

## **Role of Clinical Pharmacist in Promoting Patient Compliance through Assessment of Reasons for Non-Compliance and Minimum Maintenance Dose Titrations in Schizophrenic Patients**

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### **ABSTRACT**

**Context:** Medication non-compliance is an important area of concern in schizophrenia as it contributes to relapse and re-hospitalization of the patients. Constant advancement and study of therapeutic interventions designed to improve medication adherence and the outcome of dose titrations are required to reap the most valuable benefits from the pharmacologic treatment of schizophrenia. **Aim & Objective:** The aim of the present study is to find out the reasons for drug non-compliance and the effectiveness of treatment outcomes after dose titrations in schizophrenic patients and the main objective is to educate the patient by counseling about the disease, drugs and the importance of medication adherence. **Materials and Methods:** This study was conducted over a period of six months. All male and female subjects of age group 30-40 receiving anti-psychotic medications for a minimum of 1 year before the study starts and who were noncompliant to the prescribed medications were included. **Results:** Females were prominent in the non-adherent group and males were found to be higher in Group-B. Most of the schizophrenic patients were suffering with paranoid schizophrenia, living in the urban environment and running their nuclear families. Majority of the Subjects in the non-adherent group were illiterates and unemployed, where as in the dose titration group many have completed their primary education and were employed. Compared to first generation antipsychotics, second generation antipsychotic drugs were most commonly prescribed. Almost 56.07% do not have the support from their families. The main reasons stated by the patients to be noncompliant were difficulty in access to treatment, financial obstacles, forgetfulness. Dose titrations were made at an interval of 1 month for four antipsychotics (haloperidol, chlorpromazine, olanzapine and risperidone) and patients were benefited by the titration which was observed through the PANSS scores at each visit. **Conclusion:** Findings suggest that there is a need for identification and reduction of factors responsible for noncompliance. Strategies to improve adherence have the potential to reduce these costs. Dose titration shows beneficial effect to improve patient quality of life. Hence they should be implemented in clinical practice depending upon the individual patient.

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**Keywords:** *Schizophrenia, Non-adherence, Dose titrations, PANSS, Patient Counseling*

Schizophrenia is one of the most complex and challenging of psychiatric disorders. It represents a heterogeneous syndrome of disorganized and bizarre thoughts, delusions, hallucinations, such as hearing voices, inappropriate affect and impaired psychosocial functioning. Schizophrenia typically begins in early adulthood.<sup>1</sup>

Antipsychotic medication plays an important role in schizophrenia treatment and symptom control. Effective management of schizophrenia requires continuous long-term treatment in order to keep symptoms under control and to prevent relapse. Despite the critical importance of medication, no adherence to prescribed drug treatments has been recognized as a problem worldwide and may be the most challenging aspect of treating patients with schizophrenia.

Compliance has been defined as, “the extent to which a person’s behavior coincides with medical or health advice”. The word compliance has been condemned over the past 20 years because it signifies an idea of a paternalistic relationship between the physician and the patient, and therefore adherence has been adopted as a more equitable term .<sup>2</sup>

Clinicians face a complex task when trying to determine who will or will not adhere to medication treatment as prescribed .<sup>3</sup>

Nonadherence to medication has a negative impact on the course of illness resulting in relapse, rehospitalization, longer time to remission, and attempted suicide and also contribute to the already high costs of the disease to healthcare systems.

Reducing nonadherence to antipsychotic medications has the potential to reduce psychiatric morbidity and costs of care substantially. That would improve the welfare of patients with schizophrenia and reduce the use of resources for acute psychotic episodes.

Therefore it is important to identify the key factors contributing to nonadherence in schizophrenia, and their consequences. In addition, assessing causes and consequences of nonadherence together may highlight the importance and complexity of adherence to medication in schizophrenia. However, we are not aware of any comprehensive review of both the causes and consequences of nonadherence in schizophrenia. Furthermore, there is a need for a review that investigates whether the data allow for a quantitative assessment of the specific link between nonadherence and hospitalization.<sup>4</sup>

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<b>TABLE-1: Risk factors for non-adherence in patients with schizophrenia<sup>5</sup></b>
<p><b>Patient-related risk factors :</b>                      Socio-Demographic characteristics-age, gender and ethnicity                      Illness characteristics-age at onset and duration of illness, illness severity and subtype (e.g. Paranoid schizophrenia), cognition or memory, subjective well-being.</p>
<p><b>Medication-related factors :</b> Adverse effects, dosage, agent, route, and complexity of regimen.</p>
<p><b>General clinical factors</b>                      Drugs or alcohol consumption                      Previous non adherence</p>
<p><b>Environment related risk factors</b>                      Poor family and social support,                      Negative social perception of the disease                      Difficulty accessing health care services                      Financial burden</p>
<p><b>Physician related risk factors</b>                      Poor relationship with therapist                      Poor psychoeducation and information to patients and relatives                      Poor contact with the therapist                      Inadequate planning of the post discharge period</p>
<p><b>Treatment related risk factors</b>                      Ineffectiveness against persistent symptoms(psychotic and negative symptoms)                      Poorer adherence to oral than to intramuscular treatments.</p>
<p><b>Psychopathological symptoms</b>                      Impaired insight                      Cognitive deficiency                      Delusion of persecution, poisoning or grandeur                      Psychotic symptoms                      Negative symptoms</p>
<p><b>Psychological factors:</b>                      attitudes, beliefs and other subjective aspects                      Negative attitude toward the treatment                      Negative subjective response to treatment                      Regarding the disease as mild and/or perceived minor benefit from treatment                      Shame or stigmatization associated with the medication or the disease.</p>

**EVALUATING NON-ADHERENCE**

Evaluation methods are considered to be “direct” when they offer proof that the patient has taken their medication.<sup>5</sup>

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**Table-2: Main Adherence Evaluation Methods**

<b>DIRECT</b>	<b>INDIRECT</b>
Detection of the drug or its drug metabolites (generally in serum or urine) Direct observation of the patient	<b>Objective</b> Tablet count Electronic monitoring Pharmacy records
	<b>Subjective</b> Psychometric scales Questioning the patient Questioning the relatives Clinical judgement

**ROLE OF CLINICAL PHARMACIST <sup>(6-21)</sup>**

Schizophrenia is a mental illness about 1 % of people are affected with this illness in their lifetime. Non compliance is highly seen in the schizophrenic patients who are on antipsychotics which in turn results in the worsening of patient condition and attenuation of symptoms.

- Suboptimal attitudes of the patients towards mental illness and a lack of confidence highlights the need for different educational approaches to provide clinical pharmacy services to the patients
- pharmacist has to Communicate with the patient and Prevents the Antipsychotic polypharmacy which inturn decreases the rates of hospitalization and mortality
- As experts in pharmacotherapy, pharmacists can provide complementary skills, knowledge and attitudes to other health care professionals within a multidisciplinary team context.
- Specifically pharmacists may contribute to health care teams by detecting and resolving or preventing drug related problems; helping to ensure the safe and efficacious use of medicines; providing comprehensive drug information to patients and other health care professionals;
- Promoting medication adherence; and quality use of medicines.
- Reinforcing primary prevention and health promotion and lifestyle modification activities in the community.
- The pharmacists were able to identify people who were at high risk of the disease who had previously gone undetected, screen them and refer on to appropriate health services if required.
- Medication chart review, assessment of laboratory results and medication prescribing; and in providing education for patients and other health care professionals
- Pharmacist based intervention to improve antipsychotic adherence includes the use of unit-of-use packaging, a pharmacist education session, refills reminders and notification of clinicians when patients failed to fill prescriptions. medication reminder devices, and

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using one pharmacy for all prescriptions. Most importantly, pharmacists can assist patients with schizophrenia by showing empathy, providing encouragement and support, and reminding them that adhering to their therapy is the most effective tool in managing schizophrenia.

- As one of the most accessible health care professionals, pharmacists can positively impact patient outcomes by stressing the importance of medication adherence, as well as encouraging patients to maintain regular visits with their primary health care provider.
- When counselling patients, pharmacists should remind them about the benefits of medication therapy and educate them regarding the potential adverse effects of the selected medication.
- Successful therapy starts when patients have a thorough understanding of their therapy and the importance of therapy adherence.

### **EDUCATING THE PATIENT AND FAMILY**

It is important for the pharmacist to accurately evaluate the patient's ability to assume responsibility for taking drugs at home. The administration of antipsychotic drugs becomes a family responsibility if the outpatient appears to be unable to manage his or her own drug therapy.

#### **The pharmacist can advise the patient or family member. It includes the following points:**

- ❖ Take regular clinical appointments when necessary because close monitoring of therapy is essential.
- ❖ Report any unusual changes or physical effects to the primary health care provider.
- ❖ Take the drug exactly as directed. Do not increase, decrease, or omit a dose or discontinue use of this drug unless directed by the physician.
- ❖ Never discontinue any of the medication unless directed by their physician,
- ❖ Do not take any non-prescription drug unless use of a specific drug has been approved by the physician.
- ❖ Inform physicians, or other medical personnel about the present antipsychotic drug therapy during consultations on other medical reasons.
- ❖ Never use alcoholic beverages, cigarette or any other illicit drugs.( If quitting smoking may be difficult for patients with schizophrenia, smoking cessation strategies such as nicotine replacement methods may be recommended by the physicians.)
- ❖ Every drug has adverse drug reactions even the antipsychotics have, but these can be controlled or prevented by life style modifications and with frequent monitoring. so clinical pharmacist has a main role in educating the patients regarding their illness, medications ,adverse drug reactions ,importance of adherence, life style modifications and also about their dietary changes.

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For eg.,

- ❖ Antipsychotics may cause orthostatic hypotension, weight gain, menstrual irregularities, sedation, dry mouth in the patients on antipsychotics.
- ❖ These ADR can trouble the patients but can be managed in a simple way like
- ❖ Weight gain which is commonly observed can be prevented by intake of sweets, beverages, fast foods and by performing regular exercises. weight should be measured monthly
- ❖ To avoid constipation, take adequate fluids and if dryness of the mouth occurs, relieve it by taking frequent sips of water, chew a hard candy, or chewing gum (preferably sugarless).
- ❖ Care should be taken while suddenly standing from supine position or always take someone's help to minimize the orthostatic hypotension.
- ❖ Change in time of administration is beneficial than withdrawing the drug In patients suffering with the problem of Sedation.
- ❖ Its better educate the patient to discuss the ADR to the physician for instance, if a patient is suffering with menstrual irregularities ,then consulting psychiatrists can adjust the dose or modify the treatment plan or he may refer the patient to gynaecologist
- ❖ Inform your primary care provider if you become pregnant or intend to become pregnant during drug therapy
- ❖ Do not drive or perform other hazardous tasks if drowsiness occurs.

### AIM

- The aim of the present study is to find out the improvement of patient compliance through the assessment of reasons for the drug non-compliance in schizophrenia using the Rating of medication influences (ROMI) scale, Drug attitude inventory scale and Motivation assessment scale.
- This study also aimed at evaluating and comparing the effectiveness of treatment outcomes after dose titrations by using positive and negative syndrome scale (PANSS) and to improve the process of dose titration in routine clinical practice.

### OBJECTIVE

- To determine the percentage of patients who reached the reduction goal with dose titrations after patient education.
- To educate the patient about the disease, drugs and the importance of medication adherence.
- To compare and analyze the effect of dose titration of antipsychotic drugs(chlorpromazine, haloperidol, olanzapine and risperidone )
- To determine the effect of counseling on the patients.
- To observe and analyze the adverse drug reactions to anti-psychotic drugs.
- To improve the quality of life

## METHODOLOGY

**Study Design:** A Non Experimental prospective observational study.

**Study Period:** This study was conducted for a period of 6 months i.e., from February 2015-july 2015.

**Study Criteria :**

**INCLUSION CRITERIA:**

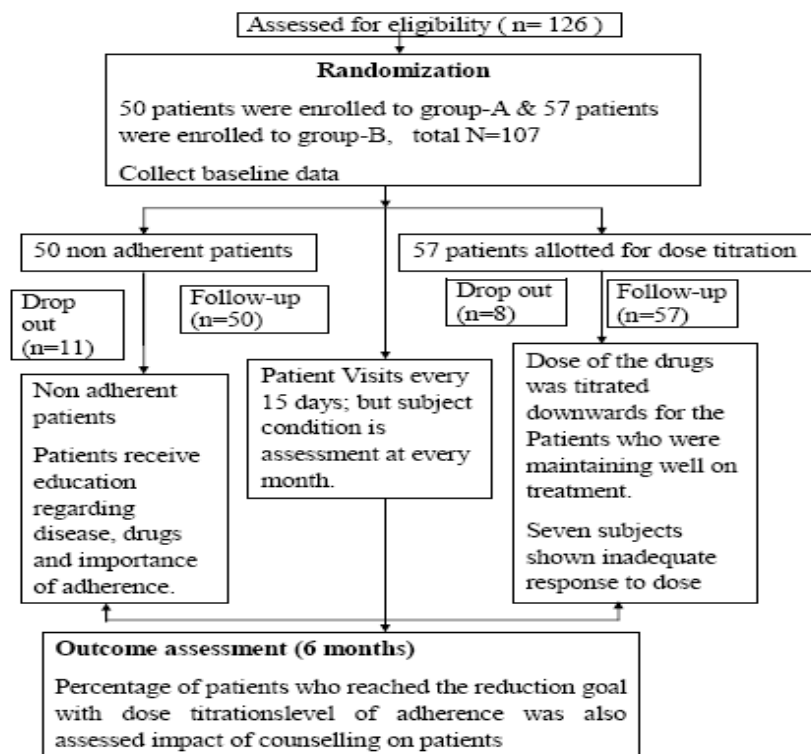
- All male and female subjects of age group 30-40 who were admitted in the inpatient ward.
- Patients having the clinical diagnosis of schizophrenia at least more than 1 year prior to study.
- Patients receiving a stable dose of anti-psychotic medications for a minimum of 1 year before the study starts and who are noncompliant to the prescribed medications.
- Patients who are willing to participate and who meets the study criteria.

**EXCLUSION CRITERIA:**

- Patients having a known history of any major systemic illness affecting quality of life (or) likely to affect participation in the study.
- Patients receiving any excluded concomitant medications.
- Patients who are not willing to participate in the study.

### STUDY DESIGN

**FIGURE 1: PATIENT RECRUITMENT AND PROGRESS THROUGH THE TRIAL**



**OBSERVATIONS & RESULTS**

The study sample consists of consecutive follow-up patients attending the outpatient services in our hospital for schizophrenia. After taking informed verbal consent, all patients were systematically interviewed along with the attendant and socio-demographic details were noted. The diagnosis of schizophrenia was reviewed in accordance to international classification of diseases-10 research diagnostic criteria. Patients were labeled as non-compliant if he was non adherent as per DAI scale. The attitude toward antipsychotic medication was assessed using DAI. Subjective reasons of medication compliance/non-compliance were assessed using ROMI scale .PANSS was used to assess the severity of the illness. The data was statistically analyzed using Microsoft office excel worksheet and graph pad prism.

**Table-3 : Description of Study Sample**

VARIABLE	NUMBER	
	GROUP-A	GROUP-B
Total patients initially considered	61	65
Patients excluded	11	8
Final study sample	50	57

Out of 126 patients,61 were grouped as non adherent but only 50 came for medication even not in the refilled dates,11 were the drop outs because they didn't consult after consenting the study . 57 were considered for the dose titrations , among them , for 50 patients , doses were titrated for their medication and are benefited where as 7 patients didn't benefit from the dose titration, as their condition worsens after the dose titration. in this group 8 members were the dropouts.

**Table-4 : Gender Wise Distribution of Study Population**

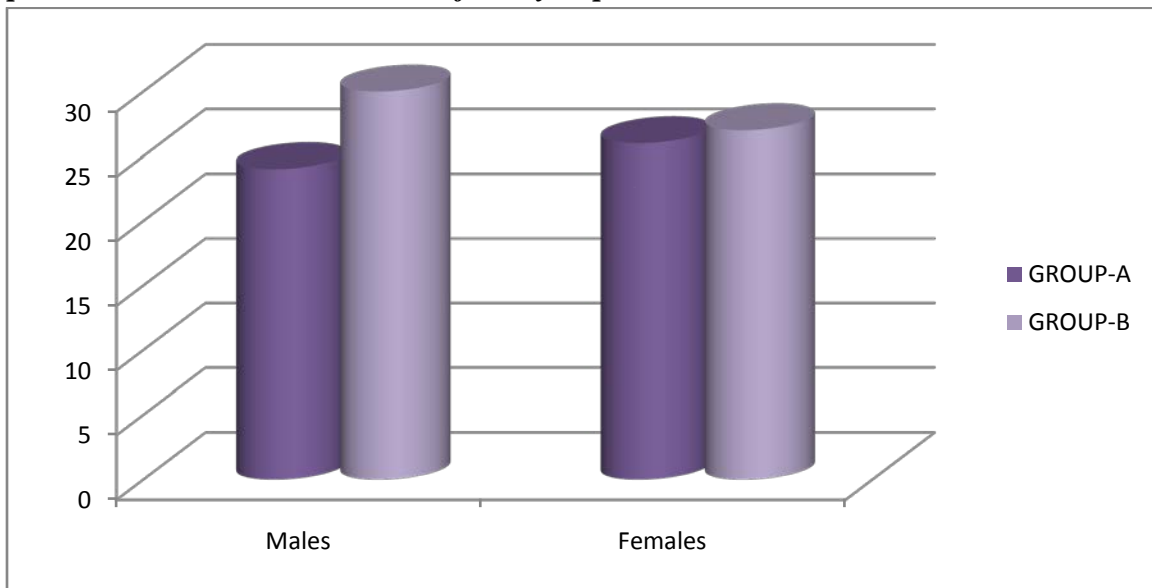
	GROUP-A (NON-ADHERENT)	GROUP-B (DOSE TITRATION)
Males	24	30
Females	26	27
Total	50	57

Females were prominent in the non-adherent group and males were found to be higher in Group-B.



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**Graph-1 : Gender Wise Distribution of Study Population**



**Table-5 : Characteristics of Sample of the Study**

CHARACTERISTIC	n=100		P-VALUE
	GROUP-A NUMBER (%)	GROUP-B NUMBER (%)	
<b>Gender</b>			
Male	27(48%)	30(52.63)	1.000
Female	26(52%)	27(47.36)	
<b>Origin</b>			
Urban	36(72%)	36(63.15%)	0.410
Rural	14(28%)	21(36.84%)	
<b>Marital status</b>			
Single	8(16%)	7(12.28%)	0.687
Married	33(66%)	42(73.68%)	
Divorced	9(18%)	8(14.03%)	
<b>Type of family</b>			
Nuclear	34(68%)	35(61.40%)	0.546
Joint	16(32%)	22(38.59%)	
<b>Education</b>			
Illiterate	18 (36%)	8(14.03%)	0.025*
Primary	15(30%)	21(36.84%)	
Secondary	14(28%)	17(29.82%)	
Graduate	3(6%)	11(19.29%)	
<b>Employment</b>			
Labour	13 (26%)	10(17.54%)	

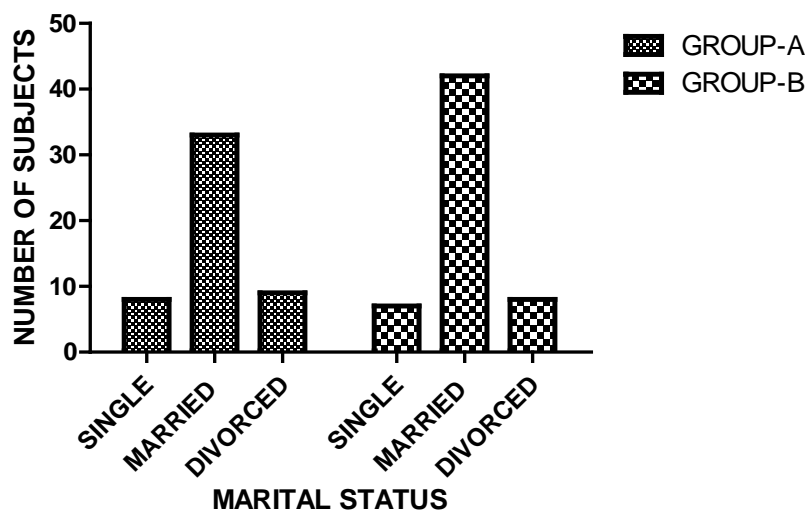
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Employed	14 (28%)	22(38.59%)	0.003**
Business	5(10%)	18(31.57%)	
unemployed	18(36%)	7(12.28%)	
<b>Family income, monthly</b>			
<6000	15(30%)	13(22.80%)	0.118
6000-10000	27(54%)	25(43.85%)	
>10,000	8(16%)	19(33.33%)	
<b>Care giver</b>			
Spouse	26(52%)	36(63.15%)	0.504
Parents	14(28%)	12(21.05%)	
Relatives	10(20%)	9(15.78%)	
<b>Exercise</b>			
Never	31(%)	6(%)	P<0.0001 ***
Occasionally	2(%)	13(%)	
<3 times per week	8(%)	24(%)	
≥ 3 times per week	5(%)	9(%)	
Daily	4(%)	5(%)	

Most of the schizophrenic patients are living in the urban environment and are married and running their nuclear families.

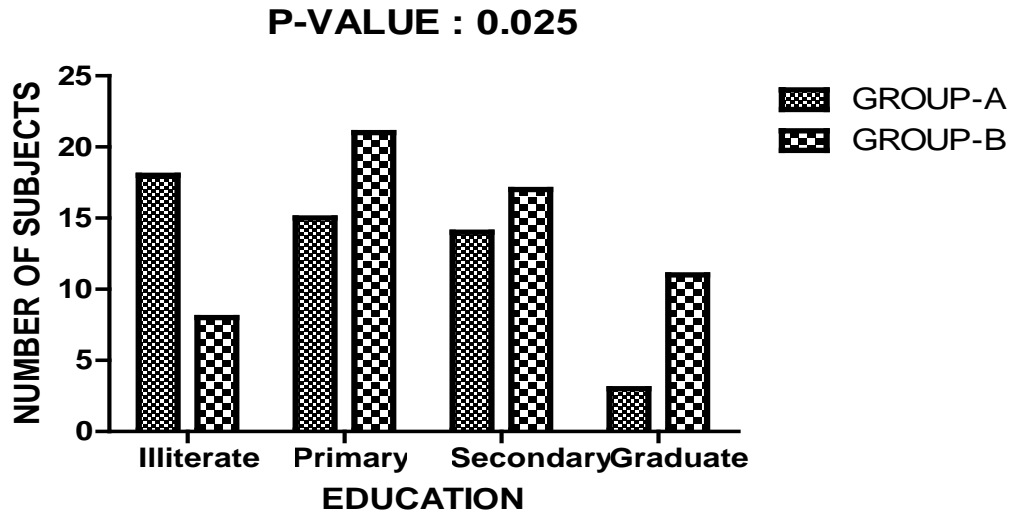
Majority of the Subjects in the non-adherent group were illiterates and unemployed ,where as in the dose titration group many have completed their primary education and were employed, having a income of 6000-10,000.many of the patients are having their spouses as care givers followed by their parents. P-value was calculated by using chi-square test ,to identify the significance between the two study groups.

**Graph-2 : Distribution of Study Population by Marital Status**

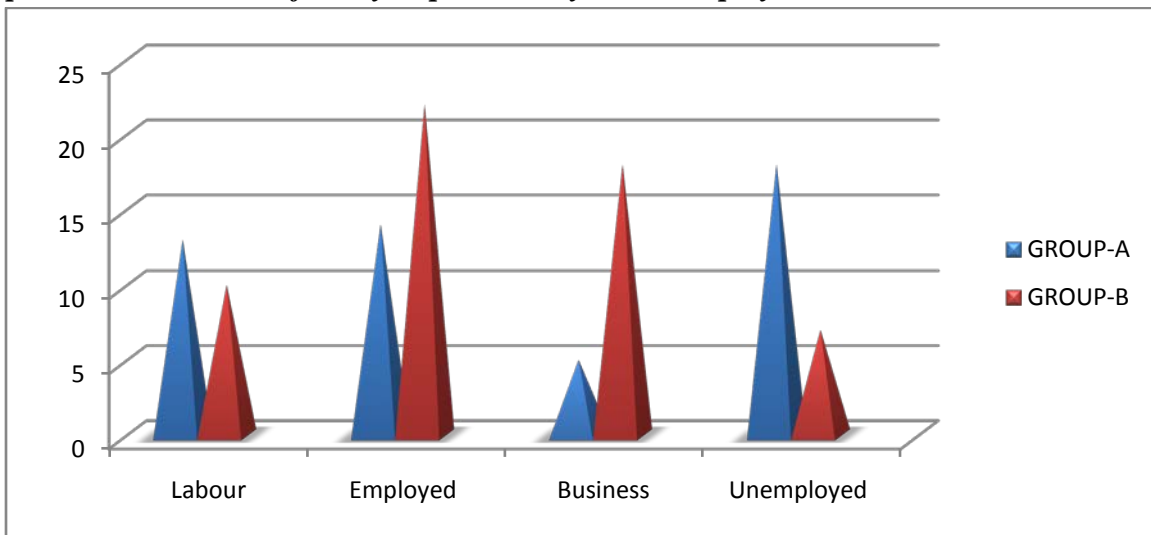


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*Graph -3 : Distribution of Study Population by Educational Status*



*Graph - 4: Distribution Of Study Population By Their Employment Status*



*Table-6: Clinical Variables of the Patients*

VARIABLE	N=100		P-VALUE
	GROUP-A	GROUP-B	
<b>Schizophrenia type</b>			
Paranoid	32 (64%)	41(71.92%)	0.6502
Catatonic	11(22%)	8(14.03%)	
Disorganized	4(8%)	4(7.01%)	
Undifferentiated	1(2%)	3(5.26%)	
Residual	2(4%)	1(1.75%)	

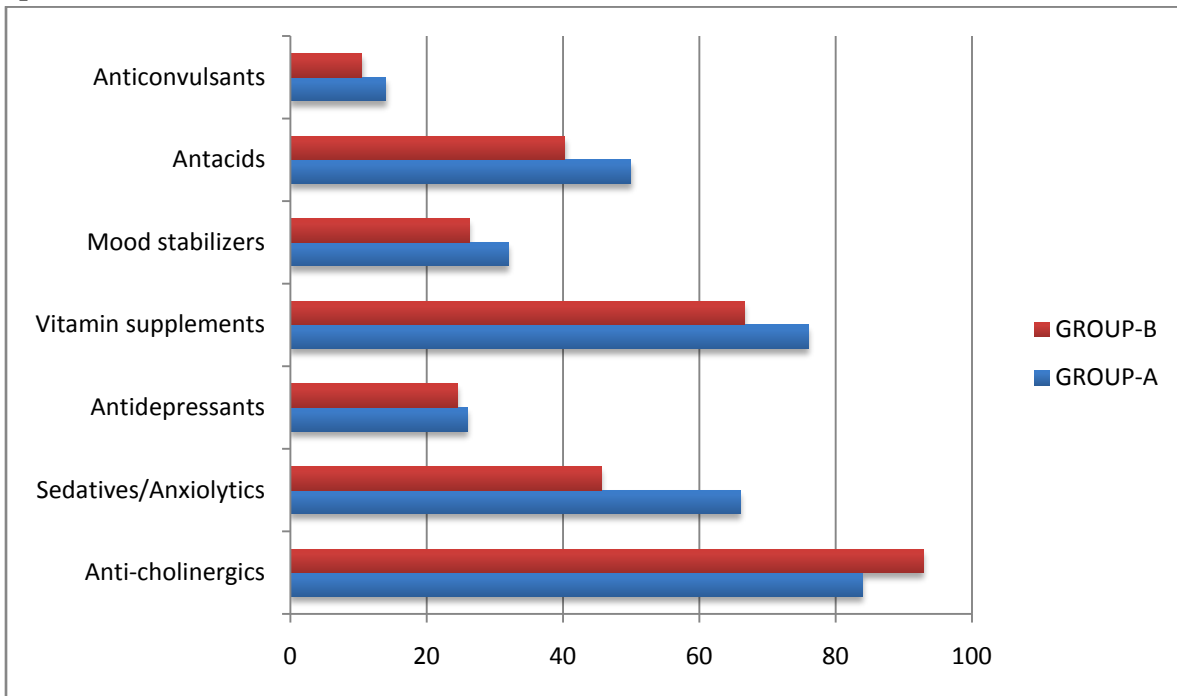
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<b>Medications added</b>			
Anti-cholinergics	42(84%)	53(92.9%)	0.886
Sedatives/Anxiolytics	33 (66%)	26(45.61%)	
Antidepressants	13(26%)	14(24.5%)	
Vitamin supplements	38(76%)	38(66.6%)	
Mood stabilizers	16(32%)	15(26.3%)	
Antacids	25(50%)	23(40.3%)	
Anticonvulsants	7(14%)	6(10.5%)	
<b>Baseline antipsychotic medications</b>			
Olanzapine alone	3 (0.06%)	4(7.01%)	0.0191*
Risperidone alone	5 (10 %)	2 (3.5%)	
Combination of olanzapine and risperidone	6 (12 %)	15(26.3%)	
Risperidone and haloperidol	5(10%)	7(12.2%)	
Olanzapine and haloperidol	9 (18%)	8(14.03%)	
Olanzapine and chlorpromazine	3(6 %)	13 (22.8%)	
Risperidone and chlorpromazine	2(4%)	3(5.26%)	
Risperidone,olanzapine and chlorpromazine	7(14%)	2(3.5%)	
Olanzapine,haloperidol,risperidone	10(20%)	3(5.26%)	
<b>Number of hospitalizations</b>			
0	3 (6%)	19(33.3%)	<0.0001***
1-5	12(24%)	32(56.1%)	
>5	35(70%)	6(10.5%)	
<b>Duration of illness,years n(%)</b>			
0-5	5 (10%)	18(31.5%)	<0.0001***
6-10	10(20%)	25(43.8%)	
11-15	12(24%)	6(10.5%)	
>15	23(46%)	8(14.03%)	
<b>Exacerbations n(%)</b>			
1-2	9 (18%)	25(43.8%)	0.0083**
3-5	14(28%)	18(31.5%)	
6-9	19(38%)	10(17.5%)	
>9	8(16%)	4(7.01%)	
Relapses	50 (100%)	31(54.3%)	
<b>Medication</b>			
First generation antipsychotics	36 (72%)	36(63.15%)	0.667
Second generation antipsychotics	50 (100%)	57 (100%)	
Insight	22 (44%)	38 (66.6%)	

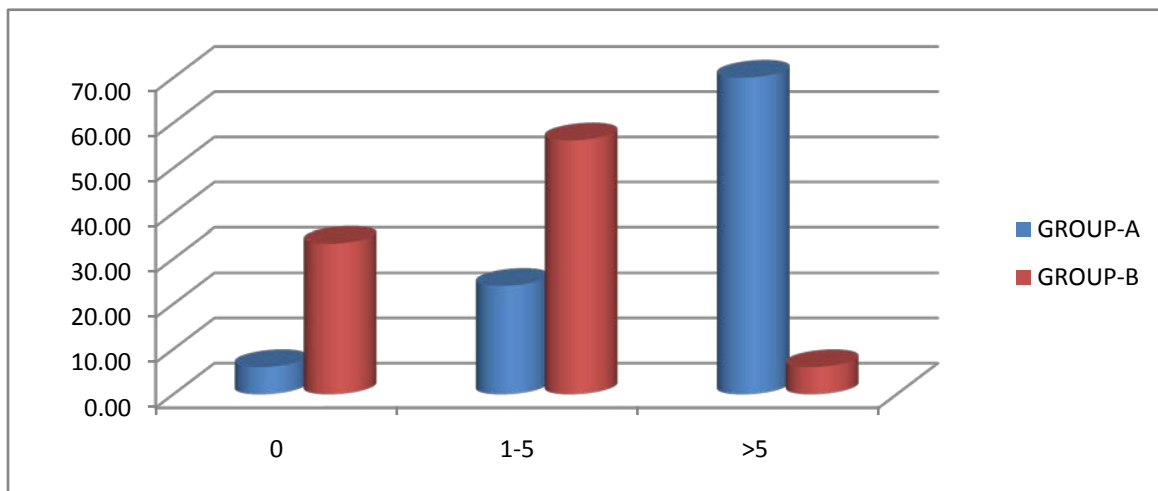
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In the present study, we found that many of the patients were suffering with paranoid schizophrenia than the other types. Anticholinergics and vitamin supplements were the main medications added along with the antipsychotics for the patients. Combination of olanzapine and risperidone was most commonly used. Patients in the non-adherent group were hospitalized many times compared to group-B. Non-adherent patients were suffering with the disease from many years and have experienced the exacerbations greater when compared to dose titration group patients. Compared to first generation antipsychotics, second generation antipsychotic drugs were most commonly prescribed.

**Graph-5 : Medications Added to the Patients**

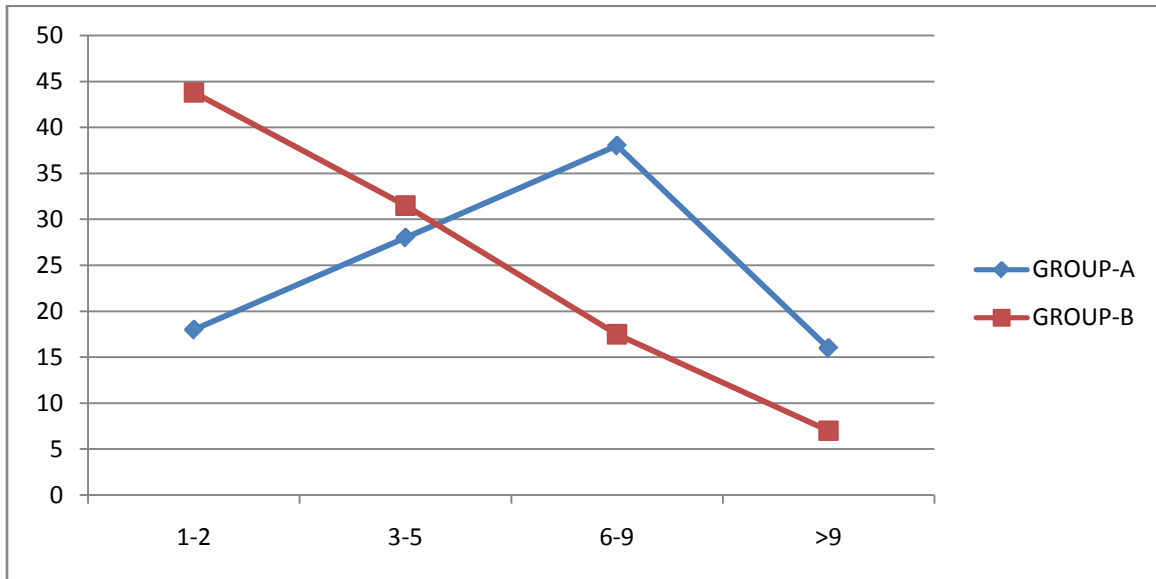


**Graph - 6 : Number of Hospitalizations for Schizophrenia in General Hospital Per 107 Patients**



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**Graph-7 : Number of Exacerbations Observed in Study Population**



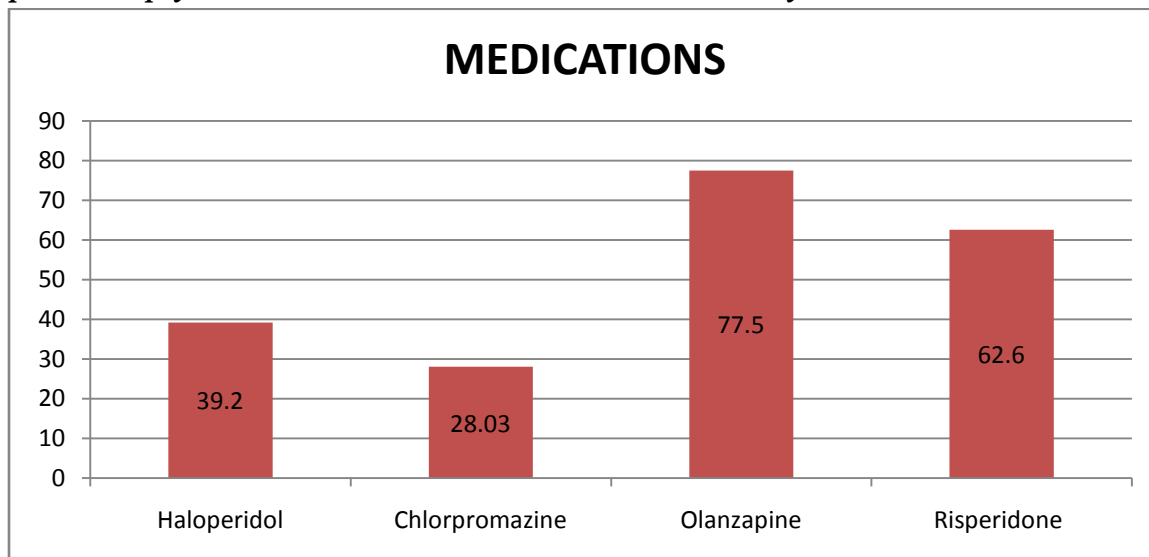
**Table-7: Antipsychotic Medication Monitored Across the Study Period**

MEDICATION	PATIENTS (n=107)	
	N	(%)
Haloperidol	42	39.2%
Chlorpromazine	30	28.03%
Olanzapine	83	77.5%
Risperidone	67	62.6%

Percentages do not sum up to 100% because of polypharmacy and change of medication during the study period.

This table suggest that the majority (77.5%) of the patients were on the medication olanzapine

**Graph-8: Antipsychotic Medication Monitored Across the Study Period**



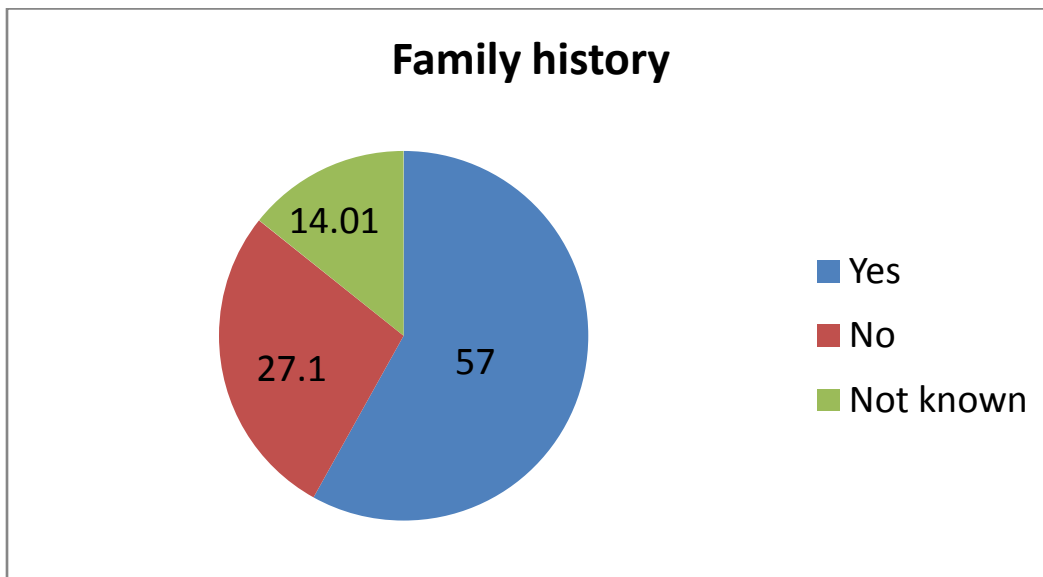
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**Table-8: Family History of Study Population**

<b>FAMILY HISTORY</b>	<b>NUMBER OF PATIENTS (PERCENTAGE)</b>
Yes	61 (57%)
No	29 (27.10%)
Not known	15 (14.01%)
Total	107

In the present study, it was found that Almost 57% of the subjects have the family history of schizophrenia.

**Graph-9: Family History of Study Population**



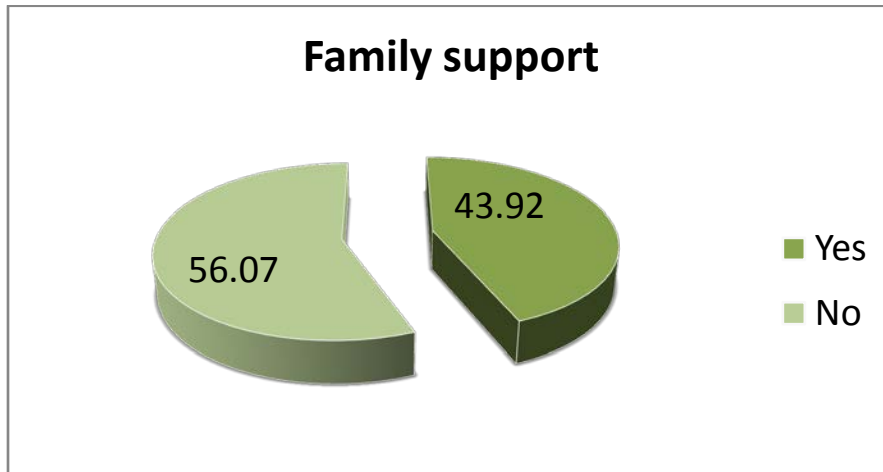
**Table-9: Family Support of Study Population**

<b>FAMILY SUPPORT</b>	<b>NUMBER OF PATIENTS (PERCENTAGE)</b>
Yes	47 (43.92%)
No	60 (56.07%)
Total	107

From the study, it was observed that 56.07% of the study population do not have the support from their families.

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**Graph-10: Family Support of Study Population**



**Table-10: Attitude of Patient towards Medication**

DAI	COMPLIANT	NON-COMPLIANT
Positive domain	6.86 ± 3.0	2.98 ±1.43
Negative domain	2.5 ±1.44	7.5 ±3.67
Total score	6.08±2.02	4.98±2.17

Analysis of the relationship between subjective attitude and reasons for compliance only revealed a direct relationship between the score obtained on the DAI Scale and the compliance subscale of ROMI.

The DAI is one of the most common measures used to assess attitude or adherence rating scales. positive attitude towards medication ,as measured by the DAI is associated with significantly higher adherence rates. The attitude towards treatment in patients has been additionally related to factors such as employment status ,duration of untreated schizophrenia, disease severity ,treatment response, hospital profile and therapeutic alliance with the medical staff.

**Table-11: Various Reasons of Compliance Using Romi Scale**

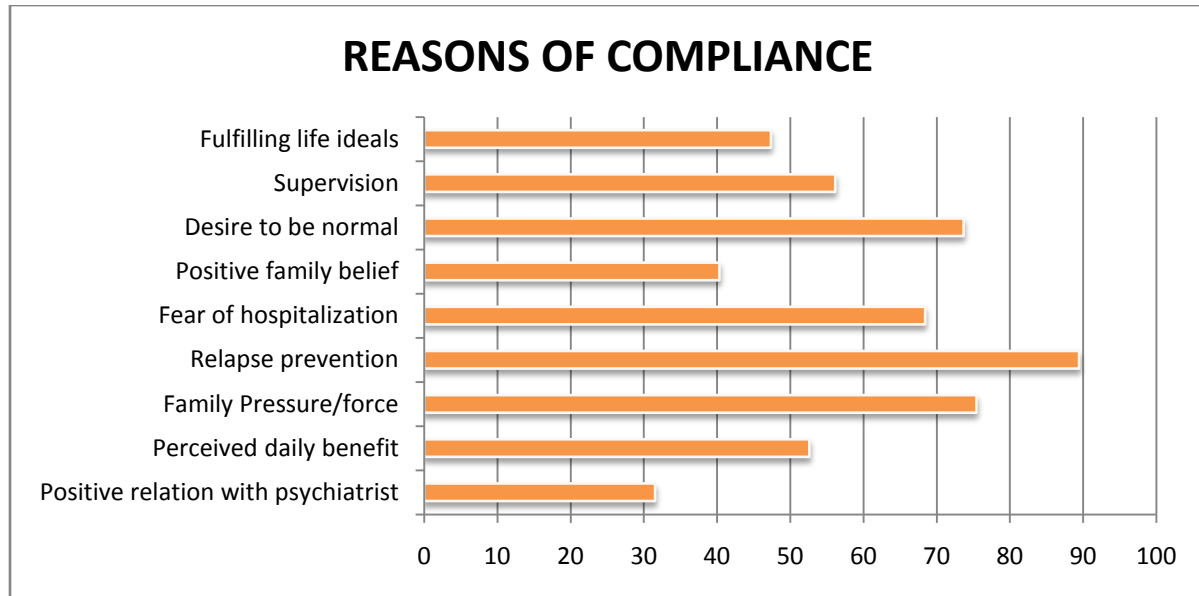
REASONS	MALES (N=30)	FEMALES (N=27)	TOTAL (%)
Positive relation with psychiatrist	7	11	18(31.57)
Perceived daily benefit	14	16	30 (52.63)
Family Pressure/force	21	22	43 (75.43)
Relapse prevention	27	24	51(89.47)
Fear of hospitalization	18	21	39(68.42)
Positive family belief	12	11	23(40.35)
Desire to be normal	23	19.	42 (73.68)
Supervision	17	15	32(56.14)
Fulfilling life ideals	14	13	27(47.36)



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The main reason stated by the patient to be compliant was to prevent the relapses followed by family pressure.

**Graph-11: Various Reasons of Compliance**



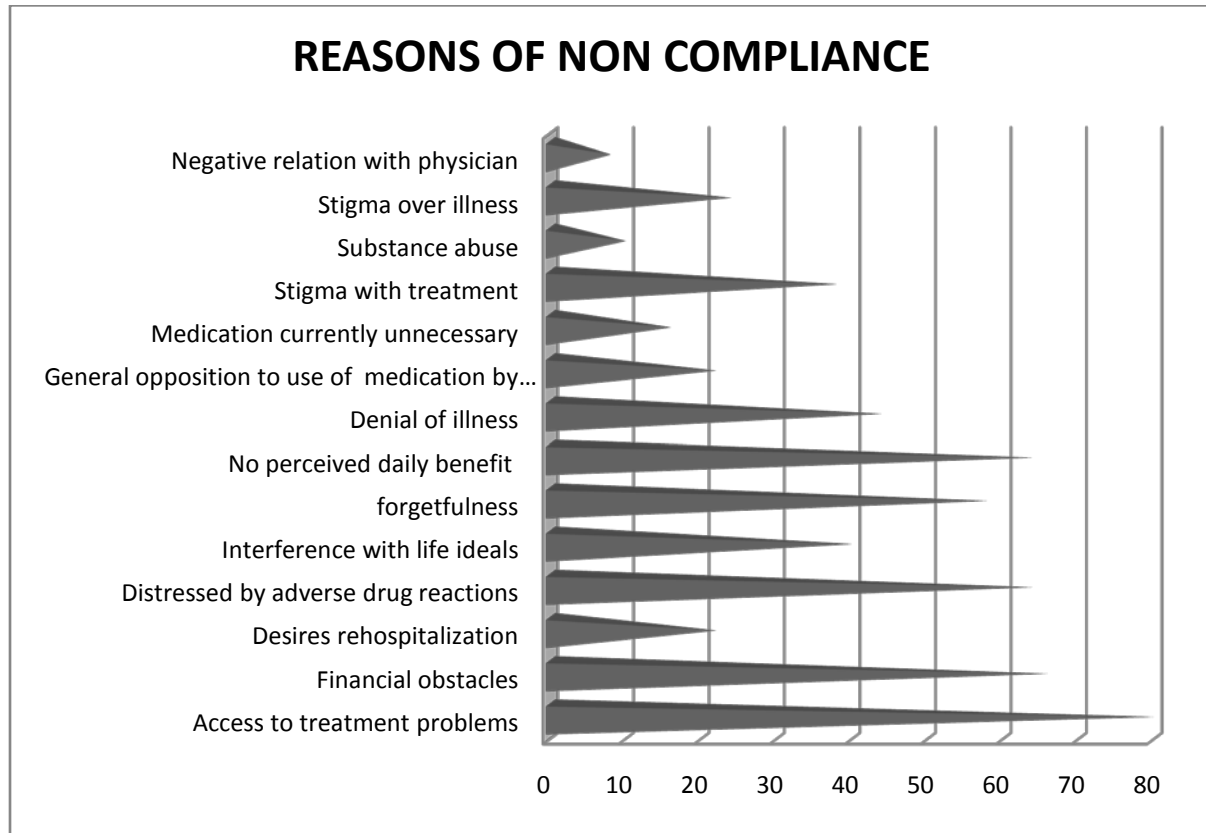
**Table-12: Various Reasons of Non Compliance Using Romi Scale**

REASONS	MALES (N=24)	FEMALES (N=26)	TOTAL (%)
Access to treatment problems	19	21	40(80%)
Financial obstacles	15	18	33(66%)
Desires rehospitalization	4	7	11(22%)
Distressed by adverse drug reactions	17	15	32(64%)
Interference with life ideals	11	9	20(40%)
Forgetfulness	13	16	29(58%)
No perceived daily benefit	18	14	32(64%)
Denial of illness	12	10	22(44%)
General opposition to use of medication by friends/family	7	4	11(22%)
Medication currently unnecessary	5	3	8(16%)
Stigma with treatment	11	8	19(38%)
Substance abuse	4	1	5(10%)
Stigma over illness	7	5	12(24%)
Negative relation with physician	3	1	4(8%)

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80% of the patients have the difficulty in access to treatment , 66% became non-complaint because of their financial obstacles and 58% were not taking their medications due to forgetfulness.

**Graph-12: Various Reasons of Non Compliance**



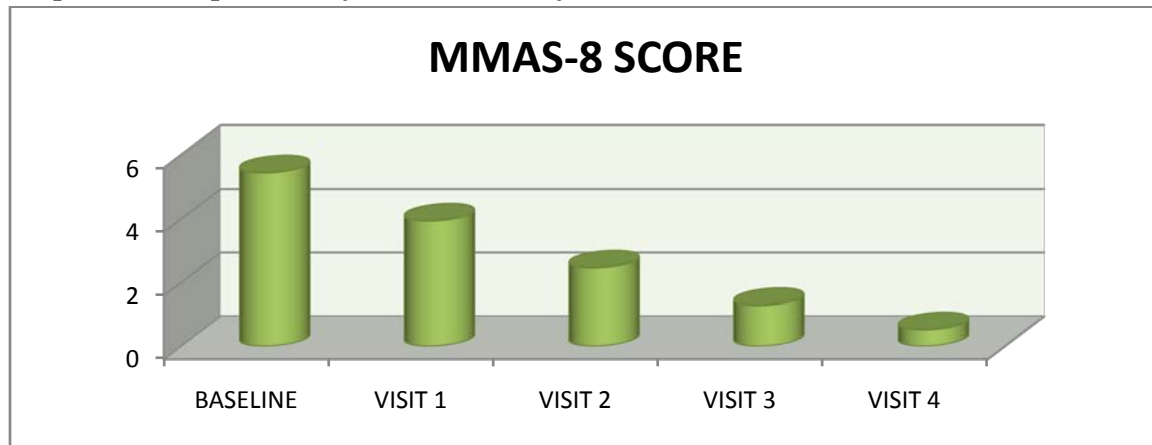
**CAUSALITY OF ADR BY NARANJO'S SCALE:** ADR'S are categorized by score in the Naranjo Adverse Drug Reaction Probability Scale. In our study, 3 definite ADR's were observed which includes sedation(57%),skin pigmentation (18%) & dystonia (33%).19 ADR's was categorized as probable which consists of events like hypotension (17%), palpitations (11%), weight gain (23%), orthostatic hypotension (15%), bleeding from rectum (5%), akathisia (24%), xerostomia(35%), vomiting(7%), dizziness(51%), constipation (38%), tremor (44%), abdominal distension (7%), galactorrhoea (8%), excessive salivation(12%), blurred vision (5%), parkinsonism (18%), hypothyroidism (7%), diabetes (8%) and somnolence (11%). 15 were observed which on assessment with naranjo's scale, categorised as possible ADR's which include headache (17%), sexual dysfunction (6%), odynophagia (4%), T.corporis infection (2%), polymenorrhoea (24%),delusion of infidelity (1%), erythroderma (3%), chestpain(14%),intertrigo (1%), burningmicturition (17%), amenorrhoea (15%), menorrhagia (4%), gastritis (7%), hypertension (13%), paronychia (3%).

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**Table-13: Comparison of Mean Scores of Mmas-8 between Visits**

ASSESSMENT PARAMETER	BASELINE	VISIT 1	VISIT 2	VISIT 3	VISIT 4
MMAS-8 SCORE	5.44 ± 1.68	3.94 ± 1.42	2.46 ± 1.32	1.28 ± 1.12	0.52 ± 0

**Graph-13: Comparison of Mean Scores of Mmas-8 between Visits**



**Table-14: Discontinuation Rates in Patients with Schizophrenia**

Reason for discontinuation	Olanzapine (n=83) N(%)	Risperidone (n=67) N(%)	Haloperidol (n=42) N(%)	Chlorpromazine (n=30) N(%)
Lack of tolerability	11(13.2%)	15(22.3%)	24(57.1%)	10(33.3%)
Lack of efficacy	7(8.43%)	13(19.4%)	5(11.9%)	3(10%)

**Table-15: Dosing Comparison of Antipsychotic Drugs in Patients with Schizophrenia from the Study**

Dose	Haloperidol	Chlorpromazine	Risperidone	Olanzapine
Dose range,mg/day	5-15 mg/day	400-1200 mg/day	2-6 mg/day	10-20 mg/day
Mean dose mg/day (total no of patients)	7.5(42)	250(30)	5(67)	15(83)
Maximum dose received (mg/day)	10	400	8	20
Number reaching maximum dose (%)	31(73.8%)	12(40%)	48(71.6%)	75(90.3%)

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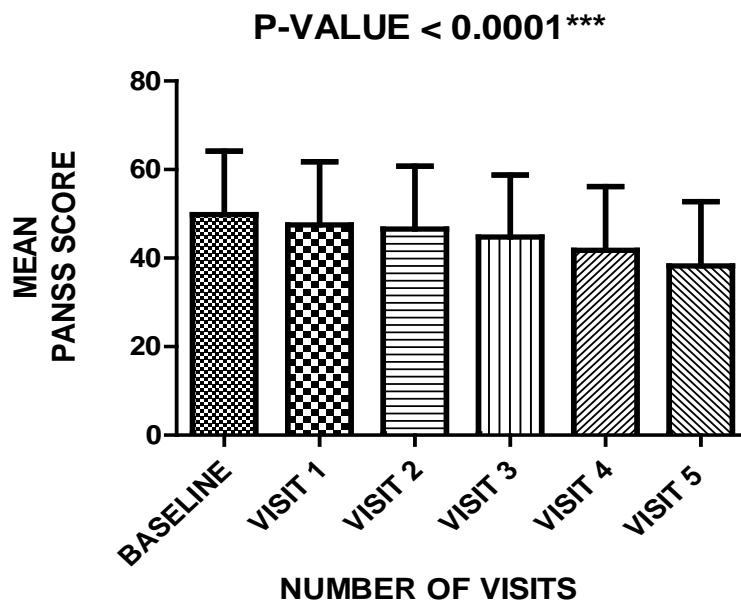
**Table-16: Initial Dose and Titration Schedule for the Schizophrenic Patients with No Complicating Condition Affecting Dosing**

ANTIPSYCHOTIC MEDICATION	USUAL STARTING DOSE (MG/DAY),RANGE	INTERVAL BETWEEN DOSE DECREASE	USUAL DOSE DECREMENT, MG
Haloperidol	10 (5-15mg)	1 month	5mg
Chlorpromazine	200 (400-1200mg)		50mg
Risperidone	4 (2-6mg)		1mg
Olanzapine	20 (10-20mg)		5mg

**Table-17: Mean Panss Positive Score, Negative Score, and General Psychopathology Score For Patients At Each Visit**

Score,mean (SD)	In treatment					
	BASELINE	VISIT 1	VISIT 2	VISIT 3	VISIT 4	VISIT 5
PANSS positive	36.28 (7.78)	33.02 (5.91)	32.68 (5.73)	30.42 (7.05)	25.18 (9.06)	23.1 (8.30)
PANSS negative	34.76 (7.20)	33.36 (6.36)	32.14 (6.16)	31.16 (4.78)	29.74 (7.53)	24.3 (8.66)
PANSS general psychopathology	78.44 (16.50)	76.02 (14.30)	74.9 (13.24)	72.78 (15.09)	70.42 (15.78)	67.32 (10.93)

**Graph-14: Comparison of Mean Panss Score for Patients at Each Visit**



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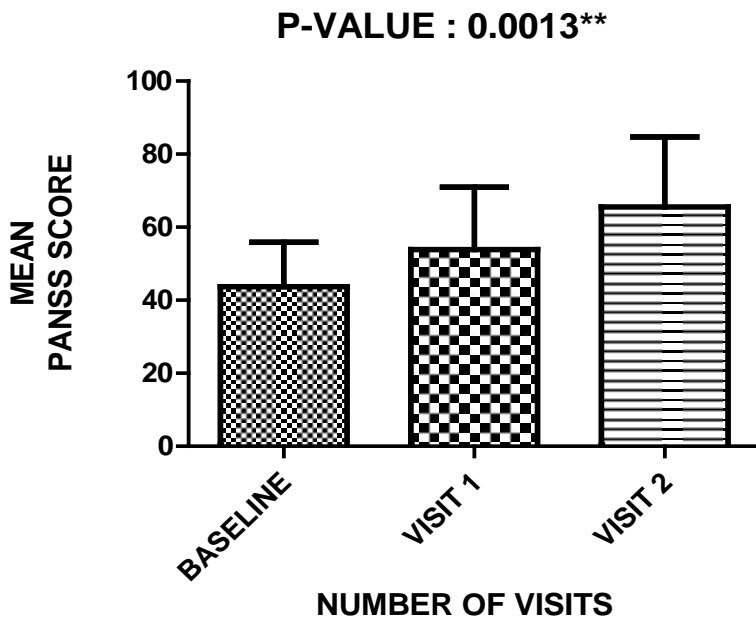
P-value was calculated by using two-way ANOVA. and the results are found to be statistically significant (P<0.0001\*\*\*)

**Table-18: Mean Panss Subscores ( Positive, Negative, General Psychopathology) for Seven Patients at Each Visit was Shown in the Table.**

Score, mean (SD)	In treatment		
	BASE LINE	VISIT 1	VISIT 2
PANSS positive	34.85(5.58)	42.14(3.38)	47.28(0.95)
PANSS negative	28.5(8.07)	31.85(7.92)	45.42(1.51)
PANSS general psychopathology	67.71(14.16)	87.57(11.34)	103.28(3.25)

As measured using the PANSS, patients condition worsen by each visits. P-value was calculated by using two-way ANOVA .and the results are found to be statistically significant(p-0.0013\*\*)

**Graph-15: Comparision of Mean Panss Score for Seven Patients at Each Visit**



**DISCUSSION**

The study is an attempt to find out the rate of non-compliance and the attitudes and reasons , it also highlights the benefits of dose titration in schizophrenic patients. Medication adherence

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plays a vital role in patients who were diagnosed with schizophrenia. Negative attitude and poor insight may lead to development of non-adherence. Beck et al <sup>22</sup>, described a direct negative relationship between concerns regarding antipsychotic drugs and adherence and an indirect negative effect as a general disturbance regarding pharmacotherapy and adherence. The authors showed a medication effect between awareness of illness and perceived necessity of antipsychotic medication on adherence. Our study is compared with shakeel ansari et al <sup>23</sup>, for the variables affecting drug compliance in schizophrenic patients which shows 37% non compliance rate and ivatury sarath Chandra et al.,<sup>24</sup> Study shows 41.9% non compliance. Whereas our study shows high prevalence of non compliance. According to Esteban Medina et al.,<sup>25</sup> study a total of 74.4% shows compliance.

Most of the previous studies conducted at various regions of the world including India showed that substance abuse is a strong predictor of non compliance, which is a contradiction to present study. According to and Ivatury sarath Chandra et al.,<sup>24</sup> Study denial of illness was the most common reason leading to non compliance. Financial burden, lack of knowledge of illness, reduced access to treatment facilities, side effects of medication and substance abuse also stand for significant contributory reasons for non-compliance. In our study accesses to treatment problems, financial obstacles, no perceived daily benefit and forgetfulness were the main reasons for non compliance. According to rosa et al <sup>26</sup> and Loffler et al<sup>27</sup>., the reasons for non compliance is mainly “inconvenience due to side effects” and “perceived daily benefit” was the reason for compliance. Statistically significant reasons for compliance and non-compliance was found by using ROMI scale. In our study the main reason for compliance was observed were relapse prevention, desire to be normal, fear of hospitalization, supervision. Where as shakeel ansari et al <sup>23</sup>., study shows positive relation with psychiatrist and perceived daily benefit are essential in improving compliance but according to ivatury sarath Chandra et al <sup>24</sup>., The factors contributing compliance were followed by positive family belief, relapse prevention and pressure or force by the family members. The point of concern coming out of these observations that there is high prevalence of non compliance to occur over compliance which is affects the management of schizophrenia. Evaluation of reasons for non compliance using the ROMI scale is mainly highlighted through five important reasons. They include

- a) Patients who do not comply are likely to feel that their medications do not help as opposed to patients who comply with neuroleptics and are more likely to report feeling better.
- b) Poor relationship with psychiatrist leading to poor compliance.
- c) Poor insight was another factor.
- d) The exponential factor is stigma related to schizophrenia.
- e) The presence of any other effect of drug (eg; ADR, side effects) was also a factor for non-compliance.

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Moreover, the Clinical Antipsychotic Trials of Interventions Effectiveness (CATIE) study found that the degree of clinical improvement due to treatment and patient quality of life are factors also related to the attitude towards medication.

In our study there is no much difference in compliance among males and females in two groups which is more likely with the study ivatury sarath Chandra et al <sup>24</sup> and concurrent with the previous findings diaz et al <sup>28</sup>.

Better compliance in employed population can be because patients suffering with schizophrenia have less chances of getting employed, which may leads to deterioration of the financial status of the family, which makes more prone to quit the course of medication. The difference was found to be statistically significant which is similar to Ivatury Sarath Chandra et al <sup>93</sup> Study. It is also mostly nearer to the findings of Atwood et al <sup>29</sup>.,Who, in a compilation analysis of 86 studies involving 23,796 psychiatric patients had found a positive association between unemployment and non-adherence indicating financially poor affordable capacity in this population.

The mean age of onset of illness in compliant and non-compliant group ( $23.5 \pm 7.7$ ) . The interruption that could be made for early onset of psychosis is prolong duration of the treatment which may leads to increased number of side effects leading to non-compliance. The other factors for burnt out syndrome in caregivers and increased financial burden with prolonged duration of illness in patients with early onset of psychosis. These findings are nearly to the findings of Ivatury Sarath Chandra et al <sup>24</sup> .the Balikci et al <sup>30</sup> study which is a 2 yr prospective study found there was a high degree of noncompliance in patients with early onset of psychosis. The DAI is one of the most common measures used to assess attitude or adherence rating scales. Positive attitude towards medication, as measured by the DAI is associated with significantly higher adherence rates. The attitude towards treatment in patients has been additionally related to factors such as employment status ,duration of untreated schizophrenia, disease severity, treatment response, hospital profile and therapeutic alliance with the medical staff.

The overall mean score of DAI was higher ( $6.08 \pm 2.02$ ) in patients who were compliant than the non-compliant group. These findings were similar to that of Ivatury Sarath Chandra et al <sup>24</sup> Study. This may be due to the high positive belief in treatment and medication of family members might be the reasons for the positive attitude of patient and compliance towards medication. The DAI is one of the most common measures used to assess attitude or adherence rating scales. Positive attitude towards medication, as measured by the DAI, was associated with significantly higher adherence rates. The attitude towards treatment in outpatient has been additionally related to factors, such as employment status, duration of untreated psychosis (DUP). disease severity, treatment response, hospital profile, and therapeutic alliance with the medical staff. Kyoko higashi et al <sup>31</sup>., Dose titration can also be problematic in clinical practice in terms of optimal number of dosage decrease steps and the time required to reach adequate efficacy and provide the required therapeutic effect. However, different titration schedules may be needed for drugs depending upon respective half-lives. Adequate dosing varies from patient

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to patient and depends upon severity and chronicity of illness, susceptibility to adverse effects. Switching of drugs is also done depending upon the patient response.

When comparing the results regarding the duration of illness in years, it was found that in Cecilia Brain<sup>83</sup> et al study, 13 are having duration of illness between 0-5, 20 are having between 6-10, 16 are having the schizophrenia from the past 11-15 years and majority of the study participants i.e., 63 are suffering with the illness from more than 15 years. Whereas in current study, 23 are having duration of illness between 0-5, 35 are having between 6-10, 18 are having the schizophrenia from the past 11-15 years and majority of the study participants i.e., 31 are suffering with the illness from more than 15 years.

In our study, 34 are having 1-2 exacerbations, 32 have experienced 3-5 exacerbations, 29 with 6-9 and 12 subjects are having >9 exacerbations. These results are correlated with the Cecilia Brain<sup>83</sup> et al study in which it was observed that 14 are having 1-2, 33 experienced 3-5, 25 suffer with 6-9 and 40 subjects have experienced >9 exacerbations.

The Mean PANSS subscores (positive, negative, general psychopathology) in the present study was compared with the results of Haya Ascher-Svanum<sup>32</sup> et al study and is found that the illness severity had improved.

The Cecilia Brain<sup>33</sup> et al study shows a mean of 14 subjects (n=81) in the adherent group and 2 subjects in the non-adherent group (n=31) were using first-generation antipsychotics. But in present study 72% of the non-adherent patients and 63.15% subjects in adherent group were on first-generation antipsychotics. In the Cecilia Brain<sup>33</sup> et al study, out of 112 outpatients, 16.1% have paranoid schizophrenia and 41.1% have undifferentiated schizophrenia, 9.8% residual schizophrenia. In our study 64%, 2% and 4% subjects in Group-A were suffering with paranoid, undifferentiated and residual schizophrenia respectively. And 71.92%, 5.26% and 1.75% were suffering with paranoid, undifferentiated and residual schizophrenia in Group-B. In present study, 39.2% of subjects were using haloperidol and 28.03% were on medication chlorpromazine and 77.5% were on olanzapine and 62.6% were taking risperidone. The results were compared to the Cecilia Brain<sup>33</sup> et al study (n=112) in which the antipsychotic medications were monitored across the study period and was found that number of patients taking haloperidol was 5.4%, olanzapine-21.4% and risperidone-15.2%. Total number of patients on olanzapine and risperidone who received the maximum doses were 90.3% and 71.6% is compared with CATIE study (Peter F. Buckley<sup>34</sup> et al) which shows 40% of patients are receiving the maximum dose for both the drugs. Discontinuation rates in our study are compared with the CATIE (the clinical antipsychotic trials of intervention effectiveness) Study. The discontinuation rate of olanzapine because of lack of tolerability was found to be 13.2% which shows decreased percentage (19%) when compared to CATIE study. The discontinuation rate of risperidone was 22.3% which shows increased percentage (10%) when compared to CATIE study. In our study, the discontinuation rate because of lack of efficacy of olanzapine and risperidone was found to be



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8.43% and 19.4% respectively, which was compared to CATIE study in which olanzapine was discontinued at a rate of 15% and risperidone at 27%.

### CONCLUSION

By assessing the reasons for non-compliance, administering the tailored doses and providing the patient education, rational therapy with increased safety and efficacy was provided to the individual patients which increases the patients quality of life and prevents the risk of relapse as well as higher economic costs for patient care.

Compliance is highly influenced by benefit with medications and positive relationship with the psychiatrists. Therefore psychiatrists should maintain a good therapeutic relationship with the schizophrenic patients.

Family pressure on the subjects for taking medicines increases compliance suggesting a need for psychoeducation to family members.

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