



Pharmacotherapy of Mental Illness in the Mental Health Centers in Kosovo During 2021

Fitim Alidema¹, Viktor Isjanovski², Arieta Hasani-Alidema^{1,3}, Behrije Halilaj-Vishi⁴, Minire Alilaj-Beqiraj^{1,4*}

¹Department of Medical Science, Faculty of Pharmacy, UBT College, Prishtina, Kosovo; ²Psychiatric Hospital, Medical Faculty, Ss. Cyril and Methodius University, Skopje, Republic of Macedonia; ³Department of Neurology, University Clinical Center of Kosovo, Prishtina, Kosovo; ⁴Department of Gynecology, Regiona Hospital, Ferizaj, Kosovo

Abstract

BACKGROUND: Treatment of mental illness with pharmacotherapy is strictly monitored in clinical centers dedicated to this purpose. While in most developed countries, this practice is well established, in Kosovo, in the absence of such a system, there is the need for further and continued investigation in this context with the aim to better monitor the therapy.

AIM: This work aims to analyze and investigate the treatment of patients with mental illness in the Mental Health (MH) Centers in Kosovo.

MATERIALS AND METHODS: The methodology of this research work is based on the specific guidelines published by the World Health Organization (WHO) - Handbook of the WHO. All patients' data were obtained from the protocol books of the treated patients. In each of MH-Centers in Kosovo, 30 patients were selected according to the theory of probability and were analyzed. A total of 209 patients were enrolled in the study. We used quantitative analysis of described drug therapy, while disorders were categorized according to the International Classification of Diseases-10R.

RESULTS: Drugs were mainly administered through the mouth, per os (82.4%). According to the clinics, there was no significant change in the administration route of the drugs ($p > 0.11$). Almost, two-third of the prescribed drugs were essential (66.1%). Considering the class of the therapeutic drugs, over half of them were antipsychotic (53.2%), whereas a percentage of 17.2% and 13.8% were anticholinergic and anxiolytic/hypnotic drugs, accordingly. These classes of drugs were 84.2% of the overall used drugs. Taken together, in the MH Centers in Kosovo, drugs are mainly administered orally, with only 17.6% of the cases treated parenterally. The majority of the drugs used are non-essential drugs, with antipsychotics being the most prescribed ones.

CONCLUSIONS: Furthermore, the study highlights the use of third-line therapy as a first choice and the use of effective drugs with low safety profiles such as clozapine. The application of the practice of drug prescribing by essential list without consideration of data by new evidence-based research for the treatment of mentally disordered patients should be addressed and considered by stakeholders and policymakers in the Ministry of Health of Kosovo for future strategies in selection and in the providing the new essential list in psychopharmacology.

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***Correspondence:** Minire Alilaj-Beqiraj, UBT College, Medical Science, UBT, Prishtina, Kosovo. E-mail: minire.alilaj@ubt-uni.net

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Introduction

In general morbidity, the prevalence of mental and behavioral disorders is 12%, with only a small proportion of patients receiving appropriate treatment. This group of diseases includes depressive disorders, affective disorders, schizophrenia, epilepsy, dementia, posttraumatic stress disorder, obsessive-compulsive disorder, panic disorder, and primary insomnia. The World Health Organization (WHO) based on evidence for the effectiveness of treatment of mental illness has concluded that the combination of psychosocial and pharmacological approaches has given the best results [1].

On a global scale, only a small number of people with mental illness consult a physician [2]. Evidence from industrialized cities shows that not all patients with mental disorders receive adequate treatment [2],

while in developing countries, the health system is often unable to provide essential mental health (MH) [3].

Antipsychotic drugs are not specific to certain types of psychosis that need to be treated. They are effective in treating acute psychoses of unknown etiology, including mania, acute idiopathic psychoses, and acute exacerbations of schizophrenia. Regarding the treatment of acute and chronic stages of schizophrenia, there are numerous results of controlled studies [4].

Antipsychotics include first-generation antipsychotics and second-generation antipsychotics, such as clozapine, risperidone, olanzapine, quetiapine, ziprasidone, and aripiprazole. Despite their therapeutic efficacy, both generations of antipsychotics can cause numerous side effects [5].

For the treatment of the above-mentioned disorders, drugs should be carefully selected, through

the assessment of the relative risk and benefit of the particular therapeutic regimen, based on the evaluation of the patients' condition and their specific needs for therapy. The research of pharmacotherapy with psychotropic drugs is of particular importance for the fact that the choice of initial treatment is crucial for the therapeutic success and compliance of the patient [6].

A large number of studies, with different research methods, have shown numerous incidents with drug interactions, often with fatal outcomes ranging from 2.2% to 30% in hospitalized patients, respectively, from 9.2% to 70%, 3% of patients in different communities [7]. This sums up the need for a better evaluate the practice of prescribing drugs, in this case in MH Centers in Kosovo. Despite the great effectiveness of psychotropic drugs in improving MH, their side effects pose a major health, social, and economic problem.

While in most developed countries, this practice is well established, in Kosovo, in the absence of such a system, there is the need for further and continued investigation in this context with the aim to better monitor the therapy.

This study aims to analyze and investigate the treatment of patients with mental illness in the MH Centers in Kosovo.

Materials and Methods

The methodology of this research work is based on the specific guidelines published by the WHO. The WHO handbook on how to research the use of medicines in health facilities [8], recommends simple quantitative screening methods to identify and evaluate the quantity of prescription and distribution. The handbook includes a summary of drug use indicators for several developing countries. The results of the indicators can be used to improve the monitoring of MH programs.

Through specific questionnaires dedicated to this purpose, data regarding the age, gender, diagnosis, and treatment of patients at MH Centers in Kosovo were collected. All patients' data were obtained from the protocol books of the treated patients. In each of the seven MH Centers in Kosovo, established in seven Regional cities of Kosovo (Mitrovica, Pristina, Ferizaj, Gjakovo, Peje, Prizren, Gjilan), based on the National Strategy for MH (2008–2013), 30 patients were selected according to the theory of probability and were analyzed. A total of 209 patients were enrolled in the study.

As a demographic characteristic, the gender structure and the average age of the patients according to the centers included in the study were analyzed. The disorders were categorized according to the International Classification of Diseases (ICD)-10.

Regarding the pharmacotherapeutic characteristics, we have analyzed the way of treatment of mental illnesses according to the groups of drugs and centers. The route of drug administration was also analyzed, which were divided into categories "PO" - oral administration of the drug and "Parenteral" - administration of the drug by injection. Furthermore, we studied the structure of the use of essential medicines, and whether the medicine was included in the list of essential medicines or not. To make a quantitative evaluation of the used pharmacotherapy, we analyzed the therapy according to the stage and order of therapy. In schizophrenia, in the therapy of stages 1, 2, and 3 we have included patients treated with one of the atypical antipsychotics (not including clozapine), which are simultaneously categorized as first-line therapy.

Moreover, we have categorized the patients treated with a conventional antipsychotic with high potency into the second stage of therapy, though they represent the second-line therapy.

In the 4th stage of therapy, we included the patients treated with conventional antipsychotics, while in the 5th 4th stage of therapy, the patients treated with clozapine were included.

Results

In the present study, a total of 209 patients with mental illness treated in seven MH Centers in Kosovo were analyzed, of which 118 (56.5%) patients were male. According to data, similar distribution of patients by sex was found (Chi-square = 35, $p > 0.24$). Excluding MH-Centers in Gjilan and Prizren where the percentage of female patients was slightly higher compared to men (55.2% and 53.3%, respectively) and in Mitrovica where the distribution of female and male patients had no differences. The average age of the patients enrolled in this study was 38 years old (38.0 ± 11.9 years old). The average age of the patients between the centers, they were treated did not have a significant change (F test = 1.49, $p > 0.18$). The lowest average age of the patients was observed in Ferizaj (35.2 ± 10.8 years old), whereas the highest was seen in Gjilan (43 ± 9.9 years old), (Table 1).

From the morbidity analysis of the patients included in the study, we have found that most of the patients (155/209, or 74.2%) had schizophrenia, schizotypal disorders, and delusional disorders. Based on the ICD, Revision - 10, these disorders are fall into F20–F29 category.

Patients with schizophrenia were 137 in total, representing 65.6% whereas with neurotic, stress disorders, and disorders with bodily manifestations

Table 1: Demographic characteristics of patients with mental illness treated in mental health-centers accordingly

Indicator	Mental Health Centers							Total
	Ferizaj	Gjakova	Gjilan	Mitrovica	Peja	Pristina	Prizren	
Number of patients	30	30	29	30	30	30	30	209
Sex* (male), n (%)	17 (56.7)	19 (63.3)	13 (44.8)	15 (50.0)	18 (60.0)	22 (73.3)	14 (46.7)	118 (56.5)
Average age** - mean \pm SD	35.2 \pm 10.8	37.4 \pm 10.5	43.0 \pm 9.9	39.0 \pm 13.0	38.6 \pm 12.3	38.0 \pm 11.6	35.2 \pm 13.8	38.0 \pm 11.9

*Chi-square test = 35, $p > 0.24$, **F-test = 1.49, $p > 0.18$ (S). SD: Standard deviation, S: Significant.

(F40–F48) were 22 (10.5%) and 14 (6.7%). Others had affective disorders, with the manifestation of non-psychotic depression, and with frequent recurrences of the disorder. With mental retardation were 11 (5.3%) patients, ten of whom had a mild degree of retardation. In a much smaller number were patients with behavioral and emotional disorders (4/209, or 1.9%) (Table 2).

Drugs were mainly administered orally (82.4%) while the 17.6% of the cases with parenteral administration. Parenteral therapy was most frequently used in MH-Centers in Ferizaj, Peja, and Gjilan (41.7%, 35%, 31.9%, respectively), while less frequently, it was used in Mitrovica (12.1%). In general, according to the centers, no significant difference was found in terms of the way of drug administration (Chi-square test = 28, $p > 0.11$) (Table 3).

Almost two-third of the prescribed drugs are essential drugs (66.1%). Whereas according to the MH-Centers, the drugs from the essential list are most often prescribed in MH-Center of Ferizaj (67.5%), Peja with (67.2%), Prizren with 66.1%, and Gjilan and Mitrovica with (55%). Most frequently nonessential drugs are prescribed by doctors in MH-Centers in Gjakova (54.8%) and Prishtina (50.4%) (Table 3).

According to the therapeutic groups, over half of the prescribed drugs belong to the group of antipsychotics (53.2%), while anticholinergics and anxiolytics/hypnotics present 17.2% and 13.8%, respectively, of the prescribed drugs. Drugs of these groups accounted for 84.2% of all drugs used.

Antidepressants accounted for 5.9% of all prescription drugs, which in structure is the same cost

as other drugs, while analgesics were prescribed less frequently (0.9%) (Table 3).

Expenditure of drugs according to therapeutic groups was similar according to the MH-Centers. Differences were in centers of Pristina, Ferizaj, Gjilan, and Gjakova with over half of the prescribed drugs being antipsychotics (66.2%, 63.7%, 57.4%, and 56%, respectively), while in the MH-center of Mitrovica, Peja, and Prizren antipsychotics were also the most consumed drugs but presented less than half of the prescribed drugs (40.2%, respectively from 42.9% for the last two centers).

Anticholinergics are most often prescribed in the MH-Center of Ferizaj (26.5% of drugs) and Gjilan (26.2%), while they are least prescribed in the MH-Center of Prizren (2%). In MH-Centers of Mitrovica and Prizren, in contrast to other centers, we found a higher expenditure on drugs from the group of anxiolytics/hypnotists (24.2% and 22.4%, respectively) (Table 3).

From the quantitative analysis of the stage of therapy used for the treatment of disorders of the subjects, we have ascertained the large number of patients who have applied the therapy of stage 5b (106/208, or 50.96%). In 29 patients (13.94%), no stage 5a therapy was applied, while in 28 (13.46%), no stage 2 therapy was applied. Four (1.92%) were treated with ineffective therapy, while 12 (5.77%) were without therapy. Table 4 shows a quantitative analysis of the therapy.

Over half of the patients (112/208, or 53.85%) were treated with third-order therapy, almost one-third of the patients (65/208, or 31.25%) were treated with second-order therapy, and with first-order therapies treated only 15 (7.21%) patients. Table 5 shows quantitative analysis

Table 2: Patients divided according to the type of the disorders (n = 209)

The disorders code	Code (ICD-Rev-10)	Disorders	n (%)	
F20 – F29	F20	Schizophrenia	137 (65.6)	
Schizophrenia, schizotypal and delusional disorders	F21	Schizotypal disorder	2 (1.0)	
	F23	Acute and transient psychotic disorders	8 (3.8)	
	F23.1	Acute psychotic disorder with symptoms of schizophrenia	6 (2.9)	
	F25	Schizoaffective disorder	2 (1.0)	
	Subtotal		155 (74.2)	
	F30 - F39	F32.2/33.2	Severe depressive disorder episode/recurrent	14 (6.7)
Affective disorders	Subtotal		14 (6.7)	
	F40 - F48	F40	Phobic anxiety disorders	1 (0.5)
Neurotic, stress-related and somatoform disorders	F41	Other anxiety disorders	10 (4.8)	
	F43.1	Posttraumatic stress disorder	2 (1.0)	
	F44	Dissociative (conversion) disorder	4 (1.9)	
	F45	Somatoform disorders	2 (1.0)	
	F48	Other neurotic disorders	3 (1.4)	
	Subtotal		22 (10.5)	
	F51	F51	Nonorganic sleep disorder	1 (0.5)
	Nonorganic sleep disorders	Subtotal		1 (0.5)
F70 - F79	F70	Mild mental retardation	10 (4.8)	
Mental retardation	F71	Moderate mental retardation	1 (0.5)	
	Subtotal		11 (5.3)	
F90 - F99	F92	Mixed disorders of conduct and emotions	4 (1.9)	
Behavioral and emotional disorders with early onset	Subtotal		4 (1.9)	
	G40	Epilepsia	2 (1.0)	
Epilepsy	Subtotal		2 (1.0)	
Total			209 (100.0)	

Table 3: Pharmaceutical characteristics of patients treated in Mental Health Centers accordingly

Indicator	Mental Health Centers							Total
	Ferizaj	Gjakova	Gjilan	Mitrovica	Peje	Pristina	Prizren	
Number of patients	30	30	29	30	30	30	30	209
Route of administration [†] (%)								
PO	58.3	84.5	68.1	87.9	65.0	76.5	82.4	82.4
Parenterale	41.7	15.5	31.9	12.1	35.0	23.5	17.6	17.6
Drug prescription (%)								
Essencial drugs ^{††}	67.5	45.2	55.0	55.0	67.2	49.6	66.1	66.1
Drug groups (%)								
AD	0.0	6.0	3.3	7.1	10.7	4.4	14.3	5.9
AL/H	0.9	17.9	8.2	24.2	11.9	16.2	22.4	13.8
AP	63.7	56.0	57.4	40.4	42.9	66.2	42.9	53.2
AC	8.8	3.6	1.6	2.0	1.2	0.0	0.0	3.0
A	0.0	0.0	3.3	2.0	0.0	0.0	2.0	0.9
Anti-Ch	26.5	14.3	18.0	11.1	26.2	13.2	2.0	17.2
Others	0.0	1.2	8.2	13.1	7.1	0.0	16.3	5.9

[†]Chi-square test = 28, p > 0.11; ^{††}Chi-square test = 28, p < 0.03. AD: Antidepressants, AL/H: Anxiolytic/hypnotics, AP: Antipsychotics, AC: Anticonvulsants, A: Analgesic, Anti-Ch: Anticholinergic, PO: per os.

of the therapy Of the conventional antipsychotics, antipsychotics with high potency of action (156/258, or 60.5%) were most often used, while antipsychotics with medium potency of action were not used for therapy. Table 6 shows quantitative analysis of the therapy.

Table 4: Analysis according to the stage of therapy (n = 208*)

Stage of therapy	n (%)
1	5 (2.40)
2	28 (13.46)
3	6 (2.88)
4	16 (7.69)
5	2 (0.96)
5a	29 (13.94)
5b	106 (50.96)
Ineffective therapy**	4 (1.92)
Without therapy***	12 (5.77)

*In the above analysis of the treatment, one of the patients was excluded which was treated with vitamin (B1 + B6 vitamins), **Ineffective therapy - nonrespondent to pharmacotherapeutic treatment, ***Without therapy - patient in stable remission who were treated with individual supportive and psychosocial approach.

The quantitative analysis of the therapy is shown in Table 7.

Table 5: Analysis according to the stage of therapy (n = 208)

Stage of therapy	n (%)
1	15 (7.21)
2	65 (31.25)
3	112 (53.85)
Ineffective therapy	4 (1.92)
Without therapy	12 (5.77)

Atypical antipsychotics serotonin-dopamine antagonist (SDA) have been used in 39 patients, with more frequent use of clozapine (33/39, or 84.62%), while risperidone and olanzapine have been applied only in 5 (12.82%), respectively in one (2.58%) case. Table 8 shows quantitative analysis of the therapy.

Table 6: The usage of conventional antipsychotics (CT) according to their potency (n = 258)

CT (potency) (n = 258)	n (%)
HPA	156 (60.5)
IPA	- (0.0)
LPA	102 (39.5)

HPA: High potency antipsychotics, IPA: Intermediate potency antipsychotics, LPA: Low potency antipsychotics, CT: conventional antipsychotics.

Discussion

The mid-1950s mark the beginning of the treatment of psychiatric disorders with proven effective

drugs. Up to date, about 10–15% of the drugs prescribed in the US are from drug groups that act to prevent mental disorders: for the purpose of calming, stimulating, or for changing moods, thinking, and behaviors [9].

Table 7: The usage of conventional antipsychotics (CT) - Drugs used for the therapy (n = 258)

Drug	n (%)
HPA	156 (60.5)
Fluphenazinum	122 (47.3)
Haloperidolum	34 (13.2)
LPA	102 (39.5)
Chlorpromazinum	50 (19.4)
Levomopromazinum	30 (11.6)
Promazinum	2 (0.8)
Thioridazinum	15 (5.8)
Sulpiridum	4 (1.6)
Lithium	1 (0.4)
Total	258 (100.0)

HPA: High potency antipsychotics, LPA: Low potency antipsychotics, CT: conventional antipsychotics.

The method of qualitative and quantitative research enables the identification of the extent of problems related to rational therapy and the identification of possible causes. There are many variations in the description of psychotropic drugs between different countries of the world, for which there is no clear explanation. Irrational use of drugs is influenced by many factors, including lack of knowledge about the prescription and use of drugs, the impact of economic factors at all levels, lack of legislation, the impact of culture, poor communication between doctor and patient, and lack of objective information of the patient about the drug. In mental disorders, errors in the description include the incorrect use of essential psychotropic drugs and the prescription of non-psychotropic drugs for the treatment of mental disorders. Such errors in the description of medicines occur in both developed and developing countries [10].

Table 8: The usage of the atypical antipsychotics (SDA-serotonin-dopamine antagonist)- drugs used for the therapy (n = 39)

SDA (n = 39)	n (%)
C	33 (84.62)
OLA	1 (2.56)
RIS	5 (12.82)

C: Clozapinum, OLA: Olanzapinum, RIS: Risperidonum, SDA: Serotonin-dopamine antagonists.

Adequate use of drugs means taking these drugs by patients according to their adequate clinical needs, in doses that meet their individual requirements, at adequate duration and at the lowest possible cost to the patients and society [11]. The regulation of essential medicines does not guarantee the rational use of medicines. Any medicine, including essential ones, can be used irrationally, both in developing countries and in industrialized countries, such as the private, public, or domestic sectors. All gains from efficient selection, procurement, and distribution may be lost due to poor patient practice and lack of adherence [12].

Anxiolytics, hypnotics, and antidepressants are the most prescribed groups of drugs, each representing approximately 20% of the total. Antipsychotics, analgesics, tonics, and herbal medicines are each prescribed in 5%–10% of cases [13], [14]. The results of studies indicate the description of a large number of drugs for mental disorders. Approximately 80% of the

drugs used are without proven clinical efficacy. Herbal medicines, tonics, analgesics, or other nonspecific medicines account for 35.6% of prescriptions, while day and night tranquilizers account for 41.3% [15], [16]. In our study, we found that 53.2% of patients were treated with antipsychotics, 13.8% with anxiolytics, 5.9% with antidepressant therapy, 17.2 % of patients were treated with anticholinergic therapy, and 5.9% of them were treated with other therapy, which is in contrast with results in other studies where anxiolytics, antidepressant, and hypnotic use is up to 20%, for each of them. The most frequent use of antipsychotics and anticholinergics found in our study can be explained by the fact that most of the patients treated in MH-Centers in Kosovo are diagnosed with chronic schizophrenia and other psychosis. Based on MH-National Strategy 2008–2013, reintegration in the community of severe mental illness patients, particularly with chronic schizophrenia was the objective of this strategy, and MH-centers as the main providers of service in the community. Furthermore, the excessive use of anticholinergic therapy can be explained by the fact that essential medicines listed for schizophrenia treatment in Kosovo for many years were second-line antipsychotics, and as an outcome, extrapyramidal side effects were more frequent.

The disease of schizophrenia progresses through three phases: the acute phase, the stabilization phase, and the stable phase. Therapeutic objectives for the treatment of schizophrenia in the acute phase are control of disordered behaviors, reduction of the intensity of psychosis, and accompanying symptoms, for example, agitation, aggression toward others and himself, negative symptoms, affective symptoms, prevention of injuries, return to normal of functioning, and adequate return of the sick to society [14], [17], [18]. In the stabilization phase, the therapeutic objective is to reduce stress, reduce the degree of reliability for relapse of the disease, adapt the patient to live in the community, accelerate the permanent reduction of symptoms and consolidation of remission, and promote the healing process. If the patient's condition improves after a certain therapeutic regimen, it is recommended to continue and monitor the treatment with the same regimen for another 6 months. Premature dose reduction, or discontinuation of therapy, may lead to the recurrence of symptoms and relapse of the disease. The goals of treatment in the stable phase are to establish remission, or control of symptoms, maintain or improve the functioning and quality of life of the patient, and to continue monitoring the side effects of medications. Atypical antipsychotics (SDAs), excluding clozapine and sertindole, due to their side effects, represent the first-line drugs for the treatment of schizophrenia. This therapy is recommended in many practice guides and according to some guidelines, SDAs are considered drugs of the first three stages of treatment because of their potent antipsychotic effect, especially on adverse symptoms, infrequent onset, or no extrapyramidal side effects (EAEP), lack of tardive dyskinesia, and

hyperprolactinemia [19], [20].

In cases of poor response to all three SDAs, it is recommended to apply a typical antipsychotic (stage 4 of treatment). Randomized clinical trials have shown the superiority of clozapine over other antipsychotics regarding the management of treated-resistant schizophrenia [21]. Clozapine, as an atypical antipsychotic, with agonist activity on a large number of receptors (dopamine, serotonin, muscarinic, alpha 1 and alpha 2-adrenergic, and H1 histamine) is distinguished from other antipsychotics due to its higher efficacy in treating positive symptoms in patients with treated-resistant diseases and lack of extrapyramidal side effects. However, clozapine causes serious and potentially fatal side effects, including agranulocytosis in 0.5–1% of patients, convulsions in 2% of patients, and the rare occurrence of myocarditis and cardiomyopathy. For this reason, the use of clozapine is reduced for patients who do not show adequate response to the two previous antipsychotics. Due to the risk of developing orthostatic hypotension, clozapine is usually titrated more slowly than other atypical antipsychotics [22].

This strategy is also recommended according to the NICE English guide (National Institute of Clinical Excellence. Health Technology Appraisal No. 43 NICE, London, 2002).

From the results obtained from this study, we found most of the patients were treated with third-line (atypical antipsychotics) such as clozapine prescription in 84.62% of cases from the SDA group in therapy as first-line antipsychotic, which is considered an effective drug, but with a low safety profile. Such a high frequency of clozapine application for the treatment of chronic schizophrenia cannot correlate with the frequency of cases treated-resistant to other antipsychotics. Moreover, ineffective drugs are used in 1.92% of, use of drugs that have not been profitable for certain diagnoses by drug treatment. Noncompliance with treatment and drug treatment indications was found in 5.77% of cases.

All guides recommend the use of depot preparations in cases where patients do not comply with the prescribed oral therapy. Before starting the use of depot preparations, it should be determined whether the patient's incompatibility is a consequence of side effects. If the incompatibility is a consequence of the appearance of side effects, before applying antipsychotics in the form of depot preparations, the use of a drug with a more favorable profile of side effects is considered. Patient motivation remains the most important factor in improving patient compliance and adherence. Conversion from oral therapy to depot therapy is most successful in patients previously stabilized with oral therapy, with the same agent, or after a short course (3–7 days). To determine the tolerance of medication by the patient without significant side effects. Certain conversion methods apply to this [23]. The advantages of long-acting injectable drugs have

been demonstrated in studies conducted by Johnson [24], conducted in the same conditions as community clinics. Long-acting injectable drugs in particular are beneficial in the stabilization phase and the stable phase. Janicak *et al.* evaluated six studies, which compare the risk of relapse of psychosis in randomized patients in the group in oral therapy, or depot. The meta-analysis of the six studies showed a significantly lower relapse rate in patients in the long-acting injectable drug group $p < 0.0002$ [25]. The prevalence of prescribing antipsychotics in the form of depot preparations shows great variability according to different centers. This is also concluded from the results of Sim *et al.*, Who analyzed the prevalence of depot preparation description in East Asia. The prevalence of prescribing antipsychotics in the form of depot preparations was 15.3% [26], which is similar to our study where we find the depot preparations drugs were administered parenterally in 17.6% of cases. Injectable preparations of typical long-acting antipsychotics are mainly represented in the content of fluphenazine decanoate and haloperidol decanoate. Although such a prevalence of depot prescriptions is consistent with the prevalence of prescriptions in East Asia, variations in this prevalence suggest that their description is not based on clearly defined principles and is more determined by local traditions and culture of description [26], while based on our findings, it depends also on the cost expensive, having into consideration that second-line depot preparations (first generation or typical antipsychotic) are cheaper than first-line depot preparations (second generation or atypical antipsychotics) such as Risperdal Consta depo.

There are numerous suggestions that justify the use of enhancement therapy, to potentiate the action of clozapine, other atypical antipsychotics, or the application of combination therapy with antipsychotics. Empowerment therapy involves the addition of a nonantipsychotic drug to patients with poor response to SDA therapy, whereas combination therapy involves the concomitant use of two antipsychotics. Theoretically, potentiation is based on the mechanism of action of the potentiating agent, which interacts synergistically with dopaminolytics to achieve efficacy [27]. Regarding the empowerment of therapy, many guidelines indicate that: (1) Empowerment therapy should be used in patients with inadequate responses; (2) fortifying agents are rarely effective when used alone; (3) positive response to tonic drugs is very rapid, and (4) if tonic therapy does not improve symptomatology, the tonic agent should be discontinued [28]. The average number of drugs applied simultaneously varies from country to country. In a pharmacoepidemiological study of the practice of prescribing antipsychotics in France, for the years 1995 and 1998, the average number of antipsychotics applied simultaneously decreased from 1.74 (± 0.02), as it was in 1995, to 1.69 (± 0.04), in 1998 ($p < 0.005$) [29]. In Austria, studies have shown that the average number of psychotropics described is higher than in France, and ranges from 2.2 to 2.9, respectively, the structure

of patients treated with ≥ 3 psychotropics has increased from 27.5% to 49.7% [30]. In a study conducted in Japan, the average number of all psychotropic drugs was 4.0, while that of neuroleptic drugs alone was 1.8, with an average treatment duration of 5.9 weeks [31].

Essential psychotropic drugs are “drugs that meet the mental health care needs of the population, selected according to public health needs, as a result of proven efficacy and comparison of safety and cost-effectiveness”. They must always be available, in the context of the functioning of the MH protection system, in the distribution system, they must be provided in appropriate quantities, in suitable pharmaceutical forms, with safe quality, adequate information, and at a price that can be afforded by the individual and the community” [32]. Essential psychotropic drugs enable the treatment of the symptoms of mental disorders, shorten the duration of many disorders, reduce disability and prevent the recurrence of the disease [4]. A large number of treatments are available for the pharmacological management of mental disorders. Many of these treatments are effective in the acute and relapsing stages of the disease; however, many uncertainties remain regarding the effectiveness of long-term treatment and day-to-day management of mental disorders [2]. It does not mean that “effective” drugs are always “essential.” This can be made clear if factors such as long-term application effectiveness, the advantages of cheaper alternatives, and cost-effectiveness are better understood. The results show that while newer psychotropic drugs have fewer side effects, they are not significantly more effective and, usually, have higher costs [4]. Although sometimes, new drugs have fewer side effects, they can help in taking the drug and reduce the need for further care and treatment [33]. Carefully selecting the essential psychotropic drugs is a prerequisite for the development of a sustainable psychotropic supply system. The selection of a limited number of essential psychotropic drugs is economical and poses a lower risk of duplication, confusion, and error. The WHO has the list of essential drugs, including psychotropics. Drugs are specified based on unprotected international names, or generic names, without reference to any particular trade name or pharmaceutical company [34].

Prescribers, distributors, and consumers find it easier to remember the therapeutic effect and side effects and do not need to deal with multiple dosing regimens and confusing nomenclature. Furthermore, careful selection speeds up the easier purchase and management of drugs (storage and distribution). This also allows for a more rational and efficient approach to the training process for prescribing and distributing medicines. Due to the significant impact on the quality of care and the cost of treatment, careful drug selection is the most important cost-effective issue for improving MH services. For example, data show that young psychotropics may have some advantages, but they

are not always more effective and are usually more expensive, while essential drugs should be selected based on consensus among experts on the type of drugs that should be available to the health-care system considering also evidence-based research on specific psychotropic guidelines for treatment and selection of essential psychotropics should be changed regularly (every 2–3 years) and accompanied by clear regulatory guidelines for procurement, distribution, and use [35].

Despite the general idea that clozapine is underutilized, little research has been done into the extent of this problem and the main indication for this drug according to guidelines is treatment-resistant schizophrenia, [36] while in our study, this is the 1st time we are in the knowledge that clozapine is overutilized, and no case was reported until now for any side effects. This can serve as a recommendation for further studies for schizophrenia-resistant treatment, as until now, these studies are scarce globally.

In our study, the structure of prescribing essential drugs was in line with essential list, while the generic name prescriptions of psychopharmacologic drugs were low.

In clinics, the tendency to prescribe tranquilizers, antidepressants, and other drugs is increasing. Research results confirm that medical treatment in general, and prescription of drugs in particular, depend not only on medical or pharmacological variables, but also on psychological, social, and cultural factors. Non-clinical factors such as age, gender, education, family status, or employment status have a significant impact on drug use.

As a limitation of our study, we consider the impossibility of critical evaluation of the factors that have influenced this practice, due to the limitation of the research in terms of other relevant nonclinical factors.

An important gap in our study was the lack of data on the prescription of drugs in other mental health care institutions in Kosovo, such as the tertiary health service institution - Clinic of Psychiatry in Pristina and other secondary health service institutions - regional hospitals with psychiatric wards. This gap can serve as an objective for further research in this area, to explain the actual situation regarding drug prescriptions and psychopharmacology treatment of patients with mental disorders and also to address a new strategy for the essential list based on our study findings and recent evidence-based research regarding effectiveness and safety profile of drugs used in MH disorders treatment.

Conclusion

Our study concludes that in the MH Centers in Kosovo, drugs are mainly administered orally (PO),

the prescribed drugs are usually essential list drugs, the most common group are antipsychotics of first-generation (atypical) and anticholinergics to treat the side effects, while parenterally administered depot preparations were also first generation-second line drugs, because of cost-effectiveness.

Furthermore, this study shows that patients are treated with third-line therapy Clozapine as a first choice and the use of this effective drug with a lower safety profile was highest in comparison with other atypical antipsychotics.

Our results demonstrate the application of the practice of drug prescribing by essential list without considering data from new evidence-based research for the treatment of mentally disordered patients, even though it has cost effects, this issue should be considered by stakeholders and policymakers in the Ministry of Health of Kosovo for future strategies in the selection and providing the essential list in psychopharmacology.

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