



Adherence to Antipsychotic Medications and Its Determinants Among Patients with Schizophrenia at a Neuropsychiatric Hospital in Maiduguri, North East Nigeria

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Abstract

Title: Adherence to antipsychotic medications and its determinants among patients with schizophrenia at a federal neuropsychiatric hospital in Maiduguri, North east Nigeria.

Introduction: Adherence to long term treatment of schizophrenia is a huge challenge to clinicians, primarily because of cognitive impairment, depression, lack of insight and social isolation. Medication adherence reduces symptoms, lower incidence of relapse and re-hospitalization and improves patient social functioning in society. Factors that influence adherence vary widely it is important to understand factors that influence it so as to guide in the design of initiatives that support adherence. **Objectives:** To evaluate antipsychotic prescription pattern, assess level of adherence and determine factors that influence adherence. **Methods:** A total of 360 patient medical records were reviewed and relevant data were extracted. A 14-item pretested questionnaire and Morisky medication adherence scale (MMAS-8) were self-administered on patients. **Data analysis:** Data were entered into SPSS 20 for descriptive and inferential statistics. Factor analysis used principal component analysis, varimax rotation with Keiser Meyer-Olkin normalization and only items with factors loadings greater than 0.4 were used for further analysis. P values ≤ 0.05 was considered statistically significant. **Results/Discussion:** Typical antipsychotic Medications were still widely prescribed in the hospital. Most patients received Trifluoperazine Monotherapy While typical accounted for about 10%. This prescription pattern is not consistent with current recommendations that atypicals should be the first line antipsychotic drug. Majority of patients reported low level of adherence (70%) and it's no surprise that medication related factors was one of the reasons for low adherence. **Conclusion:** It is important to emphasize the use of atypical antipsychotics because of their benefits of lower incidence of side effects and improvement in both negative and positive symptoms. Counseling and medication adherence support initiatives should be routinely practiced

Keywords

Schizophrenia, Adherence, Antipsychotics, Determinants, Prescription pattern.

INTRODUCTION:

Adherence to long term medications has been a huge challenge in the treatment of most chronic diseases/disorders. This is particularly more evident in mental disorders such as schizophrenia primarily due to lack of insight, cognitive impairment, depression and social isolation commonly associated the disorder. Evaluation of adherence in long term medication therapy varies widely depending on the disease, patient population and the method used in assessment¹. Medication adherence is defined as the “extent to which a patient’s medication taking matches that agreed with the prescriber². In mental disorders nonadherence is particularly pervasive compared to other chronic diseases³. The course and clinical outcomes of therapy in mental disorders is far from predictable and evidence of high inter-patient variability is well established⁴.

While some patients with schizophrenia may make full recovery often requiring little or no medication, the prognosis of others can be generally poor. Relapse rate is high and positive outcomes of therapy is often less than 50%; some reports have suggested that up to 27% of patients on antipsychotic therapy had poor outcomes⁵. While there is ample evidence that antipsychotic medication significantly reduces symptoms, lower incidence of relapse and reduces the likelihood of hospitalization; nonadherence threatens the achievement of these desirable outcomes⁶.

The rates of non-adherence associated with antipsychotic medications vary widely and results depend on assessment method, there have been suggestions that most methods tend to underestimate levels of non-adherence⁷. In a systematic review of 39 studies and using a 75% mark for adherence, rate typically averages around 41 % and may rise to 50% when rigorous assessment methods is used⁸.

There is high social and economic cost of non-adherence in areas of re-hospitalization, violence, substance abuse, aggression, persistence of symptoms and overall low quality of life. Several studies have established a link between non adherence and risk of suicide attempts, high rates of relapse and re-hospitalization⁹, self-harm¹⁰ and low quality of life¹¹ Non adherence whether intentional or unintentional can be attributed to a number of factors which includes patient related factors^{12,13}, care giver factors^{14,15}, disease factors^{16,17}, physician / service factors^{18,19,20,21} as well as stigma and provider attitudes²².

There have been suggestions that the shift from typical to atypical antipsychotics may improve

adherence due to reduced extra-pyramidal side effects and better performance in improving both negative and positive symptoms^{23,24}. While a number of studies reported that patients on atypical antipsychotics continued medication significantly longer; there was no significant difference in long term adherence levels^{25,26,27}.

Influence of socio-demographic factors on adherence have received mixed results; while some studies reported that age and gender influence adherence and that women are more adherent than men²⁸; others suggested that younger and elderly patients are likely to be less adherent²⁹. Some other studies concluded that demographic variables are not consistent predictors of adherence^{30,31}. Other common influencers of adherence reported in literature included cost of care³², family support³³ and side effects of medications.

Adherence to antipsychotic medication therapy varies widely among patients, so also are factors that negatively influence it. It is therefore critical to identify the most important negative influencers so that adherence support initiatives can be targeted to help patients maintain acceptable level of adherence.

Objectives

- To evaluate antipsychotic prescription pattern
- To assess the level of adherence to medication treatment
- To investigate influence of demographic factors on adherence

METHODS:

Setting: The study was carried out in the outpatient department of Federal Neuropsychiatric Hospital Maiduguri. It is a 200-bed hospital that offers comprehensive care service to psychiatric patients and also serves as a referral hospital to other health care facilities in the region.

Study Design:

This was a cross sectional retrospective study that used data from medical record of patients and self-administered questionnaire.

Sample Size / Sampling: A sample size of 360 was Determined using Taro Yamane formula and sampling was by systematic random sampling.

Data Collection: The medication records used for this study covered the period January 2016 – October 2017. Patients’ demographic data, diagnosis, medications, and other relevant data were extracted into specially designed forms. Patients with co-morbidities were excluded. **Questionnaire design / administration:** A fourteen item questionnaire was designed and pretested using response from twenty-

five stable patients with schizophrenia [Cronbach alpha = 0.804]. The responses used in determination of internal consistency of instrument were excluded from final analysis. The questionnaire and Morisky medication adherence scale [MMAS -8] were self-administered on randomly selected stable patients after informed consent have been obtained orally. The questionnaire which was to determine factors influencing adherence was on a five-point Likert scale, responses ranging from strongly agree to strongly disagree. Patients were to select the option that best reflect their opinion.

Data Analysis: The data was collected and entered into SPSS 20 for descriptive and inferential statistics. Factor analysis used principal component analysis with varimax rotation and factor loadings less than 0.4 were suppressed. Three components were extracted and items with high factor loading were used for further analysis. P values ≤ 0.05 was considered statistically significant.

RESULTS:

The result showed that there were more males [54.2%] compared to females [45.8%] and Their significant difference in their mean age. Most patients were on one antipsychotic medication with most attending the hospital at an average of 3 times per year [Table 1]. Majority of patients were either stay at home women, unemployed and farmers or in petty business. Interestingly students accounted for a significant percentage (11.9%) of patients [Figure 1]. Most patients were either married [57.9%] or single [29.7%] [Figure 2]. The most prescribed antipsychotic drugs were Trifluoperazine and Trifluoperazine + Chlorpromazine combination accounting for 80.9% of all prescriptions. Atypical antipsychotic drugs like Olanzapine and Risperidone accounted for 11.1% of prescriptions. Typical antipsychotic drugs were the most widely prescribed in this hospital [Figure 3] Adherence to antipsychotic medications was largely low [70.7%] to moderate [29.3%] and non-achieved high-level adherence. This is a clear indication that serious challenges exist, and patients are unlikely to achieve positive therapeutic outcomes [Figure 4]. Factor analysis using principal component analysis with varimax rotation with Kaiser normalization extracted three components. Items in the components related to provider factors [1], medication factors [2] and patient factors [3]. High factor loading indicate that the item is a significant contribute to non-adherence. [Table 2] Medication related factor affecting adherence involve patients views of medication effectiveness, feelings and perception of wellness.

So, feelings of being unwell or unhappy with drugs and disappointment with outcome contributed to non-adherence. There is no significant difference between males and female patients [Table 3]. The healthcare facility relationship with patients in areas of poor information about medications causes them to result to herbal remedies. Probably the interaction with the hospital and caregivers is cumbersome, frustrating and confusing for patients to understand the purpose of treatment and their roles in the care process [Table 4]. The inability of patients to integrate medication routine into work and social lifestyles contributed to non-adherence. This is in addition to difficulties in obtaining medication and complex instructions. There is no significant difference between males and females as to the influence of these factors on non-adherence [Table 5]

DISCUSSION:

Schizophrenia is a lifelong disabling disorder with sever social, economic and psychological implications for patients and society. Treatment offer hope the benefits of therapy will enable them function in the community and ultimately improve their quality of life and ability take care of themselves. This study result showed that males have a slightly higher prevalence of schizophrenia than females and majority of patients were young. The finding is similar to other previous studies^{34,35,36}, though other reports suggested that significant difference in gender-based prevalence is doubtful³⁷. The high number of housewives with schizophrenia found in this study may be related to the trauma of ongoing violent insurgency in this region. It may also be related to marital problems and stress arising from displacement from community life into camps. Antipsychotic drugs prescription pattern indicated that older generation antipsychotics drugs were the most prescribed similar to previous studies^{38,39}. The most widely prescribed antipsychotics included Trifluoperazine, Haloperidol while chlorpromazine accounted for less than 10% of prescriptions. There has been consensus based on results from randomized clinical trials that patients with psychotic disorders should be given newer atypical antipsychotics as first line drug^{40,41,42}, because they are associated with reduced hospitalization⁴³, shortened length of hospital admission⁴⁴, improvement in both positive and negative symptoms and overall reduction in healthcare costs⁴⁵. The use of typical antipsychotic drugs may be due to low cost and ready availability compared to

atypical which are not generally affordable by most patients.

High level adherence is required for long term control of symptoms and optimization of therapy outcomes, so where adherence is sub-optimal there is increased risk of relapse, re-hospitalization, poor symptomatic relief, poor prognosis and overall increase in cost of medical care. Majority of patients in this study had either low or moderate adherence with those in the low category accounting for the overwhelming percentage. This result is comparable to several previous studies^{36,46,47}.

Factors influencing adherence are common among patients on long term therapies and schizophrenia is no exception; low medication adherence in schizophrenia is of great concern because of cognitive impairment and lack of insight. The low-level adherence observed in this study is related to medication, patient and provider factors which are similar to earlier studies^{48,49}. Conventional antipsychotics widely used in this study are known to have severe side effects which tend to discourage patients from adherence. Adherence is reported to be better with newer generation atypical antipsychotics because of tolerable side effects compared to older generation and patients report better quality of life^{50,51}. So the widespread prescription of typical antipsychotics may be denying patients the many positive benefits of newer generation drugs one of which is lower incidence and severity of side effects.

Extra-pyramidal side effects, tardive dyskinesia, dystonias and anti-cholinergic side effects sometimes make patients on typicals to feel that there is no improvement which often makes them to voluntarily stop treatment. The low adherence level found in this study is in contrast to reports that adherence is moderately higher in patients receiving atypical antipsychotics⁴⁸, though differences between typical and atypical on long term therapy are doubtful⁵².

Patient and provider related factors have been shown to affect adherence among patients with

schizophrenia, which is similar to reports of earlier studies^{13,49,53}. These studies noted that patient factors such as level of cognitive functioning, age, ethnicity and degree of insight affect adherence. Similarly, provider and system factors such as patient –caregiver relationship, information, proper assessment and availability of adherence support programs influences level of adherence^{54,55}. Sometimes provider misconceptions that disclosure of side effects may lead to non-adherence is unfounded; it makes patients to have wrong expectations in terms of onset of therapeutic effect, severity of side effects and perceived ineffectiveness of drugs. Furthermore, prescription of drugs that is either unaffordable or unavailable pose challenges to adherence particularly in poor resource settings. When patients become clinically stable, they tend to either forget or are unable to take medication regularly due to interference with work and social lifestyles. Involvement of family members is critical to helping patients adhere to treatment.

CONCLUSION:

The result of this study further confirms previous reports of endemic low level of adherence among patients with schizophrenia. While typical antipsychotic drugs may contribute to non-adherence due to intolerable side effects, patient and provider related factors appear to significantly contribute to the low-level adherence in this study. There is no gender-based difference in the factors contributing to non-adherence. In order to improve adherence, multi-component initiatives are required with focus on patients, facility and its systems and increase in prescriptions of atypical antipsychotic medications.

Competing interests – None

Ethical approval:

Ethical approval was obtained from research ethics committee of federal neuropsychiatric hospital Maiduguri, Nigeria.

Table 1: Patient characteristics

	Male	Female	P value
Gender	54.2%	45.8%	-
Age	35.7±17.3	36.9±16.5	0.548
Number of hospital visit	3.2±2.9	3.1±2.6	0.978
Number of drugs/prescriptions	2.2±0.7	2.3±0.7	0.508
Number of antipsychotic drug/prescriptions	0.9±0.6	1.0±0.6	0.081

Table 2: Determinants of adherence Rotated Component Matrix

Items	Component		
	1	2	3
It is difficult for me to take my medicines when away from home		.550	
I am always busy with work		.521	
Sometimes I forget to take my medications		.694	
There are too many medications to take			.501
I stopped taking my medications when I use herbal remedies			.508
When I take the drugs, I feel unwell	.792		
Medication information I receive is not adequate			.795
I stopped taking my medications when I feel okay	.658		
I generally do not feel happy taking the medicine(s)	.780		
I have not seen the benefit of the medicine(s)	.649		
The medicines are difficult to find		.524	
The instructions for medicine use are too complex for me		.621	

Extraction Method: Principal Component Analysis (KMO = 0.875) Varimax with Kaiser Normalization.

Table 3: Medication related factors

	F	Male	Female	P-Value
1. When I take my drug, I feel unwell	0.792	3.15±1.19	3.14±1.08	0.933
2. I stop taking my medication when I feel okay	0.658	3.45±1.04	3.41±1.03	0.733
3. I generally do not feel happy taking the medicine	0.780	3.04±1.05	3.07±1.02	0.860
4. I have not seen the benefit of the medication	0.649	3.80±1.21	3.72±1.25	0.578

Table 4: Provider related factors

	F	Male	Female	P-Value
1. There are too many medicines to take	0.501	2.78±1.15	2.81±1.09	0.848
2. I stopped taking the medication when I used herbal remedies	0.508	3.92±0.98	3.88±0.98	0.762
3. Medication information I received is not adequate	0.795	3.89±0.91	3.70±0.39	0.099

Table 5: Patient related factors

	F	Male	Female	P-Value
It is difficult for me to take my medication when away from home	0.550	3.32±1.19	3.29±1.11	0.838
I am always busy with work	0.521	3.20±0.81	3.18±0.88	0.88
Sometimes I forget to take my medication	0.694	2.79±1.11	3.00±1.14	0.134
The medications are difficult to find	0.524	3.50±0.98	3.41±1.01	0.443
The instruction for medications used are too complex for me	0.621	3.82±0.82	3.79±0.84	0.805

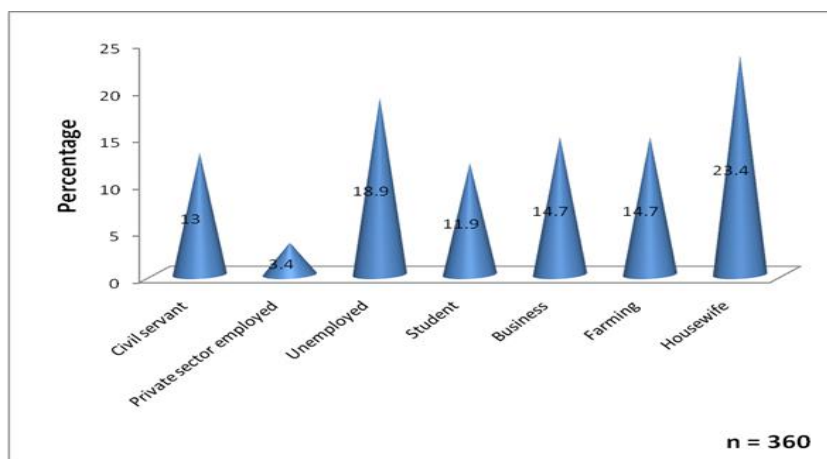


Figure 1: Occupation

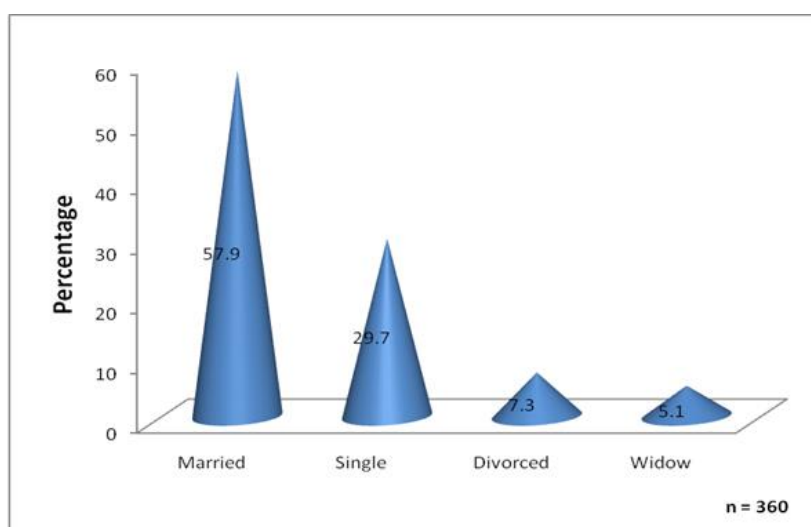


Figure 2: Marital status

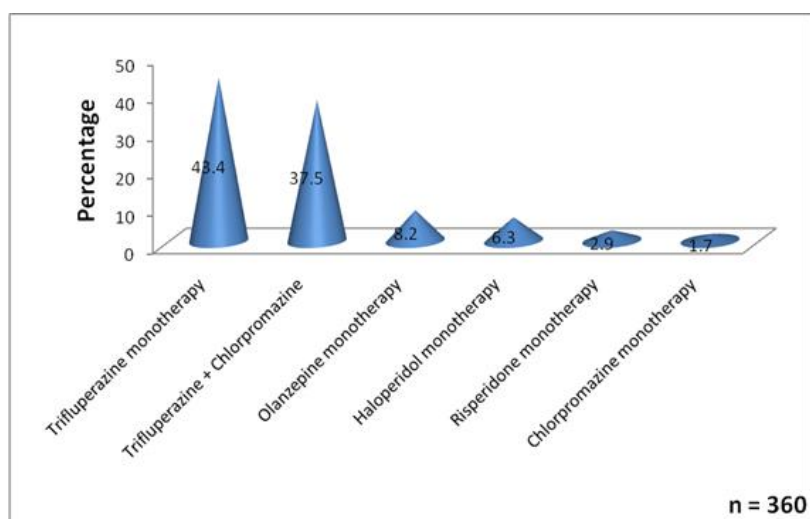


Figure 3: Antipsychotic drug prescription

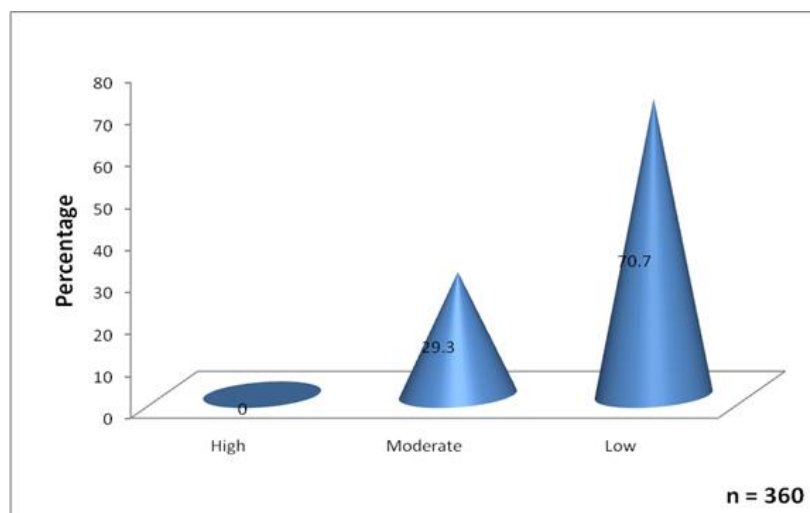


Figure 4: Adherence to antipsychotic medications

REFERENCES

- National Institute for health and clinical excellence. Medicines adherence involving patients in decisions about prescribing medicine and supporting adherence. January 2009. NICE clinical guideline 76. <http://www.nice.org.uk/guidance/CG76>
- World Health Organization. Adherence to long-term therapies; evidence for action. Geneva Switzerland. WHO 2003. <http://www.who.int/publications/2003/9241545992.pdf>
- Cramer JA, Rosenheck R. Compliance with medication regimens for mental and physical disorders. *Psychiatr Serv* 1998; 49: 196 – 201
- Ram R, Bromet EJ, Eaton WW, Pato C, Schwartz JE. The natural course of schizophrenia; a review of full class admission studies. *Schizophr Bull* 1992;18: 185 – 207
- Menezes NM, Arenovich T, Zipursky RB. A systematic review of longitudinal outcome studies of first-class episode of psychosis. *Psychol Med* 2006; 36: 1349 – 1362
- Leucht S, Tardy M, Komossa K, Heres S, Kissling W, Davis JM. Antipsychotic drugs versus placebo for relapse prevention and schizophrenia; a systematic review and meta-analysis. *Lancet* 2012; 379: 2063 – 2071
- Velligan DI, Lam YWF, Glahn DC, Barrett JA, Maples NJ, Ereshefsky L, Miller AL. Defining and assessing adherence to oral antipsychotics: a review of the literature. *Schizophr Bull* 2006; 32(4): 724 –742
- Lacro JP, Dunn LB, Dolder CR, Leckband SG, Jeste DV. Prevalence of and risk factors for medication non-adherence in patients with schizophrenia; a comprehensive review of literature. *J Clin Psychiatr* 2002; 63: 892 - 909
- Novich D, Haro DM, Suarez D, Perez V, Dittmann RW, Haddad PM. Predictors and clinical consequences of non-adherence with antipsychotic medications in the outpatient treatment of schizophrenia. *Psychiatr Res* 2010; 176: 109 – 113
- Herings RM, Erkens JA. Increased suicide attempt rate among patients interrupting use of atypical antipsychotics. *Pharmacoepidemiol Drug Safety* 2003; 12: 423 – 424
- Hayhurst KP, Drake RJ, Massie JA, Dunn G, Barnes TRE, Jones PB, Lewis SW. Improved quality of life over one year is associated with improved adherence in patients with schizophrenia. *Eur Psychiatr* 2014; 29(3): 191 – 196
- Yang J, Ko YH, Paik JW, Lee MS, Han C, Joe SH, Jung IK, Jung HG, Kim SH. Symptoms severity and attitudes towards medication: Impacts on adherence in outpatients with schizophrenia. *Schizophr Res* 2012; 134(2-3): 226 – 231
- Fenton WS, Blyler CR, Heinssen RK. Determinants of medication compliance in schizophrenia; empirical and clinical findings. *Schizophr Res* 1997; 23: 637 – 651
- Liu-Seifert H, Osuntokun OO, Feldman PD. Factors associated with adherence to treatment with Olanzapine and other atypical antipsychotic medication in patients with schizophrenia. *Compr Psychiatry* 2012; 53: 107 – 115
- de Vries ST, Keers JC, Visser R, ZeeuwDk, Haijer-Ruskamp FM, Voorham J, Denig P. Medication beliefs, treatment complexity and non-adherence to different drug classes in patients with type 2 diabetes. *J Psychosom Res* 2014; 76(2): 134 – 138
- Acosta F, Bosch E, Sarmiento G, Juanes N, Caballero-Hidalgo A, Mayans T. Evaluation of non-compliance in schizophrenic patients using electronic monitoring (MEMS) and its relationship to socio-demographic, clinical and psychopathological variables. *Schizophr Res* 2009; 107(2-3): 213 – 217
- Löffler W, Kilian R, Toumi M, Angermeyer M. Schizophrenic patients' subjective reasons for compliance and non-compliance with neuroleptic treatment. *Pharmacopsychiatry* 2003; 36: 105 – 112
- McCabe R, Bullenkamp J, Hansson L, Lauber C, Leal RM, Rossler W, Salize HJ, Svensson B, Gonzalez FT,

- Brink RVD, Wiersma D, Priebe S. Therapeutic relationship and adherence to antipsychotic medication in schizophrenia. *PlosOne* 2012. 7: e36080
19. McCabe R, Healey PG, Priebe S, Lavelle M, Dodwell D, Laugharne R, Snell A, Bremner S. Shared understanding in psychiatrist patient communication; association with treatment adherence in schizophrenia. *Patient Educ Couns* 2013. 93(1): 73 – 79
20. Zolnieriek KB, Dimatto MR. Physician communication and patient adherence to treatment: a meta-analysis. *Med Care* 2009. 47: 826 – 834
21. Haddad PM, Brain C, Scott J. Nonadherence with antipsychotic medication in schizophrenia; challenges and management strategies. *Patient related outcome measures* 2014. 5: 43 – 62
22. Teffera S, Hanlon C, Beyero T, Jacobsson L, Shibre T. Perspectives on reasons for non-adherence to medications in persons with schizophrenia in Ethiopia; a qualitative study of patients, care givers and health workers. *BMC Psychiatr* 2013. 13: 168. Doi: 10.1186/1471-244x-13-168. PMID 23773362
23. Tollefson GD, Beaseley CM Jr, Tamura RN, Tran PV, Potvin JH. Blind controlled long-term study of the comparative incidence of treatment- emergent tardive dyskinesia with Olanzapine and Haloperidol. *Am J Psychiatr* 1997. 154: 1248 – 1254
24. Jecte DV, Lacro JP, Bailey A, Rockwell E, Harris J, Caligiuri MP. Lower incidence of tardive dyskinesia with Risperidone compared to Haloperidol in older patients. *J Am Geriatr Soc* 1999. 47: 716 – 719
25. Olfson M, Mechanic D, Hansell S, Boyer CA, Walkup J, Weiden PJ. Predicting medication non - compliance after hospital discharge among patients with schizophrenia. *Psychiatr Serv* 2000. 51: 216 – 222
26. Arana GW. An overview of side effects caused by typical antipsychotics. *J ClinPsychiatr* 2000. 61: 5 – 11
27. Cabeza IG, Amador MS, Lopez CA, Chavez MG. Subjective response to antipsychotics in schizophrenic patients: clinical implications and related factors. *Schizophr Res* 2000. 41: 349 – 355
28. Lee H, Kane I, Sereika SM, Cho RY, Jolley CJ. Medication taking behaviour in young adults with schizophrenia: a pilot study. *J Psychiatr Ment Health Nursing* 2011. 18: 418 – 824
29. Oehl M, Hummer M, Fleischhacker WW. Compliance with antipsychotic treatment. *Acta Psychiatr Scand* 2000. (Suppl s407) 102: 83 – 86
30. Higashi K, Medic G, Diez T, Granstrom O, DeHert M, Littlewood KJ, Diaz T, Grainstrom O, De Hert M. Medication adherence in schizophrenia: factors influencing adherence and consequences of non – adherence: a systematic literature review. *Ther Psychopharmacol* 2013. 3(4): 200 – 218
31. Kane JM, Kishimoto T, Correll CU. Nonadherence to medication in patients with psychotic disorders; epidemiology, contributing factors and management strategies. *World Psychiatry* 2013. 12: 216 – 226
32. Taj F, Tanwir M, Aly Z, Khawajah AA, Tariq A, Syed FK et al. Factors associated with non-adherence among psychiatric patients at a tertiary care hospital, Karachi Pakistan; a questionnaire based cross sectional study. *J Pak Med Assoc* 2008. 58: 432 – 436
33. Wilk JE, West JC, Marcus SC, Countis L, Regier DS, Olfson M. Family contact and the management of medication non – adherence in schizophrenia. *Community Ment Health J* 2008. 44: 377 – 380
34. Aleman A, Kahn RS, Seltin JP. Sex differences in the risk of schizophrenia: Evidence from meta-analysis. *Arch Gen Psychiatry* 2003. 6(6): 565 – 571
35. Gureje O, Olowosegun O, Adebayo K, Stein DJ. The prevalence and profile of non-affective psychosis in the Nigerian survey of mental health and well- being. *World Psychiatry* 2010. 9: 50 – 55
36. Ibrahim AW, Yahya S, Pindar SK, Wakil MA, Garkuwa A, Sale S. Prevalence and predictors of sub-optimal medication adherence among patients with severe mental illness in a tertiary psychiatric facility in Maiduguri, North eastern Nigeria. *Pan Afr J* 2015.21: 39. 64
37. Perak J, Suvisaana J, Saarni SI et al. Lifetime prevalence of psychotic and bipolar disorder in general population. *Arch Gen Psychiatry* 2007. 64(1): 19 – 28
38. Jyothi NU, Pradeep P, Kumar MV, Sandeep K, Ramadasu P, Rao NR. Psycho-social demographic profile and drug utilization study of antipsychotics at a government medical teaching hospital. *World J Pharm and Pharm Sci* 2015. 4(9): 1036 – 1045
39. Pranab KP, Mahanjit K, Swarnamoni D. To study prescribing pattern of antipsychotic drugs in a tertiary care hospital of Assam. *Int J Pharm and Pharm Sci* 2014.6(4): 435 – 437
40. National institute of clinical excellence. Guidance on the use of newer (Atypical) antipsychotic drugs for the treatment of schizophrenia. Technology appraisal guidance 43, London NICE 2002
41. Davis JM, Chen N, Glick ID. A meta-analysis of the efficacy of second-generation antipsychotics. *Arch Gen Psychiatry* 2003. 60: 553 – 564
42. Lieberman JA. Atypical antipsychotic drugs as a first line treatment of schizophrenia; a rationale and hypothesis. *J Clin Psychiatry* 1996.57(Suppl 11): 68 – 71
43. Rabinowitz J, Lichtenberg P, Kaplan Z, Mark M, Nahon D, Davidson M. Rehospitalization rates of chronically ill schizophrenic patients discharged on a regimen of Risperidone, Olanzapine and conventional antipsychotics. *Am J Psychiatry* 2001. 158: 266 – 269
44. Finley PR, Sommer BR, Corbitt JL, Brunson GH, Lum BL. Risperidone: Clinical outcome predictors and cost effectiveness in a naturalistic setting. *Psycho pharma col Bull* 1998. 34: 75 – 81
45. Percudani M, Barbui C. Cost and outcome implication of using typical and atypical antipsychotics in ordinary practice in Italy. *J Clin Psychiatr* 2003.y 64: 1293 – 1299
46. Gurmu AE, Abdela E, Allele B, Chen E, Amogne B. Rate of non-adherence to antipsychotic medication and factors leading to non-adherence among psychiatric patients in Gondar University hospital, North east

- Ethiopia. *Advances in Psychiatry* 2014. (Article ID 475812)
47. Elicha T, Teklu A, Ali D, Solomon G, Alemayehu A. Factors associated with medication adherence among patients with schizophrenia in Makelle, Northern Ethiopia. *PlosOne* 2015. 10(3): eo120560
 48. Dolder CR, Lacro JP, Dunn LB, Jeste DV. Antipsychotic medication adherence: Is there a difference between typical and atypical agents? *Am J Psychiatry* 2002. 159: 103 – 108
 49. Valenstein M, Blow FC, Copeland LA, McCarthy JF, Zeber JE, Gillon LC, Bingham R, Stavenger T. Poor adherence among patients with schizophrenia: medication and patient factors. *Schizophrenia Bull* 2004. 30(2): 255 – 264
 50. Awad AG, Hogan TP, Voruganti LNP, Heslegrave RJ. Patient's subjective experiences on antipsychotic medications: Implications for outcome and quality of life. *Int Clin Psychopharmacol* 1995. 10(Suppl 3): 123 – 132
 51. Casey DE. The relationship of pharmacology and side effects. *J Clin Psychiatry* 1997. 58: 55 – 62
 52. Rosenheck R, Chang S, Choe Y, Cramer J, Xu W, Thomas J, Henderson W, Chainey D. Medication continuation and compliance: a comparison of patients treated with Clozapine and Haloperido. *J Clin Psychiatry* 2000. 61: 382 – 386
 53. Becker MH. Theoretical models of adherence and strategies for improving adherence. In: Shumaker, SA; Schrom EB; Ockene JR. *The handbook of health behaviour change*. New York, NY Springer Publishing, 1990. P 5 – 43
 54. Owen RR, Fisher EP, Booth BM, Cuffel BJ. Medication non - compliance and substance abuse among patients with schizophrenia. *Psychiatry Services* 1996. 47: 853 – 858
 55. Duncan JC, Rogers R. Medication compliance in patients with chronic schizophrenia: Implications for the community management of mentally disordered offenders. *J Forensic Sci* 1998. 43: 1133 – 1137