

RELAPSE EPISODES OF SCHIZOPHRENIA IN PATIENTS TREATED WITH ANTIPSYCHOTIC MEDICATIONS IN MAIDUGURI: CAUSES AND INTERVENTIONS

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ABSTRACT

Background: Relapse in schizophrenia can present with some difficulties in some settings. An understanding of factors that influence relapse episode in individuals can provide vital information to set priorities or design more effective preventive measures and institute appropriate interventions.

Objectives: The objectives were to identify factors that cause relapses among patients in the region and to quantify the extent of relapse.

Method: One hundred and thirty-four patients with schizophrenia, which comprise 72 males and 62 females with reported symptoms recurrence after first episode of the illness that lead to re-hospitalisation, were studied. Demographic data were retrieved from the patients' case notes. The causes and duration of re-occurrence as well as the interventions taken to prevent further episode were investigated.

Results: Patients who experienced first relapse episode within one month during home care were 6.7% while 11.2% of the patients reported first relapse within 2-5 months. Patients who similarly experienced first relapse within 6 months to 1 year, 1-2 years, 2-5 years, 5-10 years and those above 10 years were 20.9%, 16.4%, 24.6%, 15.7% and 4.5% respectively. Sixty-six (49.3%) patients who experienced first relapse also had second relapse while 12 (9.0%) further experienced third relapse. Several patients' related factors such as financial problems (14.9%), perceived wellness (7.5%), forgetfulness (10.5%) and breast feeding (3.0%) were identified as the cause of relapse in some patients. Lifestyle related factors like substance abuse and medication related factors such as adverse effects accounted for 17.9% and 14.2% respectively. Disease-related factors such as poor insights (6.0%) and co-morbid depression (1.5%) were other identified causes. Many patients (22.4%) linked their relapse episodes to several insurgency-related problems. Relapse due to medication non-adherence accounted for 66.4% patients. The major interventions to prevent further episodes of schizophrenia were rehabilitation (29.9%), education and counselling (26.9%), change in drug formulation (25.4%), dosage adjustment (11.9%) and change of drug (6.0%).

Conclusion: Several patients, medications, diseases and lifestyles' related factors were responsible for relapse of schizophrenia but patients' related factors such as non-adherence, substance abuse and treatment related factors particularly medication side effects were the most common causes. This study underscores the need to continually monitor drug therapy, identify factors that may cause relapse in individual and educate patients or their caregivers in order to

Keywords: Relapse, Schizophrenia, antipsychotics, substance abuse, non-compliance

INTRODUCTION

Schizophrenia is a chronic and disabling mental disorder that can relapse even after successful management of first episode. According to WHO,¹ the global burden of the illness in 2004 indicated that psychiatric disorders accounted for 3.4%. The total Disease Adjusted Life Years (DALYs) in the African region accounted for 0.5% of total DALYs. Some individuals may not experience relapse episode but several others may experience multiple relapses.² The illness is characterized by high relapse rates after treatment discontinuation or poor adherence, even after a single episode of psychosis. A longer treatment period prior to discontinuation also does not reduce the risk of relapse and many patients relapse very soon after treatment discontinuation. The transition from remission to relapse may be abrupt with some having few early warning signs. The illness recurrence may occur with symptom severity rapidly returning to levels similar to the initial psychotic episode. However, while most patients respond promptly to re-introduction of antipsychotic treatment after relapse, the response time is variable and frank treatment failure may emerge in a subset of patients.³⁻⁴

Relapse may have a devastating repercussion in patients since it can lead to worsening of symptoms, progressive deterioration of cognitive function, impaired functions and diminished quality of life.^{5,6,7,8} Relapse in psychiatric disorders may be associated with many risks particularly the risk of harming others.⁹ It is unlike the first episode of psychosis whose course may be gradual with associated prodromal period that can last from months to even years.¹⁰ Some relapse episodes occurred after early warning signs.¹¹ Signs like insomnia, social withdrawal, difficulty concentrating, irritability, hallucinations, loss of interest, and increasing paranoia are common warning signs before schizophrenic relapse occur. Relapse episode of schizophrenia can present with some difficulties in clinical settings. For instance, relapse illness recurrence may present symptom severity that rapidly returns to levels similar to the initial psychotic episode.¹² Furthermore, a better treatment response in first-episode schizophrenia than in chronic multi-episode schizophrenia has been observed.¹² Patients may also experience tolerance to medication particularly after multiple

relapses and with some medications higher doses may be required to achieve optimal clinical response as compared to the first episode.¹³ Some schizophrenic episodes may fail to remit after each episode irrespective of which episode it was. It has been observed that one in every 6 patients may fail to remit after each episode, irrespective of which episode it was but the median (SE) times to remission can be significantly longer for the second episode and third episode.¹⁴

Relapse in schizophrenia also has some effects on patients or their caregivers and the health sector as well as the entire country's economy at large. The deteriorating nature of the illness which may get worsened with each repeated episodes makes the patients to have poor performance in job thereby affecting their contributions to economic activities. Schizophrenia relapse is a major factor in generating high hospitalization rates and costs.¹⁵ According to Ascher-Svanum and associates,¹⁶ relapse of patients with schizophrenia is associated with substantial direct mental health costs that extend beyond the cost of hospitalization to other costly outpatient services and medication costs. Besides this, the burden of caregivers in taking care of patients and their bills once readmitted could lead to high economic burden. The health sector is imposed with a large burden and has to deal with the higher number of patients' re-hospitalization. The objectives of the study are to identify the various factors causing relapse among patients in the region and to quantify the extent of relapse in order to institute appropriate individualize measures for continuity of care as well as to identify the various interventions measures to prevent further relapse episode.

MATERIALS AND METHOD

The study was carried out at the Federal Neuropsychiatric Hospital, Maiduguri, Borno State, Nigeria. The city lies between latitude 11.5° North and 13.5° East in the Sudan Savannah. One hundred and thirty-four 134 patients with schizophrenia made up of 72 males and 62 females who reported first episode of the illness were studied. Demographic data such as age, gender, educational status/level, employment status, ethnic group and marital status were retrieved from the patients' case note. Relapse episodes were defined as worsening symptoms following remission of first episode that

necessitated re-hospitalisation. Only patients with relapse after first episode of schizophrenia and those with subsequent relapses described as multiple relapses are included in the study. Patients who presented with the first episodes of schizophrenia are excluded from the study. Patients with multiple relapse cases are double counted for the purpose of specific analysis. Information obtained includes duration between last discharge date and rehospitalisation, chief complaint at the time of rehospitalisation as presented by caregivers, past prescription medications, co-morbid disease, causes of relapse and noncompliance categories, and intervention measures. Descriptive statistics were used to analyse variables. Ethical approval was sought for and obtained prior to commencement of research.

RESULTS

The demographic data of the patients is presented in Table 1 and 2. The distributions for both genders are skewed toward low frequency of higher age group. The proportions of male to female cases were 0.54 and 0.46, respectively. Patients in their third decades of life accounted for 43.2% cases and those in their second and fourth decades of life were 22.4% each. The proportions of patients who are uneducated and those with an informal education or secondary levels of education are 26.9% each while those with tertiary levels of education accounted for 17.9%. The least educational level was recorded in those with primary levels of education (being 1.49%). About 49.3% of the patients were married while 43.3% were single with others being divorced (6.0%) or widowed (1.5%). In terms of the occupational status, housewives accounted for 29.9% while 17.9% were civil servants. Farmers and those in the business categories accounted for 4.5% and 13.4%, respectively. Students and unemployed groups were 16.4% and 14.9%, respectively. Artisan and labourers constituted 3.0% of the studied subjects. The major ethnic distributions of patients are Kanuri (49.3%), Marghi (11.9%), and Shuwa (10.4%).

About 6.7% cases of first relapse episode were recorded within one month while 11.2% of the patients reported relapse cases within 2-5 months (Table 3). Other duration of relapse was recorded within 6 months to 1 year (20.9%), 1-2 years (16.4%),

2-5 years (24.6%), 5-10 years (15.7%) and above 10 years (4.5%). About 49.3% (n=66) of patients who experienced first relapse also had second relapse at varying time while about 9.0% (n=12) further experienced third episode of relapse.

Fluphenazine/trifluoperazine combination was the most commonly used antipsychotic agent accounting for 34%. Other combination therapies are fluphenazine/haloperidol (10.5%), fluphenazine/chlorpromazine (11.9%), chlorpromazine/haloperidol (3.0%) and flupenthixone/haloperidol (1.5%). However, monotherapy use of agents like trifluoperazine, chlorpromazine, haloperidol, olanzapine and fluphenazine occurred in the proportions of 10.5%, 9.0%, 3.0%, 3.0% and 4.5%, respectively (Table 4).

The symptoms of relapse are similar to those experienced at the first episode but hallucination, disorganized behaviour, disorganized speech, poverty of speech and delusion occurred in 10.5%, 7.5%, 16.4%, 14.9% and 4.5% respectively (Table 5). However multiple symptoms like disorganized speech/behaviour (20.9%), disorganized speech/poverty of speech (3.0%) as well as disorganized behaviour/poverty of speech (1.5%) were recorded. Others include hallucination/poverty of speech (4.5%), loss of interest/poverty of speech (4.5%) while delusion, disorganized speech and behaviour affected 3.0% of patients. The causes of relapse (Table 6) showed several patients' related factors such as financial problems (14.9%), perceived wellness (7.5%), forgetfulness (10.5%) and breast feeding (3.0%). Lifestyle related factors (substance abuse) and medication related factors (medication side effects) accounted for 17.9% and 14.2% respectively. Disease-related factors such as poor insights (6.0%) and depression as co-morbid condition (1.5%) were observed. Insurgency-related problems affected 22.4% patients.

Several intervention measures adopted were rehabilitation (29.9%), education and counselling (26.9%), changing the drug type (6.0%), changing formulation type (25.4%), and dosage adjustment (11.9%) (Table 7). Some therapeutic manoeuvres carried out in the management of relapse cases of schizophrenia include dose increment (4.9%), dose reduction (4.9%), changing of the drug (28.4%) and

additional drug in 3.6% of the cases (Table 8).

Dosage increments were carried out with 5.6% of fluphenazine, 4.2% of chlorpromazine, and 13.3% of haloperidol while dosage reductions occurred with 7.5% of trifluoperazine and 12.5% of chlorpromazine. Changing to another therapeutic

agent affected 19.4% of fluphenazine, 7.7% of trifluoperazine, 41.7% of chlorpromazine, 40% of olanzapine, 46.7% of haloperidol and all flupenthixol. However additional drug were added to trifluoperazine (7.5%) and haloperidol (13.3%) therapies in relapse cases of patients previously placed on them.

Table 1: Age and Gender Distribution of Patients with Relapsed Schizophrenia

Age strata (Yrs)	Both genders n(%)	Male n(%)	Female n(%)
11-20	30 (22.4)	16 (22.2)	14(22.6)
21-30	58 (43.2)	30 (41.7)	28(45.2)
31-40	30 (22.4)	18 (25.0)	12 (19.4)
41-50	12 (9.0)	6 (8.3)	6 (9.7)
51-60	2 (1.5)	2 (2.8)	0 (0)
61-70	2 (1.5)	0 (0)	2 (3.2)
71-80	0 (0)	0 (0)	0 (0)
TOTAL	134 (100)	72 (100)	62 (100)

Table 2: Background Information of Patients.

Parameter	Category	Freq.n (%)	Parameter	Category	Freq.n(%)
Educational status	Uneducated	36 (26.9)	Ethnic	Kanuri	66(49.3)
	Informal Education	36 (26.9)		Marghi	16(11.9)
	Primary	2 (1.5)		Shuwa	14(10.4)
	Secondary	36 (26.9)		Yoruba	2(1.5)
	Tertiary	24 (17.9)		Babur	4(3.0)
	TOTAL	134 (100)		Bura	6(4.5)
Marital Status	Married	66 (49.3)		Kilba	4(3.0)
	Single	58 (43.3)		Hausa	8(6.0)
	Divorced	8(6.0)		Others	14(10.5)
	Widow	2 (1.5)		TOTAL	134(100)
	TOTAL	134(100)	Co-morbid conditions	None	50(37.3)
Occupation	Civil Servant	24 (17.9)		Depression	2(1.5)
	House wife	40 (29.9)		Substance	24(17.9)
	Farmer	6 (4.5)		Hypertension	14(10.5)
	Business	18(13.4)		Malaria fever	18(13.4)
	Student	22(16.4)		Bipolar	2(1.5)
	Manual Labourer	4(3.0)		Mania	12(9.0)
	Unemployed	20(14.9)		Others	12(9.0)
TOTAL	134(100)	TOTAL	134(100)		

Table 3: Duration Taken Before Relapse From Previous Remission(s)

Duration before Relapse	First Relapse n(%)	Second Relapse n(%)	Third Relapse n (%)	TOTAL N (%)
Within 1 month	9 (6.7)	0 (0)	0 (0)	9 (4.2)
2 -5 months	15 (11.2)	0 (0)	0 (0)	15 (7.1)
6 months-1 year	28 (20.9)	2 (3.0)	0 (0)	30 (14.2)
1-2 years	22 (16.4)	12 (18.2)	0 (0)	34 (16.0)
2-5 years	33 (24.6)	26 (39.4)	6 (50)	65 (30.7)
5-10 years	21 (15.7)	16 (24.2)	6 (50)	43 (20.3)
>10 years	6 (4.5)	10 (15.2)	0 (0)	16 (7.5)
Total within group	134 (100)	66 (100)	12 (100)	212
Overall Total	134 (63.2%)	66 (31.1%)	12 (5.7%)	212 (100%)

Table 4: Drug Therapy Used by Patients Before Relapses Occurred

Drug type	Frequency	Percentage
Trifluoperazine	14	10.4
Flupenthixone/Haloperidol	2	1.5
Chlorpromazine/Haloperidol	4	3.0
Chlorpromazine	12	9.0
Olanzapine	4	3.0
Haloperidol	4	3.0
Fluphenazine	6	4.5
Clozapine	4	3.0
Fluphenazine/Trifluoperazine	46	34.3
Fluphenazine/Haloperidol	14	10.4
Fluphenazine/Chlorpromazine	16	11.9
Others	8	6.0
TOTAL	134	100

Table 5: Reoccurrence of Symptoms of Schizophrenia After Remission of First Episode

Reoccurrence of symptoms	Frequency	Percentage
Hallucination	14	10.4
Disorganised Behaviour	4	3.0
Disorganized Speech	21	15.6
Poverty of Speech	13	9.7
Delusion	8	6.0
Disorganized behaviour and Poverty of Speech	7	5.2
Disorganized behaviour and disorganized speech	22	16.4
Hallucination and disorganized speech	16	11.9
Disorganized speech and Poverty of speech	4	3.0
Loss of Interest and poverty of speech	7	5.2
Delusion, disorganized speech and disorganized behaviour	14	10.4
TOTAL	134	100

Table 6: Categories and Reasons for Relapses in Schizophrenia Among Patients

Category	Reasons	Freq.	%
Patients' related factors	Financial problems	20	14.9
	Perceived wellness	9	7.5
	Forgetfulness	12	10.5
	Breast feeding,	4	3.0
Lifestyle related factor	Substance Abuse	24	17.9
Treatment related factor	Medication side effects	19	14.2
Disease related factor	Poor insights	8	6.0
	Co-morbid depression	2	1.5
Other Factors	Insurgency-related	30	22.4
	Unspecified	2	1.5
Total		134	100

Table 7: Intervention Undertaken to Prevent Further Relapse Episode

Intervention Recommended	Frequency (n)	Percentage (%)
Rehabilitation	40	29.9
Education and Counselling	36	26.9
Drug changed	8	6.0
Formulation changed	34	25.4
Dosage changed	16	11.9
TOTAL	134	100

Table 8: Therapeutic Interventions in Patients Who Experienced Relapses

Drugs used	Initial Freq	Dose Increase	Dose Reduction	Drug Changed	Additional Drug	No changes
Fluphenazine	66(33.0)	4(5.6)	0(0)	14(19.4)	0(0)	54
Trifluoperazine	52(23.9)	0(0)	4(7.5)	4(7.7)	4(7.5)	44
Chlorpromazine	48(22.0)	2(4.2)	6(12.5)	20(41.7)	0(0)	20
Olanzapine	10(4.6)	0(0)	0(0)	4(40)	0(0)	6
Clozapine	2(0.9)	0(0)	0(0)	2(100)	0(0)	0
Haloperidol	30(13.8)	4(13.3)	0(0)	14(46.7)	4(13.3)	16
Flupenthixol	4(1.8)	0(0)	0(0)	4(100)	0(0)	0
Total (%)	212(100)	10(4.9)	10(4.9)	62(28.4)	8(3.7)	140

DISCUSSION

The age distribution of all subjects is skewed toward low frequency of higher age groups with a mean and standard deviation of 28.8 ± 10.3 years. Similar distribution pattern was observed with the male patients. The highest relapse cases were observed in those who are in their third decades of life. Low cases were recorded in those above fifth decades of life. Before age 60 years, the proportions of relapse episodes of schizophrenia are higher in male than female. In general, relapse cases were higher in male than female patients. This finding is not surprising since the incidence and prevalence of the disease is said to be higher in men than women. The study by Aleman and colleagues¹⁷ supported the fact that the men had a higher incidence (ratio 1.42). In this present study this ratio is put at 1.22. Gender has also been identified as one of the factors influencing clinical remission, with relapse rates being higher in men and remission rates higher in women.^{18,19}

The influence of parameters like educational, marital and occupational status may play a role in the relapse episodes of schizophrenia. In this present study, the highest relapse episodes of the illness are among the uneducated and in those with informal and secondary levels of education. The married patients and the occupational category like housewives showed higher relapse episodes compared to their counterparts (Table 2). The high cases of relapse observed among the Kanuri, Marghi and the Shuwa ethnic groups is a reflection of the ethnic distribution of the region.

The duration of taken for symptoms to relapse after patients discontinue treatment of first episode of schizophrenia varies among individuals. This could vary from few weeks to many years. In this study, the shortest durations taken for first episode of relapse in some individuals were within the first one month of off drugs or irregular intake while it takes up to a decade or more for other patients to experience their first relapse. Majority of first episode of relapse recorded occurred between 2 to 5 years. Some authors reported that symptoms reoccurrence following treatment discontinuation after remission of first episode of schizophrenia can take within days to weeks; and onset of relapse can be abrupt²⁰ or within 2-4 weeks²¹. Other authors reported an average relapse time of 6.9 months,³ 7.8 months²² and 10.8 months²³ in some studies. Many studies reported that symptom reoccurrence rates of close to 80% at 12 months after treatment discontinuation have occurred in many regions.^{3,22,24,25} Duration of relapse as long as 20 months was reported by Henmi.²⁶ Some patients may experience warning signs before relapse occurs but even at that these signs may be very brief before relapse are observed. These relapses can be prevented if patients or their caregivers are adequately educated on factors that causes relapse and how such to avoided.

About 10-20% may never experience reoccurrence after a single psychotic episode,²⁷ but multiple relapses in schizophrenia are common incidences in various quarters³. In our study, repeated relapse episodes of schizophrenia were observed after 6

months in some few individuals and with greater incidences with prolonged duration (Table 3). The reasons for various time of relapse among individual after treatment discontinuation is not fully understood but it may appear to be a combination of various predisposing risk factors. Variation in schizophrenic threshold or psychosis de-compensation may be a contributing cause. According to Birchwood and colleagues²¹ such frequent or high relapse rates and abrupt re-emergence of symptoms may reveal reduced threshold for psychosis de-compensation particularly when the first episode has occurred.

Cases of previous admissions have been found to be associated with relapse and multiple psychiatric readmissions. Silva and associates²⁸ reported that patients with a greater number of previous admissions were more likely to relapse and hence experience multiple admissions while Yussuf and colleagues²⁹ found socio-demographic factors like young age, and clinical factors such as history of multiple admissions, longer length of stay and diagnosis of schizophrenia as factors that may predict relapse.

The causes of relapse in this study were observed to be multi-factorial, but the most outstanding reasons are non-adherences due to treatment discontinuation which was observed in nearly two-third of the cases. This pattern is similar to the 70% cases of relapse conditions associated with medication non-adherence reported by Upok and colleagues.³⁰ This result is also consistent with the 69% relapse rate arising from non-compliance to antipsychotic medications reported by Drake and colleagues.³¹ In South Africa, relapse rates of 80.4% were reported³² while in China, Germany and Finland, the rates are 56.4%, 52% and 57.8%, respectively.^{33,34,35}

Among reasons indicated as associated with non-compliance is the problem directly or indirectly linked to insurgency experienced in the region in the last few years. The region where this study was conducted has witnessed loses or disruption in several socio-economic activities that span to more than half of a decade and has resulted to displace of people from their homes and many unrest. Many people similarly reported financial problems and

possibly poor family support as accounting for non-compliance. This is not uncommon since many psychiatric patients have poor job placement.

Treatment related factors such as medication side effects are identified as the cause of non-adherence in minority of patients. This is particularly applicable to patients placed on older generation antipsychotic agents. Extra pyramidal side effects are commonly reported with such agents and have great potentials for causing treatment discontinuation if measures are not taken to prevent its occurrence in patients. Many studies generally agreed that medication side effects can often result in patients' non-adherence. For instance, relapse rates were higher when the first generation antipsychotic agents were compared with the second generation agents^{30,36,37} due to their higher side effects. Some major side effects of typical antipsychotics commonly reported in clinical practice by patients are tremors, muscle rigidity, slurred speech, restlessness, painful muscle spasms and impotence and so on; which may contribute to poor adherence. The high costs of the second generation agents often put limitation to their uses for long duration especially in resource limited areas or individuals. Proper insurance schemes and more governmental attention to psychiatric plights may reduce these problems. Perceived wellness was also identified as one of the reason for patients' non-compliance.

Lifestyle factors were identified as contributing factors to relapses. For example, the second most prominent cause of relapse in this study identified in a number of patients is substance abuse. Substance abuse has been identified as a major cause of schizophrenia, first-episode psychosis and relapse episodes of psychosis. It was identified in higher prevalence in people with schizophrenia and first-episode psychosis^{38,39,40} though the cases was reported higher in men than women^{38,41} and may possibly have made the first-episode psychosis higher in men than women^{38,41,42}. Many authors similarly identified substance abuse as one of the major causes of relapse in schizophrenia.^{5,6,43,44} Moeller and colleagues⁴⁵ indicated that stress/depression and substance abuse are the second most common causes of relapse in schizophrenia.

When the drugs used by patients were assessed, the uses of first generation agents were in much higher proportion than the second generation agents. Many factors may have influenced these observed patterns including those of socio-economic status, availability of agents, non-compliance problem that will necessitate the choice of long acting depots and a host of others. However, these agents are known to have more side effects than the second generation agents. Non-compliance because of medication side effects is always a one of the major drug therapy problems with high potentials for disease progression or relapses. Other authors have similarly identified the side effects of conventional antipsychotics as the main cause of relapse in patients with schizophrenia.^{30,36,37}

Several positive, negative and cognitive symptoms that are similar in type with the first episode of schizophrenia were presented by patients during the relapse episodes. Multiple symptoms were similarly identified in a couple of relapse cases. The positive symptoms like hallucination, delusion and disorganized speech and behaviours dominated the relapsed episode among many patients. Among the negative symptoms observed during the relapse episode, loss of interest and poverty of speech were more frequently reported by patients. No symptoms of cognitive signs were reported possibly because these signs are often missed, unassessed or ignored during the repeat episode of schizophrenia. Although the severity of these relapse symptoms were not studied, but the duration time in some relapsed cases couple with the need for hospital visit or re-hospitalization suggest that once the relapse symptoms sets in, they rapidly accelerate to the form or pattern observed with first episode of schizophrenia and may be associated with illness progression.

Several interventions were carried out to prevent repeated episodes or further relapses. For instance, rehabilitation of patients occurred in nearly one-third of patients while changing of formulation as well as patients' education and counselling was carried out in about one-quarter each of patients. In a little above one-tenth of patients, dosage changes involving either increase or decrease was carried out as interventional measures. Other interventions include change in drugs and additional drug

therapy. These therapeutic manoeuvres are common practices in pharmacotherapy. Rehabilitations are recommended component of treatment modalities in schizophrenia management and has been adopted to reduce relapse episode or disease progression.

One of the key strategies to improve adherence in both potentials and actual poor-adherent patients is to prefer the use of drugs or formulations with prolonged actions or half-life over those with shorter half-life that require frequent administrations. This is particularly important in view of the nature of the disease where most patients lack insights or have impaired memory functions.

Patients' education and counselling improves compliances to medication in many disease conditions. It is vital component of patient-focussed care in pharmaceutical care services. Family education on schizophrenia illness improves knowledge and promotes improvement in patient symptoms in a randomized controlled trial in China.³³ Similarly, patients receiving either cognitive behavioural therapy (CBT) or supportive counselling in combination with the usual treatment had better symptom recovery in one study in England.⁴⁶ Moreover, patients who understand their illnesses, medications, and treatment expectations have consistently demonstrated better adherence.⁴⁷

Dosage adjustments were carried out on patients for several reasons in other to achieve therapeutic goals. Dosage reduction may be necessary where the given doses are not tolerable to patients or in events of drug interaction that increase the plasma concentrations of other agents in concomitant use. Upward dosage review is also carried out where the lower dose is not achieving the desired therapeutic objectives and where dose increment does not cause untoward side effects. Doses of drugs may also be increased when tolerance developed to that agent.

CONCLUSION

Several factors were identified as the cause of relapse in patients with schizophrenia in the region but patients' related factors such as non-adherence

and substance abuse as well as treatment related factors such as medication side effects were topmost of these causes. The insurgency experienced in the region for more than half a decade was similarly identified as major contributory factors.

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