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Tulika Ghosh
Senior PHN of Belpahari
Rural Hospital, Jhargram,
West Bengal, India

Binapani De
Acting Principal, Govt. College
of Nursing, Rampurhat,
Birbhum, West Bengal, India

Nonadherence and reasons of nonadherence to drug regimen among schizophrenic patients at Psychiatric OPD, BSMC & H, Bankura, West Bengal

Tulika Ghosh and Binapani De

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Abstract

A descriptive research study was conducted nonadherence and reasons of nonadherence to drug regimen among schizophrenic patients at psychiatric OPD, BSMC & H, Bankura, West Bengal to investigate the nonadherence and reasons of nonadherence to drug regimen among schizophrenic patients and to find out its association with selected demographic variables among schizophrenic patients at psychiatric OPD, BSMC & H, Bankura, West Bengal. Data were collected from 120 samples by simple random sampling using semi structured demographic tool, Medication adherence rating scale (MARS) and structured interview schedule. Majority of the patients (57.50%) were non-adherent to drug regimen. Within patient related reasons majority (74%) of patients having reasons of nonadherence due to medicines are costly to buy; among hospital related reasons, 63% of the patients having hospital is far away from their home, and within miscellaneous reasons 51% unable to come to hospital due to lock down. Nonadherence among schizophrenic patients were significant with gender, education, occupation, type of family, monthly per capita income, residence, addiction status, and duration of illness at 0.05 level. Study was implicated on nursing practice, education, administration and research. An experimental study can be conducted to explore the effectiveness of awareness programme to improve adherence among schizophrenic patients.

Keywords: Nonadherence, drug regimen, schizophrenic patients, psychiatric OPD, MARS

Introduction

Schizophrenia could also be a significant mental disorder during which individuals interpret reality abnormally. Schizophrenia may be ended in some combination of hallucinations, delusions, and very disordered thinking and behavior that impairs daily functioning, and may be disabling. People with schizophrenia require lifelong treatment. Early treatment may help get symptoms under control before serious complications develop and may help improve the long-term outlook ^[1]. In a meta-analysis of 65 trials in a clinical area, patients with schizophrenia become stabilized on antipsychotic medication and it was evident that treatment with antipsychotics significantly reduces relapse rate ^[2].

Compliance is defined as “the extent to which the patient’s behavior (in terms of taking medications, following diets, or executing other lifestyle changes) coincides with medical recommendations” ^[3]. Adherence is defined as “the extent to which the patient’s behavior (in terms of taking medications, following diets, or executing other lifestyle changes) matches medical recommendations jointly agreed between patient and prescriber” ^[4]. The difference between both concepts is minimal and essentially concerns the physician’s degree of authority ^[5].

Adherence to medication regimens has been monitored since the time of Hippocrates ^[6]. The course of schizophrenia is substantially chronic consisting of recurrent relapses and unspecified continuation of treatment to sustain remission or prevent relapses is required. It is well-established that medication nonadherence is a significant obstacle in the management of many chronic disorders, and schizophrenia being no exception is also complicated by treatment adherence issues ^[7].

Despite recent progress in the treatment of schizophrenia during the last decades, non-adherence continues to be a frequent phenomenon, often associated with potentially severe clinical consequences.

Corresponding Author:
Tulika Ghosh
Senior PHN of Belpahari
Rural Hospital, Jhargram,
West Bengal, India

Non-adherence may be a complex phenomenon, with a variety of patterns. The patient might either take lower or higher doses, than the prescribed medication or follow a schedule aside from the prescribed, completely abandon the treatment. In addition, adherence may change during the patient's onset of disease; it is usually good after discharge from the hospital and tends to decrease with time. Though, the cause of non-adherence is multifactorial^[8].

Estimated non-adherence rates in schizophrenia are about 50%, widely starting from 4% to 72% (observed during a study with depot neuroleptic drugs). Factors that may account for such variability include the definition of non-adherence and criteria won't to determine it, methods for evaluating non-adherence, and observation period. Previous non-adherence, poor insight, negative attitude or negative response to treatment, current or past drug dependency, poor relationship with the therapist, shorter length of illness, and hospital discharge without an adequate follow-up plan or environment are risk factors identified for Non-adherence^[9].

In this context, the very fact of taking medication may become a distressing element, especially for patients who aren't conscious of their disease. However, for patients with psychopathological symptoms, antipsychotic drugs regimen have proven effective in reducing relapse and rehospitalization rates among patients. These findings together indicate the fact that non-adherence is considered to be preventable^[10].

Every aspect of a patient's life is suffering from schizophrenia. Non-compliance is the biggest challenge faced during long-term pharmacotherapy in schizophrenia. Noncompliance refers to the extent to which a patient's motivation is reflected by behavior that is not in accord with medical or health advice. It includes errors of omission, mistakes in dosage and timing, and taking medications that are not prescribed^[11]. However, Patients not believing that they are ill or not accepting that they experience clinical symptoms can lead to therapeutic noncompliance. The result of studies on insight in patients with schizophrenia suggests that decreased insight is associated with a greater risk of relapse, impaired social functioning, and non-compliance with medication and treatment^[12].

Numerous studies from developed countries identified many contributing factors for non-adherence to the antipsychotic drug regimen, including some qualitative studies, presented the most common factor for non-adherence to be lack of insight, low therapeutic alliance^[13], the presence of positive symptoms, being male, substance abuse, unemployment and low social functioning^[14].

Adverse effects of antipsychotic medications and their subjective tolerability by patients were also been reported as important reasons influencing adherence^[15].

Nonadherence leads to the worst patient outcome, increased relapse rate, reduced quality of life, and increased cost of treatment for rehospitalization. Therefore, nonadherence is to be considered carefully and strategies are to be addressed conveniently, as well as systematically to improve adherence, which has the potential to reduce the cost of treatment for schizophrenic patients in the clinical area. The multidimensional approach will be more effective than the Uni-dimensional approach. Improving adherence is an ongoing and dynamic process that requires the involvement of all health care professionals working with the patient towards engaging significant others for a good social

support system in favours of these long-term debilitating patients.

Therefore, this study aimed to investigate the nonadherence and reasons for nonadherence to drug regimens among schizophrenic patients. The finding of this study will helps to reveal the actual scenario of the extent of nonadherence and reasons for nonadherence to drug regimens among schizophrenic patients of the area as well as improve adherence in the region.

Statement of the problem

Nonadherence and reasons of nonadherence to drug regimen among schizophrenic patients at psychiatric OPD, BSMC & H, Bankura, West Bengal

Purpose of the study

The measures may be taken to improve adherence to drug regimen with the help of assessment of the nonadherence and identifying the reasons for nonadherence to drug regimens among schizophrenic patients.

The objective of the study

1. To assess the nonadherence to drug regimens among schizophrenic patients.
2. To identify the reasons for nonadherence to drug regimens of schizophrenia treatment among schizophrenic patients.
3. To find out the association between nonadherence to drug regimen with selected demographic variables.

Materials and Method

A descriptive survey research design was adopted applying quantitative research approach, to attain the objectives of the present at Psychiatric outdoor, BSMC & H, Bankura and West Bengal. The population of the present study comprised all schizophrenic patients who reside in West Bengal and samples were Schizophrenic patients attending psychiatric outdoor, BSMC & H, Bankura, who meet the inclusion criteria who were selected via simple random sampling with slip bag technique.

The variables of the study were Research variables including Nonadherence to the drug regimen and Reasons for nonadherence to the drug regimen. Another variables were demographic variables including age in years, sex, education, occupation and type of family, marital status, monthly per capita income and residence, addiction to substance or alcohol and duration of illness.

Data collection tools were Semi-Structured Interview schedule for demographic variables, Medication Adherence Rating Scale (MARS) to assess the non-adherence to the drug regimen and Structured interview schedule for identifying reasons for non-adherence. Data collection techniques of the three tools were interviewing.

For each item of the semi-structured interview schedule on demographic variables, reliability was done by test-retest method and the value was 1. So the tool was highly reliable.

The reliability of the Medication Adherence Rating Scale; MARS was measured by the KR20 method and the result was 0.85, so, the tool was reliable.

Medication Adherence Rating Scale is a standardized tool that consists of 10 item yes/no self-rated scale. The items are answerable by a yes/no answer, with 0 and 1 values respectively. Score 1: The answer is 'NO', Score 0: The answer is 'YES'.

The patients were considered to be 'adherent' if they had a score of 6 - 10 and 'nonadherent' if the scores were 0 - 5. The reliability of the structured interview schedule to measure the reason for nonadherence to drug regimen was measured by the KR20 method and the result was 0.81, so the tool was reliable. This tool was containing 30 questions

with two alternative options that were yes and no; which were administered to schizophrenic patients. Each statement was scored as follows, where the highest total mark was 30 and the lowest was 0. The score allotted to yes: 1, no: 0. depending on the responses of the respondent reasons for nonadherence to drug regimen were found.

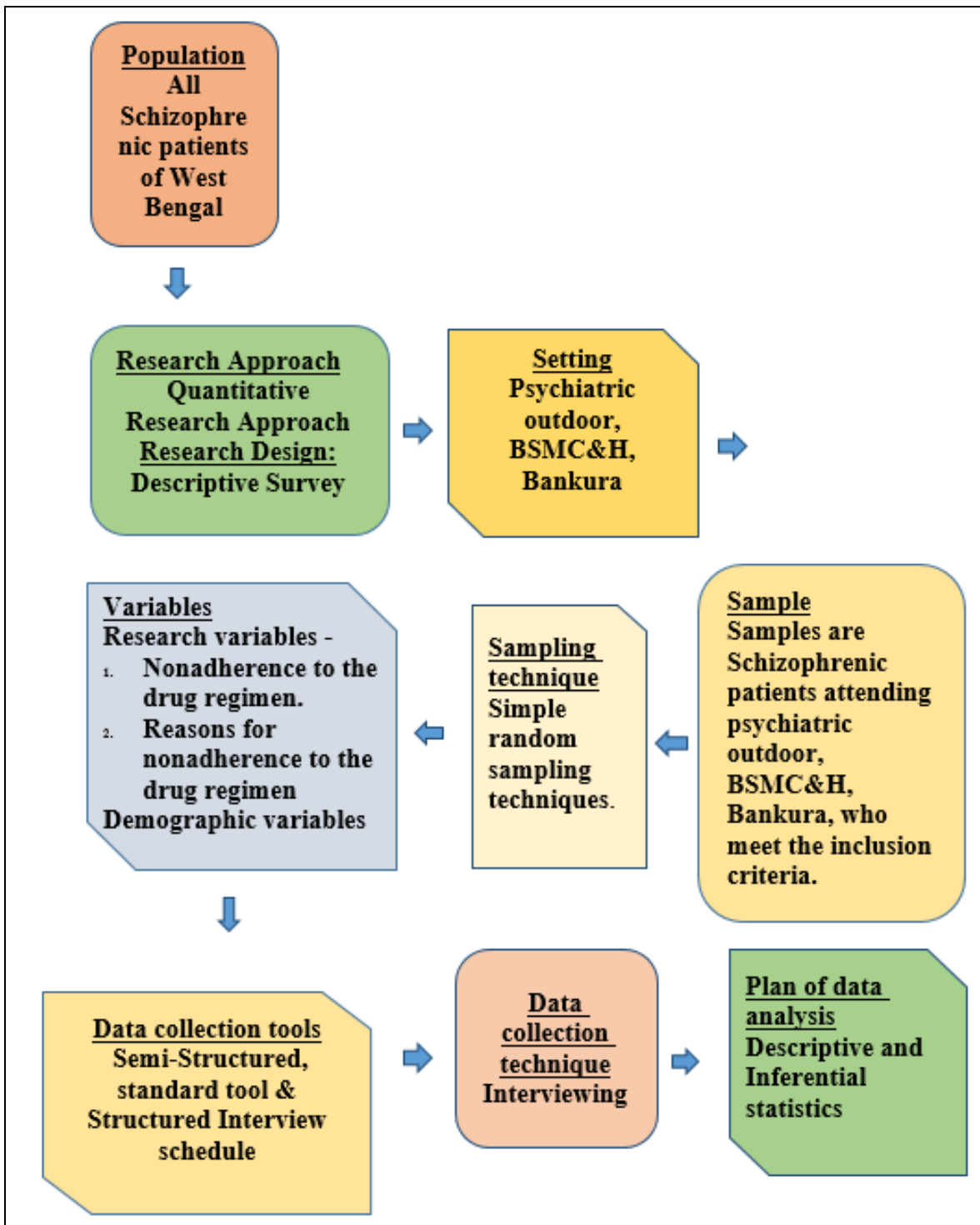


Fig 1: Schematic presentation of the research methodology

Ethical clearance was taken from the chairman, of the Institutional Ethics committee of B.S.M.C & H, Bankura. Informed consent was obtained from each schizophrenic patient after giving information about the purpose of the study, duration of involvement, voluntary willingness for participation, and possible harm and benefit of the study

participants. Privacy and confidentiality were maintained during data collection. Administrative permission was taken from the Directorate of Health Services (Nursing), Swasthya Bhawan, Principal, Govt. College Nursing and BSMC. Bankura and MSVP, Bankura Sammilani Medical College and Hospital, Bankura.

Result and discussion**Findings related to demographic characteristics of schizophrenic patients regarding non-adherence to drug regimen.****Table 1:** Frequency and percentage distribution of the schizophrenic patients according to demographic characteristics, N=120

Demographic Characteristics	Frequency (F)	Percentage (%)
Age of patients (In years)		
19-28	32	26.66%
29-38	44	36.67%
39-48	29	24.17%
49-58	12	10.00%
Above 58	03	2.50%
Sex		
Female	44	36.67
Male	76	63.33
Education		
No formal education	46	38.33
Primary	49	40.83
Secondary	23	19.17
Higher secondary	2	1.67
Graduate	Nil	00
Post graduate	Nil	00

Data presented in table 1 depicted that maximum (36.67%) patients belonged to the age group of 29-38 years, majority (63.33%) were male, maximum (40.83%) of the patients received primary education

Table 2: Frequency and percentage distribution of the schizophrenic patients according to demographic characteristics, N = 120

Demographic Characteristics	Frequency(f)	Percentage (%)
Occupation		
Daily labour	95	79.17
Business	4	3.3
Govt. Service	2	1.67
Private service	Nil	00
Farmer	19	15.83
Retired person	Nil	00
Type of family		
Nuclear	98	81.67
Joint	22	18.33
Extended	Nil	00
Marital Status		
Married	83	69.17
Unmarried	12	10
Divorce	10	8.33
Widow/ widower	15	12.5

Data presented in table 2 showed that and majority (79.17%) of them were daily labour and most (81.67%) of

the patients were belong to the nuclear family, majority (69.17%) of the patients were married.

Table 3: Frequency and percentage distribution of the schizophrenic patients according to their demographic characteristics, N = 120

Demographic Characteristics	Frequency (F)	Percentage (%)
Monthly per capita income		
Upper class (7770 and above)	2	1.67
Upper middle class (3808-7769)	Nil	00
Middle class (2253-3807)	13	10.83
Lower middle class (1166-2252)	26	21.67
Lower class(less than 1166)	79	65.83
Residence		
Rural	92	76.67
Urban	28	23.33
Addiction status		
Addicted to alcohol	15	12.50
Addicted to any substance other than alcohol	38	31.67
Both addicted to alcohol & other substance	28	23.33
Not Addiction to alcohol & other substance	39	32.50
Duration of illness (in Years)		
2-5	47	39.17
6-9	20	16.67
10-13	16	13.33
More than 13	37	30.83

Data presented in table 3 showed that majority (65.83%) monthly per capita income were less than Rs. 1166, majority (76.67%) of the patients lived in rural areas, maximum

(31.67%) were addicted to any substance other than alcohol and maximum (39.17%) of the patient's duration of illness were 2-5 yrs.

Findings related to assess the nonadherence to drug regimen among schizophrenic patients

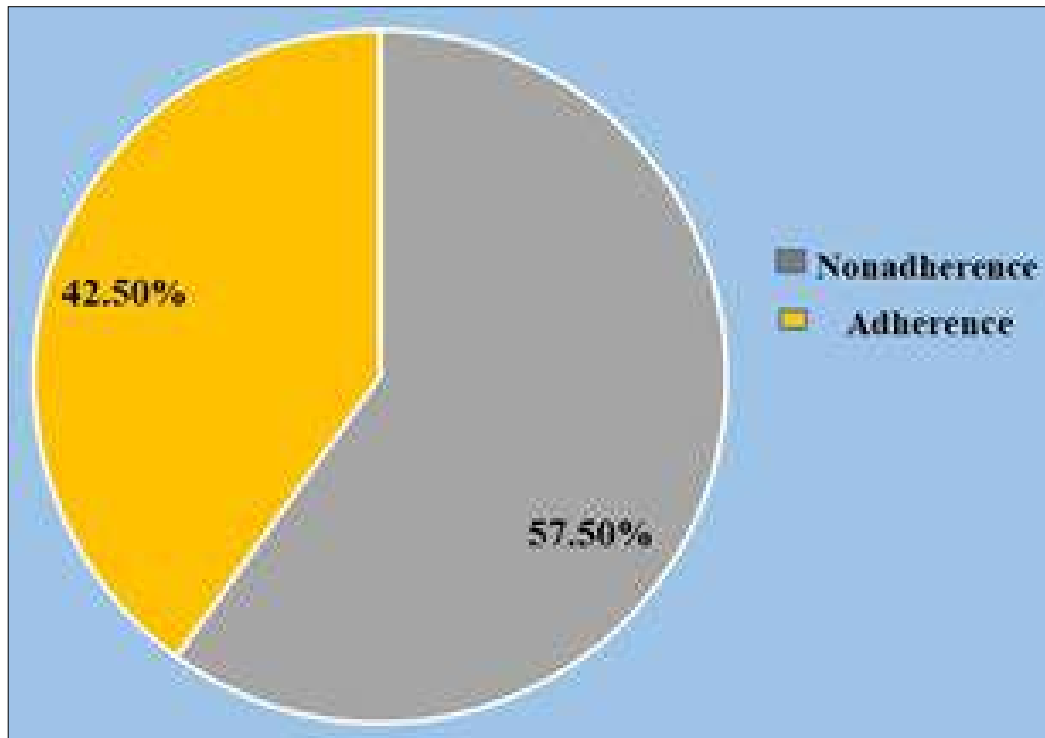


Fig 2: Pie diagram showing distribution of schizophrenic patients according to their nonadherence to drug regimen.

Data depicted in figure 2 indicated that majority (57.50%) of the schizophrenic patients were non-adherent to drug regimen whereas only 42.50% schizophrenic patients were adherent to drug regimen.

Findings related to identify the reasons of non-adherence to drug regimen of schizophrenia treatment among schizophrenic patients

Table 4: Mean and Mean % of distribution of reasons of non-adherence to drug regimen of schizophrenia treatment, N1=69

Reasons of nonadherence	Mean	Mean %
Patient related reasons	4.65	24.49
Hospital related reasons	0.88	14.73
Miscellaneous reasons	0.62	12.46

Data presented in the table 4 that maximum (24.49%) patient's reasons of nonadherence were patient related reasons followed by 14.73% of patients having hospital

related reasons and 12.46% of patients having miscellaneous reasons of nonadherence.

Table 5: Frequency and percentage distribution of nonadherent patients according to their Patient related reasons, N1=69

Patient related reasons	Response	
	Frequency	Percentage (%)
Difficulty feeling to take medicines (medication fatigue)	34	49
Problem to take medication at specified time	32	46
Forget to take medication due to too much workload at home	13	19
Stopped medicine for any religious reasons	17	25
Not enough time from work to buy medicine	4	6
Medicines are costly to buy	51	74
No one at home to remind of taking medication	8	12
Anyone at your home suggested you to stop medicine	8	12
No one to accompany to come to hospital	18	26
Feel current treatment is ineffective as longer duration of illness	31	45
stopped medicine being afraid as side-effects occurs	10	14

All data are exhaustive, and not mutually exclusive

Data presented in table 5 shows that majority (74%) of patients having reasons of nonadherence due to medicines are costly to buy, whereas 6% of them were nonadherent due to not enough time from work to buy medicine

Table 6: Frequency and percentage distribution of nonadherent patients according to their Patient related reasons, N₁=69

Patient related reasons	Response	
	Frequency	Percentage (%)
Stopped to take medicine for any other illnesses like gallbladder operation, asthma or any other disease	0	0
Believe that medicine will not improve disease condition	26	38
Someone outsider suggested to stop medicine	8	12
Unable to arrange money to come to the hospital	35	51
Believe medicine may alter body function of which afraid to stop the prescribed medication	6	8.7
Afraid of medicine dependency	17	25
Feeling worse after taking medicine	3	4.3
Not know about how and when to take medicine	0	0

All data are exhaustive, and not mutually exclusive
 Data presented in table 6 shows that majority (51%) of patients having reasons of nonadherence due to inability to arrange money to come to the hospital medicines are costly to buy, whereas only 4.3% of them nonadherence as feeling

worse after taking medicine, none stopped to take medicine for any other illnesses like gallbladder operation, asthma or any other disease, none of them not know about how and when to take medicine.

Table 7: Frequency and percentage distribution of nonadherent patients according to Hospital related reasons, N₁=69

Hospital related reasons	Response	
	Frequency	Percentage (%)
So many medicines prescribed at a time	2	3
Hospital is far away from your home	44	64
A long waiting hours in the hospital	3	4
No direct transportation to the hospital or Vehicles change many times	6	9
Treating hospital changed many times means been referred many times	4	6
Doctors unable to spend enough time in the hospital to examine patients under patient load	2	3

All data are exhaustive, and not mutually exclusive.
 Data presented in table 7 shows that majority (64%) of the patients having hospital is far away from their home whereas only 3% of patients having reasons of doctors

prescribed so many medicines at a time, Doctors unable to spend enough time in the hospital to examine patients under patient load.

Table 8: Frequency and percentage distribution of nonadherent patients are according to miscellaneous reasons, N₁=69

Miscellaneous reasons Response	Response	
	Frequency	Percentage
Medicine prescribed by Doctor not available at the local facility always	4	5.88
Due to bad weather unable to go to hospital in rainy season	1	1.45
Difficult feel in swallowing to stop prescribed medicine	1	1.45
Unavailability of prescribed medicine in medicine shops	2	2.9
Due to lock down unable to come to hospital.	35	51

All data are exhaustive, and not mutually exclusive
 Data presented in table 8 shows that majority (51%) were unable to come to hospital due to lock down, whereas

1.45% were unable to go to hospital in rainy season due to bad weather who having difficult feel in swallowing to stop prescribed medicine.

Findings related to find out the association between non-adherences to drug regimen with selected demographic variables

Table 9: Association between the nonadherence to drug regimen among Patients with their age, gender and education.

Variables	Non-adherence to drug regimen		Chi square value	DF	P-Value
	Yes	No			
Age in years					
19-38	41	35	1.07	1	0.3
>38	28	16			
Gender					
Female	31	13	4.77*	1	0.02
Male	38	38			
Education					
Upto primary	61	34	8.40*	1	0.003
Above Primary	8	17			

$\chi^2(DF_1) = 3.841, p < 0.05$ *significant

Data presented in table 9 showed that there was no association between ages, among schizophrenic patients at 0.05 level of significance. It can be concluded that nonadherence is not dependent on age of schizophrenic patients.

It also depicted that there was significant association between nonadherence among schizophrenic patients and gender, educational status, Hence, it also be concluded nonadherence was dependent on those demographic characteristics at 0.05 level of significance.

Table 10: Association between the nonadherences to drug regimen among Patients with their occupation, type of family and marital status, N=120

Variables	Non-adherence to drug regimen		Chi square value	DF	P-Value
	Yes	No			
Occupation					
Daily Labour	60	35	5.97*	1	0.01
Other than Daily Labour	9	16			
Type of family					
Nuclear	61	37	4.93*	1	0.02
Joint	8	14			
Marital status					
Married	47	36	0.08	1	0.77
Other than married	22	15			

$\chi^2(DF_1) = 3.841, p < 0.05$ *significant

Data presented in table 10 showed that there was no association between marital status and nonadherence among schizophrenic patients at 0.05 level of significance. It can be concluded that nonadherence is not dependent on marital status.

It also depicted that there was significant association between nonadherence among schizophrenic patients and occupation, type of family. Hence, it also be concluded that nonadherence was dependent on those occupation and type of family of the respondents at 0.05 level of significance.

Table 11: Association between the nonadherences to drug regimen among Patients with their monthly per capita income, residence, addiction status, and duration of illness (in years), N=120

Variables	Non-adherence to drug regimen		Chi square value	DF	P-Value
	Yes	No			
Monthly per capita income					
≥ middle class	3	12	8.2	1	0.004
< middle class	66	39			
Residence					
Rural	58	34	4.96*	1	0.025
Urban	11	17			
Addiction Status					
Addicted to alcohol, substance or both	40	41	6.72*	1	0.009
Not addicted to alcohol, substance	29	10			
Duration of illness (in years)					
2-5 Years	20	27	7.06*	1	0.007
> 6 Years	49	24			

$\chi^2(df_1) = 3.841, p < 0.05$ *significant

Yates correction done

Data presented in table 11 depicted that there was significant association between nonadherence among schizophrenic patients and monthly per capita income, residence, addiction status, and duration of illness (in years). Hence, it also be concluded nonadherence was dependent on those demographic characteristics at 0.05 level of significance.

Major findings of the present study

The major findings of the current study are encapsulated below

Findings related to the nonadherence to drug regimen among schizophrenic patients

A majority (57.50%) of the respondents were non-adherent to the drug regimen.

Findings related to the reasons for nonadherence to drug regimens among schizophrenic patients

In the area of patient-related reasons, maximum (74%) of respondents stopped medicines as those are costly to buy.

In the area of hospital-related reasons, maximum (63%) of respondents were noncompliant as hospitals were far away from their homes.

In the area of miscellaneous reasons, a maximum (51%) of respondents were unable to come to the hospital due to lockdown.

Findings related to the association between non-adherence to the drug regimen and selected demographic variables

There was a significant association between non-adherence to the drug regimen and the gender, education, occupation, type of family, family’s Monthly Per capita income,

residence duration of illness, of the patients, addiction to alcohol, substance, or both.

Discussion related to other studies

Lama A and Baruah A (2019) ^[16] conducted a quantitative non-experimental descriptive design on medication adherence and its association with subjective well-being among persons with schizophrenia. Result revealed that about maximum (38.8%) of respondents belonged to the age group 31-40 years, majority (77.6%) were male, majority (57.6%) had completed their education up to middle school, i.e., standard VIII, maximum (28.2%) of respondents were unemployed, maximum (47.1%) of respondents were married, maximum (35.3%) of the respondents' family income was between Rs. 3001 and Rs. 6000, maximum (44.7%) belonged to low socioeconomic status, majority (65.9%) of respondents belonged to nuclear family, majority of the respondents (77.6%) were from rural community, maximum (27.1%) of the respondents were suffering from the illness since 4 to 6 years, Majority of the respondents, 67.1%, had history of substance abuse ^[16].

The present study supported by the above-mentioned study findings as maximum (36.67%) patients belonged to the age group of 29-38 years, majority (63.33%) were male, maximum (40.83%) of the patients received primary education, majority (79.17%) of them were daily labour and most (81.67%) of the patients were belong to the nuclear family, majority (69.17%) of the patients were married, majority (65.83%) monthly per capita income were less than Rs. 1166, majority (76.67%) of the patients lived in rural areas, maximum (32.50%) were addicted to any substance other than alcohol and maximum (39.17%) of the patient's duration of illness were 2-5 yrs.

A quantitative research study was conducted by Sandip Subedi, Kamala Paudel, and Dev Kumar Thapa (2018) to probe the incidence and factors associated with medication non-compliance among patients suffering from schizophrenia. 94 patients were taken for the study, which was collected from psychiatric OPD of the tertiary level hospital by disproportionate stratified random sampling method. The prevalence of non-compliance was 89.4%. A significant association between noncompliance and selected demographic characteristics was identified. There was a high non-compliance rate among age group below 40 years (54.2%), among male patients (52.1%), married (64.8%) and within low economic status (52%). Medication non-compliance was more among patients with medication adverse effects like dizziness (60.6%), sedation (66%), as well as longer duration of illness (92.8%) which was significant, and having 1-3 pills (47.8%) ^[17].

The present study supported the above-mentioned study findings as 57.50% of the schizophrenic patients were non-adherent to the prescribed drug regimen.

A cross-sectional study was conducted by Ashish V. S., Deshmukh SP, and Deshmukh SB (2015) ^[18], in India on non-compliance in patients with schizophrenia to identify various factors responsible for non-compliance to the treatment regimen in a psychiatric ward and out-patient Department. The study revealed, Out of the total of 52 patients, the majority 19% had poor adherence to the drug regimen, 48 % had moderate adherence and only 33% of high compliance. Contributing factors to non-compliance were perceived cost of medicine (63%), chronic nature of disease process (52%), transportation problem (48%),

medication side effects (40%), lack of effectiveness (32%), relatives' insight towards illness (38%), lack of knowledge, misconception about psychiatric illness and patient's insight towards illness (34%).

In the present study, which was supported by the above-mentioned study that the majority (57.50%) of the schizophrenic patients were non-adherent to the prescribed drug regimen ^[18].

Velligan ID, Sajatic M, Hatch A, Kramata P and Docherty PJ conducted a systematic review of 'Why do psychiatric patients stop antipsychotic medication? To assess modifiable reasons for nonadherence to medication in patients with serious mental illnesses. Articles were taken that were published between January 1, 2005, and September 10, 2015. Articles revealed from 36 articles 11 categories of reasons for nonadherence were identified. Study result also revealed that 20 articles out of 36 represent Poor insight (55.6%), 13 articles out of 36 substance abuse (36.1%), 11 out of 36 represents a negative attitude towards medication (30.5%), 10 out of 36 showing medication side effects (27.8%), and cognitive impairment is 7 out of 36 articles (13.4%) were responsible factors for non-adherence. This systematic review suggests that a negative attitude towards medication and substance abuse were consistent reasons for nonadherence to antipsychotic medication. Adherence enhancement approaches that specifically target these reasons may improve adherence in the high-risk group ^[19].

Besides, the reasons, the majority of patients were nonadherent due to medicines are costly to buy (74%), the majority (64%) of patients are nonadherent because Hospital was far away from their home, 9% of patients were nonadherent due to transportation problem, medicine side-effects occurred (14%), maximum (45%) felt current treatment was ineffective as longer duration of illness, majority of patients (51%) were nonadherent as they were unable to arrange money to come to the hospital, anyone at their home suggested you stop medicine (12%), maximum (38%) of patients were nonadherent as believed that medicine will not improve disease condition.

Conclusion

This study revealed that nonadherence to psychotropic drug regimens was very high as a maximum portion of patients were investigated as nonadherent. This study also depicted that, prescribed medicines were costly to buy, the hospital was far away from the patient's home, and lockdown in COVID-19 period were the main reasons for non-adherence to the prescribed drug regimen. The study also represented that nonadherence was significantly associated with gender, education, occupation, type of family, monthly per capita income, residence, addiction status and duration of illness (in years) among schizophrenic patients. So, nonadherence to the prescribed antipsychotic treatment regimen is a very common problem among schizophrenic patients as long-term treatment is required for most of the patients, and even lifelong medications may be necessary in some cases.

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Researchers would like to be thankful to the author of medication Adherence Rating Scale (MARS) developed by Thompson *et al.* in 2000 which I used to investigate the nonadherence of drug regimen.

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