Evaluation of treatment adherence in outpatients with schizophrenia

**ABSTRACT**

**Background:** Treatment nonadherence is a major obstacle in the successful management of schizophrenia. Finding out factors associated with nonadherence and the reasons for nonadherence are important to improve treatment adherence in patients with schizophrenia. This study was conceived to evaluate treatment adherence in patients with schizophrenia and the factors associated with it. **Materials and Methods:** A cross-sectional study was conducted in 50 consecutive patients with schizophrenia with the help of semi-structured pro forma consisting of sociodemographic details, information regarding illness and treatment history, (PANSS), and Morisky Medication Adherence Scale-8 to assess medication adherence. Nonadherent patients were further assessed for their reasons for nonadherence. **Results:** Among the patients, 52% were low adherers (nonadherers). Factors associated with nonadherence were younger age of patients, male gender, low household income, higher PANSS score (positive, negative, and total score), lower grades of insight, lack of family history of psychiatric illness, responsibility of taking self-medications, first-generation antipsychotics, and number of drugs in prescription. Major reason for nonadherence given by patients were adverse effects of medications, treatment perceived as ineffective, financial problems, shame and stigma about illness and treatment, regarding treatment unnecessary and difficulty to access health-care facility. **Conclusion:** Our study established high proportion of nonadherence in patients with schizophrenia and also brought out factors associated and reasons for nonadherence. Adequate psychoeducation of patients and their caretakers as well as psychosocial interventions, strengthening mental health infrastructure, and community mental health services will significantly improve treatment adherence. **Keywords:** Reasons for nonadherence, schizophrenia, treatment adherence

The course of schizophrenia is characteristically chronic consisting of recurrent relapses and indefinite continuation of treatment to sustain remission or prevent relapses. It is well-established that medication adherence is a significant obstacle in the management of many chronic disorders, and schizophrenia being no exception is also complicated by treatment adherence issues.

The psychopharmacology of schizophrenia has seen remarkable growth over the years in terms of new drugs with increased efficacy against both positive and negative symptoms; drugs with decreased side effects; newer formulations of drugs including mouth dissolving tablets, liquid formulations, and long-acting formulations to increase ease of administration. But despite these recent developments, nonadherence continues to be a major concern in the management of schizophrenia. This indicates the involvement of other risk factors not related to medication efficacy or side effects in patient’s nonadherence to therapy.

It has been estimated that almost 50% of the patients with schizophrenia show nonadherence in the course of treatment. It has been seen to vary from 4% to 72% depending on the criteria for defining nonadherence, methods used to evaluate it and the observation period. There have been few studies in India exploring...
Nonadherence rates in schizophrenia. They have also shown the rates of nonadherence in schizophrenia between 37% and 58%.\cite{6,7}

Nonadherence to the treatment in schizophrenia has been shown to be the most important cause for relapse and readmission to the hospital.\cite{9} Nonadherence can lead up to four to five time’s higher chances of patients with schizophrenia to relapse.\cite{9} Nonadherence has also been shown to be associated with increased rates of involuntary admissions, slower recovery and longer hospital stay,\cite{10} higher risk of suicide,\cite{11} poorer prognosis,\cite{12} and low satisfaction with life.\cite{13} Because of these consequences, nonadherence may result in unnecessary emotional as well as financial burden on patients and their families. Above all these things, it has been proven that nonadherence can be preventable if certain modifiable risk factors are identified and timely managed.\cite{14} It is thus important to improve treatment adherence in schizophrenic patients so that their morbidity is reduced. Hence, the need to study nonadherence and the associated risk factors which is of paramount importance in the field of psychiatry research.

Treatment adherence in schizophrenia is a complex phenomenon, in which multiple factors related to patient, illness, medications, and health-care delivery system interact with one another to influence patient’s treatment taking behavior.\cite{15} Patient-related factors affecting adherence were shown to be male gender, extremes of ages, unemployment, lower socioeconomic status, financial difficulties, substance abuse, and previous history of nonadherence.\cite{5,7,16-18} Illness-related factors such as severity of illness, negative symptoms, cognitive symptoms, and impaired insight have also been linked to nonadherence.\cite{5,7,18} Ineffectivity of treatment, side effects, and complex treatment schedule was the treatment-related factors associated with nonadherence.\cite{5,7,18} Certain psychosocial factors such as shame and stigma about mental illness, patient’s different belief system about the cause of illness such as witchcraft or stressful life situations, family support, and ease of access to health-care facility have been seen to affect adherence.\cite{5,20,21}

To improve treatment outcome in schizophrenia and to reduce suffering of patients and their families the issue of treatment nonadherence has to be dealt with promptly. Hence, to identify patients at risk of nonadherence and plan appropriate strategies to improve their treatment adherence, identifying factors associated with treatment nonadherence and reasons for nonadherence is important. Hence, we undertook this study to evaluate treatment nonadherence and reasons for nonadherence in patients with schizophrenia and to evaluate sociodemographic and clinical factors associated with treatment nonadherence.

**MATERIALS AND METHODS**

A cross-sectional analytical study was conducted in the outpatient psychiatric department of a tertiary care hospital attached to a medical college. The duration of study was 3½ months from June 1, 2016 to September 15, 2016. The study sample consisted of 50 consecutive follow-up patients with schizophrenia attending psychiatric outpatient department. Only those patients who were taking treatment for schizophrenia at least for the last 6 months were included in the study. After written informed consent, patients fulfilling inclusion and exclusion criteria were interviewed along with their attendants with a semi-structured pro forma. The semi-structured pro forma consisted of sociodemographic details of the patient and information regarding his/her psychiatric and treatment history. They were also administered Positive and Negative Syndrome Scale (PANSS) to assess psychopathology of schizophrenia and Morisky Medication Adherence Scale-8 (MMAS-8) to assess medication adherence.

Patients who found to be nonadherent to medication were assessed further for reasons for nonadherence. In the initial phase, they were asked open-ended questions to describe the reasons for their nonadherence. To assist patients further in their responses, they were also interrogated about other specific factors which have been found to be related with nonadherence depending on the past literature and clinical experience in this regard. The information given by patients was corroborated with their attendants as far as possible. Many of the patients tended to give more than one reason for their nonadherence. Hence, in later phase of interview, to explore the relative contribution of these reasons in causing nonadherence, patients were asked to further provide information about the frequency of nonadherence (number of times they tended to miss medications) because of the particular reason they gave. We asked patients to state whether it was often, sometimes or rarely that they missed their medications because of the particular reason.

Institutional Ethical Committee approval was obtained before starting the study. Brief details of the scales used have been given below.

a. **PANSS**\cite{22} It is widely used scale for assessing severity of positive and negative symptoms in schizophrenia as well as global psychopathology in schizophrenia. It has total 30 items (7 items for positive scale, 7 items for negative scale, and 16 items for general psychopathology scale). Each item is scored from 1 to 7 depending on severity level of psychopathology. PANSS scale has been demonstrated to have good interrater reliability, adequate construct validity, and high internal reliability (Cronbach’s alpha for positive
scale – 0.73, negative scale – 0.83, and general psychopathology scale – 0.79)\(^{(23)}\)

b. MMAS-8\(^{(28)}\) It is a self-reported scale to assess medication adherence developed by Prof. Morisky and has been proven to be a reliable and valid instrument to estimate medication adherence. It has been used widely in various studies. It has 8 items pertaining to medicine intake behavior and attitudes toward medicine with each item having score of 1. Score of 8 indicates high adherence, score of 6–7 indicates medium adherence, and score below 6 indicates low adherence. Morisky Medication Adherence Scale has been shown to have good internal consistency (Cronbach’s alpha – 0.61), sensitivity (0.81), and specificity (0.64) for use in psychiatric patients.\(^{(24)}\)

**Inclusion criteria**

i. Patients diagnosed as having schizophrenia as per the International Statistical Classification of Diseases-10 criteria

ii. Patients’ age between 18 and 60 years

iii. Patients taking treatment at least for the last 6 months.

**Exclusion criteria**

i. Patients who were acutely psychotic at the time of interview

ii. Patients having cognitive deficits interfering with interview

Statistical analysis of data was done using SPSS 21 software software (IBM SPSS Statistics for Windows, Armonk, NY: IBM Corp). Chi-square test was applied to analyze qualitative variables and Mann–Whitney U test was applied to analyze quantitative variables. The \(P < 0.05\) was considered as significant for all statistical correlations.

**RESULTS**

A total of 50 patients with schizophrenia were interviewed, in which 26 (52\%) patients were male and 24 (48\%) were female. The mean age of patients was 35.62 ± 11.45 years (males 35.19 ± 10.83 years, females 36.08 ± 12.3 years). Among these patients, 8 (16\%) patients were high adherers, 16 (32\%) patients were medium adherers, and 26 (52\%) patients were low adherers. For the purpose of further statistical correlations, we combined high and medium adherers in one group and kept low adherers as another group. We did not differentiate high and medium adherers further as the difference between the high and medium adherence score is only 1 point, so the face validity of differentiating high and medium adherers is a bit questionable. Also low adherers, as compared to high and medium adherers, are at high risk of relapse and require interventions to improve adherence.

Among sociodemographic factors, younger age of patients (\(P = 0.05\)), male gender (\(P < 0.001\)), and low household income (\(P = 0.02\)) were significantly associated with low adherence [Table 1].

Table 2 shows the correlation of clinical- and treatment-related factors with adherence level. The higher scores on PANSS positive (\(P < 0.001\)), negative (\(P = 0.007\)), and total (\(P < 0.001\)) scales were significantly associated with low adherence. Lower grades of insight were also associated significantly with low adherence group as compared to high and medium adherence group (\(P < 0.001\)). The presence of family history of psychiatric illness was seen to be associated with high and medium adherence level while lack of family history of psychiatric illness was seen to be significantly associated with low adherence level (\(P = 0.004\)). Self-administration of medications by the patients themselves was significantly associated with low adherence and when the responsibility of giving medications was taken by some caregiver, the adherence improved to high and medium level (\(P = 0.02\)). When compared for type of antipsychotics, the first-generation antipsychotics and the combination of first-generation antipsychotics and second-generation antipsychotics were associated with low adherence as compared to second-generation antipsychotics alone (\(P = 0.012\)). More number of drugs in the prescription was also associated with low adherence in patients (\(P = 0.029\)).

The reasons given by patients for nonadherence have been shown in Table 3. The major reasons for nonadherence stated by the patients were adverse effects of medications (61.54\%), treatment perceived as ineffective (53.85\%), financial problems (46.15\%), shame and stigma about illness and treatment (42.31\%), regarding treatment unnecessary (42.31\%), and difficulty to access health-care facility (26.92\%).

**DISCUSSION**

The present study investigated the level of treatment adherence in patients with schizophrenia and the factors associated with treatment nonadherence. We found that 48\% of our patients had high and medium adherence, while 52\% of the patients had low adherence to the treatment. We considered patients with low treatment adherence only to be equivalent to nonadherent group as opposed to patients with high and medium adherence. The reasons being, as stated earlier, this group is more vulnerable for relapse and hence require attention for planning of preventive strategies. Further, this group of low adherers has only been considered as the nonadherent group. Our findings about treatment nonadherence were consistent to those of
The severity of psychopathology was one of the important predictors of nonadherence. We assessed severity of symptoms by PANSS score and found that higher positive and negative scale scores as well as higher total scale scores were correlated with nonadherence. Previous studies have also correlated higher positive PANSS scale score, negative PANSS scale score, and total PANSS scale score with nonadherence. Increased positive symptoms such as delusions, hallucinations, and aggressive behavior may reduce adherence due to paranoia or uncooperativeness while increased negative symptoms may impair adherence due to loss of volition or motivation to take treatment.

Insight into the illness was also a significant predictor of nonadherence. Low insight was associated with nonadherence. This finding was in accordance with previous findings. Patients with low insight would not perceive need for the treatment and hence would be nonadherent to the treatment.

The presence of family history of psychiatric illness was associated with good treatment adherence in our patients. Family history of psychiatric illness may improve adherence through prior sensitization of patients about morbid effects of psychiatric illness and hence importance of their treatment. For the same reasons, other family members may also keep vigilance about the treatment adherence of the patient.
Some treatment-related factors were also emerged as risk factors for nonadherence. When the drugs were supervised by some care taker adherence was better while when the drugs were self-administered by the patients, it was associated with nonadherence. The fact that availability of caretaker to supervise medication intake improves the adherence has been corroborated by other researchers also. Second generation antipsychotics were associated with better adherence as compared to first-generation antipsychotics. The study also revealed that adherence was better when the drugs were self-administered by the patients.

### Table 2: Correlation of clinical- and treatment-related factors with adherence

| Variable                              | High and medium adherence | Low adherence | Total | P     |
|---------------------------------------|---------------------------|---------------|-------|-------|
| PANSS positive score (mean±SD)         | 14.7±3.42                 | 19.6±4.91     | <0.001* |
| PANSS negative score (mean±SD)         | 17.7±6.09                 | 23.8±7.68     | 0.007*  |
| PANSS total score (mean±SD)            | 68.0±13.75                | 88.9±12.92    | <0.001* |
| Duration of illness                   | 11.3±10.57                | 11.2±10.32    | 0.683*  |
| Duration of treatment                 | 10.4±9.8                  | 9.7±9.49      | 0.726*  |
| Duration of untreated psychosis       | 0.8±1.03                  | 1.6±1.95      | 0.414*  |

- **Insight**
  - Grade 1: 2 (13.3) 13 (86.7) 15 (100) <0.001*
  - Grade 2: 0 4 (100) 4 (100)
  - Grade 3: 14 (66.7) 7 (33.3) 21 (100)
  - Grade 4: 8 (80) 2 (20) 10 (100)

- **Family history of psychiatric illness**
  - Present: 13 (76.5) 4 (23.5) 17 (100) 0.004*
  - Absent: 11 (33.3) 22 (66.7) 33 (100)

- **Substance abuse**
  - Present: 4 (28.6) 10 (71.4) 14 (100) 0.86*
  - Absent: 20 (55.6) 16 (44.4) 36 (100)

- **Medical illness**
  - Present: 7 (58.3) 5 (41.7) 12 (100) 0.411*
  - Absent: 17 (44.7) 21 (55.3) 38 (100)

- **Responsibility of taking drugs**
  - Self: 6 (25) 18 (75) 24 (100) 0.02*
  - Caretaker: 18 (69.2) 8 (30.8) 26 (100)

- **Type of antipsychotics**
  - First-generation antipsychotics: 6 (46.2) 7 (53.8) 13 (100) 0.012*
  - Second-generation antipsychotics: 16 (66.7) 8 (33.3) 24 (100)
  - Both antipsychotics: 2 (15.4) 11 (84.6) 13 (100)

- **Number of drugs in prescription**
  - 1: 18 (64.3) 10 (35.7) 28 (100) 0.029*
  - 2: 6 (28.6) 15 (71.4) 21 (100)
  - 3: 0 1 (100) 1 (100)

*Mann-Whitney U-test; *Chi-square test. P < 0.05 is statistically significant. SD – Standard deviation; PANSS – Positive and Negative Syndrome Scale

### Table 3: Reasons for nonadherence

| Reason for nonadherence (n=26) | Often | Sometimes | Rarely | Total |
|---------------------------------|-------|-----------|--------|-------|
| Adverse effects of medications  | 7 (26.92) | 5 (19.23) | 4 (15.38) | 16 (61.54) |
| Treatment perceived as ineffective | 5 (19.23) | 6 (23.08) | 3 (11.54) | 14 (53.85) |
| Financial problems              | 7 (26.92) | 4 (15.38) | 1 (3.85) | 12 (46.15) |
| Shame and stigma about illness and treatment | 3 (11.54) | 6 (23.08) | 2 (7.69) | 11 (42.31) |
| Regarding treatment unnecessary | 5 (19.23) | 4 (15.38) | 2 (7.69) | 11 (42.31) |
| Accessibility to health-care facility | 3 (11.54) | 3 (11.54) | 1 (3.85) | 7 (26.92) |
| Forgetting to take medications  | 2 (7.69) | 2 (7.69) | 2 (7.69) | 6 (23.08) |
| Improvement in previous symptoms | 3 (11.54) | 2 (7.69) | 0 | 5 (19.23) |
| Apprehension of habituation of drugs | 3 (11.54) | 2 (7.69) | 0 | 5 (19.23) |
| Hopelessness of cure            | 1 (3.85) | 2 (7.69) | 1 (3.85) | 4 (15.38) |
| Lack of caregiver               | 2 (7.69) | 2 (7.69) | 0 | 4 (15.38) |
| Lack of information about the nature of treatment | 2 (7.69) | 1 (3.85) | 1 (3.85) | 4 (15.38) |
| Regarding disease as mild       | 1 (3.85) | 1 (3.85) | 0 | 2 (7.69) |
antipsychotics or the combination of first-generation antipsychotics and second-generation antipsychotics. Previous studies comparing effects of first-generation antipsychotics and second-generation antipsychotics on adherence showed conflicting results. Some of them showed no significant difference between the two groups[34,35] while others showed better adherence with second-generation antipsychotics.[31,32] Extrapyramidal side effects such as dystonia, akathisia, and tardive dyskinesia may be particularly troublesome for patients to continue the treatment with first-generation antipsychotics.

More number of drugs in the prescription was also associated with nonadherence. More number of drugs complicates the treatment schedule and hence many times it may lead to difficulty in remembering to take drugs. In previous research, complexity of medication schedule has been associated with nonadherence.[2,16] More number of drugs in prescription may also lead to more side effects and lead to nonadherence. Furthermore, more number of drugs in prescription means patient having more psychopathology which itself is a risk factor for nonadherence.[28]

We also tried to find out the reasons for patients to be nonadherent to the treatment. The reasons for nonadherence in our patients were in concordance with the findings of previous research.[5-7] About 61.54% of the nonadherent patients gave “adverse effects of medications” to be the reason for their nonadherence. Side effects have been reported as an important factor for patients’ decision to continue or discontinue medications.[33] Side effects of first-generation antipsychotics such as dystonia, Parkinsonism, or tardive dyskinesia can be a cause of apprehension for the patients and their relatives. Second-generation antipsychotics also can cause weight gain or metabolic syndromes which are of particular concern to female patients. Hence, it becomes essential to select antipsychotic drug considering patient profile and to be vigilant for side effects in every follow-up. Furthermore, it is essential to psychoeducate the patients and relatives about side effects of medications so that they will not become apprehensive about minor side effects and make changes in their lifestyle to minimize certain side effects (e.g., diet changes or exercise).

Out of nonadherent patients, 53.85% patients reported that they “perceived treatment as ineffective” so they were missing the treatment. It has been seen in the past studies that beliefs regarding the benefits from the treatment affect adherence behavior.[34] As we know, schizophrenia will take time to respond to medications, prompt relief from symptoms may not be possible in shorter span of time. Hence, psychoeducation of patients and their relatives about the medication response and long-term nature of treatment may improve patients’ motivation to stay in treatment. Furthermore, some residual symptoms of schizophrenia may also be perceived by patients as treatment ineffectiveness. Hence, other supportive psychotherapies or social skill trainings may help patients to overcome these residual symptoms.

“Financial problems” were also reported by almost half of the patients as their reason for nonadherence. The fact is understandable as schizophrenia may make its patients morbid for long time and hence unproductive or unemployed leading them financially unsupported.[35] In this situation, bearing expenses of medications may be a difficult task for the patients.

“Shame and stigma about illness and treatment” in psychiatric illness like schizophrenia is quite a well-accepted fact globally. Especially in Indian community because of mental health unawareness and different belief systems (e.g., witchcraft, supernatural powers, etc.) in certain people, shame and stigma about psychiatric illness is quite prevalent.[36] Fear of being discriminated because of stigma or shame of taking medicines may lead patients to discontinue their treatment.[31]

Another major reason for nonadherence was “regarding treatment as unnecessary.” In previous studies also, patients’ belief about the need for treatment was found to be associated with their adherence behavior.[34] Being psychotic illness, patients with schizophrenia have problems with their insight, and hence many of them deny their illness and regard treatment unnecessary. Also because of different belief systems (e.g., witchcraft, supernatural powers, etc.) in some people, they would regard their treatment as unnecessary.

“Difficulty to access health-care facility” was also reported by patients as cause for their nonadherence. Access to a remotely placed mental health-care facility can be a problem for certain patients, especially in terms of time and money to fill their prescriptions regularly. This indicates the need for strengthening the mental health infrastructure in our country, particularly in peripheral nonurban areas and need for building community mental health services.

The study has some limitations. We used self-report as a method of assessment of nonadherence which may be unreliable and biased at times because of recall bias. Another limitation is our study design was cross-sectional so establishing causal relationship between the factors discussed and nonadherence was not possible. Furthermore, small size of sample population may limit the generalization of findings.
CONCLUSION

Our study established that the proportion of treatment nonadherence in patients with schizophrenia is quite high, and hence for the effective management of schizophrenia, it is essential to find out patients at risk of nonadherence. Patient-related, illness-related, and treatment-related factors have come out to be risk factors for nonadherence. Major reasons for nonadherence as perceived by patients were treatment-related as well as psychosocial such as stigma, financial issues, and access to health-care delivery system. Hence, as a part of preventive strategies to reduce nonadherence, adequate psychoeducation of patients and their caretakers about the nature of illness, nature of treatment, treatment response, and side effects of medications is essential. Our findings also imply need for certain psychosocial interventions to improve treatment adherence like strengthening the mental health infrastructure and treatment resources as well as building community mental health services to address financial and treatment accessibility problems.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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