Medication adherence and related psychosocial and clinical factors among schizophrenic patients: a cross - sectional analytical study in National Psychiatric Hospital 2, Vietnam

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Abstract

Background and Aims: Schizophrenia is a chronic and severe mental disorder. Treatment by antipsychotic medication is one of the main therapies to control the symptoms. Medication non/poor adherence is a one of the key factors leading to relapse and declined social and occupational function in patients. However, prevalence of schizophrenic patients with non/poor adherence to medication was quite high in previous studies. Therefore, this study aimed to identify the prevalence of medication non/poor adherence and its related psychosocial and clinical factors among schizophrenic patients. **Subjects and Method:** a cross - sectional analytical study of 126 schizophrenic patients at National Psychiatric Hospital 2 were conducted to evaluate the rate of medication non-adherence by Morisky Medication Adherence Scale 8 item (MMAS - 8). Data were collected on patients' sociodemographic factors such as sex, age, marital and economic status, level of education and clinical factors including duration of schizophrenia, clinical symptoms evaluated by Positive and Negative syndrome scale (PANSS), type, and side effects of medication. Logistic regression was used to analyze the factors associated with medication non-adherence among schizophrenic patients. **Results:** Rate of poor medication adherence among participants was 78.57% by using MMAS – 8. The associated factors with poor medication adherence among schizophrenic patients were level of education under high school; unstable job/unemployment; poor insight about schizophrenia, poor family care/support, high scores of negative PANSS and general PANSS scale, duration of schizophrenia above 5 years, treated by typical antipsychotics and having more than two side effects of antipsychotics. **Conclusion:** The rate of poor medication adherence/ non - adherence among schizophrenic patients is high. Mental health staff should be aware of this risk and screening individuals for relevant risk factors is highly recommended.

Keywords: *medication adherence, schizophrenia, social - psycho - clinical factors.*

1. INTRODUCTION

Schizophrenia is a severe and chronic mental disorder with a lifetime prevalence estimated at approximately 0.3% - 1% of the worldwide population. Clinical manifestations of schizophrenia are variable and include negative symptoms such as poverty of speech, avolition, apathy, blunted affect, social withdrawal, … and positive symptoms such as delusion, hallucination, illusion, catatonic behavior, disorganized behavior, as well as impairment of cognition. Schizophrenic treatment is a long -term process and incorporates variety of treatment modalities including pharmacotherapy, social-psychological interventions and other biological therapies such as electroconvulsive therapy (ECT) and Transcranial Magnetic Stimulation (TMS) [1,2]. Pharmacotherapy, especially antipsychotics, is a mainstay treatment for schizophrenia to control the symptoms in the acute phase and to prevent relapse in maintenance phase [1,2]. Several previous studies over the world showed that the rate of non –adherence or poor adherence to medications in schizophrenic patients was quite high [3,4]. Higashi et al. (2013) showed that 74% of schizophrenic patients discontinued medication after 18 months due to side effects, poor response to medication and other factors [3]. Kikkert M.J. and Dekker J. (2017) found that 50% of schizophrenic patients did not adhere to medications [4]. According to Widschwendter CG et al. (2018), non-adherence to medications is a major challenge in the long-term management of schizophrenia and can be viewed as a failure in the treatment of schizophrenia [5]. Previous studies have also indicated that poor adherence to medication treatment could lead to negative outcomes for schizophrenic patients such as increased relapse rates, worsening of symptoms, re-admissions, longer hospital stays and social

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and occupational impairment. Furthermore, non-compliance with treatment also aggravates the consequences of the disease such as violence, homelessness, delinquency, and suicide, adversely affecting social security. Investigating factors related to treatment adherence can reduce the rate of non-adherence, significantly reducing relapse and cost of care. This will improve the quality of treatment for schizophrenic patients and reduce financial burden on families, healthcare resources and society. This study investigated the prevalence of non – adherence to medications especially to antipsychotics among patients with schizophrenia by using Morisky Medication Adherence Scale 8 item (MMAS - 8) in National Psychiatric Hospital 2 and examined the psycho–social and clinical risk factors associated with medication non - adherence in these patients.

2. SUBJECTS AND METHODOLOGY

2.1. Subjects

A total of 126 patients over 18 years old with schizophrenia, using ICD 10 (International Classification of Diseases, 10th Revision) Schizophrenia diagnostic criteria of WHO were selected from their medical records in National Psychiatric Hospital 2, Vietnam from April, 2018 to May, 2019. This psychiatric hospital is one of the two biggest psychiatric hospitals in Vietnam and is the biggest psychiatric hospital in Southern Vietnam. Patients were invited to enroll in the study if they met the following inclusion criteria: (1) the patients had been previously diagnosed with schizophrenia and were experiencing a return of symptoms at the time of the study after a full or partial recovery, (2) signed the written informed consent form and (3) had the ability to answer the questionnaire or had relatives or caregivers who know patients' medication use well. The exclusion criteria were as follows: (1) patients with the first stage of schizophrenia, (2) schizophrenic patients who had not been previously treated, (3) outpatients, (3) inability to understand Vietnamese, (4) having acute and severe physical diseases that did not allow the participants to answer the interview questions correctly.

Eligible participants were selected by convenient sampling technique and during the time of the study we selected a total of 126 patients with schizophrenia.

2.2. Methods

Research design

This was a cross-sectional analytical study, including descriptive and statistical analyses.

Data measurement

The Vietnamese version of MMAS-8 was used to assess medication adherence in the study participants. This instrument, a self-administered questionnaire, consisted of 8 items assessing the medication-taking behavior and has been widely used in various cultures [6]. The scale consists of 8 items in which the first 7 items are answered with "yes" or "no". If the answer is "yes", the item is scored as 1, and the answer is "no", the item is scored as 0, except for item 5, in which each "yes" answer is scored as 1 and each "no" answer is scored as 0. Item 8 is rated on a 5-point scale ranging with A (never/rarely), B (once in a while), C (Sometimes), D (usually) and E (all the time/ always). If the answer is A, the item is scored as 0, the answer is from B-E, the item is scored as 1. Response options were used to calculate a continuous total score ranging from 0 to 8; scores of 3 or more indicating low adherence, 1 or 2: medium adherence, 0: high adherence [7]. When analyzing the statistical correlations, we grouped high adherence and moderate adherence into one group and the low adherence group in a separate group. To collect data on risk factors associated with medication adherence, participants were evaluated by a structured questionnaire on socio-demographic information such as age, gender, occupation, economic, marital status, and level of education, support from family and society; and clinical information including duration of schizophrenia, clinical symptoms evaluated by Positive and Negative syndrome scale (PANSS), type of medication, and side effects of medication. The Positive and Negative Syndrome Scale (PANSS) is a widely used instrument for measuring the severity level of adult patients with schizophrenia. The PANSS consists of 30 items divided into three dimensions including negative, positive and general psychopathological dimensions. Positive and negative dimension has 7 items each, while general psychopathological dimension consists of 16 items. Each item is rated on a seven-point severity scale (1=absent, 2=minimal, 3=mild, 4=moderate, 5=moderate severe, 6=severe, and 7=extreme). The lowest possible total score scales are 7 and the highest score are 49 on both negative and positive dimension of PANSS. For the general psychopathological scale, the minimum score is 16 and maximum score is 112. A higher score indicates the a more severe level of schizophrenia [8,9].

For data quality control, research team

members were psychiatrists with at least 9 years of experience and were carefully trained in a group in administering all measures.

Statistical analysis

All statistical analyses were performed using SPSS version 20.0. Frequency analyses were used to describe the sample. Chi-squared tests were applied to measure the difference of characteristics between those with high/medium and low adherence group. The odds ratio (OR) and its 95% confident intervals (Cis) were calculated. Multivariate logistic regression was used to analyze the factors associated with medication non-adherence among schizophrenic patients.

Procedure

126 schizophrenic patients admitted at National Psychiatric Hospital 2, Vietnam from April 2018 to May 2019 were invited to participate in the study. Participants and their relatives were fully explained of the study. After that they signed the written consent form. Psychiatrists who had received PANSS training accessed patients at the time of admission. This examination took about 50 minutes. If patients were calm down, they filled out a social - demographic and clinical questionnaire and MMAS - 8 with or without their relatives' help. If patients were in agitated state, they would fill out this questionnaire right after the agitation is under control.

Ethics

The research protocol was approved by the professional council and the medical ethics committee of Hue University of Medicine and Pharmacy, Hue University. This study was conducted in accordance with the Declaration of Helsinki.

3. RESULTS

A total of 126 patients with schizophrenia, with the mean age of 39.60 (SD 11.48), 56 women (44.44%) and 70 men (55.56%), participated in the study and completed the questionnaire. Among them, 7 participants (5.56%) were classified as high adherence, 20 participants (15.87%) were classified as medium adherence and 99 participants (78.57%) were classified as low adherence according to the MMAS - 8 (Table 1).

Table 1. Prevalence of medication adherence according to MMAS-8

Prevalence of medication adherence by using MMAS-8	Number (n)	Percentage (%)
Low	99	78.57
Medium	20	15.87
High	7	5.56
Total	126	100

Table 2. Socio-demographic characteristics of the participants and differences between low adherence and high/medium adherence groups

Characteristics		Adherence				Total	P
		Low		Medium/high			
		n	%	n	%		
Age (year) ± SD		40.18 ± 11.73		37.48 ± 10.44			0.28
Gender	Men	41	73.2	15	26.8	56	0.19
	Women	58	82.9	12	17.1	70	
Level of education	Secondary or less	69	87.3	10	12.7	79	**0.002**
	High school or higher	30	63.8	17	36.2	47	
Marital status	Married	43	76.8	13	23.2	56	0.661
	Single/divorced/ widowed	56	80.0	14	20.0	70	

Economic status	Average or rich	85	75.9	27	24.1	112	**0.039**
	Poor	14	100	0	0	14	
Job status	Employment	64	71.9	25	28.1	89	**0.005**
	Unemployment	35	94.6	2	5.4	37	
Support from families/ communities	Good	25	49.0	26	51.0	51	**< 0.001**
	Poor	74	98.7	1	1.3	75	

Table 2 shows that the prevalence of unemployment in low adherence group was significantly higher than in medium or high adherence group (94,6% vs 71.9%, p < 0.01). Similarly, the rates of patients with poor support from family and poor economic status as well as low education level (secondary school or less) in low adherence group were significantly higher than in medium or high adherence group (p < 0.05). There were not significant differences between the high adherence, medium adherence and low adherence groups in gender, marital status (p > 0.05).

Table 3. Clinical characteristics associated with adherence in participants

Characteristics		**Adherence**				**Total**	**P**
		Low		**Medium/High**			
		n	**%**	**n**	**%**		
Illness insight	Poor insight	41	100	0	0	41	**< 0.001**
	Good insight	58	68.2	27	31.8	85	
Duration of schizophrenia	< 5 years	17	63.0	10	37.0	27	**0.026**
	≥ 5 years	82	82.8	17	17.2	99	
Number of hospitalizations	≤ 5 times	21	47.7	23	52.3	44	**< 0.001**
	> 5 times	78	95.1	4	4.9	82	
PANSS Score	Positive	27.56 ± 3.07		26.96 ± 2.72			0.365
	Negative	29.15 ± 6.09		23.11 ± 3.31			**< 0.001**
	General psychopathological	54.20 ± 5.46		46.48 ± 4.53			**< 0.001**
Type of antipsychotics	FGA	21	58.3	15	41.7	36	**< 0.001**
	SGA	43	97.7	1	2.3	44	
	FGA + SGA	35	76.1	11	23.9	46	
Number of side effects	< 2	56	72.7	21	27.3	77	**0.045**
	≥ 2	43	87.8	6	12.2	49	

Among clinical characteristics, there were several factors associated with low adherence to medication among patients with schizophrenia including poor insight to schizophrenia (p < 0.001), duration of schizophrenia of 5 years or more (p < 0.05), number of admissions over 5 times, higher scores of negative scale and general psychopathological scales of PANSS (p < 0.001), use of typical antipsychotics, having 2 side effects or more (p < 0.01). However, score of positive scale of PANSS had no association with low adherence to medication in the participants (p > 0.05) (Table 3).

Table 4. Multivariate logistic regression model predicting low adherence (MMAS-8 score > 2) by socio-demographic and clinical factors

Characteristics		OR	95% CI	P
Level of education	Secondary or less	1.65	0.27 - 9.95	0.586
	High school or higher	1		
Job status	Unemployment	0.10	0.00 - 2.53	0.163
	Employment	1		
Support from families/ communities	Poor	30.33	2.00 - 459.08	**0.014**
	Good	1		
Duration of schizophrenia	≥ 5 years	0.32	0.04 - 2.73	0.300
	< 5 years	1		
Number of hospitalizations	≤ 5 times	1		
	> 5 times	40.68	3.87 - 427.60	**0.002**
Type of antipsychotics	SGA	1		
	FGA	3.05	0.14 - 64.78	0.475
	FGA + SGA	0.67	0.11 - 4.10	0.665
Number of side effects	< 2	1		
	≥ 2	0.31	0.02 - 4.44	0.391
PANSS score	Negative	1.05	0.84 - 1.30	0.667
	General	1.31	1.03 - 1.66	**0.027**

Multivariate logistic regression analysis found that several factors associated with low adherence to medication among schizophrenic patients including poor support from family/community (OR = 30.33, $p < 0.05$), number of admissions over 5 times (OR = 40.68, $p < 0.05$), and higher score of general psychopathological scale of PANSS (OR = 1.31, $p < 0.05$) (Table 4).

4. DISCUSSION

Previous studies showed that the prevalence of low/poor adherence to treatment was high among patients with schizophrenia. In this study, we found that 78.57% of the study population was classified as low adherence to medication according to MMAS - 8. The prevalence of non/poor compliance among schizophrenic patients varied widely in different studies. Non-adherence is estimated to range from 40% to 90% of schizophrenic patients [10]. Chaudhari B et al. (2017) studied 50 patients with schizophrenia and found that among the studied patients, 52% of patients were low adherers according to MMAS – 8 [11]. Desai R and Nayak R (2019), in a retrospective cross-sectional study with data from the Medical Expenditure Panel Surveys (MEPS) for the years 2010 - 2014, found that 71% of 1.2 million people with schizophrenia were reported as non-adherence (PDC < 80%) to treatment by using the proportion of days covered (PDC) adherence measure [12]. Valenstein et al. studied on approximately 34,000 Veterans Affairs patients with schizophrenia using Medication possession ratios (MPRs) to assess adherence to medication in patients, with good adherence defined as an MPR ≥ 0.8 during a year and poor adherence with MPR ≥ 0.8 in all years, for 4 consecutive years showed that the prevalence of poor adherence was 36% of study population in each year [13]. The criteria used to determine non/ low/poor adherence in the studies varied according to the usage of different instruments such as MMAS - 8, PDC, MPR...Thus, the difference in the rate of non - adherence in schizophrenic patients among the studies could be explained by using different assessment tools of non-adherence.

Our study results showed that the prevalence of patients with low education level (secondary or less) in low medication adherence group was significantly higher compared to those in the high or medium group in bivariate analysis (Table 2) but this factor was not a risk factor in multivariate logistic regression analysis (Table 4). Our study findings were consistent with those reported in literature. Research by Desai

R. and Nayak R. (2019) showed that people with less than 15 years of education often had poor adherence to treatment compared to those with higher education and longer study time [12]. Patients with high level of education often had better insight and awareness of importance of treatment adherence, thereby making them adhere to treatment better. The relationship between treatment adherence and education level is reciprocal. High adherence to treatment would help control symptoms in the patients, help prolong the stable time of symptoms, thereby giving the patients the opportunity to study to achieve a higher level of education. Patients with low education level often combined with other risk factors such as poor insight, unemployment, and poor economic status. All these factors lead patients to poor adherence to medication treatment. This view was supported by the data in table 2 in our study and other previous studies. Poor or lack of insight include denial of illness, rejection to taking medication because of unawareness of benefit of medication and negative medication belief; and unawareness of social consequences due to schizophrenia. Chang J.G et al (2019) studied on 81 outpatients with schizophrenia realized that there was a correlation between insight and medication adherence [14]. Higashi K et al. in their systemic review with thirty-seven papers indicated that one of the key drivers of non - adherence was lack of insight [3]. Chaudhari B et al. also found that patients from low-income households often had poor adherence to treatment [11]. The correlation between unemployment, poor economic status and adherence to treatment was a bidirectional relationship. Patients with poor adherence to treatment often have uncontrolled symptoms, short stabilization time, increased number of hospitalizations, so their possibility of finding stable jobs are very low, leading to an increased risk of unemployment. On the other hand, non-adherence to treatment increases the cost of treatment due to its consequences, thereby making economic status more difficult. In contrast, patients with difficult economic status and unemployment have more difficulty accessing health services and using good medications, thus leading them to low adherence. Lack of support from families/communities was a predictor of low adherence among patients with schizophrenia. Our result showed that the rate of patients with lack of support from their families in low adherence group was significantly higher than those in high/medium adherence group (98.7% vs 1,3%, $p < 0.05$, Table 2). This difference was also found in multivariate logistic regression (OR = 30.33, 95% CI: 2.00 - 459.08, $p < 0.05$). In Vietnam, there is a close relationship between members in each family. Family plays an important role in caring patients with chronic diseases generally and schizophrenia particularly. Families remind and control patients' medication intake. Cohen A.N and Pedersen E.R et al. studied on 801 patients with schizophrenia, and the results found that patients with good support from their families were often associated with high adherence [15]. However, in another study, Glick I.D and Davis J.M et al. (2017) reported that there was no association between support of families and medication adherence [16]. Contrasting results on the association between family/community support and treatment adherence may suggest that this factor is not an independent factor but treatment adherence may be influenced by other factors such as severity of symptoms, duration of illness, combined substance use… Our study also showed that there were no significant differences between low adherence versus high/medium adherence groups in gender, age and marital status ($p > 0.05$).

Among clinical characteristics, our study's results indicated some factors associated with medication adherence in the participants including type of schizophrenia, duration of schizophrenia, number of hospitalizations, severity of schizophrenia assessed by PANSS, type of antipsychotics and number of side effects in bivariate analysis. Evidence from other studies points to severity of positive symptoms, negative symptoms and other symptoms of schizophrenia could impact on medication adherence in patients. Bajaj V et al. (2009) found that when the score of PANSS was higher, treatment adherence was lower [17]. Chaudhari B et al. also shared this view [11]. Negative symptoms such as memory and cognitive impairment, impaired self-care could predispose patients to low adherence to treatment. Our results in table 3 showed that the mean score of negative dimension of PANSS in the low adherence was significantly higher than in medium/high adherence group (29.15 ± 6.09 vs 23.11 ± 3.31, $p < 0.01$). This result was similar with general psychopathological dimension of PANSS (54.20 ± 5.46 vs 46.48 ± 4.53, $p < 0.01$) (Table 3). But in multivariate logistic regression analysis, only higher score of general psychopathological dimension of PANSS were still risk factors (OR = 1.31, 95%, CI 1.03 – 1.66, $p < 0.05$) (Table 4). Prevalence of patients with duration of schizophrenia more than 5 years

was significantly higher in low adherence group compared to those in high/medium adherence group (82.8% vs 12.7%, p < 0.05) (Table 3). Besides that, the percentage of patients with number of admission more than 5 times was also significantly higher in the low adherence group than in the medium/high adherence group (95.1% vs 4.9%, p < 0.05) (Table 3). Number of hospitalizations was also a risk factor in multivariate logistic regression (OR = 40.68, 95% CI 3.87 - 427.60) (Table 4). An increased number of admissions usually means that the treatment was less effective, the symptoms were less improved and negative symptoms were progressively worse. All of these factors contributed to low adherence in patients with schizophrenia. Treatment by typical antipsychotics or first generation of antipsychotics was suggested as a significant predictor of poor adherence in previous studies. El Abdellati K et al. reviewed 26 studies on factors related to antipsychotics adherence revealed that patients using first-generation antipsychotics (FGA) monotherapy had poor adherence at discharge than patients using second-generation antipsychotics (SGA) either as monotherapy or in combination in some studies but this result was not consistent in other studies [18]. In bivariate analysis in our study, low medication adherence was significantly associated with using FGA (p < 0.001) (Table 3). In multivariate logistic regression analysis, this risk factor was not significant (p > 0.05) (Table 4). FGA only impact on positive symptoms but not on negative symptoms and cognitive symptoms and even make these symptoms worsen. As mentioned above, patients with negative or cognitive symptoms with poor self - care, memory and cognitive impairment was a predictor of low adherence. In addition, FGA often associated with side effects including parkinsonism, acute dystonia, tardive dyskinesia, akathisia, anticholinergic effects such as constipation, blur vision, mouth dry and side effects on cardio - vascular system such as palpitation, orthostatic hypotension. These factors lead patients to low adherence to FGA. Wubeshet Y.S et al. (2019) studied on 356 patients with schizophrenia found that 293 patients (97.7%) had side effects caused by FGA in which cardiovascular side effects occurred in 169 patients (56.3%), sedation and side effects on the central nervous system occurred in 149 patients (49.6%) and extrapyramidal side effects occurred in 114 patients (38.0%) [19]. Lee Y, Lee MS, Jeong HG, et al. (2019) studied on 81 patients with schizophrenia or bipolar found that patients' dissatisfaction attitude towards medication and their physical symptoms was associated with low post-hospitalization drug adherence in severe psychiatric patients including schizophrenia [20]. Our data in table 3 indicated that prevalence of participants having 2 or more side effects was significantly higher in low adherence group than in high/medium adherence.

There were limitations to our study. First, the sample in our study was small. Second, this was a descriptive cross - sectional study not a longitudinal follow up study so it is difficult to investigate causal relationship. Third, some potential variables that could be associated with low adherence may involve route of medication administration, substance abuse/dependence, therapeutic alliance...

5. CONCLUSION

The prevalence of low adherence to medication is high in patients with schizophrenia. Bivariate analysis indicated several factors associated with low adherence in participants including level of education below high school; unstable job/un-employment; poor insight about schizophrenia, poor caring/support from family, high scores of negative PANSS and general PANSS, duration of schizophrenia above 5 years, treated by typical antipsychotics and having more than two side effects of antipsychotics. Therefore, to improve adherence to medication among this population, following tasks should be done: (1) patients' families should support patients after discharge, (2) psychiatrists should choose and adjust dose of medication to enhance effects and reduce side effects to improve medication adherence in patients. (3) Mental health care staff should educate patients and their relatives about the important role of medication in treatment and schizophrenia.

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The authors have no conflict of interest to declare.

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