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Research Article

Prescription of antipsychotics and prevalence of metabolic syndrome in Vietnamese inpatients with schizophrenia

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ABSTRACT

Schizophrenia is a severe mental illness, characterized by psychotic symptoms including delusions, hallucinations, dystonia, adolescent behavior and language, and is accompanied by severe functional impairments. Antipsychotics, which are used mainly in the treatment of schizophrenia, have contributed to the development of metabolic syndrome. Studies on metabolic syndrome in schizophrenic patients have been still limited in Vietnam. The objective of this study was to investigate the prevalence of metabolic syndrome in Vietnamese inpatients with schizophrenia. The study population of this descriptive cross-sectional study was all patients with schizophrenia from September 2020 to June 2021 at Inpatient Department of Binh Dinh Provincial Psychiatric Hospital in Viet Nam. Three hundred and twelve patients who met the sampling requirements were enrolled in this study. The prevalence of schizophrenia in female patients was lower than in male patients (36.9% vs. 63.1%) in our study. The prevalence of metabolic syndrome was 30.4% (25.9% in men and 38.3% in women), more in patients ≥40 years old than in patients under 40 years old (the highest prevalence in patients ≥60 years). There was a significant relationship between age, body mass index (BMI), and duration of antipsychotic treatment with the frequency of metabolic syndrome. In conclusions, the prevalence of schizophrenia was higher in male inpatients than in female inpatients. However, the prevalence of metabolic syndrome was higher in female inpatients than male inpatients with schizophrenia, and increased with age, BMI, and duration of antipsychotic treatment.

Keywords:
Metabolic syndrome, Inpatients, Schizophrenia, Antipsychotics

1. INTRODUCTION

Schizophrenia is a severe mental illness, characterized by psychotic symptoms including delusions, hallucinations, dystonia, adolescent behavior and language, and is accompanied by severe functional impairments[1]. Chronic progressive schizophrenia makes the patient gradually exhausted, no longer able to work and live, becoming a burden to the family and society[2]. In Vietnam, the prevalence of schizophrenia accounts for 0.47% of the population[3]. The onset of the disease is between the ages of 15 and 35 years and is earlier in men than in women[4].

Patients with schizophrenia have a high mortality rate and a low life expectancy compared with the general population[5-6]. In recent years, studies have focused on other comorbidities in patients with schizophrenia and have found that cardiovascular risk factors are also one of the main causes of death in schizophrenia[5-7]. The prevalence of obesity, type 2-diabetes, and hypercholesterolemia in patients with schizophrenia is estimated to be 3 to 5 times higher than in the general population[8]. Antipsychotics, especially second-generation antipsychotics used in the treatment of schizophrenia, have been identified as one of the contributing causes of the development of metabolic syndrome, though increased-risk mechanisms of these drugs have not been elucidated[9]. Metabolic syndrome is a series of metabolic abnormalities that include high blood glucose levels and high blood

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pressure, elevated triglycerides, obesity, and low high-density lipoprotein (HDL). Metabolic syndrome increases the risk of cardiovascular disease, diabetes, dyslipidemia, stroke, osteoarthritis, cancer, and death rate[1].

There have been many studies on the metabolic syndrome in schizophrenic patients[10-14]. Metabolic syndrome was found very common in people with schizophrenia and having a significant cardiovascular and mortality risk. Therefore, early detection of metabolic syndrome in patients with schizophrenia would help clinicians promptly intervene in metabolic syndrome-related disorders, such as changing antipsychotic medications, changing the patient's diet, habits, etc., thereby contributing to reducing the risk of cardiovascular complications and the risk of death in these patients. However, in Vietnam, studies on this subject are still limited. The objective of this study was to investigate the prevalence of metabolic syndrome in inpatients with schizophrenia at Binh Dinh Provincial Psychiatric Hospital in order to improve quality of life as well as reduce cost of treatment in patients with schizophrenia.

2. METHODS

2.1. Study population

This descriptive cross-sectional study was approved by the Ethics Committee of Binh Dinh Provincial Psychiatric Hospital in Vietnam No.02/CN-HĐĐĐ August 31, 2020 before the collection of data.

Patients aged 18 years old and above participating in this study were diagnosed with schizophrenia according to ICD-10 criteria (F20.0-F20.9)[15]. Exclusion criteria included severe chronic diseases (cirrhosis, chronic kidney failure); psychiatric diseases outside of ICD-10 criteria (F20.0-F20.9) such as psychostimulant-related mental and behavioral disorders; malformations of the abdomen, spine, and thorax; long-term corticosteroid therapy; uncontrolled schizophrenic patients or refusal to participate in the study.

2.2. Sample size

The sample size (N) was calculated using the formula, $N=(Z_{1-\alpha/2})^2\ p\ (1-p)/d^2$, where p is the prevalence of metabolic syndrome in schizophrenic patients as 28% from the previous study[16]; d is the acceptable margin of error within 5%; Z is the confidence coefficient (Z=1.96 if the level of confidence is 95%).

Therefore, the minimum sample size was determined to be 310 patients.

2.3. Place and time

This study took place at the Inpatient Department of Binh Dinh Provincial Psychiatric Hospital from September 2020 to June 2021.

2.4. Study design

Medical information of patients with schizophrenia was collected through demographic questionnaires (age, gender, personal and family history, duration of schizophrenia, smoking, body mass index (BMI), etc.) and laboratory tests after obtaining informed consent from the patient or their legal guardian. BMI is calculated as body mass in kilograms divided by the square of body height in meters and expressed in units of kg/m². BMI was categorized into four groups according to the

Asian-Pacific cutoff points[17-18]: underweight (<18.5 kg/m^2), normal weight (18.5-22.9 kg/m^2), overweight (23-24.9 kg/m^2), and obese (≥25 kg/m^2). The metabolic syndrome was diagnosed according to the US National Cholesterol Education Adult Treatment Panel III (NCEP ATP III) criteria (2005 revision) for the Asian population[18]. Patients with three or more of the following criteria were diagnosed with metabolic syndrome: (i) waist circumference: ≥90 cm in men and ≥80 cm in women; (ii) triglycerides ≥150 mg/dL (1.7 mmol/L); (iii) HDL-cholesterol <40 mg/dL (1.0 mmol/L) in men and <50 mg/dL (1.3 mmol/L) in women; (iv) blood pressure ≥130/85 mmHg; (v) fasting blood glucose ≥110 mg/dL (6.1 mmol/L).

Patients with schizophrenia can be divided into groups according to age, gender, BMI, antipsychotic therapy, duration of illness, and duration of antipsychotic medication. The prescription of antipsychotics for inpatients with schizophrenia during admission was evaluated. The prevalence of metabolic syndrome in patients with schizophrenia in these groups during admission was determined by pharmacists. Factors influencing metabolic syndrome in patients with schizophrenia were evaluated.

2.5. Variables

The independent variables included patient characteristics (age, gender, duration of schizophrenia, antipsychotics, BMI, etc.). The dependent variable was the prevalence of metabolic syndrome.

2.6. Statistical analysis

Collected data were calculated using SPSS 22.0 software and expressed as mean±standard error (SD) with a 95% confidence interval (CI). Continuous variables with normal distributions are presented as mean± standard deviation (minimum-maximum). Categorical data were reported as percentages. Comparison of differences in prevalence of metabolic syndrome between groups of independent variables was performed using the chi -square (χ^2) test. Results would be considered

significant if the *p*-value was <0.05.

3. RESULTS

3.1. Characteristics of patient population

The study collected 312 inpatients with schizophrenia who met the sampling criteria at Binh Dinh Provincial Psychiatric Hospital from September 2020 to June 2021. Most of patients in the study were male (63.1% male vs. 36.9% female). The average age of the patient population was 35.0±20.0 years old (26-70 years old). The highest prevalence of schizophrenia was observed in patients under 40 years old. Most of patients with schizophrenia have no family history and are non-smokers. The rate of patient with schizophrenia due to accidental trauma was twice as high as that of psychological trauma. Patient group with less than five-years schizophrenia illness duration had highest rate compared to other groups. The total number of overweight and obese patients accounted for 37.82% of the study population. The proportion of patients with diabetes, dyslipidemia and hypertension accounted for 6.73%, 5.45% and 5.13% of the study population, respectively. The characteristics of the patients in this study were presented in Table 1.

Table 1. Demographic characteristics of the patients with schizophrenia.

Variables	Number (n)	Percentage (%)
Sex (N=312)		
Male	197	63.1
Female	115	36.9
Age (years) (N=312)		
<40	197	63.1
40-59	101	32.4
≥60	14	4.5
Family history (N=312)		
Family member and relatives with schizophrenia	92	29.5
Family without schizophrenia	220	70.5
Personal history (N=312)		
Psychological trauma	25	8
Accidental trauma	47	15.1
Non	240	76.9
Smoking (N=312)		
Yes	74	23.72
Non	238	76.28
Duration of schizophrenia (N=312)		
<5 years	120	38.5
5-<10 years	50	16.0
10-<20 years	111	35.6
≥20 years	31	9.9
BMI (kg/m^2) (N=312)		
Underweight (<18.5)	21	6.73
Normal (18.5-22.9)	173	55.45
Overweight (23-24.9)	62	19.87
Obese (≥25)	56	17.95
Diseases associated with metabolic syndrome (N=312)		
Diabetes mellitus	21	6.73
Dyslipidemia	17	5.45
Hypertension	16	5.13

3.2. Prescription of antipsychotic drugs for inpatients with schizophrenia

Risperidone was the most prescribed antipsychotic drug for patients with schizophrenia, accounting for 51.3%. The antipsychotics amisulpride and clozapine were also widely prescribed at 46.8% and 43.3%, respectively, to patients with schizophrenia. The drug chlorpromazine is indicated at least for patients with schizophrenia (7.1%). Doses of most antipsychotic drug were within the recommended dosage range for schizophrenic patients according to the guidelines of the Ministry of Health of Vietnam, except for 22 patients received olanzapine 30 mg/day (higher than the recommended dosage range of 10 to 20 mg/day), two patients received chlorpromazine 25 mg/day and 11 patients received chlorpromazine above 1000 mg/day (exceeding the recommended dose range of 50-200 mg/day) (see Table 2).

Table 2. Frequency of antipsychotic use in patients with schizophrenia.

Number	Antipsychotics (Recommended Daily Dose (mg))	Frequency of use (Percentage %) (n=827)	Mean Daily Dose (min-maximum dose used) (mg)
1	Risperidone (2-8)	160 (51.3)	4 (2-6)
2	Amisulpride (400-1200)	146 (46.8)	370 (200-800)
3	Clozapine (200-400)	135 (43.3)	219 (100-300)
4	Olanzapine (10-20)	117 (37.5)	17 (10-30)
5	Levomepromazine (25-300)	106 (34.0)	84 (25-125)
6	Haloperidol (2-12)	92 (29.5)	6 (3-9)
7	Quetiapine (300-800)	49 (15.7)	457 (400-600)
8	Chlorpromazine (50-200)	22 (7.1)	797 (25-1100)

Among 312 inpatients with schizophrenia, 297 patients (95.2%) were prescribed combination antipsychotic therapy; only 15 patients (4.8%) used monotherapy. Triple therapy was most used to treat schizophrenia (50%) (see Figure 1).

Treatment regimens for 312 patients with schizophrenia were diverse to effectively control the disease for each individual. For monotherapy, Olanzapine was the most indicated for schizophrenia patients with the rate of 53.3%. For dual therapy, the combination of Olanzapine and Amisulpride accounted for the highest rate of 27.8%. For the triple therapy, the combination of Clozapine + Amisulpride + Quetiapine and Risperidone + Levomepromazine + Amisulpride accounted for the highest rate of 13%. For quadruple therapy, the combination of Clozapine + Risperidone + Amisulpride + Olanzapine accounted for the highest rate of 57.1% (see Table 3).

3.3. Evaluation of metabolic syndrome in inpatients with schizophrenia

The prevalence of metabolic syndrome in schizophrenic patients in this study was 30.4%. The rate of metabolic syndrome in women was significantly higher than in men (p=0.022<0.05).

There was a significant difference in the rate of metabolic syndrome between age groups (p=0.011 < 0.05). The prevalence of metabolic syndrome was highest at age 60 and older (50%).

The prevalence of metabolic syndrome in the groups of schizophrenic patients classified by BMI and duration of antipsychotic treatment was significantly different (p<0.05). The highest prevalence of metabolic syndrome was found in obese patients (69.6%) and in patients taking antipsychotics for more than 10 years (40.2%).

The incidence of metabolic syndrome was increased in patients receiving multiple antipsychotic combinations, but not significantly (p>0.05) (See Table 4).

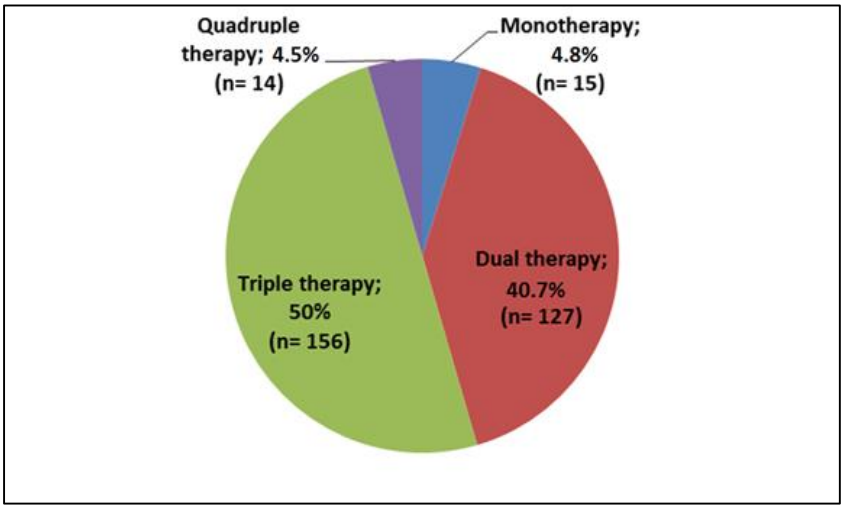

Figure 1. Prevalence of different types of treatment regimens for schizophrenia.

Table 3. Antipsychotic therapies in patients with schizophrenia.

Therapies	Combination of drugs	Frequency of use (n)	Percentage (%) (n/N)
Monotherapy (N1=15)	Olanzapine	8	53.3%
	Clozapine	4	26.7%
	Levomepromazine	3	20.0%
Dual therapy (N2=127)	Olanzapine+Amisulpride	35	27.8%
	Olanzapine+Risperidone	24	19.0%
	Clozapine+Amisulpride	17	13.5%
	Haloperidol+Levomepromazine	13	10.3%
	Haloperidol+Clozapine	9	7.1%
	Clozapine+Risperidone	8	6.3%
	Chlorpromazine+Haloperidol	7	5.6%
	Risperidone+Levomepromazine	7	5.6%
	Risperidone+Quetiapine	6	4.8%
Triple therapy (N3=156)	Clozapine+Amisulpride+Quetiapine	21	13.0%
	Risperidone+Levomepromazine+Amisulpride	21	13.0%
	Clozapine+Risperidone+Levomepromazine	17	10.6%
	Chlorpromazine+Haloperidol+Levomepromazine	16	9.9%
	Risperidone+Levomepromazine+Quetiapine	16	9.9%
	Olanzapine+Clozapine+Risperidol	14	8.7%
	Haloperidol+Clozapine+Amisulpride	14	8.7%
	Clozapine+Risperidone+Quetiapine	11	6.8%
	Haloperidol+Levomepromazine+Amisulpride	10	6.2%
	Olanzapine+Haloperidol+Amisulpride	9	5.6%
	Clozapine+Risperidone+Amisulpride	7	4.3%
	Olanzapine+Risperidone+Amisulpride	5	3.1%
Quadruple therapy (N4=14)	Clozapine+Risperidone+Amisulpride+Olanzapine	8	57.1%
	Chlorpromazine+Clozapine+Risperidone+Amisulpride	6	42.9%

Table 4. The relationship between metabolic syndrome and gender, age, BMI, antipsychotic therapies and duration of antipsychotic treatment.

Variables	Metabolic syndrome, n (%)		*p*-value
	Yes	No	
Sex			
Male	51 (25.9)	146 (74.1)	0.022
Female	44 (38.3)	71 (61.7)	
Total	95 (30.4)	217 (69.6)	
Age (years)			
<40	48 (24.4)	149 (75.6)	0.011
40-59	40 (39.6)	61 (60.4)	
≥60	7 (50.0)	7 (50.0)	
BMI (kg/m^2)			
Underweight (<18.5)	4 (19.0)	17 (81.0)	<0.001
Normal (18.5-22.9)	27 (15.6)	146 (84.4)	
Overweight (23-24.9)	25 (40.3)	37 (59.7)	
Obese (≥25)	39 (69.6)	17 (70.4)	
Antipsychotic therapies			
Monotherapy	4 (26.7)	11 (73.7)	0.636
Dual therapy	38 (29.9)	89 (70.1)	
Triple therapy	48 (30.8)	108 (69.2)	
Quadruple therapy	5 (35.7)	9 (64.3)	
Duration of antipsychotic treatment (years)			
<1 year	7 (17.1)	34 (82.9)	0.004
<5 years	15 (19.5)	62 (80.5)	
<10 years	26 (33.8)	51 (66.2)	
≥10 years	47 (40.2)	70 (59.8)	

4. DISCUSSION

4.1. Characteristics of study population

The age of inpatients with schizophrenia in this study ranged from 18 to 74 years (a mean age of 35 years). Previous studies have shown that the rate of schizophrenia in men and women is nearly equal[19-20]. However, the prevalence of schizophrenia in female patients was lower than in male patients (36.9% vs. 63.1%) in our study. This difference may be due to population fluctuations, migration, mortality, and genetic characteristics of the study population[21-22].

Currently, it has not been possible to determine with certainty what genetic factors determine the development of schizophrenia. In this study, the proportion of patients with a family history of schizophrenia was 29.5%. The prevalence of schizophrenia in the first-degree relatives of the study subjects such as father, mother, brother, sister was 2 times higher than the rate of second-degree relatives of the study subjects such as aunt, uncle, and cousins (20.8% versus 8.7%). Sadock B.J. showed that the prevalence of schizophrenia in first-degree relatives of patients accounted for 18%. Therefore, our study results were higher than those of Sadock B.J.[20].

Regarding to personal history, the results of our study are similar to some previous studies. Some authors have suggested that the prevalence of schizophrenia was related to factors such as psychological trauma and accidental trauma and ranged from 15 to 79%[23].

Smoking and BMI are among the risk factors for metabolic syndrome[24]. In our study, the prevalence of smoking in schizophrenic patients accounted for 23.72%, in which the percentage of male patients who smoked was higher than that of female patients. The prevalence of obese inpatients with schizophrenia at Binh Dinh Provincial Psychiatric Hospital was lower than in some other Asian countries[25]. This could be due to the different quality of health care, lifestyle, and physical condition among ethnic groups. Patients with schizophrenia are at risk of obesity due to side effects of antipsychotic drugs, eating habits, inactivity, etc.[11,26].

4.2. Prescription of antipsychotic drugs for inpatients with schizophrenia

Risperidone, Amisulpride, and Clozapine were the most prescribed antipsychotics for patients with schizophrenia at Binh Dinh Provincial Psychiatric Hospital in Viet Nam. The prevalence of patients using multi-therapy regimens for schizophrenia at Binh Dinh Psychiatric Hospital was very high (95%). Hiroto et al. showed that the proportion of schizophrenic patients receiving multi-therapy in 2008 was 50.5% in China, 33.3% in Hong Kong, 65.9% in Japan, and 46.9% in South Korea[27]. It is possible that the patient in our study was an inpatient, primarily using combination therapy for the treatment of acute or recurrent schizophrenia. A meta-analysis showed that combination therapy was superior to monotherapy in efficacy and adherence in patients with schizophrenia[28]. However, schizophrenia patients treated with long-term combination antipsychotics have a higher risk of adverse events, drug overdose, and death. Furthermore, combining more than two drugs increases drug interactions, even leading to disease recurrence[7,29].

4.3. Prevalence of metabolic syndrome in inpatients with schizophrenia

Many studies have reported the incidence of metabolic syndrome in schizophrenic patients in different countries and ethnicities[12,14,30]. Most studies have used the NCEP ATP III criteria to estimate prevalence. The sample sizes in these studies ranged from 20 to 2,270 patients, and the prevalence of metabolic syndrome varied widely from 11% to 69%[31].

We used the NCEP ATP III (2005 revision) diagnostic criteria to assess the prevalence of metabolic syndrome in this study, as it required three or more of the five existing criteria in the patient's medical record. Metabolic syndrome is common in the Vietnamese population (accounting for 16% of the adult population), including high-risk groups such as women, people living in urban areas, and obese people[32]. However, patients with schizophrenia are at high risk for metabolic syndrome. The prevalence of metabolic syndrome in our study was 30.4%, higher than that of De Hert et al. with 27.5% and lower than in other studies[12,14,30]. The difference in the prevalence of metabolic syndrome in schizophrenic patients between studies may be due to many influencing factors such as mean age, sex, lifestyle, diagnostic criteria for metabolic syndrome, and antipsychotic drugs.

In our study, the prevalence of metabolic syndrome in female patients (38.3%) was higher than in male patients (22.6%), similar to the results of previous studies[33-34]. However, other studies have reported no difference in the incidence of metabolic syndrome between men and women[34], while some studies showed that the incidence of metabolic syndrome was higher in men than in women[34,36].

Duration of schizophrenia has been associated with a higher prevalence of metabolic syndrome in previous studies[10,13,33]. However, other studies have not shown an association between the prevalence of metabolic syndrome and the duration of schizophrenia[36-37]. In this study, we found that the prevalence of metabolic syndrome was highest in patients with schizophrenia over 20 years and ≥60 years old as a high-risk age group for cardiovascular diseases. Our study showed the highest prevalence of metabolic syndrome in the most obese

group. Therefore, metabolic syndrome should be monitored in patients with schizophrenia, especially the elderly, the obese, and those on long-term therapy.

Researches on the prevalence of metabolic syndrome in Vietnamese schizophrenic patients are still very limited. Therefore, the sample size in this study was calculated based on the prevalence of metabolic syndrome in outpatients with schizophrenia in a previous study in Vietnam[16]. Our study is the first study of the prescription of antipsychotics and prevalence of metabolic syndrome in Vietnamese inpatients with schizophrenia.

We have collected information from inpatient medical records and checked against patients' electronic records on the hospital's computer system to ensure reliability and accuracy.

However, our study only investigated metabolic syndrome in one medical facility, so it cannot be extrapolated to all patients with schizophrenia in Vietnam. The hospital collects data with a high rate of multi-drug regimens, so it has not been able to assess the side effects as well as the level of influence of each antipsychotic drug on patients with schizophrenia.

5. CONCLUSION

The prevalence of metabolic syndrome was higher in women than men patients with schizophrenia, and increased with age, BMI, and duration of antipsychotic treatment.

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Conflict of interest

The authors declare that there was no conflict of interest.

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None to declare

Ethics approval

This study was approved by the Ethics Committee of Binh Dinh Provincial Psychiatric Hospital issued together with Decision No.02/CN-HĐĐĐ August 31, 2020.

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