# **Original Research Article**

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# Medication compliance in schizophrenic out patients with psychoactive substance use co-morbidity: a cross-sectional study

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# ABSTRACT

**Background**: Medication adherence is an important issue in the treatment and management of persons with psychiatric disorders including schizophrenia. Apart from side effects and inefficient outcomes of psychiatric medications, substance abuse also complicates the adherence pattern to the prescribed medications. Present study was designed to estimate the magnitude of medication non-adherence and its correlates in patients with schizophrenia having co-morbid psychoactive substance use.

**Method**: The 60 schizophrenic patients with active substance use were taken from OPD of institute of mental health and hospital, Agra. Positive and negative syndrome scale (PANSS), alcohol, smoking and substance involvement screening test (ASSIST), medication adherence rating scale (MARS) and Morisky 8-item medication adherence questionnaire (MMAQ-8) were used to gather relevant clinical data along with a proforma for recording socio-demographic characteristics.

**Results**: The results revealed an alarming level of medication adherence. The 91.7% sample (55 patients) met the criteria for medication non-adherence. Majority of the patients were using alcohol (58.3%) and cannabis (51.7%). **Conclusions**: Given the high rate of medication non-compliance it is suggested that specific intervention aimed at compliance to prescribed medication is needed in this population.

Keywords: Medication adherence, PANSS, Schizophrenia, Substance use, MARS, MMAQ-8

# INTRODUCTION

Schizophrenia is a major psychiatric disorder with distinctive signs and symptoms such as altered behaviour, speech and an inability to understand veracity, lasting for a large proportion of time which cause significant social and occupational dysfunction.<sup>1</sup> The life time prevalence of schizophrenia is 1% and currently the general accord regarding treatment is the use of antipsychotic medications.<sup>2,3</sup>

Schizophrenic patients are susceptible to psychoactive substance use.<sup>4</sup> Psychoactive substance users use those substances which when administered lead to changes in the brain affecting mental processes like cognition and

affect and includes the whole gamut of substances, legitimate or illegitimate, which are of significance to drug policy.<sup>5</sup> These substances are found in numerous medications as well as in various no medicinal substances like alcohol, nicotine, caffeine etc. and cause harm in excess.<sup>6</sup> Term psychoactive substance use does not automatically mean that it is addictive, however most of them do show such properties when taken for period of time.

It is not uncommon that most of these patients meet the criteria of a substance use disorders. Concerning explicit substance use; tobacco, alcohol, cannabis and cocaine use disorders are most frequently found in patients of schizophrenia with rates as much as three times more than the general population.<sup>7,8</sup> The lifetime prevalence for smoking and alcohol use is 60-90% and 21-86% respectively, along with 17-83% for cannabis use and 15-50% for cocaine use.<sup>7,9</sup> This leads to a higher chance of reversion, poor global functioning, clinical exacerbations, poor medication compliance, suicide and rehospitalization.<sup>10</sup>

Prevalence studies of psychoactive substance use in patients of schizophrenia suggested the overall prevalence of psychoactive substance use are 41% to 51%.<sup>11,12</sup>

Other studies on prevalence of psychoactive substance use in schizophrenic patients reported that cannabis is the most frequently used substance (26%-69%) followed by alcohol (14%-42%) and other stimulants (5%-14%).<sup>11,13</sup> Mueser et al in his study suggested a prevalence of alcohol use 47%, 42% for cannabis use, 25% for stimulants, 18% for hallucinogens and 7% for sedatives.<sup>14</sup>

Poor Medication compliance is very common and an important obstacle to treatment especially in patients of schizophrenia who require long term management with antipsychotic medication.<sup>15</sup> Almost half the patients showed poor medication compliance when they are using psychoactive substances.<sup>16,17</sup> This leads to a higher chance of reversion with a poor outcome. However, as far as research is concerned there is very little information regarding compliance use as a co-morbidity.<sup>18</sup>

Several studies have evaluated the medication compliance in psychiatric patients, specifically to schizophrenia and reported that psychoactive substance user groups were more likely to have poor medication compliance.<sup>18-20</sup> Various demographic as well as clinical factors such as age, unemployment, psychopathology, reduced insight, psychoactive substance use, lack of treatment access, stigma and financial constraints were all found to be connected with poor medication compliance.<sup>21,22</sup> Kovasznay et al also reported psychoactive substance use was associated with high symptom score but was not linked to medication compliance.<sup>23</sup>

There are various conflicting evidences that suggest the role of symptoms (especially negative symptoms) in medication compliance. The same can be said about psychoactive substance use. Thus, a major goal of this study is to find out whether psychoactive substance use affects medication compliance or not and whether any symptoms associated with schizophrenia lead to poor medication compliance or not as literature on the subject are very sparse and conflicting.

# Aim and objectives

Aim and objectives of the study were to estimate medication compliance among outpatients of

schizophrenia who have psychoactive use co-morbidity and to find out the relationship between medication compliance and socio-demographic and clinical profile of patients.

# **METHODS**

The study was conducted at institute of mental health and hospital, Agra. It is a tertiary referral center and a postgraduate teaching hospital which imparts training in psychiatry, clinical psychology, psychiatric social work and psychiatric nursing. The hospital has a wide catchment area which includes states of Uttar Pradesh, Madhya Pradesh, Rajasthan, Haryana and Uttarakhand.

# Sample

It was a cross-sectional hospital-based study. The subjects were recruited for the study by the purposive sampling technique. A total of 60 patients diagnosed with schizophrenia according to diagnostic criteria for research accompanying the ICD-10 (DCR-10) having psychoactive substance use as a co-morbidity from the out-patient department of institute of mental health and hospital, Agra (IMHH) with the following inclusion and exclusion criteria were selected for the study.

# Inclusion criteria

Patients diagnosed with schizophrenia according to ICD-10 DCR within the age range of 18-60 years of either sex having minimum illness duration of 5 years. Only clinically stable co-operative patients who gave their consent were taken. Patients with minimum education of up to 10<sup>th</sup> class and who understand English. Patients having any psychoactive use (except nicotine) as their comorbidity. Patients who were prescribed any antipsychotic medication except Clozapine and patients who were not taking medications for psychoactive substance use disorder were included in the study.

# Exclusion criteria

Patients who had a co-morbid psychiatric illness such as a depressive episode, suicidal ideation and an unstable general medical condition and patients who had cognitive disorders such as dementia or having memory deficits and mental retardation were excluded from the study.

# Tools

# Socio-demographic and clinical data sheet

Semi-structured Pro-forma was used for recording demographic details like age, sex, marital status, education, occupation, family income and family type, as well as clinical data such as age of onset of illness, duration of illness, family history of the psychiatric illness.

# The PANSS<sup>24</sup>

The PANSS is a widely used research tool to measure psychopathology in schizophrenia. It is a 30-item, 7-point (1-7, from absent to extremely severe) scale rated with the help of a semi-structured interview. It has 3 subscales to measure the severity of the positive symptoms (7items), the severity of the negative symptoms (7items) and to measure the general psychopathology

# The ASSIST version 3.0

The ASSIST was developed for the world health organization (WHO) by an intercontinental group of substance abuse researchers to perceive psychoactive substance use and connected problems in principal care patients. It consists of 6 questions. It enquires about the life time use of substances, frequency, dependence symptoms and related problems, current use of substances craving, pre-occupation with psychoactive substance use, intravenous drug use etc. The scoring is No use 0; one or two times use 2; monthly use 3; weekly use 4; and almost daily use 6. The total score of 0 to 3 indicates no intervention, a score of 4 to 26 requiring short term intervention and score >26 requiring long term intensive intervention.

# The MARS<sup>25</sup>

The MARS was developed primarily for assessing medication adherence in schizophrenia (Thompson et al).<sup>25</sup> It consists of a 10-item questionnaire with a simple scoring chart that assesses medication compliance during the past one week. Patients are regarded as complaint during the past week if they give "NO" responses to questions 1-6 and 9-10 and "YES" to questions 7 and 8. It examines medication taking behavior and attitudes towards medications with higher reliability and validity.

# The Morisky 8-item MMAQ-8<sup>26</sup>

The MMAQ-8 assesses compliance up to 2 weeks. The first seven items are yes/no responses while the last item is a 5-point Likert response. The additional 4 questions

incorporate items which are related to medication taking behaviors especially related to underuse. MMMAQ-8 has been reported to have good reliability and validity for both acute and chronic illnesses and thus is an excellent report of medication compliance. The participants are labeled as having low compliance if scores of >2 are found on MMAQ-8 while high compliance is labeled if patients obtain a score of 0 and a score of 1 or 2 indicates medium adherence.

# Procedure

The study was conducted at IMHH, Agra after getting proper ethical and scientific clearance from the institutional ethics committee and scientific committee. Subjects were taken from IMHH outpatient department as per the inclusion and exclusion criteria. While a written and informed consent was taken from the patients after explaining the objective and procedure of the study. Socio-demographic details of each patient were entered in the socio-demographic data sheet. PANSS was used to psychopathology. measure Information about psychoactive substance use was taken from the patient by using the ASSIST scale. Lastly, information about medication compliance was taken and recorded on the MARS and MMAQ-8 scales. Participants were labeled as having good MA if the patient scored >2 on the MMAQ-8 and "YES" responses on question 7 and 8 of MARS scale while others were labeled as having poor MA.

# RESULTS

Table 1 shows frequency and percentages of demographic and clinical variables of the subjects. Large no of patients was male, Hindu, married, skilled workers and belonged to joint family. The mean and SD of the age was  $37.68\pm9.01$  years, PANSS positive mean score was  $12.03\pm5.78$ , PANSS negative score was  $16.58\pm3.43$  and PANSS general psychopathology was  $30.86\pm6.61$ . Table 2 shows frequency of psychoactive substances among patients of schizophrenia excluding nicotine. Alcohol used disorder was most commonly found psychoactive substance (58.3%) followed cannabis used disorder (50%), sedatives (11.7%) inhalants, opiods (5%).

Categorical variables		Frequency	Percentage (%)
Gender	Male	54	90.0
	Female	6	10.0
Religion	Hindu	48	80.0
	Muslim	8	13.3
	Others	4	6.7
Marital Status	Single	12	20
	Married	35	58.3
	Divorced	6	10.0
	Separated	7	11.7
Occupation	Skilled worker	48	80
	Unemployed	12	20
Residence	Rural	37	61.7

# Table 1: Sample characteristics.

Continued.

# Ahlawat S et al. Int J Res Med Sci. 2022 Jan;10(1):167-172

Categorical variables		Frequency	Percentage (%)
	Urban	23	38.3
Family Income	0-4999	19	31.7
	5000-9999	36	60.0
	15000-19999	5	8.3
	Matriculate	25	41.7
Education	Inter	30	50.0
	Graduate	5	8.3
Family type	Nuclear	11	18.3
	Joint	49	81.7
Continuous variables		Mean	S. D.
Age (years)		37.68	9.01
PANSS positive symptoms		12.03	5.78
PANSS negative symptoms		16.58	3.43
PANSS general psychopathology		30.86	6.61

# Table 2: Percentages of psychoactive substances.

Type of substances	Frequency	Percentage (%)
Alcohol	35	58.3
Cannabis	31	51.7
Sedatives	7	11.7
Inhalants	3	5
Opioids	3	5
Others	1	1.7
Cocaine	0	0
Amphetamines	0	0
Hallucinogence	0	0

# Table 3: Percentages of cases requiring intervention for psychoactive substances.

ASSIST	No use (%)	No intervention (%)	Short term intervention (%)	Long term intervention (%)
ASSIST, alcohol	25 (41.7)	5 (8.3)	30 (50)	-
ASSIST, cannabis	29 (48.3)	-	25 (41.7)	6 (10)
ASSIST, opioids	57 (95)	-	-	3 (5)
ASSIST, inhalants	57 (95)	-	-	3 (5)
ASSIST, sedatives	53 (88.3)	-	6 (10)	1 (1.7)
ASSIST, cocaine	60 (100)	-	-	-
ASSIST, amphetamines	60 (100)	-	-	-
ASSIST, hallucinogence	60 (100)	-	-	-
ASSIST, others	58 (96.7)	-	2 (3.3)	-

Table 3 suggests that short term intervention was required by 50% cases of alcohol use, 41.7% cases of cannabis use, 6% cases of sedative use and 3.3% cases of other substances. Whereas, long term intervention was required by 10% cases of cannabis use, 5% cases of inhalants and opiods each and 1.7% cases of sedatives. Others did not need an intervention for substance abuse.

# Table 4: Percentages of patients with psychiatric medication adherence.

Adherence	Frequency	Percentage (%)
Poor adherence	55	91.7
Good adherence	5	8.3
Total	60	100.0

Table 4 indicates that 55 patients (91.7%) had poor medication adherence. Only five patients (8.3%) had good medication adherence which is quite low.

# DISCUSSION

Poor medication compliance is the single major reason leading to relapse and continuation of psychopathology in schizophrenic patients.<sup>27</sup> The addition of substance abuse along with schizophrenic psychopathology further complicates the scenario.<sup>28</sup> The present study was an attempt to study the pattern of medication adherence and its correlates in patients of schizophrenia with co-morbid psychoactive substance abuse. The results were highly disappointing because 91.7% patients had poor medication compliance as determined by the scores on

MARS and MMAQ-8. Only a few patients 5 (8.3%) were continuing their prescribed treatment. Given this disproportionate amount of medication non-adherence, it was not possible to statistically determine the sociodemographic and clinical correlates of medication adherence. A direct comparison is warranted to determine if the magnitude of medication non-adherence is greater in schizophrenic patients with psychoactive substance abuse vs the patients of schizophrenia without any such substance.

The present study did not sample the patients without substance. Hence, the exiting researches were considered to compare the results. In a review study, Julius et al reported that 20-72% patients had poor adherence to medication in the studies included in the review.<sup>29</sup> Lieberman et al reported that 74% patients had discontinued their medications within one and a half year mainly due to unpleasant side effects and insufficient efficacy.<sup>30</sup> Eticha et al reported 26.5% as non-adherent to their medications. Semahegn et al in a meta-analytic study reported that 56% patients of schizophrenia were non-adherents.<sup>31,32</sup>

In an Indian study, Chaudhari et al observed that 52% of schizophrenic patients were non-adherers.<sup>33</sup> Following factors were found to be associated with non-adherence; high scores on PANSS, low income, poor insight, adverse side effects of medications, ineffective treatment, shame and stigma of being mentally ill and seeking its the treatment. These studies support the position that the nonadherence is even greater in schizophrenic patients with co-morbid substance abuse which was 91.7% in the index sample which is at alarming level. Many of these patients consider that taking psychiatric medications along with substance of abuse will aggravate their condition. They tend to skip the medications in favor of the psychoactive substance. The results clearly suggest that these patients need intensive psychosocial support for continuing the prescribed treatment. Schoeler et al reported that 20-36% of the adverse effects on outcome in psychosis was mediated by continued cannabis use. Intervention specifically focused on medication adherence could help in resolving part of the problem.<sup>28</sup> Alcohol and cannabis were found to be most prevalent substance of abuse in this group as shown in the Table 2 and majority of these patients needed short term intervention for their substance as per the findings of ASSIST as shown in the Table 3. Only a few patients of cannabis and other nonalcoholic substance required intensive intervention. At the time of assessment, the patients had mild to moderate level of psychopathology scores on PANSS. Given this, it can be construed that substance use contributed more to severity the non-adherence than the of the psychopathology.

# Limitations

The results of the study should be considered given the limitations such as small sample size, non-random

sampling, selection of the sample from single psychiatric hospital, and cross-sectional nature of the study.

# Implications of the study

In a developing country like India poor medication compliance leads to frequent relapse and hospitalization in patients with Schizophrenia and hence a poor outcome, still remains a big issue to be solved. This study is important from the viewpoint that the patient being treated and interventions to improve Medication compliance should be specialized.

# CONCLUSION

To develop clear understanding of the role of substance abuse in the non-adherence, it would be better to design a study which includes group of patients without substance abuse so that a comparison can be done on various demographic and clinical variables for determination of factors associated with medication non-adherence in this population of co-morbid disorder. Also, specific assessment should be done to find out the perceived reasons for non-continuation of prescribed treatment.

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