

Predicting medication noncompliance among patients with schizophrenia after hospital discharge

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ABSTRACT

Background: Medication noncompliance (NC) after hospital discharge is the main reason for poor outcomes of the clinical course of the schizophrenic subjects. In the present study we assess the patients with diagnosis of schizophrenia and predict the reason for medication noncompliance after hospital discharge on follow up period. **Methods:** A total of 70 patients (C=35, NC=35) with schizophrenia at 1 month follow-up were interviewed using self-designed tools to assess sociodemographic data, insight, clinical symptoms, attitudes, therapeutic alliance, side-effects experienced and substance use disorder were assessed at baseline and 6 month follow-up. **Results:** Mean age with \pm SD in compliance (C) and noncompliance (NC) group is 32.45 ± 11.07 and 35.29 ± 13.45 respectively. Significant correlation between C and NC group in education level, SES ($p = 0.011$). Majority of patients in both groups are male (C=72.7%, NC=70.3%). NC is higher in illiterate, unmarried, joint family and Low SES. At 1 month follow up, in NC group most patients are need of treatment (45.9%), reports of difficulty relabeling their symptoms (18.9%). Clinical symptoms in Mean \pm SD, BPRS Score differ in C and NC group ($p=0.052$). At 6 month follow up, 66 no's of subjects came (C=35, NC=31). Significant reduction in the severity of the psychopathology BPRS score ($P=0.000$) and perceived side-effects ($P=0.015$). Improved quality of therapeutic relationship. Substance abuse, lack of awareness, attitudes and belief system, social isolation are reason for noncompliance. **Discussion:** As inpatient care, medication taking behavior is closely supervised by hospital staff, so compliance is high. Post-discharge follow-up is important for continued medication compliance in schizophrenic patients. NC increase the risk of relapse, rehospitalization, self-harm, lower quality of life. **Conclusion:** Public awareness concerning stigma to illness and antipsychotic medicine noncompliance should be further studied. With the current available pharmacological and psychological approaches that lowers risk of medication noncompliance should be encouraged in every patient, family members and medical personnel.

Keywords: Noncompliance, Compliance, Schizophrenia, Medication, Acute Hospitalization, Drug attitude, Therapeutic alliance.

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Compliance towards medications is essential and pharmacotherapy is the mainstay in the treatment of schizophrenia spectrum disorders.

Noncompliance can be defined primarily as one not buying or receiving the medicines and secondarily other group is the one not following the instruction as prescribed regarding drug dosages, frequency, duration of medication¹ and follow-up visit. Compliance is the extent to which the patients behavior matches the prescribers recommendations³. Medication non-compliance is thought to be a major factor in psychiatric hospitalizations. The first few weeks after hospital discharge represent a critical period in the course of recovery from exacerbations of chronic schizophrenia. After stabilization still symptomatic patients make transitions from inpatient to outpatient care, they typically assume some amount of independency and control over several aspects of their daily lives. As the patients move from secondary/tertiary care to primary care they move from an environment where compliance is carefully supervised to one where compliance is almost entirely dependent on the patient¹⁹. Noncompliance can take different form from either avoidance of prescription, taking less or more medication than prescribed, taking someone else medication, failing to comply with time²⁸.

A large number of factors have been studied as possible determinants of medication noncompliance among patients with schizophrenia. Patients, medication noncompliance is the primary focus of this article. In this study, we consider the possible predictors of medication noncompliance like role of severity of illness, substance use, insight, treatment alliance, social support system, family involvement and aspects of medication management.

Comorbid substance use disorders(SUD) are common among patients with schizophrenia who are noncompliant with antipsychotic medications. There is a strong correlation of SUD and medication noncompliance among schizophrenic patients. Intoxication may impair judgement, reduce motivation. Impair cognitive functions on a number of levels from basic motor coordination to more complex executive function tasks occur depending on the type and duration of substance use. Impairment in executive function have been found to be associated with trouble learning and applying the skills required for successful recovery, reducing motivation, and devaluation of the protection offered by antipsychotic medications, putting them at increased risk for relapse.

Lack of family support is another major contributor to noncompliance. Various cross-sectional studies have demonstrated lower rates of medication noncompliance among patients with schizophrenia who live with family members or primary caregiver who supervise their medications^{40,41,42}. At the same time whose families are ambivalent about the antipsychotic medications are at increased risk of medication noncompliance after hospital discharge⁴³. Patients whose families refused to participate in treatment were at high risk for stopping their medications³⁰.

Another common cause of noncompliance is the lack of awareness of the patient to realize their diseases. Patients who denied of being mentally ill have higher rates of medication noncompliance than patients with insight to their illness. Insight and attitude towards treatment are important variable predicting compliance. Longitudinal research suggests that the relationship between insight and compliance may not be straightforward⁴⁴. Attitudes

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towards treatment were predicted by insight, relationship with the physician prescriber and patient's experience during hospitalization.

The quality of relationship between physician and patients during acute admission is determinant of patient's attitude towards compliance of medications. Enhancing such relationship yields better compliance both as an outpatients and inpatients. Patients with strong alliances with their therapist more likely to comply to prescribed medications. The development of good rapport and trusting clinical relationship may lead patients to perceive practical advantages of continuing the medications. A poor relationship with prescriber, experience of force, threats during admission, compulsion to take medications and low insight predicted a negative attitude towards treatment. It was confirmed that important therapeutic alliance with clinician was important^{33,34}.

In a descriptive study, side effects of medication were the most common reason for medication noncompliance. In some cases, the patients preferred the experiences of symptoms related to the disease than the medication side effects³⁵. Opposition to the idea of taking medication due to belief of lack of medication activity and occurrence of physical side effects were the most frequent reasons for discontinuing medication intake³⁷. Also fear of addiction to medication, inappropriate and inadequate dosing of medication leading to poor compliance.

METHODOLOGY

Participants

Medical records of all patients discharged from active treatment as inpatient care in psychiatry department of a tertiary hospital, one month before the study were recorded. A total of 70 patients with diagnosis of schizophrenia according to ICD-10, were assessed. Inclusion criteria were patients of both gender with a minimum age of 15years and maximum 64years having a primary diagnosis of schizophrenia admitted as inpatients, treatment with oral antipsychotics and signed informed consent formed the study sample. Exclusion criteria were patients who are discharged against medical advice, patient who are transferred to another department inpatient facility, patients who received depot injection and Severe general medical conditions.

Assessment and measures

In our study, medication noncompliance was assessed in a sample of patient with schizophrenia who are interviewed within 1 month after discharge from acute hospitalization and 6months later as outpatient follow-up. Assessment of medication compliance and noncompliance and reasons for noncompliance, drug attitudes, severity of illness, level of insight, substances use disorder in self and family members, family support, therapeutic alliance quality were performed in Noncompliance (NC) and compliance(C) sample via a set of semi-structured clinical interviews and rating scales. Sociodemographic data, details of illness, and treatment history were noted for each participant in a semi-structured proforma specially designed for the study.

Within 1month following discharge from acute hospitalization, later at 6months after discharge from hospital, patients complete structured assessment of the reasons for noncompliance were done. Insight into illness was assessed by the Schedule for the Assessment of Insight(SAI)⁴, is a structured clinical interview providing 3 components of

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insight – recognition of illness, treatment adherence and symptoms re-labelling. Higher the total score better the insight¹⁰.

Clinical symptoms at hospital discharge were assessed by The Brief Psychiatric Rating Scale (BPRS)³¹, 24 items. It measures the psychopathology and treatment related symptom change³².

Drug attitudes was assessed by The Drug Attitude Inventory 10(DAI -10) consists of 10 yes or no statements reflecting patients experience of and attitudes towards medication^{16,29}. A positive total score predicts higher adherence means compliance to treatment¹⁶.

Therapeutic alliance was measured using six items The Helping Alliance Scale(HAS), a self-rating scale measuring patients views of therapeutic relationships with health care professionals^{33,34}. Family involvement was evaluated by any family members present during admissions, giving attendant to patient, how much they are involved into the patient care, any family members visited during hospital stay.

Substance used disorder were assessed at the time of hospital admission from history, taken from patient and family members, ICD-10¹⁷

Side-effects perceived from used of antipsychotics were asked to patients and attendants. It is a subjective experience, focusing on the previous treatment profiles (prescriptions, any documentation available) before admission.

Brief Medication Questionnaire, a self-report tool is used assessing the noncompliance and barriers in compliance. It includes a 5-item regimen screen that asks patients about there each medication intake in the past week, a 2-item Belief Screen that asks about drug effects and bothersome features, and a 2-item Recall Screen about potential difficulties remembering⁴⁵.

Follow-up assessment

At 1 month and 6 months' interval after hospital discharge, patients were interviewed using the instruments to assess change in target symptoms, use of antipsychotics, any perceived side-effects, on time follow-up or not. At follow-up patients and family members if present were asked if they had stopped medication for 1 week or more, during 6 months period since hospital discharge. During the medications free period any reappearance of symptoms? any reason for discontinuation, subsequently restarted medications or not?

Compliant patients were defined as those who took medications for at least 80% of the days post discharge from hospitalization. The rest were considered as noncompliant.

Statistical methods - Statistical analysis was done by using SPSS Version 21. Mean and SD were calculated. Comparison of mean values between 2 groups (NC & C) were done using students t-test, Fisher's exact test. Comparison were considered statistically significant at P-value ≤ 0.05 .

RESULTS

A consecutive total sample of 70 patients with schizophrenia, discharged from acute hospitalization were contacted within a month after hospital discharge for follow up and follow up again at 6 month interval.

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Table 1 summarizes socio-demographic variables, no significant group differences were noted in age, sex, domicile, occupation, marital status, religion and type of family. Mean age with \pm SD in compliant group and noncompliant group is 32.45 ± 11.07 and 35.29 ± 13.45 respectively. The majority of patients in both groups is male (72.7%) in compliant group and (70.3%) in noncompliant group. Most of patients in each group live in joint family, NC (54.5%), and C (56.8%). Compliance was more in middle socio-economic status (48.5%). Significant correlation seen between NC and C group in education level, socio-economic status and distance to hospital in km ($P = 0.011$).

Table no. 1 Socio-demographic characteristics of the patients in Compliance and Noncompliance group.

Sociodemographic variables	Compliant group(n=33)	Noncompliant group(n=37)	Statistical analysis and p value
Age (mean \pm SD)	32.45(11.07)	35.29(13.45)	P = 0.497
Sex			
Male	24(72.7%)	26(70.3%)	P = 0.820
Female	9(27.3%)	11(29.7%)	
Education			
Illiterate	7(21.2%)	14(37.8%)	P = 0.011 *
1-12 th standard	11(33.3%)	13(35.1%)	
Undergraduates	13(39.4%)	9(24.3%)	
Graduates and above	2(6.1%)	1(2.7%)	
Domicile			
Urban	18(54.5%)	21(56.8%)	P = 0.853
Rural	15(45.5%)	16(43.2%)	
Occupation			
Student	3(9.1%)	10(27%)	P = 0.262
Daily laborer	11(33.3%)	13(35.1%)	
Unemployed	6(18.2%)	5(13.5%)	
Employed	4(12.1%)	2(5.4%)	
Businessmen	2(6.1%)	0(0%)	
Household	7(21.2%)	7(18.9%)	
Marital status			
Single	15(45.5%)	20(54.1%)	P = 0.473
Married	18(54.5%)	17(45.9%)	
Socioeconomic status			
Lower class	8(24.2%)	21(56.8%)	P = 0.011 *
Middle class	16(48.5%)	13(35.1%)	
Upper class	9(27.3%)	3(8.1%)	
Religion			
Hindu	19(57.6%)	16(43.2%)	P = 0.231
Islam	14(42.4%)	21(56.8%)	
Type of family			
Nuclear	15(45.5%)	16(43.2%)	P = 0.853
Joint	18(54.5%)	21(56.8%)	
Distance to hospital (in km)			
1-20km	10(30.3%)	8(21.6%)	P = 0.011 *
21-40km	3(9.1%)	15(40.5%)	
40km and above	20(60.6%)	14(37.8%)	

Table 2, shows follow up at 1 month after discharge from acute hospitalization.

Insight- At 1 month follow up, study group did not differ significantly in the mean \pm SD, SAI score, 2.00 ± 0.87 in compliant group and 1.83 ± 0.72 in noncompliant group. Most patient in both age group were aware of having mental illness, few know their diagnosis as schizophrenia. In noncompliance group most patients are need of treatment (45.9%).

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Medication noncompliance, because patient in noncompliant group reports of difficulty in relabeling their symptoms (18.9%).

Symptoms at 1month follow up- Clinical symptoms differ significantly in the mean \pm SD of BPRS score in both C and NC group, of 51.27 ± 11.54 and 77.7 ± 16.04 respectively. The P-value is 0.052

Table no. 2:- At 1 month follow up after discharge

VARIABLE	Scale	At 1month follow-up after discharge from acute hospitalization N=70		P VALUE <0.05 significant
		COMPLIANCE N=33	NONCOMPLIANCE N=37	
Insight -illness awareness -need of treatment -symptoms re-labelling	SAI, Mean(SD) 1.914(0.793)	2.00(0.87)	1.83(0.72)	0.165
Clinical symptoms	BPRS Mean(SD) 65.28(19.33)	51.27(11.54)	77.7(16.04)	0.052*
Attitudes	DAI-10 Mean(SD) 0.742(3.56)	0.72(3.92)	0.75(3.26)	0.256
Therapeutic alliance	HAS Mean(SD) 76.61(19.54)	74.48(20.35)	78.51(18.87)	0.658
Side effects -Experienced before admission -Experienced after taking antipsychotics	Mean(SD) 1.44(0.500)	1.54(0.50)	1.35(0.48)	0.103
Substance Use -Alcohol -Multiple substance use	Mean(SD) 1.32(0.47)	1.24(0.43)	1.40(0.49)	0.147

Attitudes - Attitudes in both groups does not differ significantly in the mean \pm SD, DAI-10 score, (0.742 ± 3.56 , Pearson chi square value = 15.880 and df=13, P-value = 0.256). In C and NC group mean \pm SD is 0.72 ± 3.92 AND 0.75 ± 3.26 respectively.

Therapeutic alliance- Patients with medication NC have mean \pm SD, HAS score of 78.51 ± 18.87 , compared to C group of 74.48 ± 20.35 .

Side-effects and Substance use disorder - More number of patients in NC group experienced side-effects due to antipsychotics before admissions and more number of patients in C group experienced side effects after talking antipsychotics. However, no significant trend (P =0.103) was noted in C and NC group with newer antipsychotics. Substance use in both groups had non-significant association (P= 0.147), whether its alcohol or multiple substance use, NC group has more number of subjects abusing multiple substances.

Table 3, shows follow up at 6 months after discharge from acute hospitalizations. At the end of follow-up period only 66 numbers of patients came for follow up, 35 patients are

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compliance to treatment and 31 patients are treatment noncompliance. 2 patients could not be contacted, 1 patients came early due to physical comorbid condition, and other one reminder call was given but did not come. There is significant association with the mean value of the studied variables at 6month follow-up.

There is significant reduction in the severity of the psychopathology, BPRS score ($P = 0.000$) and perceived side effects ($P = 0.015$). Patients reported improve quality of therapeutic relationship at 6month ($P = 0.000$) compared to 1month ($P = 0.658$) follow up in HAS score. Attitudes towards medication (Total DAI-10 score, $P = 0.000$) and level of insight (total score on the SAI, $P = 0.012$) differed significantly in the C and NC groups at 6 month follow up. 37.1% can re-label their symptoms in C group compared to 6.5% in NC group. Level of insight(SAI)having a Pearson chi-square value of 8.832 and likelihood ratio of 9.750 and $df = 2$, have significant relation ($P = 0.000$) in 6month follow up.

Table 3 - At 6month follow-up after discharge

VARIABLE	Scale	At 3month follow-up after acute hospitalization N= 66		P VALUE <0.05 significant
		COMPLIANCE(35)	NONCOMPLIANCE(31)	
Insight -illness awareness -need of treatment -symptoms re-labelling	SAI, Mean(SD) 1.84(0.76)	2.05(0.83)	1.61(0.61)	0.012*
Clinical symptoms	BPRS Mean(SD) 70.33(17.27)	57.22(12.01)	85.12(7.49)	0.000*
Attitudes	DAI-10 Mean(SD) 0.80(3.43)	3.57(1.68)	-2.32(1.81)	0.000*
Therapeutic alliance	HAS Mean(SD) 76.93(19.70)	92.94(8.83)	58.87(10.79)	0.000*
Side effects -Experienced before admission Experienced after taking antipsychotics	Mean (SD) 1.45(0.50)	1.31(0.47)	1.61(0.49)	0.015*
Substance Use -Alcohol -Multiple substance use	Mean(SD) 1.57(0.49)	1.37(0.49)	1.80(0.40)	0.000*

At 6month follow up, side-effects experienced before admission in compliance group is 68.6% and non-compliance group is 38.7%. and side effects experienced after admission in compliance and non-compliance is 31.4% and 61.3% respectively. While in substance use disorder in compliance group 62.9% abuse alcohol and 80.6% in non-compliance group abuse multiple substances.

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figure 1:-Side-effects experienced at 1m and 6m follow-up

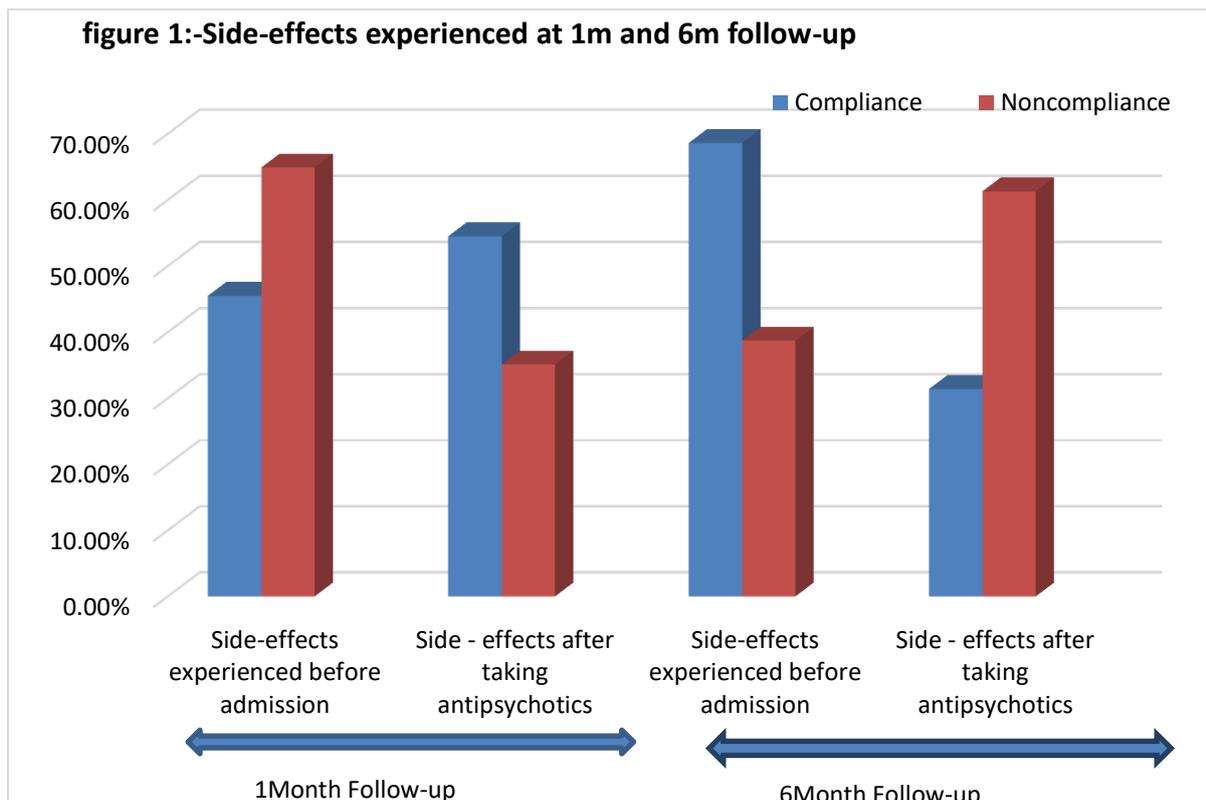
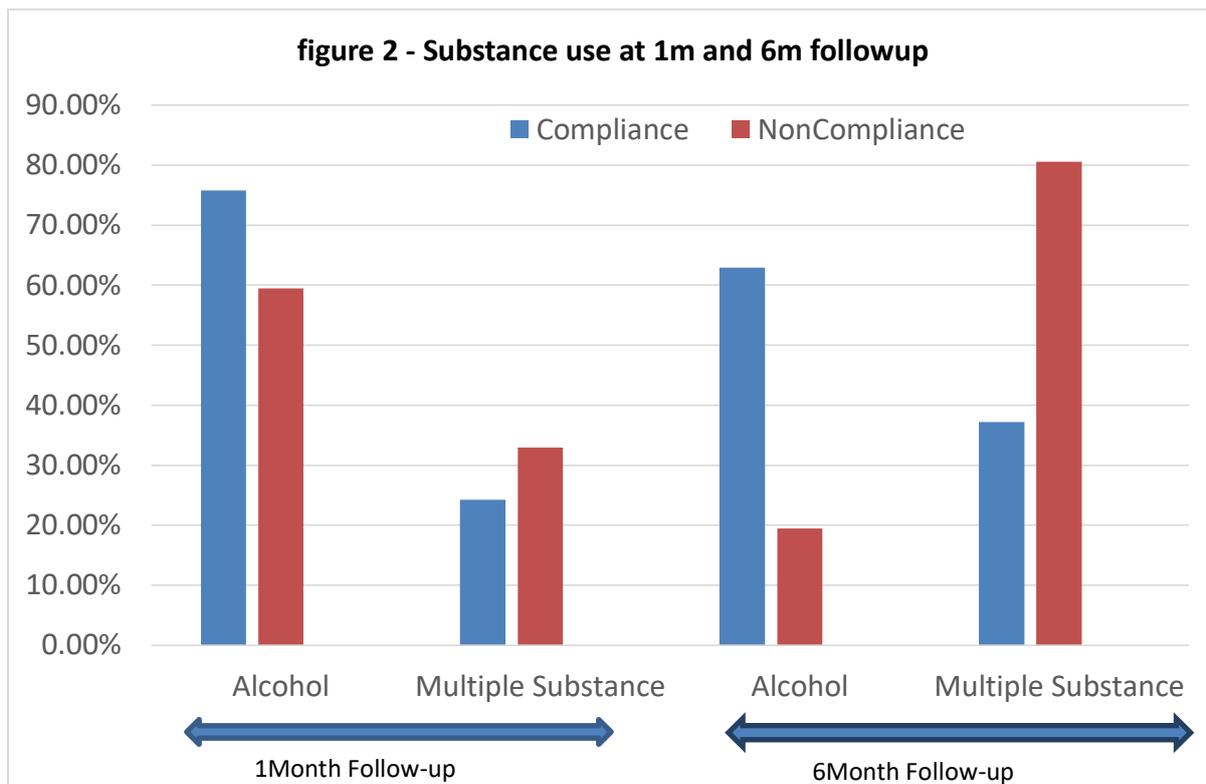


figure 2 - Substance use at 1m and 6m followup



DISCUSSION

The present study was conducted in 70 schizophrenic patients discharged after acute hospitalization. The study focused on the medication non-compliance and predictors of medication non-compliance in schizophrenia. In this study, there was no significant difference between compliance and non-compliance group with respect to age, occupation, religion and domicile. The mean age of the subjects in compliance and non-compliance group is 32.45 ± 11.07 and 35.29 ± 13.45 respectively. A similar study reported mean age 32.36 ± 7.59 in non-compliance and 37.69 ± 11.59 in compliance group¹⁸. In this study, higher non-compliance is observed in illiterate, unmarried, joint-family and lower socio-economic status (SES). Similar to previous studies where unmarried, lower educational qualification, joint family and lower SES are associated with non-compliance.

As inpatient care following acute hospitalization, medication taking behavior is closely supervised by hospital staff and compliance was high about 90%. But after discharge, on 1 month follow up decrease in medication compliance (47.1%). In an Indian study by **Ansari et al**⁵, 37% are non-compliance (n=100). Study by **Yalamova et al**³⁹ at 1 month follow up (n=40) 32.5% were adherent to medication. In our study higher compliance rates was found in 6 months after hospital discharge (53.03%) in contrast to **Yalamova et al**³⁹ (16.7%) at 6 month follow up. The possible explanation would be complete medication discontinuation is rare in chronic cases, they use to have medication on and off with irregular follow up. With exacerbation of symptoms, they restart medication and could benefit them depending on therapeutic range and dosage of medication.

The compliance rate at 1 month is low compared to 6 month follow up. **Berger et al**⁶ found that during 6-month period following hospitalization, patient with schizophrenia (n=43) received an average of 101 therapy-days and mean medication possession ratio is 55.1%. Psychopathology decreases further during follow up. This may be so because after initiating treatment it takes time for antipsychotics efficacy to develop. Positive effects of treatment results in decrease psychopathology. In some schizophrenic subgroups who continue to function well for a number year without treatment¹⁵.

Insight exists in several levels. Recognition of illness and need of treatment is the main reason for treatment compliance. With 6 month follow up, patients were more aware of illness and need of treatment in the present study. Patient who have difficulty in recognition of illness are less likely to seek treatment. In a study by **Olfson et al**³⁰, reported that in noncompliance group, they have found it somewhat or very difficult to recognize their clinical symptoms. Poor insight was an important factor in an Indian study by **Ansari et al**⁵. Insight is not a stable trait and often improved during the course of treatment²¹

Positive attitude of the patient and family members towards medication lead to treatment compliance. Overall mean DAI score was higher in patient of compliant group (5.60) in this study. In study by **Freudenreich O et al**¹⁴ also overall mean DAI score found to be higher in compliant group (p=0.03).

Therapeutic alliance is considered widely as a common therapeutic factor, which is critical for treatment success across different treatment and patient groups²⁵. Therapeutic alliance is important in schizophrenic patients and related to important aspects of their treatment such as better medication compliance, lower drop-out rates, fewer rehospitalization, improved symptoms levels and better outcomes¹³.

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Self-report of medication compliance is most common method for assessing compliance and noncompliance behavior. On Brief Medication Questionnaire in our study, we have found that 52% are compliance in 5-item regimen screen at 1 month follow up and 48.5% at 6 month followup. In a prospective study, one-third of patients are non-compliance at 6 months afterwards following hospital admission after acute episodes of schizophrenia⁴⁶. And also in a 2-year prospective study, it seen that 33.4% of patients stopped follow up visits and difficulty continuing treatment⁴⁷.

Most of the previous studies showed that substance abuse is a strong predictor of noncompliance^{24,30}, which was consistent with present study. Previous studies reported that side effects of medicines as a barrier to compliance^{27,36,37} as in case of present study. Active engagement of family and positive family support and attitudes of family members are significantly associated with higher compliance³⁰ concurrent with present study.

Factors associated with noncompliance

Illness factors – insight, cognitive impairment, psychopathology, substance use disorder. Physician related – therapeutic alliance, language barrier, inadequate time, drug attitudes. Medication factors – effectiveness, side-effects profile, drug attitudes, dosing, formulations, past experience of the medication, availability and cost of medicines. Familial factors – attitudes towards illness and medications, social stigma, financial, physical and psychological burden, lack of primary caregivers. Service factors – communication problem, distance to hospital, lack of adequate primary mental health facilities in locality.

Limitations

Non-compliance to medications is widespread, so predicting the reason behind is even more challenging, and so of management of psychiatric illnesses. First the questionnaire used to elicit compliance and non-compliance were patient-rated and self-rating scales. So there might be every possibility of underestimation or overestimation of the actual compliance and noncompliance. Secondly small sample size, and consisted only of patients after discharge from acute hospitalization. Non-compliance might be quite high and differ significantly from those patients receiving outpatients care and in stabilized schizophrenic patients. Thirdly, psychological intervention not mentioned in the study.

CONCLUSION

Medication non-compliance as outpatient in schizophrenic increases substantially after discharge from acute hospitalization. But 6 month follow up compliance was higher 53.03% in this study. Due to short duration of hospital stay and initiating antipsychotic treatment takes time to achieved desire level of efficacy of antipsychotics. With subsequent follow up psychopathology improves, insight to illness improves. There is good therapeutic alliance, less side effects experience after admission, positive attitudes towards drugs and less no. of patients in multi-substance abuse group at 6 month visits in compliance group. Medication non-compliance in schizophrenics places the patients in chronic debilitating condition with cognitive decline, acute exacerbations of symptoms, disability adjusted life, drop out from outpatient care. More research to be done regarding medication noncompliance. Public awareness concerning stigma to illness and antipsychotic medicine noncompliance should be further studied. With the current available pharmacological and psychological approaches that lowers risk of medication noncompliance should be encourage in every patient, family members and medical personnel.

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Conflict of Interest

The author declared no conflict of interests.

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