin et al., 2014).

In Turkey, a large number of psychiatric prescriptions have been written by nonspecialist physicians, who may not have enough knowledge of the potentially adverse effects of the psychiatric medications, especially in case of prescribing for unlicensed indications and in the presence of comorbidity. A panel of 44 000 subjects conducted in France showed that for 60% of the subjects, the antidepressant treatment was prescribed by a general practitioner and one quarter (25%) presented with a diagnosis of a characterized psychiatric disease, outside of the marketing authorization indications for the product taken (Olie et al., 2002). These findings are consistent with reports from the United States that showed that approximately 1 in 10 adults were treated with an antidepressant, usually by a general medical provider (73.6%) (Mojtabai & Olfson, 2008). So, appropriate monitoring for side effects and treatment response and the liaison between specialist physicians and primary care physicians are very important issues to improve quality and safety of health care services provided to patients and to ensure rational use of health care resources.

4.Conclusion

This study must be understood in light of its limitations. Since it used mentions of recommended medications as a proxy of actual pharmacological treatment, it was not possible to assess if the drug was actually consumed by patient. The major strength of this study is the fact that it is a large multiregional study. Data from TMI is based on a national sampling strategy that identifies representative samples of different socio-demographic and geographic settings.

Psychotropic medications are one of the most common and costly classes of prescription drugs in Turkey. While their increasing use has been widely reported, far less is known regarding the evolution of their clinical uses. Psychotropic medications are frequently prescribed for a wide range of psychiatric and nonpsychiatric conditions. When the use of drugs for the new and untested clinical indications reaches a substantial volume,

additional efforts may be needed to generate evidence that demonstrates the safety and efficacy of the new uses. The substantial extent of prescription written by family physicians is of great concern, also. In order to improve quality and safety of health care services provided to patients and to ensure rational use of health care resources, it is essential to know the reasons why psychotropic medications are prescribed to patients.

References

Azermai, M., Elseviers, M., Petrovic, M., Van Bortel, L., & Vander Stichele, R. (2011). Geriatric drug utilisation of psychotropics in Belgian nursing homes. Hum Psychopharmacol, 26(1), 12-20.

Bhuvaneswar, C. G., Baldessarini, R. J., Harsh, V. L., & Alpert, J. E. (2009). Adverse endocrine and metabolic effects of psychotropic drugs: selective clinical review. CNS Drugs, 23(12), 1003-1021.

Brijnath, B., Xia, T., Turner, L., & Mazza, D. (2017). Trends in GP prescribing of psychotropic medications among young patients aged 16–24 years: a case study analysis. BMC Psychiatry, 17, 214.

Campayo, A., de Jonge, P., Roy, J. F., Saz, P., de la Camara, C., Quintanilla, M. A., ... Lobo, A. (2010). Depressive disorder and incident diabetes mellitus: the effect of characteristics of depression. Am J Psychiatry, 167(5), 580-588.

Chang, K. J., Hong, C. H., Lee, Y., Lee, K. S., Roh, H. W., Back, J. H., ... Son, S. J. (2015). Effect of Psychotropic Drugs on Development of Diabetes Mellitus in Patients With Alzheimer's Disease. Medicine (Baltimore), 94(23), e919.

Dworkin, R. H., O'Connor, A. B., Audette, J., Baron, R., Gourlayi G. K., Haanpaa, M. L., ... Wells, C. D. (2010). Recommendations for the pharmacological management of neuropathic pain: an overview and literature update. Mayo Clinic Proc, 85(3), S3-S14.

FDA. Medication Guide Antidepressant Medicines, Depression and other Serious Mental Illnesses, and Suicidal Thoughts or Actions. https://www.fda.gov/media/72995/download

Franzen, P. L., & Buysse, D. J. (2008). Sleep disturbances and depression: risk relationships for subsequent depression and therapeutic implications. Dialogues Clin Neurosci, 10(4), 473-481.

Friedman, R. A. (2014). Antidepressants' Black-Box Warning - 10 Years Later. N Engl J Med, 371, 1666-1668.

Gareri, P., Segura-Garcia, C., Manfredi, V. G. L., Bruni, A., Ciambrone, P., Cerminara, G., ... De Fazio, P. (2014). Use of atypical antipsychotics in the elderly: a clinical review. Clin Interv Aging, 9, 1363-1373.

Gill, S. S., Bronskill, S. E., Normand, S. T., Anderson, G. M., Sykora, K., Lam, K., ... Rochon, P. A. (2007). Antipsychotic Drug Use and Mortality in Older Adults with Dementia. Ann Intern Med, 146, 775–786.

Gulla, C., Selbaek, G., Flo, E., Kjome, R., Kirkevold, O., & Husebo, B. S. (2016). Multi-psychotropic drug prescription and the association to neuropsychiatric symptoms in three Norwegian nursing home cohorts between 2004 and 2011. BMC Geriatr, 16, 115.

Guo, J. J., Keck, P. E., Corey-Lisle, P. K., Li, H., Jiang, D., Jang, R., & L'Italien, J. R. (2006). Risk of diabetes mellitus associated with atypical antipsychotic use among

patients with bipolar disorder: A retrospective, population-based, case-control study. J Clin Psychiatry, 67(7), 1055-1061.

Hamilton, M. (1989). Frequency of symptoms in melancholia (depressive illness). Br J Psychiatry, 154(2):201-206.

Kharadi, D., Patel, K., Rana, D., & Patel, V. (2015). Off-label drug use in Psychiatry Outpatient Department: A prospective study at a Tertiary Care Teaching Hospital. Journal of Basic and Clinical Pharmacy, 6(2), 45-49.

Larkin, I., Ang, D., Avorn, J., & Kesselheim, A. S. (2014). Restrictions on pharmaceutical detailing reduced off-label prescribing of antidepressants and antipsychotics in children. Health Aff (Millwood), 33(6),1014-1023.

Mojtabai, R., & Olfson, M. J. (2008). National patterns in antidepressant treatment by psychiatrists and general medical providers: results from the national comorbidity survey replication. J Clin Psychiatry, 69(7), 1064-1074.

Muneer, A. (2016). Pharmacotherapy of Acute Bipolar Depression in Adults: An Evidence Based Approach. Korean J Fam Med, 37(3), 137-148.

Olie, J. P., Elomari, F., Spadone, C., & Lepine, J. P. (2002). Antidepressants consumption in the global population in France. Encephale, 28(5 Pt 1), 411-417.

Patten, S. B., Esposito, E., & Carter, B. (2007). Reasons for antidepressant prescriptions in Canada. Pharmacoepidem. Drug Safe, 16, 746–752.

Perlis, M. L., Giles, D. E., Buysse, D. J., Thase, M. E., Tu, X., & Kupfer, D. J. (1997). Which depressive symptoms are related to which sleep electroencephalographic variables? Biol Psychiatry, 42(10), 904-913.

Pringsheim, T., & Gardner, D. M. (2014). Dispensed prescriptions for quetiapine and other second-generation antipsychotics in Canada from 2005 to 2012: a descriptive study. CMAJ Open, 2(4), E225–E232.

Ranga, K., & Krishnan, R. (2005). Psychiatric and medical comorbidities of bipolar disorder. Psychosomatic Medicine, 67, 1-8.

Steinberg, M., & Lyketsos, C. G. (2012). Atypical Antipsychotic use in patients with dementia: Managing safety. Am J Psychiatry, 169(9), 900-906.

T.C. Sağlık Bakanlığı. Türkiye İlaç ve Tıbbi Cihaz Kurumu. Endikasyon Dışı İlaç Ek 4. https://www.titck.gov.tr/dinamikmodul/45.

Tsuno, N., Besset, A., & Ritchie, K. (2005). Sleep and depression. J Clin Psychiatry, 66(10), 1254-1269.

Vigen, C. L. P., Mack, W. J., Keefe, R. S. E., Sano, M., Sultzer, D. L., Stroup, T. S., ... Schneider, L. S. (2011). Cognitive effects of atypical antipsychotic medications in patients with Alzheimer's disease: outcomes from CATIE-AD. Am J Psychiatry, 168(8), 831-839.

WHO. (2010). International Statistical Classification of Diseases and Related Health Problems 10th Revision Volume 2, Instruction manual 2010 Edition. https://www.who.int/classifications/icd/ICD10Volume2_en_2010.pdf.