A STUDY OF FACTORS ASSOCIATED WITH RELAPSE IN SCHIZOPHRENIA

Dissertation Submitted to

THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY

in partial fulfillment of the regulations

for the award of the degree of

M.D. (Psychiatry)

BRANCH – XVIII

MADRAS MEDICAL COLLEGE

THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY

CHENNAI, INDIA

APRIL 2011

CERTIFICATE

This is to certify that the dissertation entitled "A STUDY OF FACTORS ASSOCIATED WITH RELAPSE IN SCHIZOPHRENIA" is the bonafide original work of **Dr. SOWMYA BHASKARAN T.S.** in partial fulfillment of the requirements for **M.D. (Psychiatry) BRANCH–XVIII** Examination of the Tamilnadu Dr. M.G.R. Medical University to be held in April 2011. The period of study was from May to October 2010.

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DECLARATION

I **Dr. SOWMYA BHASKARAN T.S.** solemnly declare that the dissertation titled, **"A STUDY OF FACTORS ASSOCIATED WITH RELAPSE IN SCHIZOPHRENIA"** is a bonafide work done by me at Madras Medical College during 2008-2011 under the guidance and supervision of **Dr. R. SATHIANATHEN, M.D., D.P.M. M.P.H.,** Professor of Psychiatry, Madras Medical College.

The dissertation is submitted to Tamilnadu, Dr. M.G.R. Medical University, towards partial fulfillment of requirement for the award of **M.D. Degree (BRANCH – XVIII) in Psychiatry.**

Place : Chennai.

Date :

(Dr. SOWMYA BHASKARAN T.S.)

ACKNOWLEDGEMENT

I wish to thank immensely **Prof. Dr. J. Mohanasundaram, M.D; DNB; Ph.D**; Dean, Madras Medical College, for giving me an opportunity to do this study.

My sincere thanks to Professor **Dr. R. Sathianathan, M.D; D.P.M; M.P.H;** Director, Institute of Mental Health, for his encouragement and guidance throughout the study.

I thank Professor **Dr. Jeyaprakash M.D., D.P.M;** Deputy Superintendent, Institute of mental health, for his valuable suggestions and advice.

I am grateful to **Dr. A. Kalaiselvan M.D., D.P.M.,** Associate Professor, Institute of Mental Health for the support given to me.

I express my gratitude to **Dr. Krishnan, M.D., D.P.M;** Associate professor, Institute of Mental Health for his timely guidance in refining the study and the draft of the thesis

I am deeply indebted to **Professor Dr. S. Nambi, M.D.,** (retired) Addl prof, and professor **Dr Shanthi Nambi M.D**., Associate professor, Institute of Mental Health, for providing direction and encouragement during the study.

My special thanks to **Dr Poornachandrika M.D., DCH** and **Dr Shanthi Maheshwari M.D** for their advice and suggestions.

I am grateful to **Dr Shanmugiah M.D.** and **Dr. Vimal Doshi M.D.,** for their valuable insights and immense help in conceptualizing the study.

I am also grateful to **Dr. Venkatesan Ph.D;** H.O.D. Dept of statistics, **Mr**. **Srinivasan,** statistician and my friend **Dr. Pradeep Menon** from Indian Council of Medical Research, Tuberculosis Research Centre, Chennai, and for helping me with the statistical part of the study.

I would like to thank my fiercest critic **Arun** for bringing out the best in me.

I wish to thank my husband for his patience, support and immeasurable help with the technical know-how, my in-laws for their encouragement and profound understanding and my parents-my pillars of strength.

I thank all the patients who participated in the study without whose co-operation; the study would not have been possible.

CONTENTS

A STUDY OF FACTORS ASSOCIATED WITH RELAPSE IN SCHIZOPHRENIA

INTRODUCTION

Schizophrenia is a complex and puzzling disease because it is characterized by a multiplicity of symptoms affecting most aspects of human cognition, emotion, and behaviour.

Emil kraeplin gave the conceptual framework that defines schizophrenia. His description of dementia praecox included a broad range of symptoms but he perceived negative or deficit symptoms like emotional dullness, failure of mental activity, loss of mastery over volition and ability of independent action as the most fundamental abnormality in schizophrenia. He characterised dementia praecox as a group of profound mental disturbances inescapably associated with progressive deterioration. He stressed that although the general course of dementia praecox was very variable, the usual outcome was a state of apparent dementia.

Paul Eugen Bleuler conceptualised “loss of unity of personality” as the most important sign of the illness he coined as schizophrenia. He classified the symptoms of schizophrenia into two broad categories, fundamental and accessory symptoms. He believed that the fundamental symptoms were present in all patients and tended to occur only in schizophrenia, the accessory symptoms on the other hand occurred in a variety of disorders. He identified

loss of continuity of association, loss of volition, ambivalence and autism as the pathognomonic symptoms. He concluded that schizophrenia was not invariably incurable and did not always progress to full dementia and nor did it always and only occur in young people.

Adolf Meyer believed that schizophrenia was the natural result of a life history that could be clearly traced to various physical, social, and psychological factors in the patient's past. He stressed the importance of psychological and environmental factors in addition to biological causes and maintained a positive prognosis for the illness. He concluded that the illness was episodic and recurrent, relapses representing new attacks of underlying illness.

Schizophrenia is a chronic and disabling illness that affects approximately 1% of the world's population. Relapse remains common in schizophrenia despite the best combination of biological and psychosocial interventions.[1]

Each relapse results in the growth of residual symptoms[2] and accelerates social disablement.[3] It predicts poor prognosis, deteriorates occupational, functional status and increases burden on the family. Relapse is one important secondary prevention target after the onset of first episode psychosis because increases the risk of treatment resistance and economic burden for the wider community because of increased costs of treatment.[4]

It is vitally important to determine the socio-demographic and clinical predictors of relapse to identify patients at a higher relapse risk and implement effective measures and appropriate intervention programmes aimed at preventing relapses.

REVIEW OF LITERATURE

The dictionary definition of relapse is “the return of a disease after apparent recovery, total or partial” and this could cover relapses during the course of schizophrenic illness.

THE COURSE OF SCHIZOPHRENIA

Relapse in schizophrenia is not inevitable[5].A five year follow up study by Shepherd et al suggested that almost a quarter of patients with first episode suffer no further relapses, a third have several episodes without impairment, the remainder having episodes without return to normality.[2]Another follow up study by Crow et al of 120 first admission schizophrenia patients who were randomly assigned to either neuroleptics or placebo on discharge revealed that 54% in the medicated group did not relapse while the proportion in the placebo group was 38%[6].Madras longitudinal study also studied the course of schizophrenia in detail and identified four basic patterns in the 20 year follow up. It was found that 8.2% of patients’ attained complete remission, 39.3% of the patients had relapse with complete remission in between, 44.3% of patients’ experienced relapse with partial remission in between and 8.2% had continuous illness[7].

DEFINITIONS OF RELAPSE

Although the measurement of the course of schizophrenic disorder has heavily relied upon the concept of relapse, there has been paucity in clear definitions of relapse.

An examination of the criteria used in various studies of relapse revealed a wide variation. They included hospital readmission, exacerbation of all symptoms, exacerbation of symptoms of schizophrenia, and the need for major change in clinical management.

HOSPITALIZATION

The usual definition used hospital admission as a central criterion for relapse. Some investigators have used hospitalization as the sole criterion for relapse regardless of the symptom presentation or the severity[8-10].Although a major proportion of hospital admissions in a patient diagnosed with a schizophrenic illness are probably due to worsening or reappearance of symptoms of schizophrenia, it may not be the only reason for such an admission. It has been observed that hospital admissions were associated with affective symptoms. At times the decision to admit the patient is determined by the tolerance of the support system[11] and thus does not exclusively determine severity. In present day psychiatry where rapid return to the community is advocated, hospital stay may be very brief and represent a relatively small aberration during the course of illness rather than a significant event.

CLINICAL DETERIORATION

Certain others have defined relapse as “clinical deterioration of such magnitude that hospitalization seems imminent”[12].Another common method of defining relapse is “significant deterioration of mental state” without mention of the specific symptoms being evaluated in tracing the course of deterioration. The inclusion of many types of clinical deterioration has resulted. For example exacerbations of depressive symptoms[12, 13], occurrence of suicide attempts[12] have been included as relapses in studies of schizophrenia. In several data analyses hypo manic episodes, situational reactions and toxic drug effects were among the episodes included in the broad definition of relapse.

CLINICAL DETERIORATION: SPECIFIC TO PSYCHOTIC SYMPTOMS

Few studies studying relapse restricted its definition to include patients exhibiting clinical deterioration of schizophrenic phenomenology[14-16] and some others included patients showing increase in psychotic symptoms[13].

CHANGE OF MANAGEMENT

In clinical trials of maintenance therapy the definition is often that the patient’s condition has deteriorated to such an extent that the double blind research procedures have to be terminated in order to ensure that active medication is given. Among these, in a study by Kane et al, signs of imminent relapse were sufficient for termination[17].In another by Leff et al, the criterion used was clinician’s concern about the patient s mental state requiring

confirmation if the patient was on active drug[15] while another drug study by Schooler et al provided specific dosage adjustment limits that, when exceeded as a result of clinical deterioration necessitated termination[18].Such studies largely employ the therapist's discretion and apprehension and may not correlate very well with the severity of schizophrenia. Also it has been reported that many of the prodromal symptoms of impending relapse may be as much an indicator of affective disturbance as an exacerbation of schizophrenia.

SOCIAL IMPAIRMENT

The level of social functioning is an important aspect in evaluation of outcomes in schizophrenia. Deterioration in work and interpersonal roles are associated with florid schizophrenic symptoms. Hogarty et al and Quitkin et al have included marked or significant social impairment as major criteria[12, 13].The difficulty that arises in taking social impairment as one of the criteria is the fact that premorbid adjustment, coping ability and baseline levels of social functions are very important determinants of social impairment.

TYPES OF RELAPSE

Based on the behaviour and symptomatology , several types of relapse have been analysed.

SEVERITY

It is the most common parameter to study relapse. Severity is a continuous variable which can be quantified using rating scales[19]and a

longitudinal measurement may be done . Such a measurement is vital as relapse cannot be viewed as an all or none phenomenon and so that prodromal symptoms do not get mixed up with that of relapse.

NON PSYCHOTIC AND PSYCHOTIC

Subotnik and Neuchterlein defined psychotic relapses as characterized by rating of severe or very severe on unusual thought content, hallucinations or conceptual disorganization items of BPRS.[19] Non psychotic relapses were characterized by ratings of severe or very severe on items like depression and hostility.

RELAPSE WITH RESPECT TO POSITIVE AND NEGATIVE SYMPTOMS

Relapse may be with reference to increase in the positive symptoms or the negative symptoms of schizophrenia. A patient who displays withdrawn, non communicative behaviour is just as ill as the person who is aggressive and exhibits bizarre behaviour. At times, adverse effects of medication also can be confused with negative symptoms of schizophrenia. Depression also appears like relapse of negative symptoms but is more closely linked with positive symptoms[20].

NATURAL AND INTERVENTIONAL RELAPSE

Many schizophrenia patients continue to relapse in spite of receiving medication while a few may not relapse at all or may do so less frequently.

Antipsychotic medication tends to double the interval between relapses compare to patients on placebo[5].

EARLY WARNING SIGNS AND STAGES OF RELAPSE

Studies have revealed that subtle changes in thought, affect and behaviour precede the onset of psychosis[21].First the non psychotic phenomena like withdrawal, insomnia, loss of appetite occur followed by increasing levels of emotional disturbance and then finally frankly psychotic symptoms occur[22,23]. This progression occurs over a period of less than four weeks[24].

Studies have shown that psychotic relapse can be predicted with a sensitivity of 50-70% and specificity of 75-81% when standardised measures of neurotic or dysphoric symptoms combined with those of low level psychotic symptoms and ratings are conducted fortnightly[19, 23, 24].Birchwood et al have described a set of 55 non specific and psychotic symptoms constituting of early warning signs of psychotic relapse.

STAGES OF RELAPSE

Donlon et al have described four stages of psychotic phenomena in relapse or decompensation [25].

STAGE 1: A massive psychological conflict not solved by neurotic methods, or by mental changes, impinges upon an emotionally sensitive individual.

Stage 2: The individual attempts to ward off impending psychological disintegration by increasingly utilizing ego defences.

Stage 3: Failure to contain the psychotic process is seen by loss of control of thought process and conceptual mechanism.

Stage 4: Compensatory process such as idiosyncratic thinking provides relief to the individual.

CONCEPTUAL BASIS FOR RELAPSE

Nuechterlein et al have proposed a vulnerability stress model of schizophrenic relapse [26].According to this model of schizophrenic relapse and illness course, increase in vulnerability factors like dopaminergic dysfunction, reduced available information processing resources, autonomic hyperactivity or environmental stressors like critical or emotionally over involved parent, over stimulating social environment, stressful life events or a decrease in protective factors like coping and self efficacy, anti psychotic medication may lead to movement from remitted to prodromal states. Critical mediating roles are hypothesized for increased autonomic activation and fragmentation in allocation of resources for effortful, attention- demanding cognitive processes. Patient's own prodromal symptoms might often contribute to environmental stressor level and may cause increases in personal vulnerability factors.

Thus, this model of relapse hypothesizes that genetic factors influence the development of certain vulnerability characteristics, which interact with relevant environmental factors to modify the course of schizophrenia.

FACTORS ASSOCIATED WITH RELAPSE IN SCHIZOPHRENIA

AGE

Mortensen et al reported that readmission rate decreased with increasing age at first schizophrenic admission till fifth discharge but no effect was found at later admissions.[27]Moller et al reported that age > 40 years reduced the risk of re hospitalization and age > 30 reduced the risk of relapse in patients on maintenance treatment.[28] Madras longitudinal study found that there was a slight but significant effect of onset after 25 years in predicting poor prognosis. It also found that younger patients had better outcome.[29]

GENDER

Angermeyer et al reported that female gender was connected with significantly lower readmission risk[92] whereas Mortensen at al found that male gender was associated with lower readmission risk.[27]

MARITAL STATUS

Certain studies have shown that living in partnership predicted a better outcome [28, 30] however other studies predicted that marital status did not predict readmission risk.[31, 32]In a study by Doering et al being married coincided with higher rehospitalisation rate in one group of patients while being unmarried predicted the same in another group of patients.[33]

EDUCATION

Higher educational level is protective against first readmission.[34]Educational level was found to be an important factor in secondary prevention of schizophrenic episodes in a study in Japan.[35] It is possible that this reflects a problem of social function such as school refusal or being the object of bullying, as well as being a problem of intelligence. This social dysfunction may be ascribable to a premorbid state or onset of schizophrenia

SUBTYPES OF SCHIZOPHRENIA

Readmission risk was lower after first discharge for simple, paranoid and latent subtypes than for other groups.[27]Diagnosis of residual type decreased the risk of relapse.

ONSET OF ILLNESS

Acute or sub acute onset have been found to be predictors of good outcome[36]. Insidious onset of illness has been found to be suggestive of poor outcome in the course of the illness.[31, 32]

SOCIAL ADJUSTMENT

Social competence was significantly correlated to good outcome in a long term follow up study, in the same it was observed that social isolation and avoidance behaviour were measures significantly related to poor long term

outcome.[36] A study by Rajkumar et al also showed that social contacts were more among non relapsers.[40]

PREMORBID PERSONALITY

A schizoid premorbid personality was associated with poor outcome in a study by Valliant et al.[37]A study by Robinson et al indicated that premorbid social isolation predicted initial relapse independent of medication adherence and that poor adaptation to school also predicted relapse in first episode patients.[38]Kane et al found a significant association between social isolation in childhood and relapse in first episode patients taking placebo but not in patients taking antipsychotic drugs for maintenance.[39] Personality deviation in adolescence and introversion were components related to poor outcome.

PSYCHOPATHOLOGY

Affective symptoms were found in 21% of the relapsers in a three year prospective follow up study at Chennai. [40]Subjective feelings of depression during first admission, number of depressive episodes, depression developing within one year of recovery from a schizophrenic episode were associated with early relapse in various studies.[33, 34, 41] IPSS has also shown that depression /elation during an episode is one of the predictors of relapsing course. This could imply that the presence of affective symptoms could predispose a patient to relapse or that depression manifests during acute phases of decompensation.

Depressed mood in the first episode has been shown to be a predictor of good outcome.[42] Depressive delusions at baseline were associated with lower risk of readmission. Certain other studies have shown that mania or elation predict better outcome.[43]

Robinson et al reported that despite a possible relationship between mood symptoms and relapse, neither the severity of baseline symptoms nor the presence of mood symptoms was related to relapse or had any prognostic value.[38]

Suicide attempts were not found to be increased in the relapsing group in the three year follow up study by Rajkumar et al.[40]However a suicide attempt in the case history seemed to be a significant predictor of greater rehospitalisation rate in a two year German follow up study.[33]

Flat affect is a less common but consistent finding which predicts poor outcome. Grandiose delusions were also associated with poor prognosis in Madras longitudinal study.[7]

EMPLOYMENT

A longer period of unemployment was seen to be a reliable predictor of lower rehospitalisation rate.[28, 44] Work during the last year before admission was a predictor of good outcome whereas lowered efficiency at work was an item related to poor outcome.[36]

It is likely that repeated relapses had interfered with their occupational functioning. However it is also possible that the relapsed group may have been retrospectively magnifying their occupational dysfunction.

RELIGIOUS FAITH

A strong religious faith predicted a negative outcome in a study by Doering et al. Religious activity was followed up in an Indian study and it was seen that observance of religious activity increased during the stage of acute decompensation and reduced activity was noted among the relapsers.[40] The results must be interpreted with caution as there is a problem of validly operationalizing religious faith and there is difficulty in differentiating between true religious beliefs and symptoms of illness since religious delusions may be a part of schizophrenia and reduced religious activity may be a reflection of generalized psychomotor slowing and chaotic disruption of routines.

SUBSTANCE ABUSE

Substance abuse is common among patients with schizophrenia. The life time prevalence is estimated to be as high as 47% with approximately 33% of the patients having an alcohol dependence disorder. Commonly abused substances include nicotine, alcohol and cannabis.

Patients who regularly took their medication but also abused substances were readmitted to hospital sooner compared to compliant patients who did not use substances. For noncompliant patients, time to first readmission was shorter

for patients with a dual diagnosis compared to patients with a singular diagnosis of schizophrenia. These data indicate that much of the benefit that antipsychotic medication has on increasing community survival is reduced by substance abuse.[45]

Substance abuse also leads to relapse in patients of schizophrenia independent of its effects on medication adherence. In a study evaluating relapse in 22 patients with schizophrenia, comparing substance abusers with non abusers by Gupta et al, medication compliance was ensured as all subjects. Substance abusers had a significantly higher readmission rate to the hospital compared to non abusers. These data suggest that in the presence of documented medication compliance substance abuse continues to remain a major factor contributing towards relapse.[46]

A study by Warner et al did not show significantly higher rates of substance use among the patients with relapses.[47]

TREATMENT ADHERENCE

The medication compliance for psychiatric illnesses is 58% which is much lower than that for non psychiatric illness.[48] More specifically, about half of the patients with schizophrenia are non-adherent to treatment.[49] This non-adherence may be due to factors that are patient-related (e.g. substance abuse, forgetfulness, anxiety about side-effects, inadequate knowledge, lack of insight, lack of motivation, fear of stigma); health care-related (e.g. poor patient/ health care provider relationship, poor services and access to services, poor staff

training); socio-economically-related (e.g. illiteracy, low level of education) or treatment-related (e.g. poly-pharmacology, complex treatment regimens).

Data from a five year follow up of first episode schizophrenia patients show that medication discontinuation substantially increases the relapse risk.[38] Mc Evoy et al found that non compliant relapsed patients had gradual onset of episode with prominent psychotic features, required involuntary commitment, and remained in hospital longer. Compliant patients had a rapid onset of symptoms with prominent affective features which were frequently associated with environmental stressors independent of the patient. Compliant patients were usually voluntary admissions and recovered quickly with minimal or no change in their antipsychotic pharmacotherapy.[50]

Sullivan *et al* revealed that medication non compliance to be a strong indicator of rehospitalisation .[51]Madras longitudinal study also discovered a shorter time to relapse and slower time to remit among non compliant individuals.[7]The hazard ratio in a study by Laan et al has shown that the risk of relapse is decreased when a patient is properly adherent to antipsychotic therapy.[52] Compliance with maintenance medication has been shown to be important in preventing relapses.[53]

On the other hand Herz et al in their detailed study on relapses in schizophrenia found that only 2% of the patients attributed relapse to stopping or incorrectly using their medication.[21] Poor medication compliance was not significantly correlated with rehospitalisation in a Japanese case control study. [35]

DURATION OF UNTREATED PSYCHOSIS

It has said that the longer the psychotic symptoms proceed unchecked by medication the greater the likelihood of profound clinical deterioration.

One hypothesis is that treatment closer to onset may dampen the activity of deficit processes and delay, attenuate, or prevent the development of chronicity. Here, shorter duration of untreated psychosis results from earlier treatment and the earlier treatment is causally connected to a better course of disorder.

The major alternate hypothesis is that shorter duration of untreated psychosis (i.e., earlier treatment) is a reflection of prognosis rather than its determinant. This hypothesis contends that patients with a better prognosis to start with present or behave in such a way that they receive treatment earlier in the course of their illness. The apparent relation here of early treatment with better outcome is actually a sampling effect. Conversely, patients with a poor prognosis, i.e., those with poor premorbid functioning who have an insidious onset of illness laden with negative symptoms, behave in such a way that they deny illness and/or avoid treatment until well after onset. Here later treatment and long duration of untreated psychosis are results of poor prognosis rather than vice versa.[54]

In a study by Owens et al, those with long duration of untreated psychosis exhibited more behaviour threatening to others and more bizarre behaviour, were more likely to be single, to live alone or dependently, to be

unemployed and to have experienced more adverse life events prior to admission. Logistic regression showed that bizarre behaviour and unemployed status independently increased the risk of relapse, bizarre behaviour making the single biggest contribution.[55]

On the other hand a study by Ho et al showed that despite the fact that many patients experienced long periods of untreated initial psychosis, this delay in seeking treatment does not appear to significantly impair subsequent outcome for the average patient with schizophrenia.[56]

The association between duration of untreated psychosis and poor outcome may be spurious, confounded by the fact that poor premorbid functioning is independently associated with both duration of untreated psychosis and poor outcome with no direct causal link between these two latter variables. Duration of untreated psychosis may also be that causal pathway between poor premorbid functioning and poor outcome, poor adjustment leading to delays in access of care, subsequently increasing the risk of presenting with a non remitting course of illness. [57]

EXPRESSED EMOTIONS

The crucial components of the expressed emotions construct are criticism, emotional over involvement and hostility.

Expressed emotions in relation to short term relapse

Two studies in Britain found that schizophrenia patients who left the hospital to live with one or more relatives who made many critical comments

about the patient during a private interview or who displayed a marked degree of emotional overinvolvement in the patient's life had a significantly greater risk of relapse within 9 months of hospital discharge than did patients living with relatives who were less critical and less emotionally overinvolved [58, 59]

Expressed emotion in relation to long term relapse

A study about the relevance between expressed emotion and rehospitalisation over seven years has shown that index expressed emotion status is associated significantly with time to both first and second readmissions during 7 years after discharge. Also high criticism was prospectively related to higher and longer length of hospitalizations.[60]

The Nithsdale schizophrenia survey showed that expressed emotion was not causally related to schizophrenic relapse as the relapse rate in patients living in consistently low expressed emotion homes was as great as that of patients living in high expressed emotions homes.[61]

In a study in Chandigarh by Wig et al, the global expressed emotion index was significantly related to one year relapse rate at first contact but in the two year data this relationship attenuated and lost its significance. However hostility in relatives remained significantly associated with relapse for both one year and two year follow up.[62]

STRESSFUL LIFE EVENTS

Retrospective design based studies

Brown and Birley found that schizophrenic patients reported an increased frequency of stressful life events that were independent of the patient's illness in the 3-week period just prior to the datable onset of an episode and concluded that life events play a role in "triggering" the onset or relapse of psychotic symptoms in schizophrenia [63]

Socioenvironmental stressors may precipitate schizophrenic attacks and such events tend to cluster in the two to three week period immediately preceding illness onset.[64]

Prospective design based studies

A study by Malla et al indicated a more frequent occurrence of independent life events in the lives of patients who relapsed over a period of one year when followed prospectively. There was a temporal relationship between the frequency of exposure to independent life events and relapse amongst schizophrenic subjects, thus providing support to a causal influence of life events on the course of schizophrenia. However, this relationship becomes significant only when major and minor events are considered together.[65]

Another prospective study by Ventura et al showed that a significantly higher number of independent life events occurred in the month preceding relapse. This increase was apparent relative to either the analogous month of a

"nonrelapse" period in the same patient or the average number of independent events per month during a 1-year standardized medication period for non relapsing patients.[66]

It must also be considered that at least 50% of instances of schizophrenic relapse occur without any increase in major life events in the preceding one month period.[67]

INSIGHT

In England, Drake *et al* examined a sample of patients with first-episode non-affective psychosis recruited for a trial of cognitive–behavioural therapy and observed poor insight to be an independent predictor of relapse and readmission .Re labelling of symptoms was the aspect of insight that was best related to outcome. It was based on the assumption that poor insight is significantly associated with poor adherence which in turn could explain the readmissions to the hospital.[68] However, the assumption that insight predicts future adherence is itself not clearly supported and, it has been argued, that it possibly holds only for patients who do not have substance misuse problems and who are not maintained on long-acting injectable medications.[69]

Insight into treatment was associated with less hospitalization and better social functioning but insight into mental illness or psychotic illness was not found to be correlated in a one year prospective study in Taiwan.[70] A study in India regarding the effect of insight and psychopathology on outcome of first

episode schizophrenia found that improvement in level of insight into illness during the early part of the illness predicted good outcome.[71]

On the other hand a study by Soskis et al failed to find an association between insight and hospitalizations.[72]

AIM AND OBJECTIVES

AIM

To study the factors associated with relapse in schizophrenia

OBJECTIVES

1. To evaluate the differences in clinical features between the patients with relapse in schizophrenia and patients in remission

2. To assess the differences in the two groups in terms of the following variables

   a) Education

   b) Employment

   c) Marital status

   d) Background

   e) Family history of psychosis

   f) Duration of untreated psychosis

3. To compare the two groups in terms of

   a) Insight

   b) Adherence to medication

   c) Stressful life events

HYPOTHESES

The following null hypotheses were generated in the study:

1. There is no significant difference in the psychopathology between patients in relapse and remission
2. There is no significant difference in educational qualification, marital status, and background between patients with relapse and remission.
3. There is no significant difference in relation to family history of psychotic illness between patients with relapse and remission.
4. There is no significant difference in duration of untreated psychosis between patients with relapse and remission
5. There is no significant difference in terms of insight between patients in relapse and remission.
6. There is no significant difference in terms of treatment adherence between patients with relapse and remission.
7. There is no significant difference in terms of stressful life events between patients in relapse and remission

METHOD AND MATERIALS

THE SETTING

The study was carried out in the Institute of Mental Health, Chennai over a period of six months from May 2010 to October 2010.

SUBJECTS

Cases: 30 consecutive patients suffering from relapse of schizophrenia attending the Review OPD for treatment.

Controls: 30 patients under remission matched for age, sex, duration of illness and subtype of schizophrenia attending the Review OPD for treatment.

STUDY DESIGN: The study is a cross sectional comparative study

INCLUSION CRITERIA

CASES: Patients with relapse in schizophrenia

Relapse was defined as[44]

(i) Presence of $\geq$ 1 criterion from the A–D group or presence of $\geq$ 2 criteria from the E–H group of ICD-10 criteria for schizophrenia lasting for at least 1 week;[73]

(ii) Socio-Occupational Functioning Assessment Scale (SOFAS) level of $\leq$ 70 ;[74]

(iii) Positive and Negative Syndrome Scale for Schizophrenia (PANSS) positive subscale $\geq$ 13;[75]

(iv) Following a period of remission of at least 2 months in which there was absence of any A–D criteria and $\geq$ 2E–H criteria for schizophrenia in ICD-10.

(v) With the current relapse not being the first expression of schizophrenia psychosis.

CONTROLS: Patients with remission of schizophrenia matched for age, sex, duration of illness and subtype of schizophrenia.

Remission was defined as[44]

(i) absence of A–D criteria and absence of $\geq$ 2 E–H criteria for schizophrenia in ICD-10;

(ii) SOFAS >70;

(iii) PANSS positive subscale score <12;

(iv) no hospitalization; and

(v) Duration of at least 2 months.

All the five criteria had to be fulfilled for the identification of relapse or remission.

All patients with relapse or remission are evaluated within 6 months of onset of relapse.

EXCLUSION CRITERIA

1. Organic brain syndrome
2. Mental retardation
3. Co morbid psychiatric illness
4. Co morbid substance abuse(except tobacco)

MATERIALS

1. Semi structured proforma to collect socio demographic details
2. PANSS (Positive and Negative Syndrome Scale)
3. SOFAS (Social and Occupational Functioning Assessment Scale)
4. PSLES (Presumptive Stressful Life Events Scale)
5. DAI (Drug Attitude Inventory)
6. SAI-E (Schedule For Assessment of Insight- Extended)

Semi Structured Proforma

It includes the socio demographic details of the patient, family history, duration and type of schizophrenia, duration of untreated illness. (Appendix I)

Positive and Negative Syndrome Scale (Kay et al 1987)[75]

The 30 items PANSS in a drug sensitive, operationalized instrument that provides balanced representation of positive and negative symptoms and gauges the relationship to one another and the global psychopathology.

It consists of 4 scales measuring positive and negative symptoms, their differential and general severity of the illness. Of the 30 items included in the PANSS, 7 constitute a positive scale, 7 a negative scale and the remaining 16 a general psychopathology scale. Therefore, the potential ranges are 7 to 49 for the positive and negative scales and 16 -112 for the general psychopathology scale. In addition to these measures, a composite score is scored by subtracting the negative score from the positive score. This yields a bipolar index that ranges from +42 to -42 which is essentially a difference score is reflecting the degree of prominence of one syndrome over the other.

The time frame for rating the PANSS is within the past week before the rating.

A number of studies have established a good to excellent reliability with PANSS. On the items that constitute the positive syndrome scale, ICCs range from 0.81-0.93.for negative items ICCs range from 0.63-0.90. (Appendix II)

Social and Occupational Functioning Assessment Scale[74]

It is a scale that exclusively focuses on the individual s level of social and occupational functioning and is not directly influenced by the severity of the individual s psychological symptoms. The SOFAS is usually used to rate functioning in the current period and is a clinically useful measure for adaptive functioning. It has better predictive and concurrent validity that GAF. It has an excellent reliability of >0.74. (Appendix III)

Presumptive Stressful Life Events Scale (Gurmeet Singh et al 1984)[76]

It is a 51 item scale with proven reliability and validity that has been standardized for the Indian population. It is a standardization of social readjustment rating schedule by Holmes and Rahe. The items are chosen to represent the life changes frequently experienced in individuals of general population. The items are further categorized into personal/impersonal, desirable/undesirable or ambiguous events. It is administered in the form of a semi structured interview, where events are assessed as present or absent. The test retest reliability and content validity are found to be satisfactory. (Appendix IV)

Schedule for Assessment of Insight-Extended (David et al 1990)[77]

David (1990) reported that insight was not an all-or-nothing phenomenon and developed this scale to quantitatively evaluate insight based on 3 components: therapy compliance, awareness of illness, and relabeling of

psychotic symptoms. It is a semi-structured, clinician-rated scale that consists of 8 questions. The highest total score for the first 7 questions is 14. The eighth question is a hypothetical question and it is up to the discretion of interviewer to ask the question or not. With the addition of the last question, the highest total score is 18. Higher scores indicate higher levels of insight. In the original reliability study of SAI, from which SAI-E derives, the ICC found was 0.72.It has an excellent validity. (Appendix V)

Drug Attitude Inventory-30.(Hogan et al 1983)[78]

It is a 30 item self report measure predictive of compliance in people with schizophrenia. Each statement is rated as being true or false. The measure produces a total score from+30 to -30.A positive score is predictive of compliance while a negative score of non compliance.

It has shown good discriminate value with 99% agreement between DAI and clinical rating of whether patient is compliant or non compliant. It also correlates with biochemical measures of adherence. It has good internal reliability of 0.93 and test- re test reliability of 0.82. (Appendix VI)

Approval was obtained from Ethical committee of Madras Medical College, Chennai. (Appendix VII)

The cases were selected from a screened sample of 50 consecutive relapsed patients of schizophrenia. The diagnosis was made by a medical officer in charge. But 20 were excluded as 5 expressed unwillingness to

participate, 9 had co morbid alcohol dependence, 2 had a history of stroke, 3 had co morbid depressive disorder and 1 had co morbid anxiety disorder. Finally a sample of 30 patients constituted the study group.

The control group consisted of patients with remission in schizophrenia .Each control was matched with case with regard to age, sex, duration of illness and subtype of schizophrenia. Hence a group of 30 patients constituted the control group.

Informed consent was obtained in written form for participation in the study from the patients. (Appendix VIII)

The patients were administered semi structured proforma, Positive and Negative Syndrome Scale, Social and Occupational Functioning Assessment Scale, Drug Attitude Inventory, Presumptive Stressful Life Events Scale and Scale For Assessment of Insight-Extended.

These scales took about two hours to complete and it was especially tedious to administer SOFAS to score the occupational functioning.

The data thus collected were tabulated and discussed with reference to the aims and objectives of the study. (Appendix IX)

STATISTICAL ANALYSIS

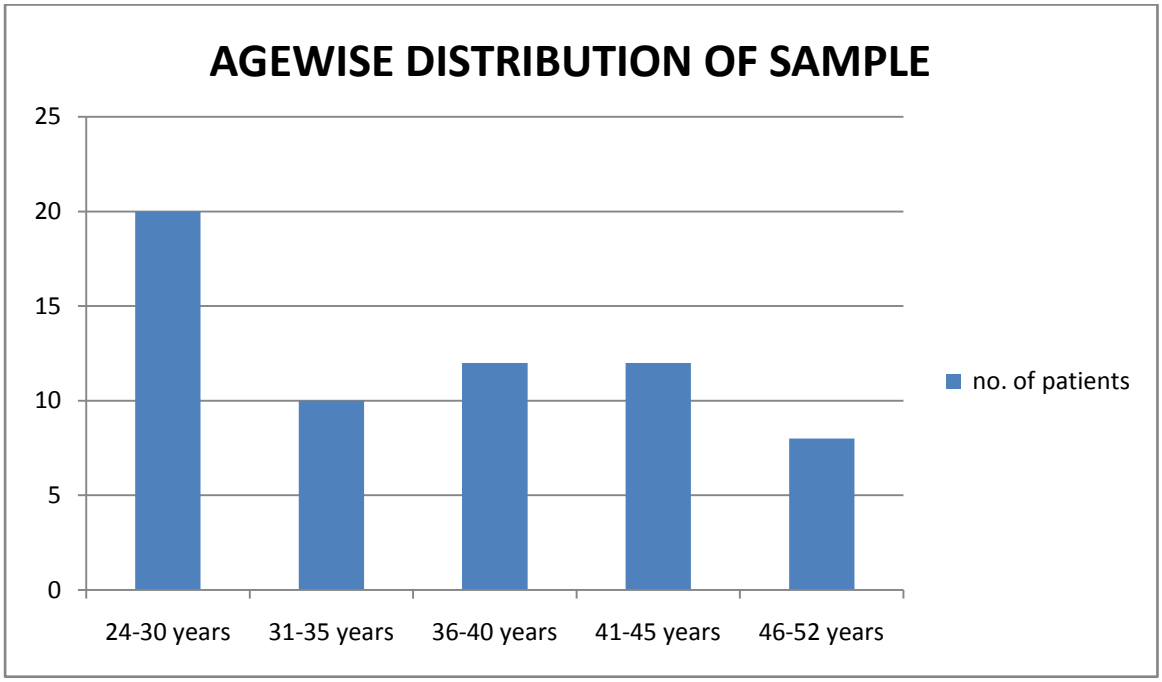
Statistical analysis was done using Chi square test for categorical variables and Independent t test for continuous variables. Logistic regression was used to find the predictive value of the variables. Statistical analysis was done using SPSS version 14.

RESULTS

AGE

The age of the patients in the sample ranged from 24 to 52 years with the mean of 36.9±7.76years.

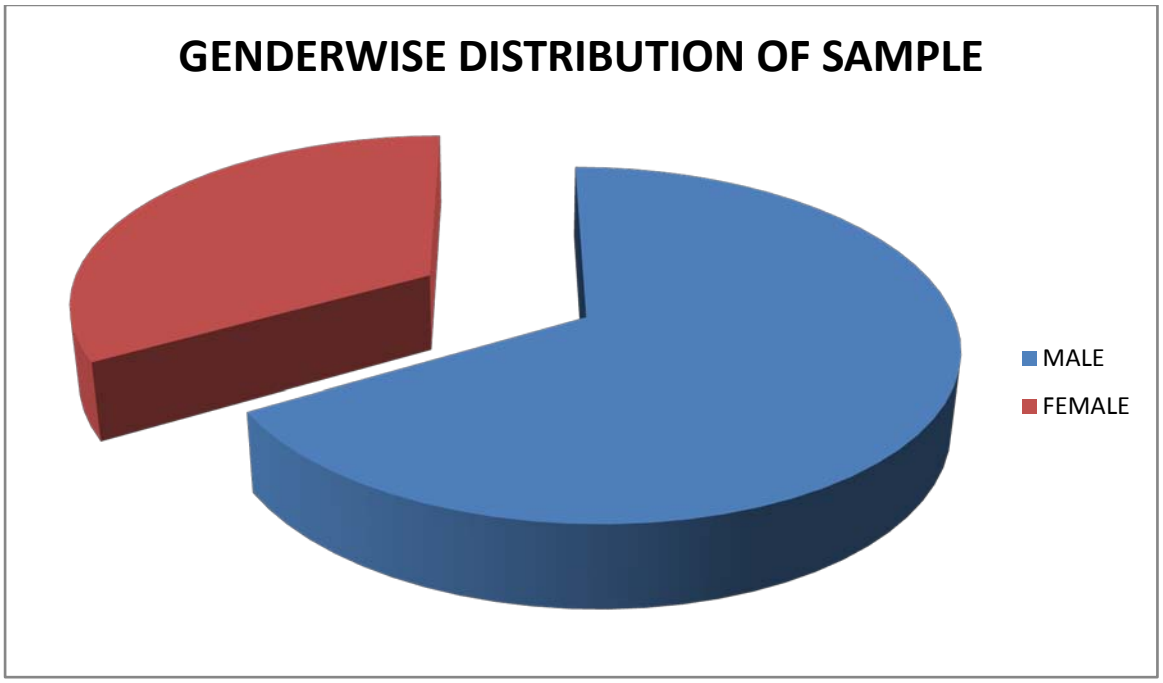
Figure 1



GENDER

The majority of patients in the relapsed and the remitted group were male. Males accounted for 66.7% of the study population.

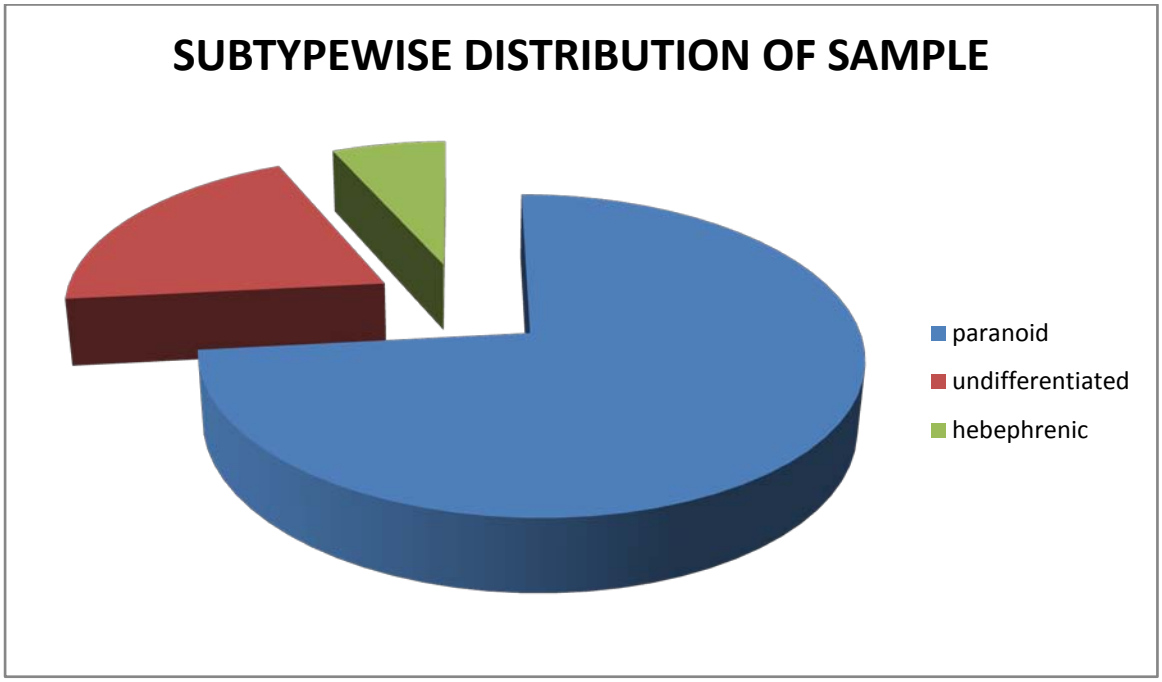
Figure 2



SUBTYPE OF SCHIZOPHRENIA

In the sample 73.3% belonged to the paranoid subtype, 20% to the undifferentiated subtype and 6.7% to the hebephrenic subtype.

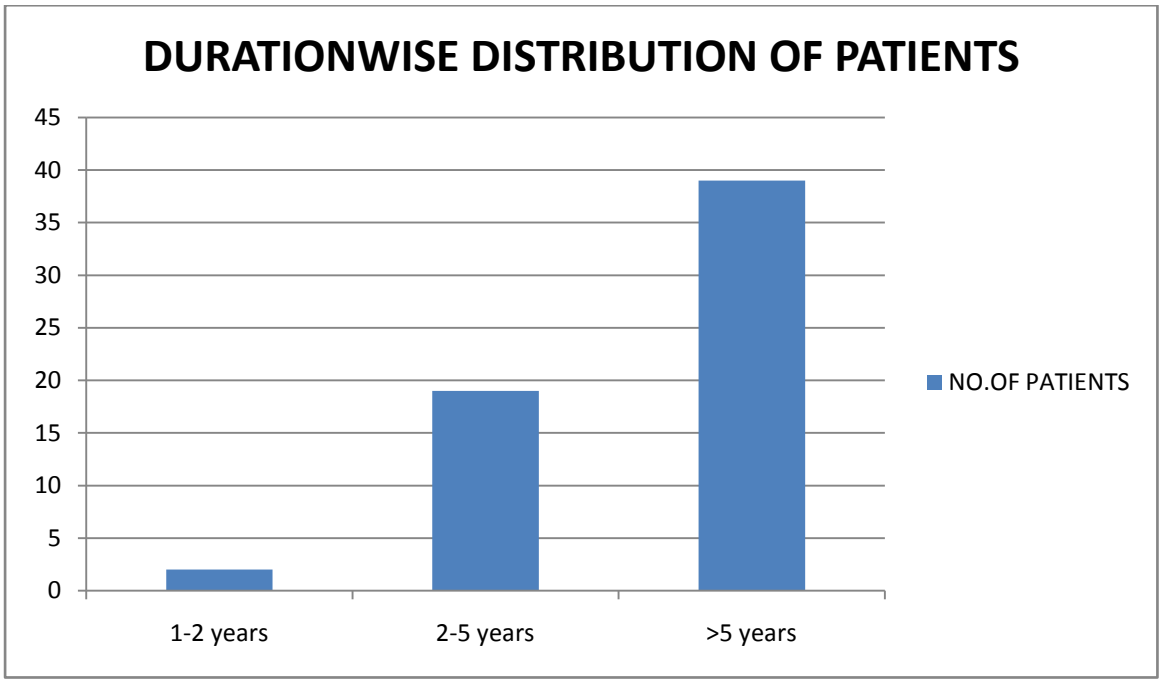
Figure 3



DURATION OF ILLNESS

In the sample 3.3% had duration of illness ranging from 1-2 years, 33.3% had duration ranging from 2-5 years and 63.3% had illness ranging from 5-10 years.

Figure 4



COMPARISON OF RELAPSED AND REMITTED GROUP ON THE BASIS OF BACKGROUND

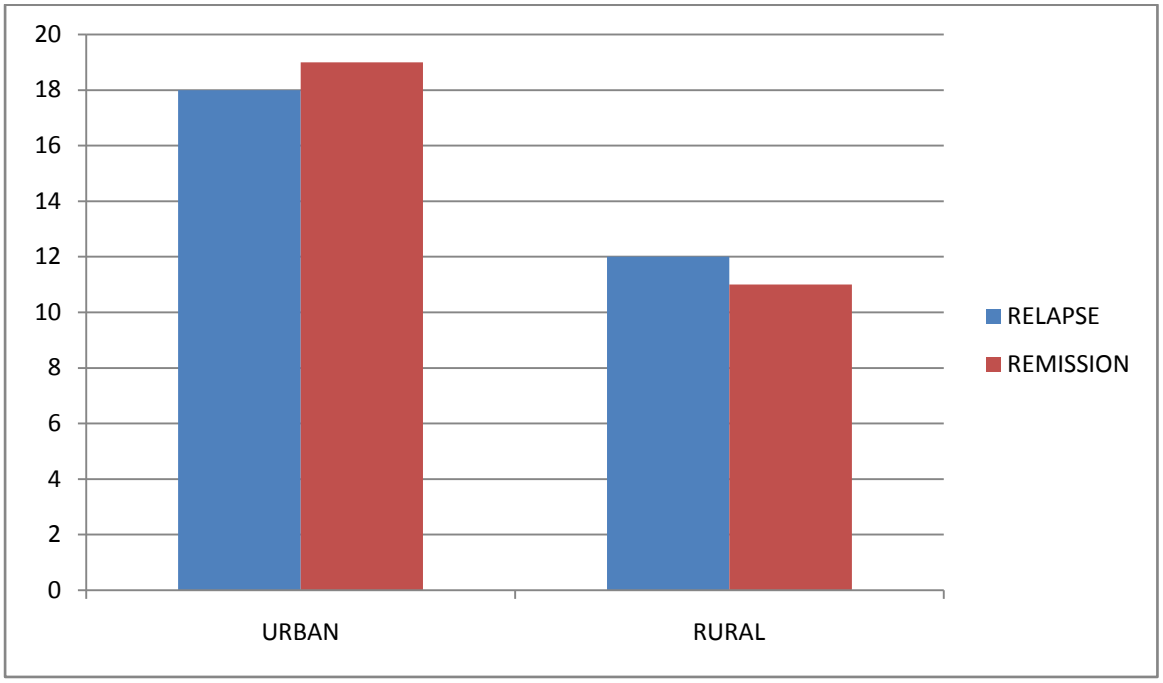
CASE / CONTROL	BACKGROUND		TOTAL
	URBAN	RURAL	
RELAPSE	18	12	30
REMISSION	19	11	30
TOTAL	37	23	60

	VALUE	P VALUE	SIGNIFICANCE
CHI SQUARE	0.71	0.791	NOT SIGNIFICANT

Among the relapsed group 60% belonged to urban background while 40% belonged to the rural background. In the remitted group 63.3% were from urban background while 36.7% were from rural background. The difference was not statistically significant.

COMPARISON OF RELAPSED AND REMITTED GROUP ON THE BASIS OF BACKGROUND

Figure 5



COMPARISON OF RELAPSED AND REMITTED GROUP BASED ON MARITAL STATUS.

CASE / CONTROL	UNMARRIED	MARRIED	SEPERATED	DIVORCED	TOTAL
RELAPSE	15	13	1	1	30
REMISSION	10	13	5	2	30
TOTAL	25	26	6	3	60

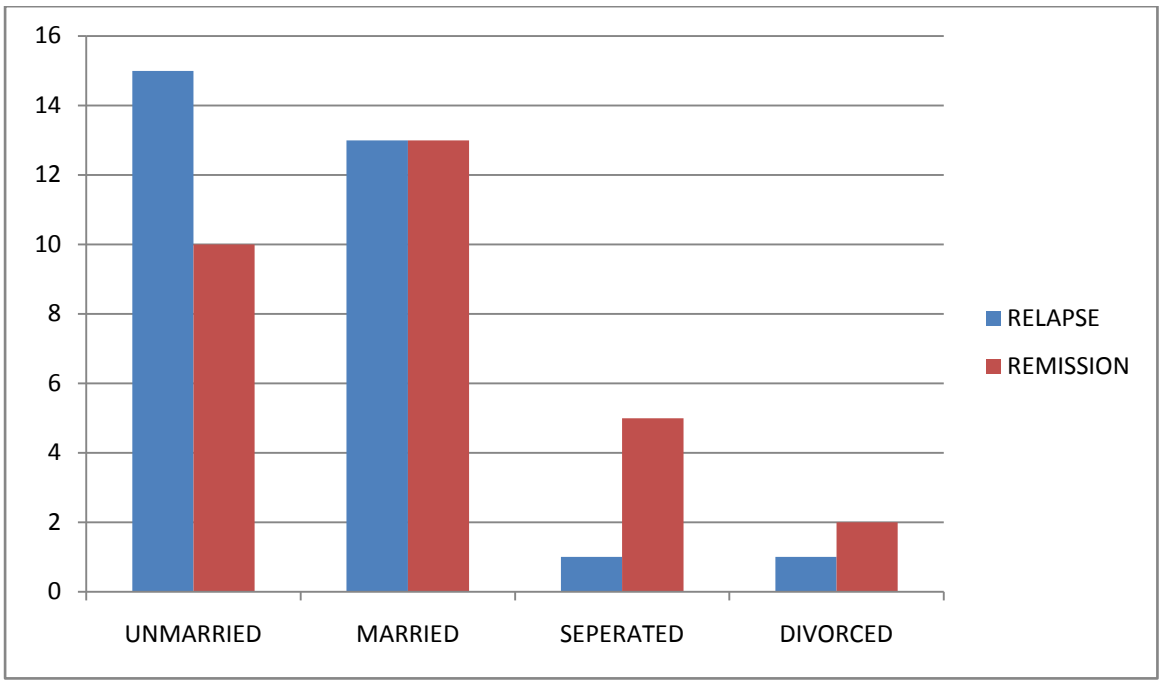
	VALUE	P VALUE	SIGNIFICANCE
CHI SQUARE	4.00	0.2615	NOT SIGNIFICANT

In the relapsed group 50% were unmarried, 43.3% were married, 3.3% were separated and 3.3% divorced. In the remitted group 33.3% were unmarried, 43.3% were married, 16.7% were separated and 6.7% were divorced.

The difference was not statistically significant.

COMPARISON OF RELAPSED AND REMITTED GROUP BASED ON MARITAL STATUS

Figure 6



COMPARISON OF RELAPSED AND REMITTED GROUP BASED ON EDUCATION

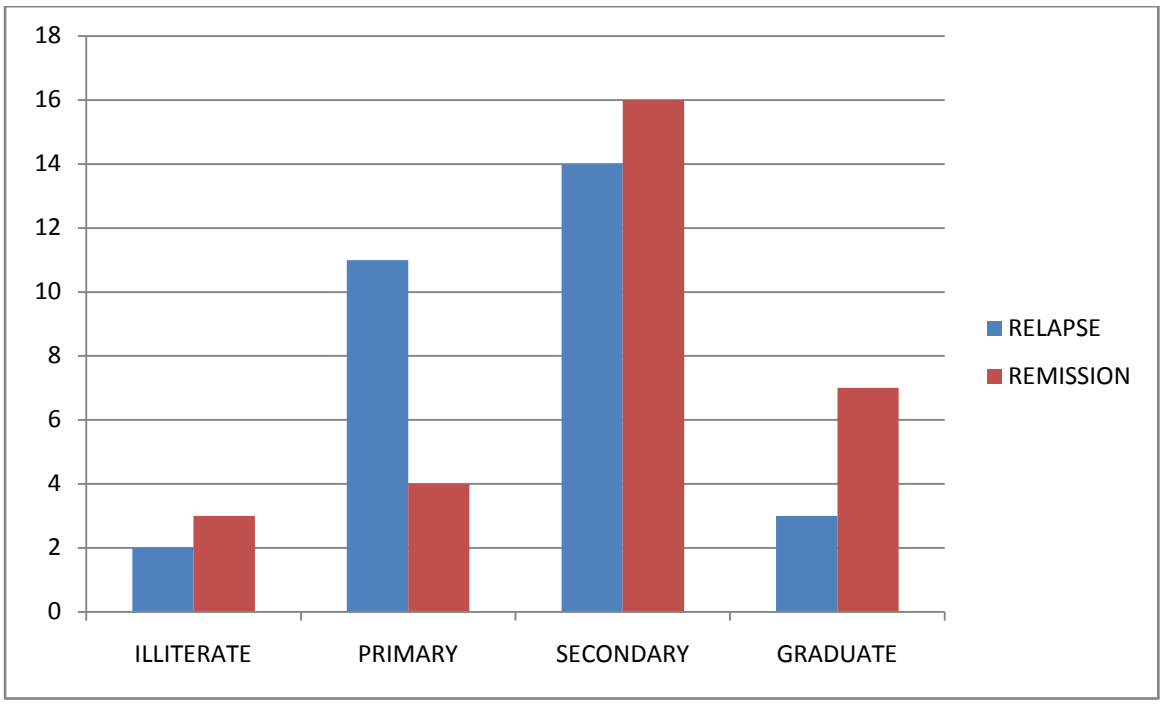
CASE / CONTROL	ILLITERATE	PRIMARY	SECONDARY	GRADUATE	TOTAL
RELAPSE	2	11	14	3	30
REMISSION	3	4	16	7	30

CHI SQUARE	VALUE	P VALUE	SIGNIFICANCE
	5.2	0.158	NOT SIGNIFICANT

In the relapsed group 6.7% were illiterate, 36.7% were educated up to primary level, 46.7% up to secondary level and 10% were graduates. In the remitted group 10% were illiterate, 13.3% were educated up to primary level, 53.3% were educated up to secondary level and 23.3% were graduates. The difference was not statistically significant.

COMPARISON OF RELAPSED AND REMITTED GROUP BASED ON EDUCATION

Figure 7



COMPARISON OF RELAPSED AND REMITTED GROUP ON THE BASIS OF EMPLOYMENT

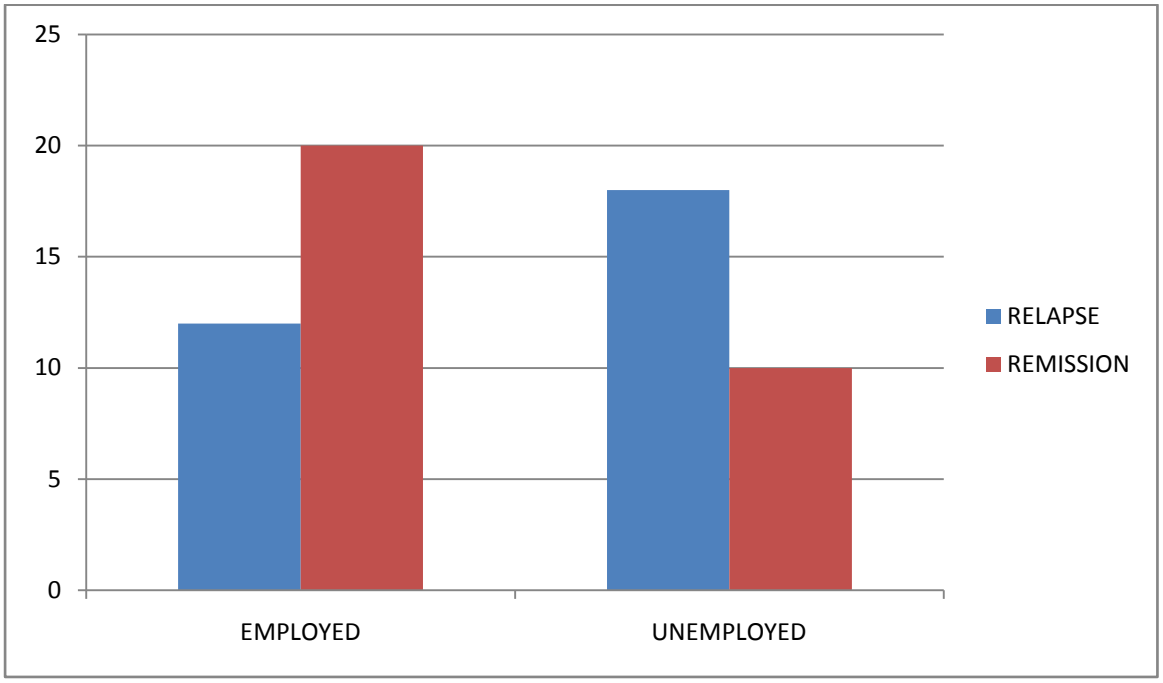
CASE/CONTROL	EMPLOYED	UNEMPLOYED	TOTAL
CASE	12	18	30
CONTROL	20	10	30
TOTAL	32	28	60

CHI SQUARE	VALUE	P VALUE	SIGNIFICANCE
	4.214	0.0401	SIGNIFICANT

In the relapsed group 40% of the patients were employed while 60% of them were unemployed, on the other hand in the remitted group 66.7% were employed while 33.3% were unemployed. The difference was statistically significant.

COMPARISON OF RELAPSED AND REMITTED GROUP ON THE BASIS OF EMPLOYMENT

Figure 8



COMPARISON OF RELAPSED AND REMITTED GROUP ON THE BASIS OF DURATION OF UNTREATED PSYCHOSIS

CASE/CONTROL	DUP < 6 MONTHS	DUP-6-9 MONTHS	DUP 1-2 YEARS	DUP >2 YEARS	TOTAL
RELAPSE	5	3	19	3	30
REMISSION	10	7	8	5	30
TOTAL	15	10	27	8	60

DUP	RELAPSE		REMISSION		P VALUE
	MEAN	S.D	MEAN	S.D	
MONTHS	17.17	10.452	14.87	12.445	0.441

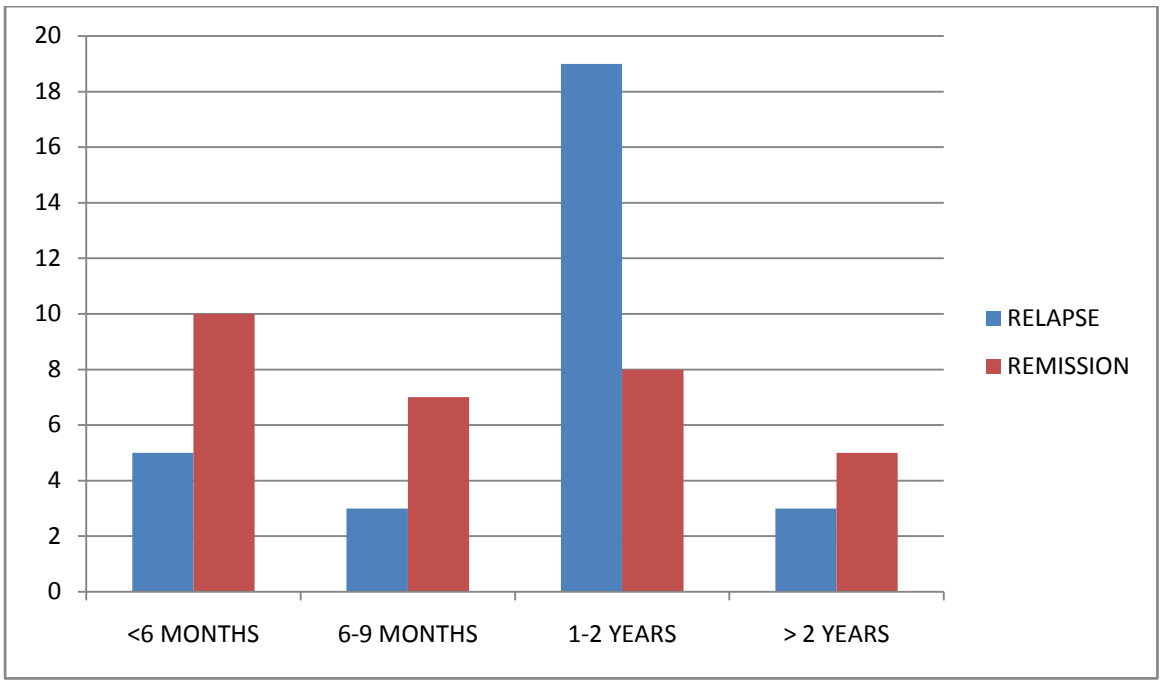
In the relapsed group 16.7% had DUP less than 6 months, 10% had DUP ranging from 6-9 months, 63.3% had dup of 1-2 years and 10% had DUP of more than 2 years.

In the remitted group 33.3% had dup of less than 6 months, 13.3% had dup from 6-9 months, 36.7% had dup of 1-2 years and 16.6% had dup of more than 2 years.

The difference was not statistically significant (p=0.441) on t test.

COMPARISON OF RELAPSED AND REMITTED GROUP ON THE BASIS OF DURATION OF UNTREATED PSYCHOSIS

Figure 8



COMPARISON OF RELAPSED AND REMITTED GROUP BASED ON NUMBER OF HOSPITALIZATIONS

CASE/CONTROL	0	1	2	3	4	5	TOTAL
RELAPSE	2	3	15	4	3	3	30
REMISSION	10	12	4	4	0	0	30
TOTAL	12	15	19	8	3	3	60

CHI SQUARE	VALUE	P VALUE	SIGNIFICANCE
	22.716	0.0004	SIGNIFICANT

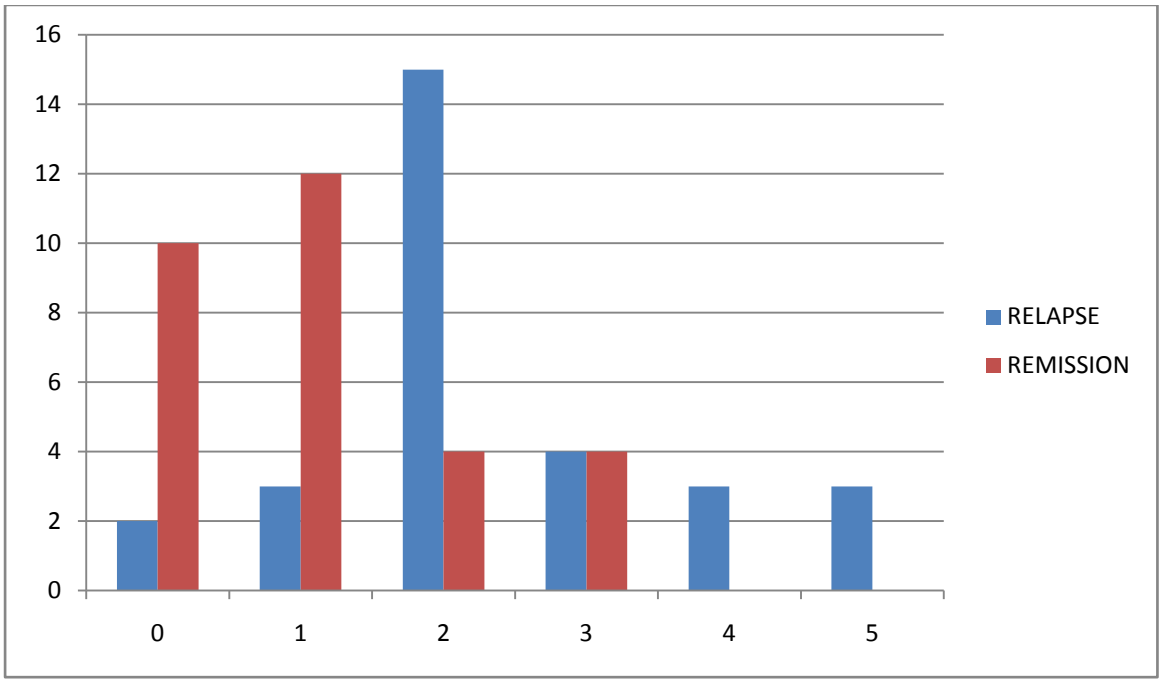
In the relapsed group 6.7% had no hospitalization, 10% had 1 hospitalization, 50% had 2 hospitalizations, 13.3% had 3 hospitalizations and 10% had 4 and 5 hospitalizations each.

In the remitted group 33% had no hospitalizations, 40% had 1 hospitalization, 13.3% had 2 and 3 hospitalizations each.

The difference was statistically significant. On logistic regression the number of hospitalizations were highly predictive of relapse (p=0.017).

COMPARISON OF RELAPSED AND REMITTED GROUP BASED ON NUMBER OF HOSPITALIZATIONS

Figure 9



COMPARISON OF RELAPSED AND REMITTED GROUP BASED ON FAMILY HISTORY OF PSYCHOSIS

CASE/CONTROL	FAMILY HISTORY PRESENT	FAMILY HISTORY ABSENT	TOTAL
RELAPSE	18	12	30
REMISSION	15	15	30
TOTAL	33	27	60

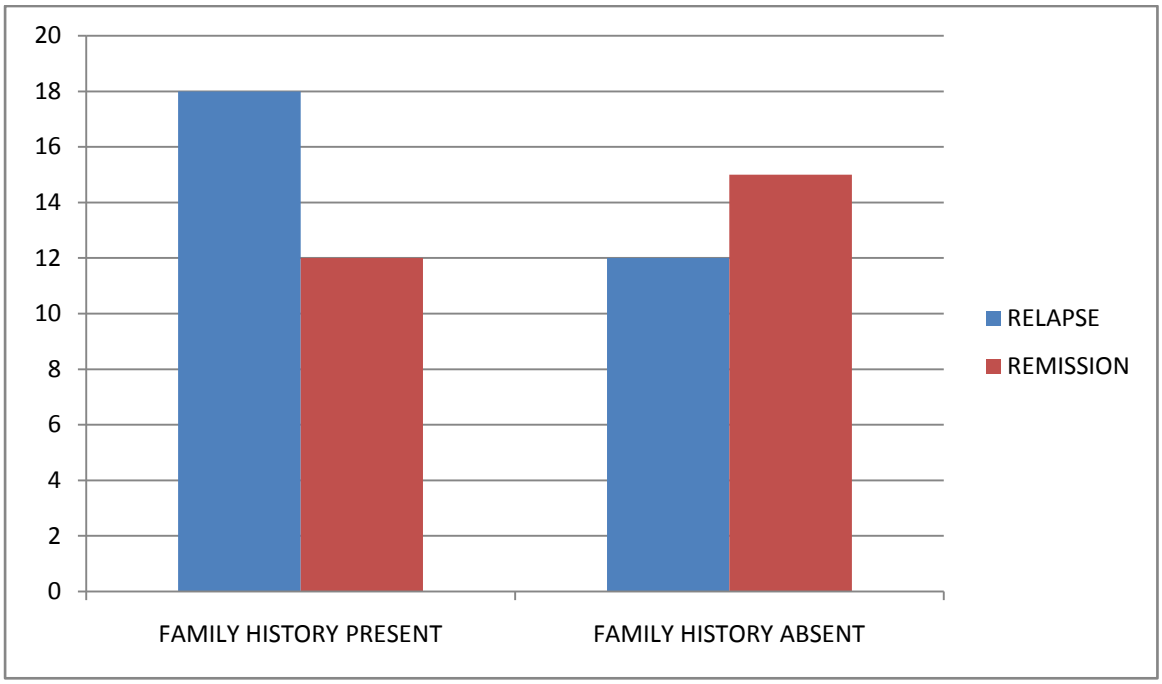
CHI SQUARE	VALUE	P VALUE	SIGNIFICANCE
	0.596	0.440	NOT SIGNIFICANT

In the relapsed group 60% of the patients had family history of psychosis while the remaining 40% did not have a family history of psychosis.

In the remitted group 50% of the patients had a family history of psychosis while the other half did not have a family history of psychosis. The difference was not statistically significant.

COMPARISON OF RELAPSED AND REMITTED GROUP BASED ON FAMILY HISTORY OF PSYCHOSIS

Figure 10



COMPARISON OF RELAPSED AND REMITTED GROUP ON POSITIVE SYMPTOMS BY PANSS SCALE

SCALE	RELAPSE		REMISSION		P VALUE
	MEAN	S.D	MEAN	S.D	
PANSS POSITIVE SUBSCALE SCORE	24.13	4.049	9.33	1.900	0.000

The mean score on the positive subscale of PANSS was 24.13 (S.D±4.049) for relapsed group and the mean score on positive subscale of PANSS for the remitted group was 9.33(S.D±1.90).

The difference was statistically significant (p-.000) in t test.

COMPARISON OF RELAPSED AND REMITTED GROUP ON NEGATIVE SYMPTOMS BY PANSS SCALE

SCALE	RELAPSE		REMISSION		P VALUE
	MEAN	S.D	MEAN	S.D	
PANSS NEGATIVE SUBSCALE SCORE	17.30	6.608	15.67	5.726	0.310

The mean score on negative subscale of PANSS for the relapsed group was 17.30(S.D±6.608) and the mean score on negative subscale of PANSS for the remitted group was 15.67(S.D±5.726)

The difference was not statistically significant (p-.310) on t test.

COMPARISON OF RELAPSED AND REMITTED GROUP ON GENERAL PSYCHOPATHOLOGY BY PANSS SCALE

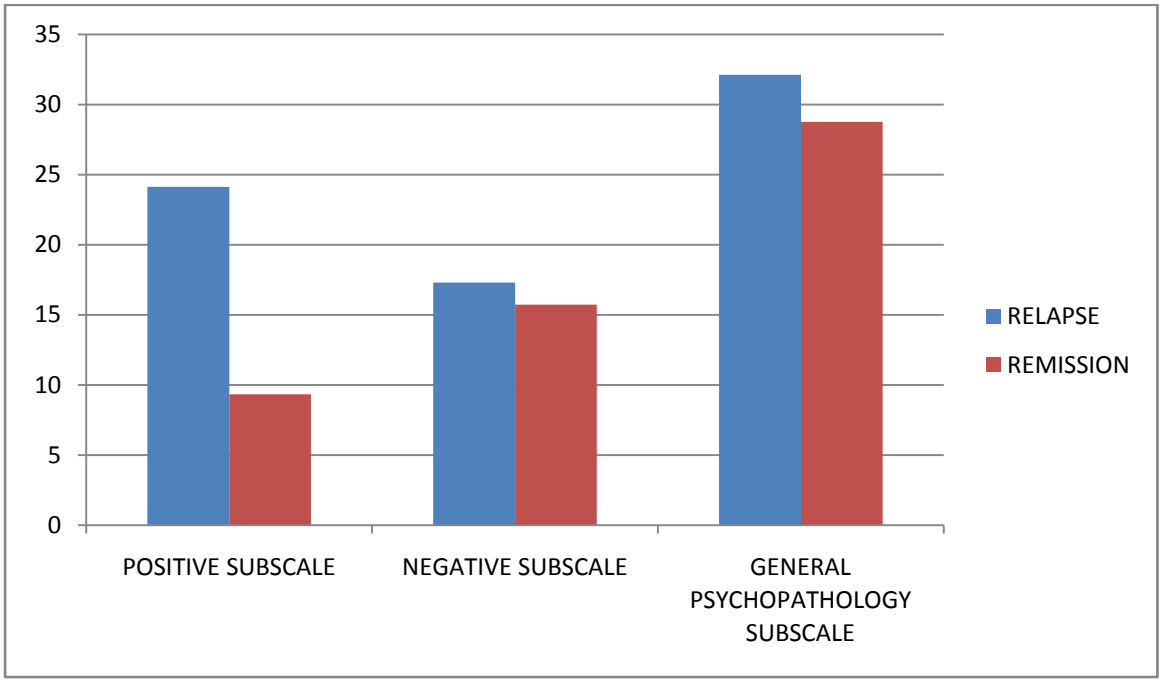
SCALE	RELAPSE		REMISSION		P VALUE
	MEAN	S.D	MEAN	S.D	
PANSS GENERAL PSYCHOPATHOLOGY SUBSCALE SCORE	32.13	6.61	28.77	6.66	0.54

The mean score on general psychopathology subscale of PANSS for relapsed group was 32.13(S.D±6.61) and the mean score on the same scale for the remitted group was 28.77(S.D±6.66)

The difference was not statistically significant (p-0.54) on t test.

COMPARISON OF RELAPSED AND REMITTED PATIENTS ON PANSS SCORES ON POSITIVE NEGATIVE AND GENERAL PSYCHOPATHOLOGY SUBSCALE

Figure 11



COMPARISON OF RELAPSED AND REMITTED SUBGROUP ON DELUSIONS IN PANSS

SCALE	RELAPSE		REMISSION		P VALUE
	MEAN	S.D	MEAN	S.D	
PANSS DELUSION SCORE	5.27	1.437	1.73	1.081	0.000

In the relapsed group, 3.3% of the sample had mimimal delusions,10%-mild delusions,16.7%-moderate delusions,20%-moderately severe delusions,26% - severe and 23.3% had extremely severe delusions.

In the remitted group,60% of the sample had absence of delusions,16.7%-minimal and moderate delusions each,3.3% had moderate and moderately severe delusions each.

The mean score on delusions for relapsed group was 5.27 (S.D±1.437) and the mean score on the same for the remitted group was1.73 (S.D±1.081). The difference was statistically significant (p-0.00) on t test.

COMPARISON OF RELAPSED AND REMITTED GROUPS ON HALLUCINATIONS IN PANSS

SCALE	RELAPSE		REMISSION		P VALUE
	MEAN	S.D	MEAN	S.D	
PANSS HALLUCINATION SCORE	4.70	1.988	1.63	0.999	0.000

In the relapsed group, 13.3% have absent and mild auditory hallucinations each,10% have moderate auditory hallucinations, 30% have moderately severe auditory hallucinations,6.7% have severe and 26.7% have extremely severe auditory hallucinations.

In the remitted group, 63.3% did not have auditory hallucinations, 16.7% had minimal and moderate hallucinations each and 3.3% had moderately severe auditory hallucinations.

The mean score on hallucinations for relapsed group was 4.70 (S.D±1.988) and the mean score on the same for the remitted group was1.63 (S.D±0.99). The difference was statistically significant (p-0.00) on t test.

COMPARISON OF RELAPSED AND REMITTED GROUPS ON DEPRESSION SCORE IN PANSS.

SCALE	RELAPSE		REMISSION		P VALUE
	MEAN	S.D	MEAN	S.D	
PANSS DEPRESSION SCORE	3.07	1.680	3.03	1.450	0.935

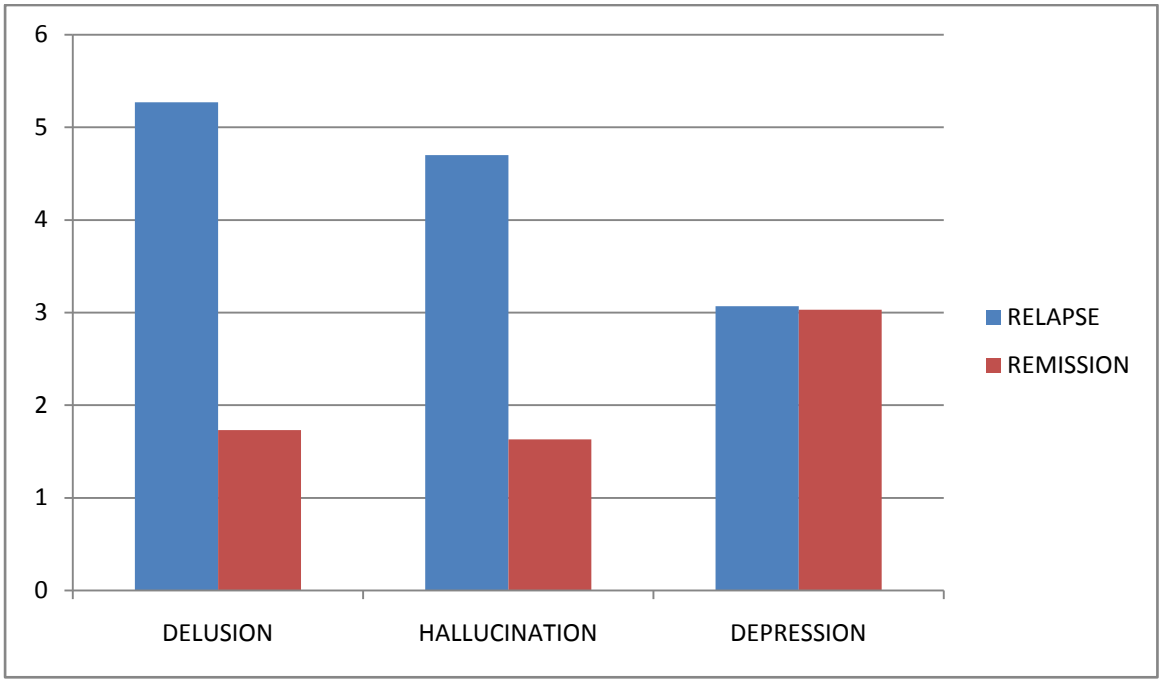
In the relapsed group 30% had no scoring in depression,3.3% minimal depression,23.3% mild depression,26.6% showed moderate depression, 10% moderately severe and 3.3% showed severe and extremely severe degree of depression.

In the remitted group, 20% had no scoring in depression subscale, 16.7% minimal depression, 23.3% mild and moderate scores,13.3% showed moderately severe depression and 3.3% showed severe depression.

The mean score on depression for relapsed group was 3.07 (S.D±1.680) and the mean score on the same for the remitted group was 3.03 (S.D±1.450). The difference was not statistically significant (p-0.935) on t test.

COMPARISON OF RELAPSED AND REMITTED PATIENTS ON PANSS SCORES ON DELUSIONS, HALLUCINATIONS AND DEPRESSION.

Figure 12



COMPARISON OF DRUG ATTITUDE INVENTORY SCORES IN RELAPSED AND REMITTED GROUPS

CASE/CONTROL	COMPLIANT	NON COMPLIANT	TOTAL
RELAPSE	12	18	30
REMISSION	27	3	30
TOTAL	39	21	60

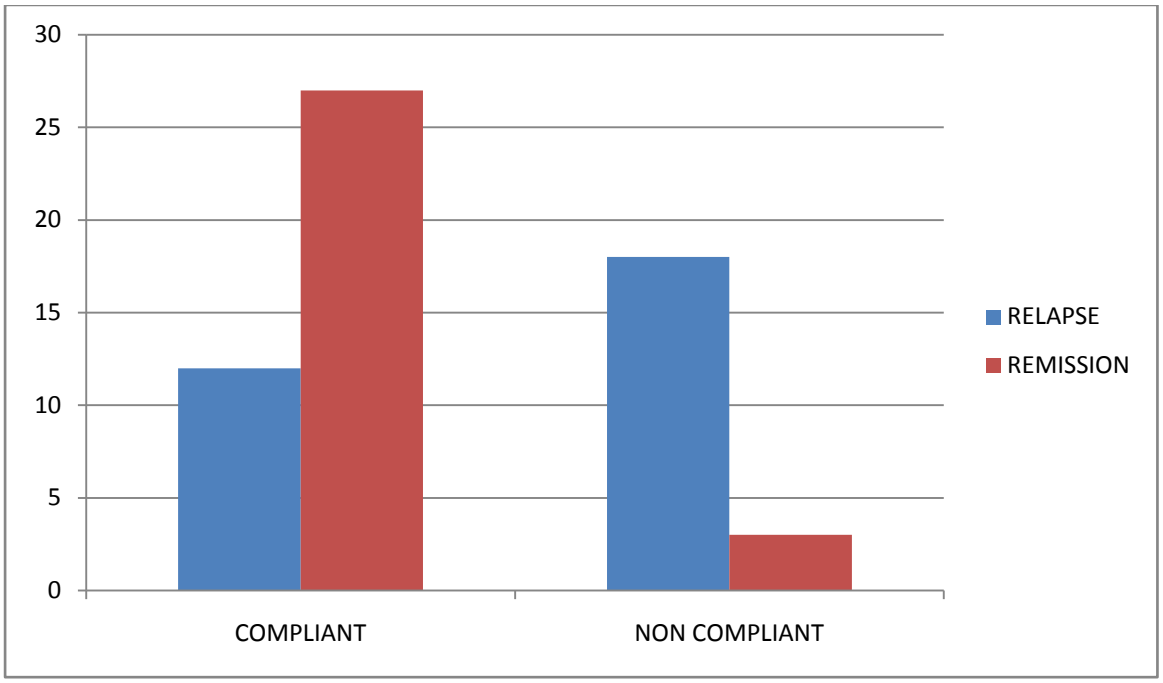
CHI SQUARE	VALUE	P VALUE	SIGNIFICANCE
	16.20	0.0001	SIGNIFICANT

In the relapsed group, 60% of the sample showed a negative subjective response while 40% gave a positive objective response.

In the remitted group, 10% of the sample gave a negative subjective response while 90% of the sample gave a positive subjective response. The difference was statistically significant

COMPARISON OF DRUG ATTITUDE INVENTORY SCORES IN RELAPSED AND REMITTED GROUPS

Figure 13



COMPARISON OF RELAPSED AND REMITTED GROUPS BASED ON STRESSFUL LIFE EVENTS IN THE PRECEDING SIX MONTHS

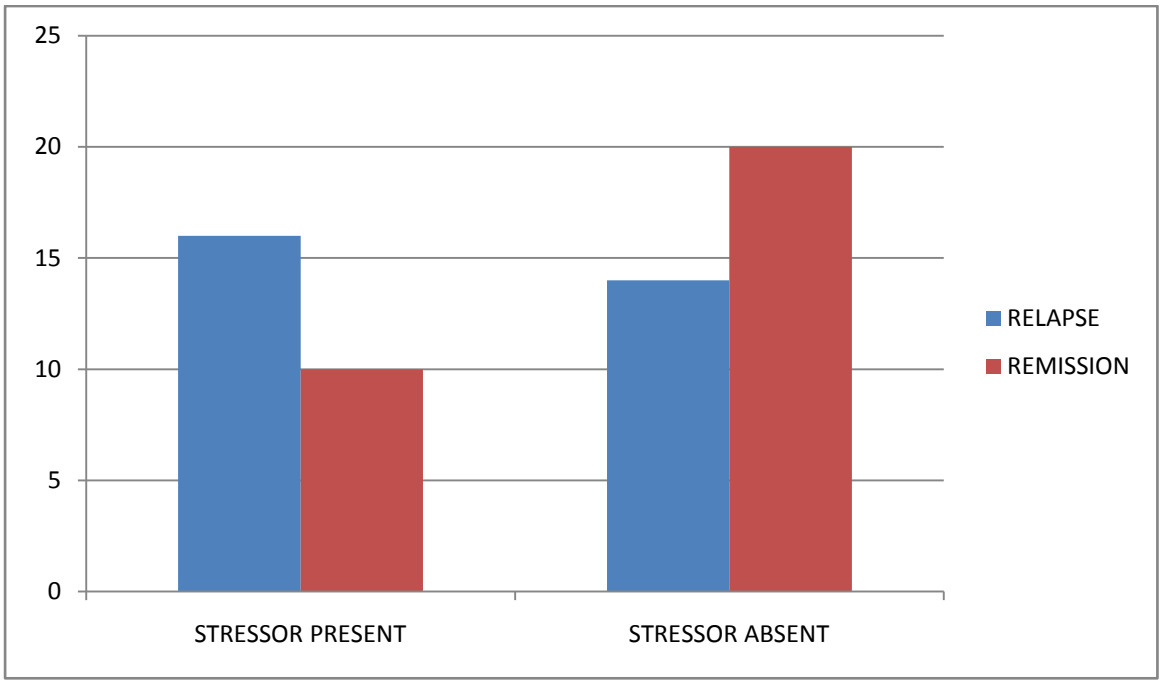
CASE/CONTROL	STRESSOR PRESENT	STRESSOR ABSENT	TOTAL
RELAPSE	16	14	30
REMISSION	10	20	30
TOTAL	26	34	60

CHI SQUARE	VALUE	P VALUE	SIGNIFICANCE
	2.40	0.1211	NOT SIGNIFICANT

In the relapsed group, stressor was present in the preceding six months in 53.3% of the group while it was absent in 46.7% of the group. In the remitted group stressor was present in 33.3% of the group while it was absent in 66.7% of the group.The difference was not statistically significant.

COMPARISON OF RELAPSED AND REMITTED GROUPS BASED ON STRESSFUL LIFE EVENTS IN THE PRECEDING SIX MONTHS

Figure 14



COMPARISON BETWEEN THE RELAPSED AND REMITTED GROUPS IN TERMS OF INSIGHT

SCALE	RELAPSE		REMISSION		P VALUE
	MEAN	S.D	MEAN	S.D	
SAI-E SCORE	4.20	4.003	9.23	3.602	0.000

The mean score on SAI-E for relapsed group was 4.20 (S.D±4.003) and the mean score on the same for the remitted group was9.23 (S.D±3.602). The difference was statistically significant (p-0.00) on t test.

On logistic regression insight was highly predictive of relapse (p=0.21).

COMPARISON BETWEEN THE RELAPSED AND REMITTED GROUPS IN TERMS OF INSIGHT

Figure 15

DISCUSSION

This study found no significant difference in marital status between relapse and remission groups. This finding is in contrast to the findings of Moller et al and Biehl et al which predict better outcome in persons who live in partnership.[28, 30] This finding could be explained by the fact that it is possible that unmarried people may be in a new partnership and that in these groups lots of people have stable relationships without being married. It may also be due to the higher rates of marriage and lower rates of divorce in the Indian population.

When work status was compared, more people from the relapsed group had not been working in the past 6 months than in the remitted group. Chi square test showed a significant difference (p=0.0401) with regard to occupational status. Jonsson et al documented that a longer period of employment could be viewed as a reliable predictor of lower rehospitalisation rate.[36]Buchkremer et al found that there was a low rehospitalisation risk among patients holding down a job paid at standard rates.[79] Significantly more relapsed patients had become unemployed due to their mental illness in comparison to the remitted group. It is likely that repeated relapses had interfered with their occupational functioning. However, it is also possible that the relapsed group may be retrospectively magnifying their occupational dysfunction.

In this study, an association was found between the number of hospitalizations and relapse (p value -0.001).Logistic regression findings also find this measure as highly significant in predicting relapse in our study (p=0.017) This is consistent with findings of many authors. Doering et al found that the absence of hospitalization in the preceding year was the most significant predictors for rehospitalisation rate.[33] The number of admissions in the hospital has shown to be a significant predictor of outcome in a study by Biehl et al.[30]But in contrast is the finding of Chabungbam et al where they failed to find an association between numbers of previous hospitalization and relapse. They explain that it is probably because of the fact that most of the psychotic relapses are treated on an outpatient basis in India unlike in the west where there is a closer correspondence between hospitalizations and relapse. [44]

In terms of education, in a prospective study by Biehl et al, higher educational level corresponded with better outcome.[30]Suzuki et al reported that educational level is an important factor in secondary prevention of schizophrenic episodes.[35] In our study we found no association between educational levels and relapse. (p=0.158). The results of our study are similar to that of Kazadi et al who reasoned that schizophrenia tends to have an early onset and leads to a declining level of functioning that may have contributed to the early school dropout.[80]

In the context of duration of untreated psychosis, Ucok at al found that patients with longer duration of untreated psychosis were rehospitalized earlier and had more relapses during one year follow up. These findings may indicate that duration of untreated psychosis is partially related with a more severe course. [81] Our study did not find an association between duration of untreated psychosis and relapse (p=0.441). This result is similar to the study by Barnes et al who reported that longer duration of untreated psychosis was not associated with poor outcome or greater worsening of illness.[82] Our findings are probably due to the fact that most of the patients in our study have had illness for around 5 years or more and Marshall et al have reported that the relationship between duration of untreated psychosis and the clinical course is clearer in the earlier phase. [83]

While comparison was made between the relapsed group and the remitted group in terms of family history of psychosis no significance was found in our study. These findings are similar to that of Xiang et al who also did not find an association between family history of psychiatric disorder and relapse in schizophrenia.[84]

The occurrence of significant difference between relapsed and remitted groups (p= 0.000) in positive syndrome score was mandated by our definition of relapse but there was no significant difference between the scores on general psychopathology and negative syndrome between the relapsed and remitted

groups. This was contrary to the findings of Chabungbam et al, who found a significant association difference between relapsed and remitted patients on general psychopathology, negative syndrome, anergia and paranoid features which attested that the symptom cluster of schizophrenia is syndromal in nature.[44]

Several studies have found a significant peak of life events in the month preceding a relapse [63, 66]. Pallanti et al found that 61% of those that relapsed had a severe event in the month prior to relapse. [85]On the other hand Hirsch et al and Bebbington et al found no support for the earlier contention that life events had a triggering role in psychosis.[86, 87] In our study, we found no significant association between relapse and stressful life events (p=0.121).Bebbington and Kuipers speculated that the lack of identifiable life events before relapse in people with schizophrenia may be due to the fact that they were abnormally sensitive to relatively minor stressors that were difficult to detect.[88] Also it is truly impossible to apply an experimental design to life events research as one cannot ensure that all subjects across and within research groups will experience similar life events.

In our study, we looked at the drug attitudes of relapsed and remitted patients and there was a highly significant difference (p=0.0001). We found that non compliance was highly correlated with the relapsed group. These findings are similar to that of Kane et al and Leucht et al, who found that

negative attitudes were correlated with relapse and rehospitalisation.[89, 90] Fenton et al found that relapse rates were an average of 3.7 times higher in patients who were rated as noncompliant. Morken et al concluded that non-adherence with oral or depot antipsychotic medication combined were associated with increased frequencies of relapses, being persistent psychotic and an increased risk of being admitted to hospital.[91]

On the other hand, logistic regression findings in our study do not show drug attitudes as a major predictor of relapse. This could be due the fact that several authors have noted that relapse among medication compliant out patients averages around 40% in a year following hospital discharge[50].These results are similar to the results obtained in the study by Suzuki et al where poor drug compliance was associated with hospitalization on bivariate analysis but not on logistic regression.[35] This may be due to the limitation in the way in assessing compliance by means of the drug attitude inventory rather than using external validating factors like urine tests or serum neuroleptic levels.

In our study, a significant difference was found in the insight scores between the relapsed and the remitted groups (p=0.000). Logistic regression findings indicated that it was a significant predictor of relapse (p=0.021).These results were similar to those in the study by Drake at al where those with the best insight scores had an estimated rate of relapse that was 39% of that of those with the worst scores .Readmission was highly correlated with relapse, so

poor insight also predicted readmission .Insight predicted both relapse and readmission. [68]

On the other hand Yen at al, found that there was no significant difference in insight between hospitalized and non hospitalized patients. They explained that insight correlated with treatment compliance and this confirmation to drug schedules led to decrease in risk for relapse.[70] Thus insight plays an important role in influencing course and contributing to the prevention or triggering of relapse. Poor insight is one aspect of lack of concern, which reduces the likelihood of presenting for help. Poor insight is also likely to have effects subsequent to onset, such as influencing attitudes toward treatment, whether medication or psychological interventions.

CONCLUSIONS

In our study, demographic factors like education, marital status, background and clinical features like family history of psychosis, duration of untreated illness and adverse life events were not associated with relapse in schizophrenia.

Patients with relapse have more positive features but did not differ from remitted patients in terms of negative features or general psychopathology.

The findings of our study suggest that negative attitude towards psychiatric medication which indirectly indicated non compliance, severe illness characterized by number of hospitalizations, unemployment and poor insight may be causally related to relapse in schizophrenia.

The identification of these specific factors will help in reducing the risk of relapse in patients with schizophrenia. Various measures like psycho education can be given to improve drug compliance, attempts can be made to increase insight as an early intervention strategy to aid successful treatment and reduction in hospitalization can be brought about.

Relapse prevention is a major goal of treatment for patients with schizophrenia. Lowering rates of relapse decreases patient suffering, the disruption of relationships between patients and their families, and the societal costs of providing care for patients with schizophrenia. With the successful prevention of relapse, patients with schizophrenia can achieve their full potential with regard to work and social relationships. The societal costs of

treating patients with schizophrenia can be lessened by employing these strategies that decrease relapse and the need for rehospitalisation, the costliest treatment alternative.

LIMITATIONS

1) An optimal study of relapses would use a prospective design. Causal inferences are generally more tenuous. Also in this study, subjects and informants had to recall their experiences over the past several weeks or months, which could have caused a recall bias.

2) The sample size is small

3) The sample consisted of patients referred to a tertiary service, our patients could be more severely ill and therefore it might not be possible to generalize these results to community samples.

4) The role of predictors needs to be validated by a prospective design

5) The study did not include patients who had co morbid substance dependence which could have lead to exclusion of a proportion of patients.

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Appendix I

PROFORMA

Name :	
Age :	
Gender : Male (1) / Female (2)	
Address : Urban (1) / Rural (2)	
Marital Status	Unmarried(1) Married(2) Separated(3) Divorced(4)
Education	Illiterate (1) Primary(2) Secondary(3) Graduate(4)
Income	<1000(1), 1000-5000 (2), >5000 (3)
Employment	Yes (1) /No (1)
Age Of Onset Of Illness	
Duration Of Untreated Psychosis	
Age At First Hospitalization	
Number Of Hospitalization	
Duration Of Illness	<1yr (1), 1-2 Yr(2), 2-5yr (3), >5yr (4)
Family History Of Psychosis	Yes (1), No (2)
Subcategory Of Schizophrenia	Paranoid (1), Undifferentiated (2), Hebephrenic (3)
Primary Caregiver	
Stressor in PSLES	Present (1) Absent (2)
DAI	Compliant (1) Non compliant (2)

Appendix II

PANSS

O=Absent l=MinimaI 2=Mild 3=Moderate 4=Moderate severe 5=Severe 6=Extreme

POSITIVE SCALE (P)

P1 Delusions [_]

Beliefs which are unfounded, unrealistic, and idiosyncratic. Basis for rating: Thought content expressed in the interview; and its influence on social relations and behavior.

P2 Conceptual disorganization [_]

Disorganized process of thinking characterized by disruption of goal-directed sequencing, e.g., circumstantiality, tangentiality, loose associations, non sequiturs, gross illogicality, or thought block. Basis for rating: Cognitive-verbal processes observed during the course of interview.

P3 Hallucinatory behavior [_]

Verbal report or behavior indicating perceptions which are not generated by external stimuli. These may occur in the auditory, visual, olfactory, or somatic realms. Basis for rating: Verbal report and physical manifestations during the course of interview as well as reports of behavior by primary care workers or family.

P4 Excitement [_]

Hyperactivity as reflected in accelerated motor behavior, heightened responsivity to stimuli, hypervigilance, or excessive mood lability. Basis for rating: Behavioral manifestations during the course of interview as well as reports of behavior by primary care workers or family.

P5 Grandiosity [_]

Exaggerated self-opinion and unrealistic convictions of superiority, including delusions of extraordinary abilities, wealth, knowledge, fame, power, and moral righteousness. Basis for rating: Thought content expressed in the interview and its influence on behavior.

P6 Suspiciousness/persecution [_]

Unrealistic and exaggerated ideas of persecution, as reflected in guardedness, a distrustful attitude, suspicious hypervigilance, or frank delusions that others mean one harm. Basis for rating: Thought content expressed in the interview and its influence on behavior.

P7 Hostility [_]

Verbal and nonverbal expressions of anger and resentment, including sarcasm,

passive-aggressive behavior, verbal abuse, and assaultiveness. Basis for rating: Interpersonal behavior observed during the interview and reports by primary care workers or family.

NEGATIVE SCALE (N)

Nl Blunted affect [_]

Diminished emotional responsiveness as characterized by a reduction in facial expression, modulation of feelings, and communicative gestures. Basis for rating: Observation of physical manifestations of affective tone and emotional responsiveness during the course of interview.

N2 Emotional withdrawal [_]

Lack of interest in, involvement with, and affective commitment to life's events. Basis for rating: Reports of functioning from primary care workers or family and observation of interpersonal behavior during the course of interview.

N3 Poor rapport [_]

Lack of interpersonal empathy, openness in conversation, and sense of closeness, interest, or involvement with the interviewer. This is evidenced by interpersonal distancing and reduced verbal and nonverbal communication. Basis for rating: Interpersonal behavior during the course of interview.

N4 Passive/apathetic social withdrawal [_]

Diminished interest and initiative in social interactions due to passivity, apathy, anergy, or avolition. This leads to reduced interpersonal involvements and neglect of daily activities.

N5 Difficulty in abstract thinking [_]

Impairment in the use of the abstract-symbolic mode of thinking, as evidenced by difficulty in classification, forming generalizations, and proceeding beyond concrete or egocentric thinking in problem-solving tasks. Basis for rating: Responses to questions on similarities and proverb interpretation, and use of concrete vs. abstract mode during the course of interview.

N6 Lack of spontaneity and flow of conversation [_]

Reduction in the normal flow of communication associated with apathy, avolition, defensiveness, or cognitive deficit. This is manifested by diminished fluidity and productivity of the verbal-interactional process. Basis for rating: Cognitive-verbal processes observed during the course of interview.

N7 Stereotyped thinking [_]

Decreased fluidity, spontaneity, and flexibility of thinking, as evidenced in rigid, repetitious, or barren thought content. Basis for rating: Cognitive-verbal processes during the course of interview.

GENERAL PSYCHOPATHOLOGY SCALE (G)

Gl Somatic concern **[_]**

Physical complaints or beliefs about bodily illness or malfunctions. This may range from a vague sense of ill being to clear-cut delusions of catastrophic physical disease.

G2 Anxiety **[_]**

Subjective experience of nervousness, worry, apprehension, or restlessness, ranging from excessive1 concern about the present or future to feelings of panic. Basis for rating: Verbal report during the course of interview and corresponding physical manifestations.

G3 Guilt feelings **[_]**

Sense of remorse or self-blame for real or imagined misdeeds in the past. Basis for rating: Verbal report of guilt feelings during the course of interview and the influence on attitudes and thoughts.

G4 Tension **[_]**

Overt physical manifestations of fear, anxiety, and agitation, such as stiffness, tremor, profuse sweating, and restlessness. Basis for rating: Verbal report attesting to anxiety and, thereupon, the severity of physical manifestations of tension observed during the interview.

G5 Mannerisms and posturing **[_]**

Unnatural movements or posture as characterized by an awkward, stilted, disorganized, or bizarre appearance. Basis for rating: Observation of physical manifestations during the course of interview as well as reports from primary care workers or family.

G6 Depression **[_]**

Feelings of sadness, discouragement, helplessness, and pessimism. Basis for rating: Verbal report of depressed mood during the course of interview and its observed influence on attitude and behavior.

G7 Motor retardation **[_]**

Reduction in motor activity as reflected in slowing or lessening of movements and speech, diminished responsiveness to stimuli, and reduced body tone. Basis for rating: manifestations during the course of interview as well as reports by primary care workers or family.

G8 Uncooperativeness **[_]**

Active refusal to comply with the will of significant others, including the interviewer, hospital staff, or family, which may be associated with distrust, defensiveness, stubbornness, negativism, rejection of authority, hostility, or belligerence. Basis for rating: Interpersonal behavior observed during the course of interview as well as reports by primary care workers or family.

G9 Unusual thought content **[_]**

Thinking characterized by; strange, fantastic, or bizarre ideas, ranging from those which are remote or atypical to those which are distorted, illogical, and patently absurd. Basis for rating: Thought content expressed during the course of interview.

G10 Disorientation **[_]**

Lack of awareness of one's relationship to the milieu, including persons, place, arid time, which may be due to confusion or withdrawal. Basis for rating: Responses to interview questions on orientation.

G11 Poor attention **[_]**

Failure in focused alertness manifested by poor concentration, distractibility from internal and external stimuli, and difficulty in harnessing, sustaining, or shifting focus to new stimuli. Basis for rating: Manifestations during the course of interview.

G12 Lack of judgment and insight **[_]**

Impaired awareness or understanding of one's own psychiatric condition and life situation. This is evidenced by failure to recognize past or present psychiatric illness or symptoms, denial of need for psychiatric hospitalization or treatment, decisions characterized by poor anticipation of consequences, and unrealistic short-term and long-range planning. Basis for rating: Thought content expressed during the interview.

G13 Disturbance of volition **[_]**

Disturbance in the willful initiation, sustenance, and control of one's thoughts, behavior, movements, and speech. Basis for rating: thought content and behavior manifested in the course of interview.

G14 Poor impulse control **[_]**

Disordered regulation and control of action on inner urges, resulting in sudden, unmodulated, arbitrary, or misdirected discharge of tension and emotions without concern about consequences. Basis for rating: Behavior during the course of interview and reported by primary care workers or family.

G15 Preoccupation **[_]**

Absorption with internally generated thoughts and feelings and with autistic experiences to the detriment of reality orientation and adaptive behavior. Basis for rating: Interpersonal behavior observed during the course of interview.

G16 Active social avoidance **[_]**

Diminished social involvement associated with unwarranted fear, hostility, or distrust. Basis for rating: Reports of social functioning by primary care workers or family.

Appendix III

SOCIAL AND OCCUPATIONAL FUNCTIONING ASSESSMENT SCALE (SOFAS)

Code (Note: Use intermediate codes when appropriate, e.g., 45, 68, 72.)

91-100	Superior functioning in a wide range of activities.
81-90	Good functioning in all areas, occupationally and socially effective.
71-80	No more than a slight impairment in social, occupational, or school functioning (e.g., infrequent interpersonal conflict, temporarily falling behind in schoolwork).
61-70	Some difficulty in social, occupational, or school functioning, but generally functioning well, has some meaningful interpersonal relationships.
51-60	Moderate difficulty in social, occupational, or school functioning (e.g., few friends, conflicts with peers or co-workers).
41-50	Serious impairment in social, occupational, or school functioning (e.g., no; friends, unable to keep a job).
31-40	Major impairment in several areas, such as work or school, family relations (e.g., depressed man avoids friends, neglects family, and is unable to work; child frequently beats up younger children, is defiant at home, and is failing at school).
21-30	Inability to function in almost all areas (e.g., stays in bed all day; no job, home, or friends).
11-20	Occasionally fails to maintain; minimal personal hygiene; unable to function independently
1-10	Persistent inability to maintain minimal personal hygiene. Unable to function without harming self or others or without considerable external support (e.g., nursing care and supervision).
0	Inadequate information

APPENDIX IV

PRESUMPTIVE STRESSFUL LIFE EVENTS SCALE (Gurmeet Singh et al. 1984)

Rank on Stress score	Life events	Mean
1.	Death of spouse	95
2.	Extra marital relation of spouse	80
3.	Marital separation / divorce	77
4.	Suspension or dismissal from job	76
5.	Detention in jail of self of close family member	72
6.	Lack of Child	67
7.	Death of close family member	66
8.	Marital conflict	61
9.	Property or crops damaged	61
10.	Death of friend	60
11.	Robbery or theft	59
12.	Excessive alcohol or drug use by family member	58
13.	Conflict with in laws (other then dowry)	57
14.	Broken engagement or love affair	57
15.	Major personal illness or injury	55
16.	Son or daughter leaving home	55
17.	Financial loss or problems	54
18.	Illness of family member	52
19.	Trouble at working with colleagues / superior or subordinates	58
20.	Prophecy of astrologer or palmist etc.	52
21.	Pregnancy of wife (wanted of unwanted)	51
22.	Conflict over dowry (Self or Spouse)	51
23.	Sexual problems	51
24.	Self or family member unemployed	51
25.	Lack of son	51
26.	Large loan	49
27.	Marriage of daughter / dependent sister	49
28.	Minor violation of law	46
29.	Family conflict	47
30.	Break up with friend	47
31.	Major purchase or construction of house	46
32.	Death of pet	51
33.	Failure in examination	43
34.	Appearing for an exam or interview	43
35.	Getting married and engaged	43
36.	Trouble with neighbour	40
37.	Unfulfilled commitments	40

38.	Change of residence	39
39.	Change or expansion of business	37
40.	Outstanding personal achievement	37
41.	Begin or end of schooling	36
42.	Retirement	35
43.	Change in sleep, working conditions or transfer	33
44.	Change in sleeping habits	33
45.	Birth of daughter	30
46.	Gain of new family member	30
47.	Reduction in no of family function	29
48.	Change in social activities	28
49.	Change in eating habits	27
50.	Wife begins or stops work	25
51.	Going on pleasure trip or pilgrimage	20

Appendix V

Schedule for assessing the three components of insight

la. Does patient accept (includes passive acceptance) treatment (medication and/-or admission and/or other physical and psychological therapies)?

Often-2 (may rarely question need for treatment)

Sometimes =1 (may occasionally question need for treatment)

Never = 0 (ask why)

If 1 or 2, proceed to

lb. Does patient ask for treatment unprompted?

Often = 2 (excludes inappropriate requests for medication (etc)

Sometimes = 1 (rate here if forgetfulness/disorganization leads to occasional requests only)

Never = 0 (accepts treatment after prompting)

2a. Ask patient: "Do you think you have an illness?" or

"Do you think there is something wrong with you?"

(mental, physical, unspecified)

Often = 2 (thought present most of the day, most days)

Sometimes = 1 (thought present occasionally)

Never = 0 (ask why doctors/others think he/she does)

If 1 or 2 proceed to:

2b. Ask patient: "Do you think you have a mental/psychiatric illness?"

Often = 2 (thought present most of the day, most days)

Sometimes = 1 (thought present occasionally, minimum once per day)

Never = 0

If 1 or 2 proceed to:

2c. Ask patient: "How do you explain your illness?"

Reasonable account given based on plausible mechanisms

(appropriate given patient's social, cultural and educational background, e.g. excess stress, chemical imbalance, family history, etc) = 2

Confused account given, repetition of overheard explanation without adequate understanding or "don't know" = l

Delusional explanation = 0

3a. Ask patient: "Do you think the belief that... [insert specific delusion] is not really true/happening?" or "Do"; you think that . . . [insert specific hallucination] is not really there/happening?"

Often = 2 (thought present most of the day, most days)

Sometimes = 1 (thought present occasionally, minimum once per day), / Never = 0 If 1 or 2 proceed to:

3b. Ask patient: "How do you explain these phenomena [the belief that . . . hearing that voice/seeing that image, etc]'

Part of my illness = 2

Reaction to outside event/s (e.g. 'tiredness', 'stress', etc) = 1

Attributed to outside forces (may be delusional) = 0

Maximum score =14.

Supplementary question (hypothetical contradiction)

"How do you feel when people, don't believe you [when, you talk about... (delusion or hallucinatory experience)] ?"

They're lying = 0

I’m still sure despite what others say= 1

I'm confused and don't know what to think = 2

I wonder whether something's wrong with me = 3

That's when I know I'm sick = 4.

Appendix VI

DRUG ATTITUDE INVENTORY - 30

1.	I don't need to take medication once I feel better	T F
2.	For me, the good things about medication outweigh the bad	T F
3.	I feel strange, "doped up", on medication	T F
4.	Even when I am not in hospital I need medication regularly	T F
5.	If I take medication, it's only because of pressure from other people	T F
6.	I am more aware of what I am doing, of what is going on around me, when I am on medication	T F
7.	Taking medications will do me no harm	T F
8.	I take medications of my own free choice	T F
9.	Medications make me feel more relaxed	T F
10.	I am no different on or off medication	T F
11.	The unpleasant effects of medication are always present	T F
12.	Medication makes me feel tired and sluggish	T F
13.	I take medication only when I feel ill	T F
14.	Medications are slow-acting poisons	T F

15.	I get along better with people when I am on medication	T F
16.	I can't concentrate on anything when I am taking medication	T F
17.	I know better than the doctors when to stop taking medication	T F
18.	I feel more normal on medication	T F
19.	I would rather be ill then taking medication	T F
20.	It is unnatural for my mind and body to be controlled by medications	T F
21.	My thoughts are clearer on medication	T F
22.	I should keep taking medication even if I feel well	T F
23.	Taking medication will prevent me from having a breakdown	T F
24.	It is up to the doctor to decide when I should stop taking medication	T F
25.	Things that I could do easily are much more difficult when I am on medication	T F
26.	I am happier and feel better when I am taking medications	T F
27.	I am given medication to control behaviour that <u>other</u> people (not myself) don't like	T F
28.	I can't relax on medication	T F
29.	I am in better control of myself when taking medication	T F
30.	By staying on medications I can prevent myself getting sick	T F

Appendix VII

INSTITUTIONAL ETHICAL COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI -3

Telephone No: 04425305301
Fax : 044 25363970

CERTIFICATE OF APPROVAL

To
Dr. B. Sowmya
PG in MD Psychiatry
Institute of Mental Health
Kilpauk , Chennai -10.

Dear Dr. B. sowmya

The Institutional Ethical Committee of Madras Medical College reviewed and discussed your application for approval of the project / proposal / clinical trail entitled " A study of predictive factors associated with relapse in schizophrenia" No 54082010.

The following members of Ethical committee were present in the meeting held on 24.08.2010 conducted at Madras Medical College, Chennai -3.

1. Prof. S.K. Rajan, MD	– Chairperson
2. Prof. J. Mohanasundaram, MD,Ph.D,DNB Dean, Madras Medical College, Chennai -3	– Deputy Chairman
3. Prof. A. Sundaram, MD Vice Principal , MMC, Chennai -3	– Member Secretary
4. Prof R. Nandhini, MD Director, Institute of Pharmacology, MMC, Ch-3	– Member
5. Prof. C. Rajendiran , MD	– Member
Director, Institute of Internal Medicine, MMC, Ch-3	– Member
6. Prof. Md. Ali, MD, DM	– Member
Professor & Head ,,Dept. of MGE, MMC, Ch-3	– Member
7 Prof. Shantha Ravishankar, MD Professor of Neuro Pathology, MMC, Ch-3	– Member
8. Tmt. Arnold Soulina	-- Social Scientist

We approve the trail to be conducted in its presented form.

Sd /. Chairman & Other Members

The Institutional Ethics Committee expects to be informed about the progress of the study, any SAE occurring in the course of the study, any changes in the protocol and patient information / informed consent and asks to be provided a copy of the final report

Member Secretary, Ethics Committee

Appendix VIII

CONSENT FORM

I, the undersigned have been explained the following in the language I understand.

1. I have been explained about the nature and details of the study and I give my full consent to participate in it freely, without any bias or coercion.

2. I understand that the purpose of this study is to find further information regarding the nature of relapse in schizophrenia and the factors associated with it.

3. The finding of this study can be used in a thesis or research paper.

4. Personal information will be kept strictly confidential.

Name and signature of patient

Name and signature of the doctor

Name and sign of witness

PATIENT INFORMATION SHEET

As you know schizophrenia is an illness which is characterized by relapses and remissions. In this study we are investigating certain aspects associated with relapse of illness with the help of certain questionnaires. We shall assess the medication adherence, psychopathology, insight, stressful life events, social and occupational functioning. We will compare it with patients having remission in schizophrenia. We seek your consent to take part in this study. If you consent we will examine your functioning and symptoms by interviewing you in detail. These tests will take around two hour to complete. We will show you how the tests are done before taking the assessment. After understanding the nature of the assessment if you choose not to undergo the tests your decision is respected by us. Taking part in the study does not involve any risk to your health. Please be informed that you have the right to refuse to take part in the study at any point of time.

Signature of patient:

Date:

Place:

Appendix - IX

name	age	case/control	sex	background	marital status	education	employment	income	DUP	No. of hosp	subtype of schizophrenia	duration of illness	F/H/O PSY	PANNS P	PANNS N	PANNS GP	panns deln	panns hallucination	panns abstraction	panns depression	panns judgementntnt and insight	DAI	STRESSOR	SA insight compliance	SA insight awareness	SAinsight relabelling	insight total
1	40	2	1	1	1	3	1	1	24	1	1	4	2	7	9	30	1	1	1	1	5	1	2	4	3	1	11
2	42	2	1	1	2	4	2	0	24	1	2	4	1	11	19	25	5	1	5	3	4	1	1	4	3	1	9
3	52	2	1	1	3	3	2	0	24	0	2	4	1	12	18	39	3	3	3	5	4	1	2	3	3	2	9
4	35	2	2	2	2	2	2	0	1	1	2	3	1	12	11	26	1	5	2	4	6	1	2	4	1	0	5
5	38	2	2	2	2	1	2	0	24	0	1	4	1	7	13	19	1	1	1	1	2	1	2	4	2	2	10
6	36	2	1	1	1	3	1	3	36	2	2	4	1	7	15	28	1	1	4	4	5	1	2	4	3	1	8
7	38	2	1	1	1	3	2	0	5	1	3	4	1	8	16	25	1	1	3	3	3	1	2	4	1	2	9
8	30	2	1	2	2	4	1	2	24	1	2	3	1	10	14	23	3	2	3	3	3	1	1	4	5	3	14
9	40	2	1	1	4	3	2	0	26	2	2	4	1	11	14	25	3	1	4	3	3	1	1	4	2	1	8
10	51	2	2	1	2	3	1	1	6	3	1	4	1	7	15	28	1	1	4	2	7	1	2	4	1	1	7
11	32	2	2	1	3	3	2	0	3	0	1	2	1	9	20	27	1	1	3	2	6	1	2	4	0	0	4
12	43	2	1	1	2	4	1	3	36	2	1	3	2	7	9	23	1	1	3	2	5	1	2	4	0	0	5
13	52	2	1	1	2	3	2	0	24	3	1	4	1	7	7	18	1	1	1	1	3	1	2	4	4	4	14
14	24	2	1	2	1	3	2	0	1	0	2	4	1	7	8	22	1	1	1	2	4	1	2	4	4	4	16
15	35	2	1	1	1	3	2	0	24	1	1	4	2	9	22	28	1	1	5	3	4	1	2	4	1	2	9
16	44	2	2	1	1	3	1	2	2	1	1	3	2	10	15	28	2	3	4	4	4	1	2	4	3	2	11
17	42	2	1	1	1	3	1	3	36	3	1	4	2	7	13	23	1	1	3	1	4	1	2	4	4	2	12
18	30	2	1	1	1	3	1	2	12	1	1	4	2	12	20	26	4	3	4	5	4	1	2	4	3	2	11
19	30	2	1	1	3	2	1	1	2	0	1	3	2	11	23	34	2	2	3	3	2	1	2	3	3	4	13
20	26	2	1	2	1	4	1	2	3	3	1	3	2	10	8	29	1	3	1	3	4	1	1	4	2	3	13
21	47	2	1	1	1	4	1	2	36	2	1	4	2	11	11	25	1	1	4	1	7	2	1	4	0	0	4
22	29	2	1	2	2	4	1	3	12	0	1	4	1	7	14	24	1	1	2	1	1	1	2	4	6	4	4
23	30	2	1	2	2	1	1	1	2	1	1	4	2	7	17	45	1	1	3	4	2	2	1	0	3	2	7
24	30	2	1	1	2	3	1	2	6	0	1	3	2	11	19	44	2	1	3	5	3	1	1	4	2	2	11
25	41	2	2	2	3	1	1	1	24	1	1	4	2	11	19	39	2	2	3	4	5	1	1	3	4	2	11
26	29	2	2	2	4	4	1	3	2	1	1	3	2	11	12	33	2	2	3	5	4	1	2	4	6	3	17
27	32	2	2	1	2	3	1	2	2	0	1	3	2	9	13	34	1	2	3	6	4	1	1	2	2	2	8
28	40	2	1	2	3	2	1	2	6	0	3	4	1	11	26	33	1	3	5	2	5	2	1	2	1	2	7
29	41	2	2	1	2	3	1	1	12	1	1	4	2	11	17	26	3	1	4	4	2	1	2	4	3	2	2
30	28	2	2	2	2	2	1	2	7	0	1	3	1	10	33	34	3	1	4	4	4	1	2	2	3	2	8
31	40	1	1	1	2	3	1	3	6	2	1	4	1	24	8	33	7	1	1	4	3	1	1	0	2	2	6
32	41	1	2	2	2	2	2	0	24	2	1	4	1	23	14	27	6	5	7	2	5	2	1	1	1	0	3
33	29	1	1	1	1	4	1	2	6	2	1	4	2	18	22	36	5	4	6	3	3	2	1	0	3	2	5
34	30	1	1	2	1	3	1	1	12	2	1	4	2	24	22	32	6	5	6	3	4	1	1	3	3	1	8

Appendix - IX

name	age	case/control	sex	background	marital status	education	employment	income	DUP	No. of hosp	subtype of schizophrenia	duration of illness	F/H/O PSY	PANNS P	PANNS N	PANNS GP	panns deln	panns hallucination	panns abstraction	panns depression	panns judgementnt and insight	DAI	STRESSOR	SA insight compliance	SA insight awareness	SAinsight relabelling	insight total
36	47	1	1	2	1	3	1	1	12	5	1	4	1	25	19	29	6	7	6	3	5	1	1	4	2	0	7
37	51	1	2	1	2	3	1	3	3	4	1	4	1	26	23	31	6	7	5	3	7	2	2	0	0	0	0
38	32	1	2	2	1	2	1	2	2	3	1	2	2	19	15	43	7	1	4	7	7	2	1	0	0	0	0
39	35	1	2	2	2	2	2	0	24	1	2	3	1	24	11	33	6	7	4	4	7	2	1	0	0	0	1
40	30	1	1	1	1	2	1	2	1	0	1	3	1	26	9	25	6	7	3	1	5	2	1	1	2	0	4
41	29	1	2	2	2	3	2	0	12	2	1	3	1	20	12	28	7	1	3	6	7	2	2	4	4	0	8
42	38	1	1	2	1	3	2	0	24	2	3	4	2	24	22	39	3	5	7	1	7	2	2	0	0	0	0
43	43	1	1	1	2	3	2	0	12	1	1	3	1	21	9	27	5	5	1	3	5	2	2	3	3	0	7
44	52	1	1	1	4	1	2	0	24	0	1	4	1	19	13	24	4	4	5	3	4	1	1	2	3	0	6
45	41	1	2	1	2	3	2	0	36	4	1	4	2	20	10	43	6	1	2	3	7	2	2	0	1	0	2
46	42	1	1	2	2	4	1	2	24	2	2	4	2	20	22	20	4	3	3	1	3	1	2	3	4	2	11
47	38	1	2	1	2	1	2	0	24	5	1	4	1	27	7	25	7	7	1	4	3	1	1	4	4	1	11
48	24	1	1	1	1	2	2	0	9	3	1	4	1	26	21	33	5	5	6	1	7	2	2	0	0	0	0
49	40	1	1	1	1	3	2	0	24	5	2	4	2	27	26	26	4	5	5	1	5	2	1	4	6	2	14
50	30	1	1	2	1	2	2	0	3	3	2	3	1	25	26	30	3	4	5	1	5	2	2	0	0	0	1
51	26	1	1	1	1	3	1	2	12	2	1	3	1	30	10	29	7	6	3	4	5	2	2	0	1	0	3
52	44	1	2	1	2	2	2	0	5	4	1	4	1	28	16	40	5	5	4	4	7	2	1	0	1	0	1
53	28	1	2	1	1	3	2	0	12	1	1	3	1	21	16	27	5	3	2	1	2	2	1	0	0	0	1
54	30	1	1	1	1	2	2	0	36	2	1	3	2	21	13	26	2	7	3	5	2	1	2	4	3	2	11
55	52	1	1	1	2	2	1	1	24	2	2	4	2	20	22	36	3	3	5	1	7	2	2	0	0	0	0
56	36	1	1	2	1	4	2	0	24	3	2	4	2	20	27	46	4	3	6	5	7	2	2	0	0	0	1
57	42	1	1	1	2	3	1	2	24	2	1	4	2	35	29	37	7	7	7	4	7	1	2	0	1	0	1
58	35	1	1	1	3	3	2	0	36	2	1	4	1	28	16	33	6	7	6	4	6	1	1	0	0	0	0
59	32	1	2	2	2	2	2	0	12	2	1	3	2	30	23	41	5	5	6	5	7	1	1	4	0	0	4
60	40	1	1	1	1	2	2	0	24	2	3	4	1	24	26	39	4	5	4	4	5	1	2	2	2	0	6