

## ORIGINAL RESEARCH

## A Cross-Sectional Study of Association between Treatment Adherence & Medication in Patients with Schizophrenia

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### ABSTRACT

**Background:** Schizophrenia is the most incapacitating mental disorder, with a lifetime prevalence of 1% and symptoms often appearing in late adolescence or early adulthood. It is characterised by delusions, hallucinations, disorganised speech, grossly disorganised behaviour or catatonic behaviour, negative symptoms. Antipsychotic (neuroleptic) medications are an essential part of schizophrenia treatment. To keep symptoms under control and prevent relapse, effective care necessitates long-term treatment. Medication adherence can be defined as the extent to which the patient's medication taking matches that agreed with the prescriber. The current study focusses on medication adherence & various illness related factors. To study relationship between medication adherence & severity of schizophrenia, antipsychotic medication & its adherence, antipsychotic medication & its side effects in patients with schizophrenia.

**Materials and Methods:** It is a cross sectional study conducted in 60 subjects aged 18 – 55 yrs fulfilling the criteria for schizophrenia as per ICD-10 classification. Information collected was intake proforma, Positive and Negative Syndrome Scale (PANSS) scale to assess symptoms severity, Drug Attitude Inventory (DAI-30) to assess positive or negative attitude towards treatment adherence, Udvalg for Kliniske Undersogelser (UKU) side effect scale to assess the side effects of antipsychotics. To assess overall severity of schizophrenia PANSS was compared with CGI scale (clinical global impression scale). A score of (58-74) was considered minimally ill, (75-94) as mildly ill, (95-115) as moderately ill & ( $\geq$  116) as severely ill. The antipsychotics used by the patients in our study are Olanzapine (n=23), Risperidone (n=18), Amisulpride (n=15), clozapine (n=2), Cariprazine (n=1), Trifluoperazine (n=1).

**Results:** In the current study patients with minimal illness & mild illness has more positive attitude towards medications adherence (71%, 61%) respectively, when compared to moderately ill patients who had only 33% positive attitude towards medication adherence. Among the antipsychotics used in the study there is significant positive attitude towards medication adherence with Risperidone (P=0.001) & negative attitude towards medication adherence with olanzapine (P=0.005). The medication side effect significant in current study are concentration difficulties (P=0.014), memory failure (P=0.032), Depression (P=0.032), headache (P=0.04), constipation (p=0.00), weight gain (p=0.004), galactorrhea (P=0.00), orgasmic dysfunction (p=0.26).

**Conclusion: The current study supports the inverse relation between illness severity & positive attitude towards medication adherence. Improving adherence plays a crucial role in symptom reduction & further relapse prevention.**

**Keywords: Schizophrenia, Adherence, antipsychotics, Medication side effects.**

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## INTRODUCTION

Schizophrenia is the most incapacitating mental disorder, with a lifetime prevalence of 1% and symptoms often appearing in late adolescence or early adulthood.<sup>[1-3]</sup> It is characterised by delusions, hallucinations, disorganised speech, grossly disorganised behaviour or catatonic behaviour, negative symptoms. Although there are a variety of cognitive, behavioural, and emotional dysfunctions associated with schizophrenia, no single symptom is pathognomonic of the disorder.<sup>[4]</sup> In 2017, an estimated 1.1 million new cases were reported, with a total of 20 million cases reported in 2019.<sup>[5,6]</sup> It imposes a disproportionately large economic burden on society. Based on scientific evidence for the management of schizophrenia antipsychotics are the first line agents.<sup>[7]</sup> To keep symptoms under control and prevent relapse, effective care necessitates long-term treatment with antipsychotics.<sup>[8]</sup> Antipsychotic drug's benefits are occasionally overshadowed by their side effects. These side effects range from minor tolerability issues (e.g., mild sedation or dry mouth) to extremely unpleasant (e.g., constipation, akathisia, sexual dysfunction) to painful (e.g., acute dystonias) to disfiguring (e.g., weight gain, tardive dyskinesia) to life threatening (e.g., myocarditis, agranulocytosis).<sup>[7]</sup> Atypical antipsychotics cause metabolic changes that increases the risk of morbidity and mortality over time, particularly cardiovascular disease and Type 2 diabetes, as well as the requirement for medical supervision.<sup>[9]</sup> According to the CATIE study, 74% of patients stopped taking their medications after 18 months due to insufficient efficacy, unacceptable side effects, or other factors.<sup>[10]</sup> Nonadherence to prescribed drug treatments has been recognized as a problem worldwide and also the most challenging aspect of treating patients with schizophrenia. Thus, nonadherence can have a substantial negative impact on patient's health and functioning as well as a financial impact on society. Adherence with treatment will reduce catastrophic repercussions, including hospitalization and suicide. Medication adherence can be defined as the extent to which the patient's medication taking matches that agreed with the prescriber.<sup>[8]</sup> Objective of the current study is to assess relationship between medication adherence & severity of schizophrenia, antipsychotic medication & its adherence, antipsychotic medication & its side effects in patients with schizophrenia.

## MATERIAL AND METHOD

It is a cross-sectional study, carried out at Mallareddy Narayana multi-speciality Hospital, a tertiary care hospital attached to Mallareddy medical college for women, Hyderabad. The study was conducted from June 2021- May 2022 (1 year). The study was conducted in 60 participants selected by simple consecutive sampling fulfilling the study criteria. The study-protocol was approved by the Research and Ethics committees of the institute. Written informed consent was obtained from all participants prior to inclusion; other ethical safeguards were also maintained during the study.

### **Inclusion criteria:**

a. Age 18–55 years

b. Patients meeting diagnostic criteria for schizophrenia as per ICD-10 classification.

**Exclusion criteria:**

Psychiatric illness other than schizophrenia.

Data collection tools: Intake proforma, Positive and Negative Syndrome Scale (PANSS) scale to assess symptoms severity in schizophrenia, Drug Attitude Inventory-30(DAI-30) to assess positive or negative attitude towards treatment adherence, Udvalg for Kliniske Undersogelser (UKU) side effect scale to assess the side effects of antipsychotics.

The following assessments were carried out:

1. Psychopathology: The positive and negative syndrome scale (PANSS). 30 items included in the PANSS, 7 constitute a Positive Scale, 7 a Negative Scale, and the remaining 16 a General Psychopathology Scale. The scores for these scales are arrived at by summation of ratings across component items. Therefore, the potential ranges are 7 to 49 for the Positive and Negative Scales, and 16 to 112 for the General Psychopathology Scale. To assess overall severity of schizophrenia PANSS was compared with CGI scale ( clinical global impression scale). A score of (58-74) was considered minimally ill, (75-94) as mildly ill, (95-115) as moderately ill & ( $\geq$  116) as severely ill.<sup>[3]</sup>
2. Adherence: The drug attitude inventory-30 (DAI-30) item version was used as a patient-report measure of adherence. Though the DAI-30 primarily measures subjective response and attitudes toward medication, scores on this scale are highly predictive of adherence. The DAI- 30 contains 15 item, a patient who is fully adherent to their prescribed medication (and so would be expected to have a 'positive' subjective response to medication) would answer as 'True', and 15 items such a patient would answer as 'False'. The total score for each patient is calculated as the sum of the positive scores, minus the negative scores. A positive total score indicates a positive subjective response (adherent) and a negative total score indicates a negative subjective response (non-adherent).
3. Side-effects: Overall rating was carried out with the Udvalg for Kliniske Undersogelser side- effect rating scale (UKU). The UKU Side Effect Self-Rating Scale (UKU-SERS-Pat) comprises 48 symptoms considered suitable for self-rating .the items are clustered into four subgroups: Psychic, Neurological, Autonomic and Other side effects. Each symptom is scored on a scale of 0-3 (0= absent, 1=mild, 2=moderate, 3=severe).

**Data analysis:**

The data was entered in SPSS 21; Descriptive statistics were calculated to describe the patient demographic characteristics, drug adherence, severity of illness, different antipsychotics. Pearson chi square test is applied to assess relationship between severity of illness & drug adherence, antipsychotics & medication adherence, medication side effects & antipsychotics. The level of statistical significance was  $P < 0.05$ .

**RESULTS**

The study sample consisted of 60 patients with schizophrenia who reported they were currently taking a medication to treat their condition. The mean age of the sample was 31.8 years, approximately half of the sample was Female, majority of them were Hindu. 41% were educated up to intermediate, 20% were unemployed, and among the working individuals most of them were employed in semiskilled job. More than half of the sample was married (56.7%) & belonged to lower middle socio-economic status (43.3%). Majority (91%) of the patients were not under supervision for treatment. 78.3 % of the study population had a family history of psychiatric illness.

**Table 1: Age**

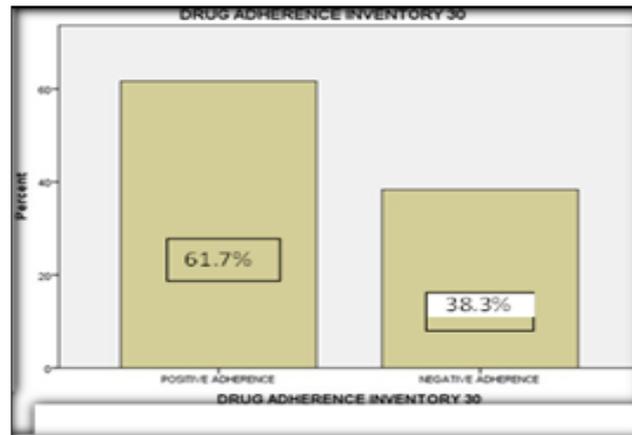
	<b>N=60</b>	<b>Percentage</b>
Gender	Male -28	46
	Female - 32	53
Religion	Hindu - 49	81.7
	Muslim - 11	18.3
Education	Primary School Certificate - 8	13.3
	Middle School Certificate -2	3.3
	High School Certificate - 10	16.7
	Intermediate - 25	41.7
	Graduate Or Post Graduate - 15	25.0
Occupation	Unemployed - 12	20.0
	Unskilled Worker - 1	1.7
	Semi-Skilled Worker - 12	20.0
	Skilled Worker - 11	18.3
	Clerical, Shop Owner, Farmer -7	11.7
	Semi-Profession - 8	13.3
Marital Status	Student - 9	15
	Single - 25	41.7
	Married - 34	56.7
Socio Economic Status	Divorced - 1	1.7
	Upper Lower - 6	10
	Lower Middle - 26	43.3
	Upper Middle - 12	20
Treatment Under Supervision	Upper Class - 16	26.7
	Yes – 5	8.3
Family History of Mental Illness	NO - 55	91.7
	Yes - 13	21.7
	No - 47	78.3

Mean age of illness onset is 23.2 years; mean duration of illness is 8.27yrs. Mean treatment duration is 7.9yrs.

**Table 2: ?**

	<b>Mean</b>	<b>Minimum</b>	<b>Maximum</b>	<b>Standard Deviation</b>
Age	31.8	18	55	9.9
Age of Illness Onset	23.2.	12	42	6.8
Duration of Illness	8.27	1	32	7.5
Duration of Treatment	7.9	1	32	7.4

In this current study with 60 patients overall positive attitude towards medication adherence is 61.7% & negative attitude towards medications is 38.3%.

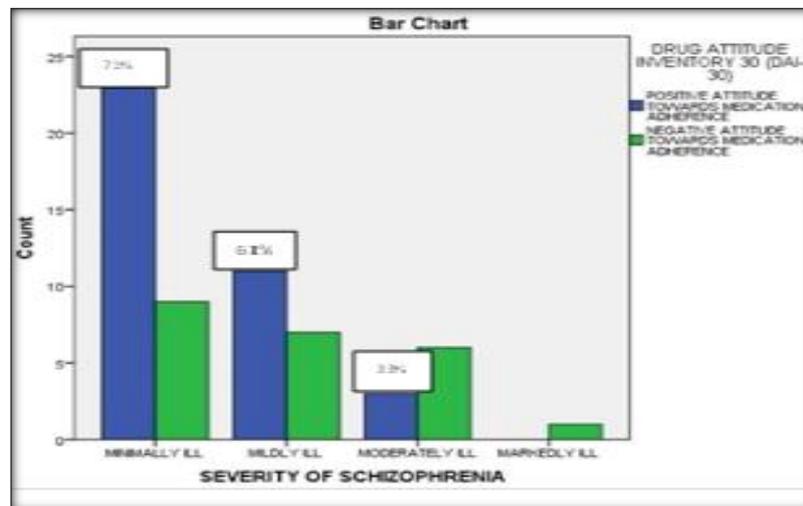


**Figure1: Drug adherence inventory**

In current study patients with minimal illness & mild illness has more positive attitude towards medications adherence (71%, 61%), when compared to moderately ill patients who had only 33% positive attitude towards medication adherence. This clearly depicts severity of illness is inversely related to positive attitude towards medication adherence is decreased.

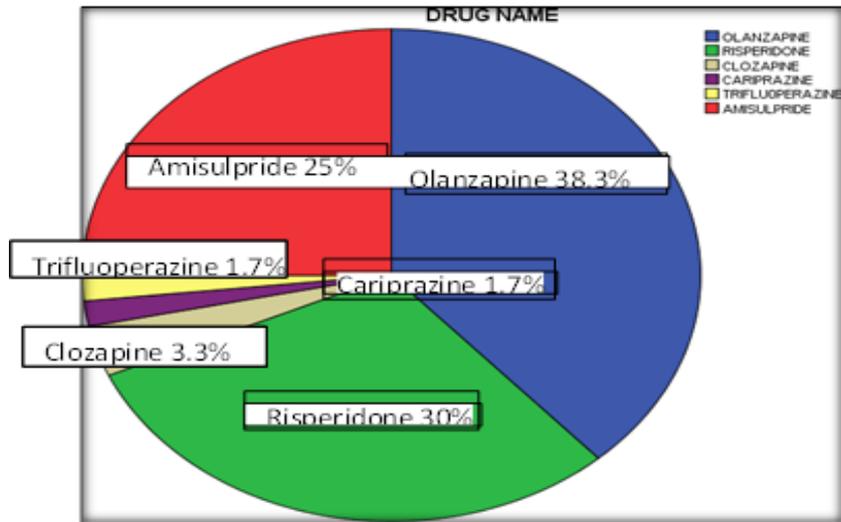
**Table 3: Severity of schizophrenia**

	Severity of schizophrenia (PANSS CGI score)	Positive attitude	Negative attitude	Total
1	Minimally ill (58-74)	23 (71%)	9 (28%)	32 (53.3%)
2	Mildly ill (75-94)	11 (61%)	7 (38%)	18 (30%)
3	Moderately ill (95-115)	3 (33%)	6 (66%)	9 (15%)
4	Markedly ill ( $\geq$ 116)	0	1	1 (1.7%)



**Figure 2: Severity of schizophrenia**

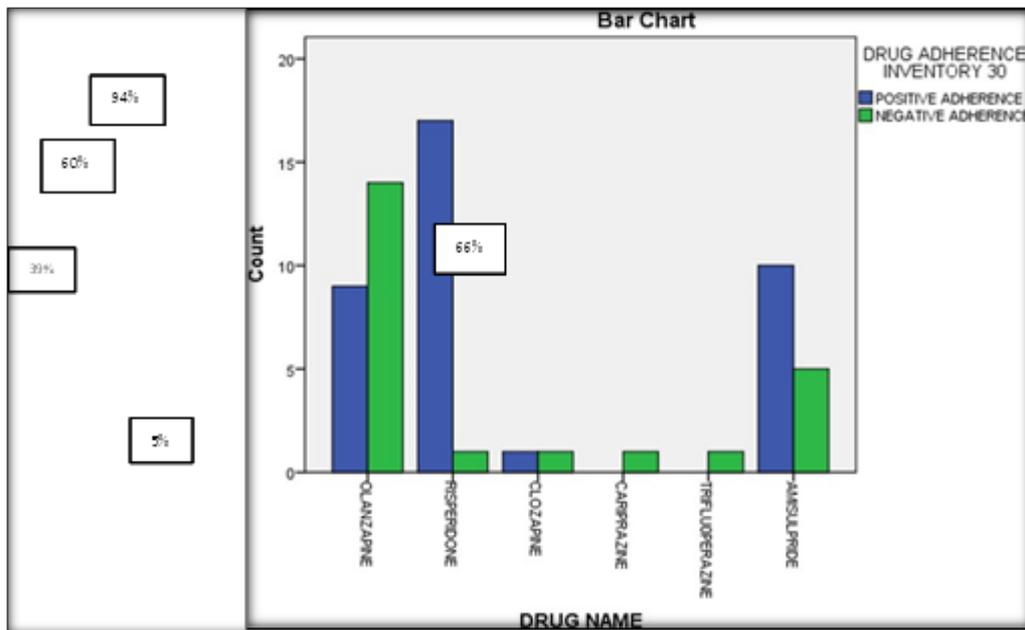
The antipsychotics used by the patients in our study are Olanzapine (n=23), Risperidone (n=18), Amisulpride (n=15), clozapine (n=2), Cariprazine (n=1), Trifluoperazine (n=1). In the current study risperidone (p=.001) has a statistically significant positive attitude toward medication adherence, while olanzapine (p=.005) has a statistically significant negative attitude toward medication adherence.



**Drug attitude inventory**

**Table 4: Drug attitude inventory**

Antipsy Chotics	Drug Attitude Inventory		Total	P
	Positive Attitude	Negative Attitude		
Olanzapine	9	14	23	.005*
Risperidone	17	1	18	.001*
Clozapine	1	1	2	.730
Cariprazine	0	1	1	.201
Trifluoperazine	1	1	2	.201
Amisulpride	10	5	15	.646
Total	37	23	60	



**Figure 4: Drug count**

**Table 5: Drug and its psychic side effect**

<b>Psychic Side Effect</b>	<b>Olanzapine-23</b>	<b>Risperidone-18</b>	<b>Clozapine-2</b>	<b>Cariprazine-1</b>	<b>Trifluoperazine-1</b>	<b>Amisulpride-15</b>	<b>P</b>
Concentration Difficulties	0.818	.062	.009*	.578	.578	0.014*	0.014*
Asthenia/Lassitude/Increased Fatigability	.738	.070	.159	.672	.672	.06	.2
Sleepiness/Sedation	.106	.185	.573	.692	.692	.380	.545
Failing Memory	0.014*	0.002*	.80	.394	.394	.880	0.032*
Depression	.07	.111	.847	.249	.249	.035*	.032*
Tension/Inner Unrest	.553	.063	.962	.329	.297	.179	.306
Increased Duration of Sleep	.106	.185	.573	.692	.692	.380	.145
Reduced Duration of Sleep	.98	.610	.665	.761	.761	.178	.76
Emotional Indifference	.604	.495	.847	.378	.249	.764	.751
<b>Neurological Side Effects</b>	-	-	-	-	-	-	-
Dystonia							
Rigidity	-	-	-	-	-	-	-
Hypokinesia	-	-	-	-	-	-	-
Hyperkinesia	-	-	-	-	-	-	-
Tremors	.580	.211	.847	.378	.249	.035*	.242
Akathisia	-	-	-	-	-	-	-
Seizures	-	-	-	-	-	-	-
Paresthesia	-	-	-	-	-	-	-
Headache	.822	.01*	.089	.394	.233	.096	.04*
<b>Autonomic Side Effects</b>							
Accommodation Disturbances	-	-	-	-	-	-	-
Increased Salivation	.382	.492	.489	.526	.526	.869	.839
Decreased Salivation	.42	.123	.851	.896	.896	.560	.796
Nausea/Vomiting	.353	.26	.281	.614	.044*	.456	.205
Diarrohea	.257	.346	.789	.851	.851	.013*	.287
Constipation	.000*	.000	.068	.427	.427	.646	.000*
Micturation Disturbances	-	-	-	-	-	-	-
Orthostatic Dizziness	0.017*	.619	.121	.692	.692	.079	.124
Palpitations/Tachycardia	-	-	-	-	-	-	-
Increased Tendency To Sweat	.427	.509	.851	.896	.896	.081	.997
<b>Other Side</b>							

<b>Effects</b>							
Rash	-	-	-	-	-	-	-
Pruritis	-	-	-	-	-	-	-
Photosensitivity	-	-	-	-	-	-	-
Increased Pigmentation	-	-	-	-	-	-	-
Weight Gain	.006*	.001*	.364	.068	.578	.290	.004*
Weight Loss	.257	.028*	.789	.851	.851	.406	.437
Menorrhagia	-	-	-	-	-	-	-
Metrorrhagia	-	-	-	-	-	-	-
Amenorrhea	.761	.053	.366	.526	.109	.013*	.051
Galactorrhea	.427	.509	.851	.896	.000*	.560	.000*
Gynecomastia	-	-	-	-	-	-	-
Increased Sexual Desire	-	-	-	-	-	-	-
Decreased Sexual Desire	.619	.366	.701	.788	.788	.232	.838
Erectile Dysfunction	.427	.123	.851	.896	.896	.560	.075
Ejaculatory Dysfunction	-	-	-	-	-	-	-
Orgasmic Dysfunction	.066	.000*	.665	.761	.761	.178	.026*
Dry Vagina	-	-	-	-	-	-	-

## DISCUSSION

In the current study overall positive adherence is 61.7% & majority of the study population was on atypical antipsychotics which is supported by Valenstein et al. 2004 patients on atypical antipsychotics had better adherence.<sup>[11]</sup>

The overall negative adherence rate in this study is 38.3%, which is consistent with a systemic evaluation by Lacro et al, who observed a mean rate of medication nonadherence in schizophrenia of 41%.<sup>[12]</sup>

Patients with minimal illness and mild illness exhibited a higher positive attitude toward medication adherence (71 percent and 61 percent, respectively) than moderately ill patients, who only had a 33 percent positive attitude toward medication adherence in the current study. Two prospective studies back this up. There was a directional association between symptom severity and poor adherence, according to Hudson et al. (2004) and Acosta et al. (2009).<sup>[13,14]</sup>

Memory loss, weight gain, constipation, orthostatic dizziness, and a statistically significant negative attitude toward medication adherence ( $p=0.005^*$ ) were all reported as major negative impacts of olanzapine in the current study. According to Velligan et al. (2009), chronic side effects such as weight gain in women, severe sedation, and cognitive impairment worsen adherence problems.<sup>[15]</sup> In the current study, 66 percent of participants had a positive attitude toward medication adherence with amisulpride which is confirmed by Leucht's meta-analysis, which found that when compared to placebo, amisulpride was the most tolerable, with fewer discontinuations due to side effects.<sup>[16]</sup>

In our study, there were statistically significant failing memory with olanzapine ( $p=0.014$ ), risperidone ( $p=0.002$ ) & concentration difficulties ( $p=0.014$ ), depressive symptoms ( $p=0.035$ ) with amisulpride, which is supported by the CATIE study, which observed that atypical antipsychotics are not more effective than typical antipsychotics in reducing negative or cognitive symptoms.<sup>[17]</sup>

Risperidone caused considerable orgasmic dysfunction ( $p < .01$ ) in the current study, which was also found by Cutler in 2003. Sexual dysfunctions were the most severe; they affect both sexes and are often overlooked in research and clinical practise, despite the fact that they may have a detrimental impact on adherence.<sup>[18]</sup>

## CONCLUSION

The current study supports the inverse relation between illness severity & positive attitude towards medication adherence. Improving adherence plays a crucial role in symptom reduction & further relapse prevention. Health care professionals can increase the likelihood of adherence by employing relatively basic measures. Good communication, joint medicine decision-making and focused yet non-judgmental adherence questioning are some of these. Involving the family or a key caregiver in the medication decision-making is typically beneficial.

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