A STUDY ON THE SHORT - TERM OUTCOME IN SCHIZOPHRENIA WITH REFERENCE TO DURATION OF UNTREATED PSYCHOSIS

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CERTIFICATE

This is to certify that the dissertation titled, **"A STUDY ON THE SHORT - TERM OUTCOME IN SCHIZOPHRENIA WITH REFERENCE TO DURATION OF UNTREATED PSYCHOSIS"**, submitted by **Dr. Sudhakar S,** in partial fulfillment for the award of the **MD degree in Psychiatry** by the Tamil Nadu Dr. M. G. R. Medical University Chennai, is a bonafide record of the work done by him in the Institute of Mental Health , Madras Medical College during the academic years 2005 – 2008

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INTRODUCTION

Schizophrenia is a chronic, disabling disorder for most affected individuals. Despite historical pessimism about prognosis, more recent studies suggest that early intervention can improve outcome. Efforts at early identification and treatment are based in part on the assumption that through an as- yet unknown process, illness duration causally influences treatment responsivity and outcome.

A large number of studies have examined the prognostic value of premorbid, sociodemographic, and psycho- pathological factors on outcome in schizophrenia.More recently, several groups of investigators have proposed that a long duration of untreated initial psychosis may also affect long- term outcome in schizophrenia.

Wyatt was the first to suggest that psychosis may be “biologically toxic” and that long-term morbidity in some patients with schizophrenia may be prevented if patients are treated with neuroleptics

Some investigators have found an association between longer duration of untreated initial psychosis and poor outcome in schizophrenia and have explained such an association with the “toxic psychosis” hypothesis.

Understanding the causes and consequences of untreated psychosis is important for at least two reasons. First, the duration of untreated psychosis

(DUP) is a potentially modifiable prognostic factor, and understanding its relation to outcome could lead to improved therapeutic strategies and public health initiatives. Second, a relationship of duration of untreated psychosis to outcome may indicate a neurodegenerative process and so have important implications for understanding the pathophysiology of schizophrenia.

Alternatively, the length of initially untreated psychosis may be related to the severity of illness and thus may be a marker rather than a determinant of outcome.

However, despite the knowledge of such factors, the prediction of outcome in schizophrenia has remained a challenging task and is generally poor. One of the well established facts and consistent finding about outcome of schizophrenia is that patients from developing countries including India have better outcomes than those from the developed countries (Lieberman, 1996).

Though there is no definitive evidence as to whether reduction of DUP will alter the course of schizophrenia for better, this issue has considerable public health importance. Given the low psychiatrist to population ratio and difficulties in reaching a psychiatrist, it is unlikely that patients from developing countries have shorter DUP than those from the developed countries.

There is a need to study the influence of duration of untreated psychosis on outcome of schizophrenia in the Indian context, hence this study.

REVIEW OF LITERATURE

Schizophrenia has been with us as an identified illness for over a century. Kraeplin described it as ‘dementia praecox’ in 1896 separating it from the broad spectrum of psychoses seen within his clinic, and Bleuler renamed it as schizophrenia in 1908. Illness are usually identified and defined in terms of their clinical presentation, course and outcome.

Kraeplin’s identification of what we now call as schizophrenia rested almost exclusively on course and outcome. He found a very pessimistic view of the outcome in schizophrenia, and was convinced that recovery was very rare, or even impossible, and deterioration almost inevitable.

Kraeplin’s gloomy appraisal of the outcome has been challenged, most convincingly by careful follow-up studies.

Some of the commonly measured outcomes in schizophrenia are symptom outcomes, cognitive and neurobiological outcomes, patient related outcomes, adverse drug effects, social outcomes, hospitalization, duration of untreated psychoses and economic outcomes.

Duration of untreated psychoses:

In the past two decades, duration of untreated psychoses(DUP) has been an intense focus of clinical and research interest, with the recognition that not only is long DUP associated with poor outcome, but that as a potentially

malleable prognostic factor, reducing it at the population level might have a significant public health importance(Swaran&Singh et al 2007).

Angst and Schulz reviewed 10 studies performed in the 1950s that studied both acute and chronic patients who had not received drug treatment. Poorer response to neuroleptics was found among chronic patients in six studies, suggesting that delay in treatment may lead to a significantly poor outcome.

Lo Lo et al (1977) in a retrospective 10 year follow-up study of 133 chronic schizophrenic patients found that shorter duration of untreated illness prior to the initial acute episode was significantly associated with favorable outcome.

By the 1980s, studies had begun to demonstrate the importance of the time period between the onset of psychoses and initiating treatment in determining outcome in schizophrenia.

May et al in 1981 randomly assigned 228 first admission schizophrenic patients to five treatment groups, three of which did not include drug treatment (psychotherapy, milieu therapy and ECT group). Patients from the above three groups who did not respond were subsequently treated with antipsychotic drugs. In this study the drug treatment groups showed the best response and, together with ECT group showed the best outcome for up to three years (as measured by clinical, social and psychological criteria). Thus the groups

initially not treated with medication were found to have a poor outcome over the following period.

Inoue et al (1986) in a retrospective evaluation of 19 treated schizophrenic and schizophreniform patients noted that the time interval between onset of illness and first outpatient treatment varied from 1 to 6 years. Less favorable outcome in the form of poor occupational and scholastic achievement at 3year follow up was predicted by long duration of illness (4 years or more).

Rabiner et al in 1986 studied a group of 64 first episode subjects with varied diagnosis and found that 36 schizophrenic subjects had a mean duration of illness of 14.5months. This study also found that the longer the duration of illness, the poorer the outcome, as measured by the presence of remission or relapse over a 1 year follow up period.

In a prospective study of 120 first episode schizophrenic patients who were followed up for 2 years in a randomized controlled trial of maintenance neuroleptic treatment, relapse subsequent to initial hospital discharge was substantially more common in those whose pretreatment illness lasted more than 1 year. Only 18% of the patients who were given active treatment and none who were given placebo remained free of relapse after 2 years (Crow et al).

The Northwick Park study of first-episode of schizophrenia found that the most important determinant of relapse was duration of illness prior to starting antipsychotics (John stone et al 1986).

Wyatt has shown that patients who had not been treated with neuroleptics and who were discharged within six months of hospitalization required significantly more rehospitalization and as much subsequent neuroleptic treatment as patients who had neuroleptics.

Loebel et al (1992) did a year 3 year prospective study in 70 schizophrenic patients and found that the mean duration of psychotic symptoms before initial treatment was 52 weeks. The effect of duration of illness was found to be significantly associated with time to remission as well as with level to remission .DUP was not correlated with age at onset, mode of onset, premorbid adjustment or severity of illness at entry into the study.

Haas et al in 1998 in his prospective study of 103 schizophrenia patients found that those with one or more years of untreated psychoses displayed a more severe poverty syndrome at the time of admission and discharge and a more severe reality distortion syndrome at discharge from index hospitalization, thus concluding that failure to initiate treatment early in the course of illness may be associated with a recurrent pattern of poor treatment response and more severe and persistent positive and negative symptomatology.

In the West London first episode study of schizophrenia by Barnes et al in 2000, there was little evidence of any association between DUP and progressive deterioration in schizophrenic illness. Patients in the long DUP (>26 weeks) were more likely to be employed and living alone or homeless.

Drake et al in 2000, did a 12 month follow up study in 248 consecutive first admissions with schizophrenia, and found that median DUP was 12 weeks. Long DUP was predicted by poor insight, social isolation and preserved coping skills, but not by demographic factors. Even allowing for these for variables, long DUP predicted poor outcome. He thus concluded that DUP's relationship to outcome is strongest in the initial months of psychoses.

Beng and Andreasen et al in 2000 evaluated 74 neuroleptic-naïve schizophrenic patients for 6 months and found that earlier age at illness onset was associated with long duration of untreated prodromal psychotic symptoms. After controlling the effect of age at onset, the DUP did not significantly impair subsequent the quality of life, symptom severity, or remission of positive symptoms.

In the above mentioned study, there were no significant association between DUP and premorbid functioning, nor were there any significant gender differences in DUP.

A two year follow-up study of 65 first admitted subjects with psychoses had found that the association between DUP and poor outcome may be

spurious; confounded by the fact that poor premorbid functioning is independently associated with both DUP and poor outcome, with no direct causal link between these two later variables (Verdoux et al).

Craig and his colleagues in 2000 did a 24 month follow-up study in first admission schizophrenic in-patients and found that the median duration of untreated psychoses was 98 days and duration of untreated psychoses was not significantly associated with 24-month illness course or clinical outcome.

Harris et al (2005) in a prospective, naturalistic study of 318 first episode psychoses patients found that shorter DUP correlated moderately with decreased severity of positive symptoms, and enhanced social and occupational functioning and quality of life. DUP exceeding 1 year was associated with a poor outcome and there was no association with DUP and negative symptoms.

In a systematic review of 26 first-episode studies, Marshall et al in 2005 found that a longer DUP was not associated with worse symptoms or poorer functioning at first presentation, at 6 and 12 months following treatment. Longer DUP was associated with more severe overall symptoms and with worse overall functioning. Patients with long DUP were also less likely to experience remission at 6, 12, and 24 months.

Perkins et al did a review of 43 studies and found that longer DUP was associated with more severe negative but not positive symptoms or neurocognitive functioning, shorter duration of untreated psychoses was thus

associated not only with greater treatment responsiveness but also with greater reduction in negative symptoms.

Norman and his colleagues did a systematic review and found that there is a substantial evidence of DUP being an independent predictor of treatment outcome, particularly remission of positive symptoms, over the first year or so of treatment.

Indian studies on Duration of untreated psychoses and outcome:

Studies from the West have shown that the duration of untreated psychoses is associated with poor outcome, with the relationship being strongest in the initial months of psychoses. This is particularly relevant in low- and middle income countries where a significant number of patients come late to treatment.

The reasons for delay in treatment were due to lack of awareness, a strong belief in magical or religious causes, poor accessibility to health care systems and lack of community care (Isaac et al, 1981; Padmavathi et al, 1991).

A cross-cultural study on pathways to psychiatric care replicated these findings (Gater et al 1991). Most patients are brought for treatment after a significant delay from the onset of symptoms.

Philip et al in 2003 did a study on the influence of duration of untreated psychosis on the short term outcome of drug-free schizophrenic patients and

found that DUP was longer in the unimproved group. In a logistic regression model, only DUP emerged as a significant predictor.

Tirupati et al in 2004 did a prospective follow-up study of 75 drug naïve patients out of which 60% had a DUP of over 5 years and 36% over 12 years. Following treatment for one year, patients with a DUP of 5 years or less had shown good clinical outcome. An encouraging observation was the notable treatment response despite many years of untreated illness.

Isaac et al in 2007 have described factors apparently contributing to good prognosis of schizophrenia in low-and middle-income countries.

Established

- Less expressed emotion
- Good social support
- Tolerance of odd behavior by society and family
- Marriage

Doubtful

- Less industrialization and urbanization
- Early death of those with bad outcome
- Increased prevalence of acute psychosis

Needs to be established

- Co morbid substance use
- *Duration of untreated psychosis*
- Pharmacological interventions

Can duration of untreated psychosis be reliably measured?

Onset of psychosis is a nebulous phenomenon that evades close scrutiny. Establishing onset has become important for early identification and intervention of psychosis. Yet there is no consensus definition of onset of psychosis and the literature yields few standardized replicable methods for measuring onset (Singh et al, 2005).

Clinically it is difficult to identify a precise time when a certain behavior or symptom makes the transition from non-psychotic to a psychotic domain, with considerable arbitrariness introduced in both identifying and dating the phenomenon.

Definitions of onset thus vary from the interval between first sign of illness and the appearance of florid psychotic symptoms (Valliant, 1964) to the interval between appearance of psychotic symptoms to the initiation of treatment (Day et al 1987).

The end of the period of untreated psychosis is conceptually simpler to date, but 'the start of treatment' is in a reality a similarly complex construct.

Does 'untreated psychosis' end when any treatment begins, when anti-psychotics are started, treatment at an adequate dose has been adhered for an adequate period, or when psychosis itself remits? Many studies do not make these distinctions clear in their measure of DUP and scales do not include a precise definition of treatment adequacy.

The Nottingham Onset Schedule is a short, guided interview and rating schedule to measure onset in psychosis. Onset is defined as the time between the first reported/observed change in mental state/behavior and the development of psychotic symptoms (Singh et al 2005).

Marshall et al (2005) in his systematic review found that only 12 out of 26 studies reported a systematic method to assess DUP.

Confounding factors associated with DUP

It is important to examine whether any relationship that does exist between duration of untreated psychosis can be explained by other confounding factors which have in the past been found to predict treatment outcome.

Gender

Loebel et al (1992) and Larsen et al (1996) report that males have a long duration of untreated psychosis than females. Five other studies do not find any gender differences to be associated with DUP.

Age at onset:

Ho et al (2000) in his follow-up study has found that longer DUP was significantly related to younger age at onset of illness while many other studies do not show any such difference (Haas et al, Loebel et al, Larsen et al, Blake et al).

Symptoms at baseline

Several studies have reported longer DUP to be associated with higher levels of at least some aspects of negative or deficit symptoms at presentation (Larsen et al, Browne et al, Malla et al, Blake et al). DUP was associated with the severity of negative symptoms but not with the severity of positive symptoms or general psychopathology. (Perkins et al).

Drake et al (2000) found a relationship between longer DUP and higher positive but not negative symptoms at presentation, but others have found no relation to initial positive symptoms (Larsen et al, Malla et al).

Premorbid adjustment

The interpretation of findings with respect to premorbid adjustment as a possible explanation for any relation between DUP and treatment outcome is potentially complex. Harrigan et al (2003) demonstrated that in a large sample of patients with first-psychosis, the effects of DUP on several dimensions of outcome are independent of premorbid adjustment prior to the onset of

prodromal or psychotic symptoms. DUP remained as a significant predictor of outcome at 12 months following a multiple regression analysis that included premorbid adjustment.

Very few studies have found lower premorbid adjustment to be significantly associated with longer duration of untreated psychosis (Verdoux et al, Malla et al). Poor premorbid function could confound the relationship between DUP and outcome, because both could lead to delays in recognizing illness.

In a 10 year follow-up study by White et al, he found that both premorbid adjustment and DUP to be independent predictors of symptomatic and functional outcomes.

Treatment response

Shorter duration of untreated psychosis was associated with a greater response to antipsychotic treatment as measured by improvement or end point severity of symptoms.(Perkins et al).

Studies examining the relationship between duration of untreated psychosis and outcome

Associated with poor outcome	**Not associated with poor Outcome**
Johnstone et al (1086)	Linszen et al (1998)
Makanjoula et al (1087)	Craig et al (2000)
Helgason et al (1990)	Ho et al (2000)
Moscarelli et al (1991)	de Haan et al (2000)
Loebel et al (1992)	Barnes et al (2000)
Waddington et al (1995)	
Wyatt et al (1997)	
Scully et al (1997)	
Haas et al (1998)	
Carbone et al (1999)	
Larsen et al (2000)	
Drake et al (2000)	
Browne et al (2000)	
Harris et al (2003)	
Philip et al (2003)	
Tirupati et al (2004)	
Marshall et al (2005)	
Perkins et al (2005)	

AIMS AND OBJECTIVES

1. To study the clinical and social determinants of duration of untreated psychosis in drug naïve schizophrenic patients.

2. To assess the influence of duration of untreated psychosis on the short-term outcome in schizophrenia.

3. To study the relationship of premorbid social adjustment on the duration of untreated psychosis and outcome.

HYPOTHESIS

1) There is no significant association between duration of untreated psychosis and age, gender.

2) There is no significant correlation of marital status, occupational status and socioeconomic status with duration of untreated psychosis.

3) There is no significant association of duration of untreated psychosis and the mode of onset.

4) There is no significant association between duration of untreated psychosis and the type of family.

5) There is no significant association of duration of untreated psychosis and the severity of symptoms at baseline.

6) There is no significant association between the improved and the unimproved groups with regard to the sociodemographic variables.

7) There is no significant association between improved and unimproved groups in terms of the duration of untreated psychosis.

8) There is no significant association of premorbid social adjustment and duration of untreated psychosis and outcome at 8 weeks.

MATERIALS AND METHODS

This study was done at The Institute of Mental Health, Chennai.

SAMPLE

100 consecutive patients admitted as in-patients in the institute of mental health, fulfilling the ICD-10 criteria for schizophrenia, who were never treated were included in the study.

INCLUSION CRITREIA

1. Age 18-45 years.
2. Patients with a diagnosis of schizophrenia as per ICD-10 criteria.
3. Drug naïve patients.

EXCLUSION CRITERIA:

1. A medical condition that might influence the current state of psychiatric presentation.
2. History of head injury
3. Current substance use disorder or history of substance dependence disorder.
4. Mental retardation

MATERIALS USED

1. Semi-structured proforma.
2. SAPS (Scale for assessment for positive symptoms)
3. SANS (Scale for assessment of negative symptoms)
4. Clinical Global Impression –Schizophrenia Scale(CGI-SCH)
5. Global assessment of functioning (GAF)
6. Premorbid Social Adjustment Scale (PSA)

A Semi-structured Proforma to include the socio-demographic and clinical data, family history, subtypes of schizophrenia, treatment, hospitalization.(Appendix I)

Clinical interview for diagnosis of ICD-10 criteria for schizophrenia.

Ascertainment of Duration of untreated psychosis

Data relating to the onset of psychosis were collated from interviews with the patient and a close relative of the patient. After explaining psychosis in clear language, we asked when the patient first experienced or when the family members first noticed psychotic symptoms.

In line with the previous studies (Craig et al, 2000 and Morgan et al, 2006), onset of psychosis defined as the presence for 1 week or more of the following psychotic symptoms: delusions; hallucinations; marked thought

disorder; marked psychomotor disorder; and bizarre, grossly inappropriate and/or disorganized behavior with a marked deterioration in function. A rating of onset was made only when there was a clear, unequivocal description from any source of symptoms meeting the criteria. In this study the end point was considered as admission to the hospital.

SAPS (Scale for the Assessment of positive Symptoms) and SANS (Scale for the Assessment of negative symptoms) were used. These scales were sourced from the University of Iowa press, 1983. These scales are used for the assessment of positive and negative symptoms, principally those occurring in schizophrenia. Both the instruments are used in a way complimentary to each other. They have been widely used in many studies and well tested for reliability and validity. The SAPS contains 35 items divided into 5 domains i.e. Hallucinations, Delusions, Bizarre behavior, Positive formal thought disorder and inappropriate affect. The SANS contains 24 items divided into 5 domains i.e. Affective flattening or blunting, Alogia, Avolition-apathy, Anhedonia-asociality and Attention. Items in both the scales are scored between 0 (none) and 5 (severe).

Three dimensions were used to summarize symptom severity, based on previous studies. The negative symptom dimension was defined as the sum of the global ratings of alogia, anhedonia, avolition and affective flattening (range=0-20). The psychotic symptom dimension was defined as the sum of the global ratings of delusions and hallucinations (range=0-10). The disorganized

symptom dimension was the sum of the global ratings of bizarre (disorganized) behavior, positive thought disorder, and inappropriate affect (range=0-15). Higher scores represent greater symptom severity.(Appendix II & III).

Clinical Global Impression-Schizophrenia scale: (CGI-SCH)

This Scale was adapted from the CGI scale and the CGI-bipolar Patients scale by Haro et al in 2003. This scale is a reliable and a valid instrument to evaluate severity and treatment response in schizophrenia. It consists of only 2 categories; severity of illness and the degree of change. The severity of illness category evaluates the situation during the week previous to the assessment, while the degree of change category evaluates the change from previous evaluation. Each category contains five different ratings (positive, negative, depressive, cognitive and global) that are evaluated using a seven point ordinal scale. (Appendix IV)

The Premorbid Social Adjustment Scale

This scale was an adapted version of the cannon-spoor scale (1992), was used to assess five areas of adjustment; sociability, peer relations; scholastic performance; adaptation to school and interests. Each subject received a score for each item, rated on a 7 point Likert scale that Ranged from 1 (excellent adaptation) to 7 (extremely poor adaptation). Each item was rated separately for childhood (5-11 years) and adolescence (12-16 years). The total Premorbid

Adjustment Scale score is obtained by summing up the two sub scores. Higher scores indicate poorer premorbid functioning. (Appendix V)

Global Assessment of Functioning Scale: (GAF)

The GAF scale is used to assess psychiatric patients at the time of admission to an inpatient or an outpatient program as part of the multiaxial evaluation recommended by the APA DSM classifications. The GAF scale is a 100-point single-item scale with values ranging from 1 to 100 representing the hypothetically sickest person to the healthiest. The scale is divided into 10 equal 10-point intervals with the 81 to 90 and 91 to 100 intervals for individuals who exhibit superior functioning. The 71 to 80 interval is for persons with minimal psychopathology. Most patients in outpatient settings will receive ratings between 31 and 70, and most inpatients between 1 and 40. (Appendix VI)

METHOD

Consecutive patients fulfilling the ICD-10 criteria for schizophrenia, admitted as inpatients in the Institute of Mental Health, Chennai from June 2006 to August 2006 were evaluated. Those satisfying the inclusion and exclusion criteria were taken into the study. The diagnosis was obtained from the case records and re-confirmed by 2 psychiatrists, one of them a senior consultant.

Informed consent in a written form was obtained for participation in the study from the patients as well as the relatives.

The patients were administered the Semi-structured proforma, Scale for the Assessment of Positive Symptoms (SAPS), Scale for Assessment of Negative symptoms (SANS), Clinical Global Impression-Schizophrenia Scale, Global Assessment of Functioning Scale (GAF) and the Premorbid Social Adjustment Scale at the time of admission or within few days. Treatment in the ward was given by a psychiatrist in charge of the ward according to the patient's symptoms and needs. The treating psychiatrist was completely blind to the study sample.

Follow up assessment was done after a period of 8 weeks by administering SAPS, SANS and GAF. All those who completed 8 weeks of follow-up were enquired from their caregivers about compliance to medication.

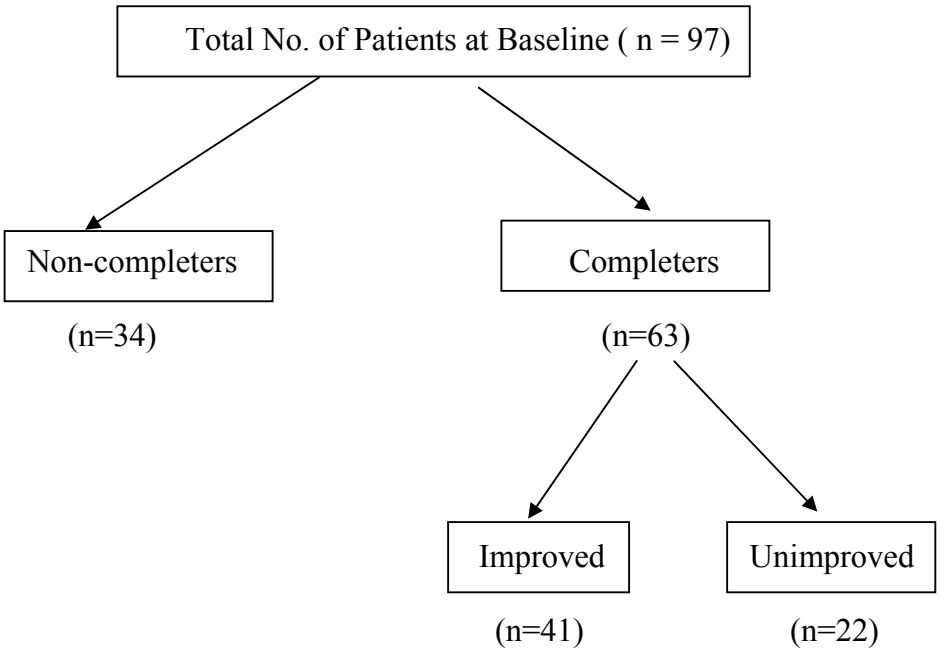
The outcome was assessed using the Clinical Global Impression-schizophrenia scale and GAF. The outcome variable was converted into dichotomous, unimproved (>4 on CGI-SCH scale which includes no change, minimally worse, much worse and very much worse; GAF>60) and improved (<3 on CGI-SCH scale which includes minimally improved, much improved and very much improved; GAF<60).

The data collected thus were tabulated and discussed with reference to the aims and objectives of the study. Statistical analysis was done using the chi-square test, t-test and correlation methods. In measuring DUP there is more chances of right skew, hence after initial data analysis DUP was normalized by taking the logarithm to base 10 (log DUP) to allow the use of parametric statistics (Pearson's r, t-tests) and these results were presented. Data was analyzed using SPSS 11.0. $P< 0.05$ is considered as a statistically significant value.

Approval was obtained from the Ethics committee of the Institute of Mental Health, Chennai.

RESULTS

100 consecutive patients were screened, evaluated and entered into the study out of which 3 patients were excluded, one patient was found to be HIV positive and 2 patients were found missing from the ward. Hence the total number of sample at baseline assessment was 97. At the end of 8 weeks follow up assessment was done for 63 patients who reported along with their caregivers. The remaining 34 patients who did not complete the follow up were categorized as 'non-completers'.



Sample characteristics at admission: (n=97)

The baseline sample included 97 patients among which 43 (44.3%) were men and 54(55.67) were women. Mean age of the patients was 29.7(6.7) years. More than 90% of the patients were in the low and middle socioeconomic status.

11.34% were uneducated, 24.74% up to primary school, 35.05% in high school, 13.4% up to higher secondary level and 15.4% were graduates. 39(40.2%) patients were married, 8(8.2%) were married and separated, 1patient was a divorcee, 4 patients were widowed and 45(46.3%) were unmarried. 66(68.1%) patients were in a joint family system and 31(31.9%) were in the nuclear type of family. 69.1% were employed and 30.1% were unemployed among the sample.

Age at onset of illness was 27.94 ± 6.2 years. The mean duration of untreated psychosis was 22.33 ± 28.8 months. 40(41.2%) patients had a DUP between 1-6 months, 17(17.5%) between 6-12 months, 3(3.1%) had a duration between 13-18 months, 4 patients between 19-24 months and 33(34.1%) had a DUP greater than 2 years (Table 1).

Family history of schizophrenia was present in 31(31.9%) patients and there was no such illness in 66(68.1) patients.

TABLE NO. 1

DURATION OF UNTREATED PSYCHOSIS OF THE WHOLE SAMPLE (N = 97)

DUP (Months)	Frequency	Percentage
1 – 6 Months	40	41.24%
7 – 12 Months	17	17.53%
13 – 18 Months	3	3.09%
19 – 24 Months	4	4.12%
> 24 Months	33	34.02%

TABLE NO. 2

CORRELATION OF DURATION OF UNTREATED PSYCHOSIS WITH AGE AT FIRST PRESENTATION AND AGE AT ONSET OF ILLNESS

DUP (Months)	Correlation coefficient	P
Age	0.346	0.001
Age at Onset	0.003	0.971

There is a positive correlation between the age at first presentation and the duration of untreated psychosis with the p value being significant (P< .05). There is no significant correlation between DUP and the age at onset of illness.

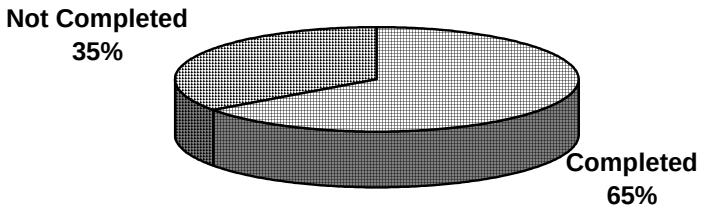
TABLE NO. 3

CORRELATION OF SYMPTOMS AND PREMORBID FUNCTIONING WITH DUP

Log DUP	Correlation Coefficient	p Value
Psychotic domain	0.021	0.838
Disorganized	0.192	0.061
Negative	0.256	0.011
Premorbid social Adjustment score (Total)	0.334	0.001

The correlation of logDUP with psychotic and disorganized symptom domain was non significant (P> .05). There is a significant correlation between DUP and negative symptom domain at baseline presentation (P< .05).

FIG. 1 COMPARISON BETWEEN PATIENTS WHO COMPLETED FOLLOW UP AND NON-COMPLETERS.



The total number of patients who completed 8 weeks of follow up and who were regular on medication were categorized as 'completers'. Those who did not turn for follow up were categorized as 'non-completers'. There was no statistically significant difference among the socio-demographic and clinical variables. No significant difference was found between the two groups with regard to the duration of untreated psychosis, symptom domains and premorbid functioning (Table 4).

TABLE NO. 4

COMPARISON OF THOSE WHO COMPLETED 8 WEEKS OF FOLLOW-UP WITH NON-COMPLETERS

Variables	Completed n = 63	Non-Completers n = 34	p
Age	30.20 ± 6.8	29.02 ± 6.6	1.43
Age at onset	28.11 ± 6.3	27.61 ± 6.1	0.71
Psychoticism	3.76 ± 2.1	3.23 ± 1.7	0.22
Disorganization	3.22 ± 2.4	2.64 ± 1.7	0.23
Negative	2.52 ± 3.5	3.11 ± 3.4	0.42
Premorbid Social Adjustment	27.88 ± 7.1	27.52 ± 4.8	0.79
Log DUP	1.05 ± 0.55	1.02 ± 0.48	0.73

TABLE.NO.5

GENDER WISE COMPARISON BETWEEN IMPROVED AND UNIMPROVED GROUPS

Gender	Improved		Unimproved		Total
	n	%	n	%	
Male	21	51.2	11	50.0	32
Female	20	48.8	11	50.0	31
Total	63	100	22	100	63

$\chi^2 = 0.008$ p=0.92

Among the improved group of patients, 51.2% were males and 48.8% were females. In the unimproved group 50% were males and 50% were females. The difference was not statistically significant.

FIGURE 2

GENDER WISE COMPARISON BETWEEN IMPROVED AND UNIMPROVED GROUPS

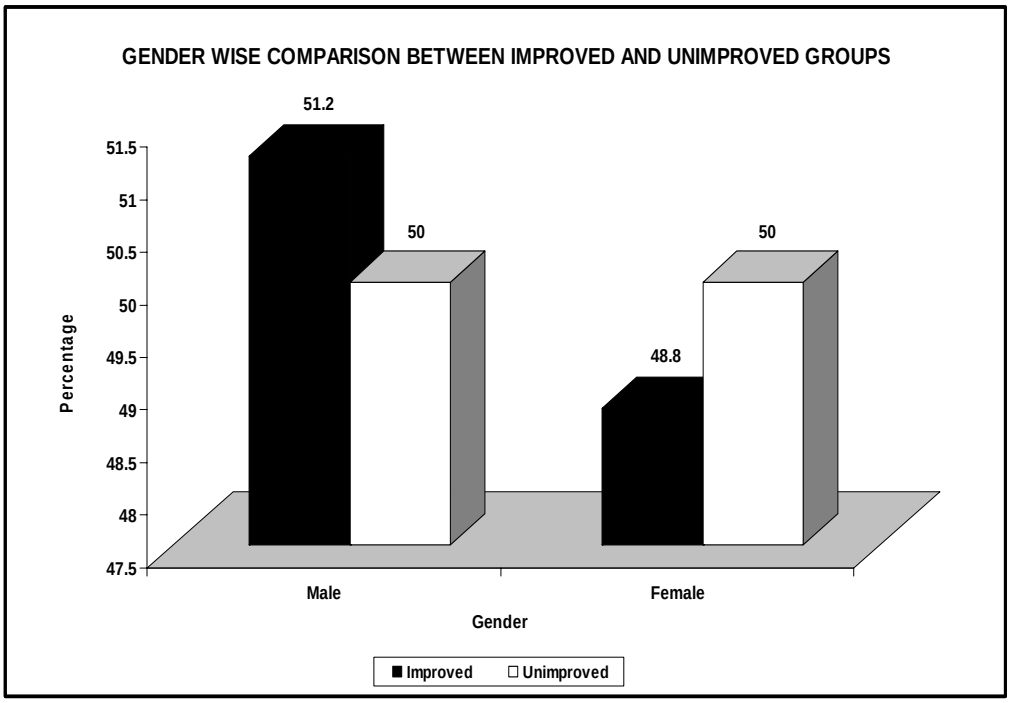


TABLE.NO.6

COMPARISON OF THE GROUPS BY EDUCATION

Education	Improved		Unimproved		Total
	n	%	n	%	
Uneducated	5	12.2	3	13.6	8
Primary	10	24.4	7	31.8	17
Secondary	12	29.3	6	27.3	18
High school	3	7.3	4	18.2	7
Graduate	11	26.8	2	9.1	13
Total	41	100	22	100	63

$\chi^2 = 4.04$ $p = 0.40$

Among the improved group, 12.2% were uneducated, 24.4% were educated upto primary level, 29.3% upto secondary level, 7.3% upto high school and 26.8% were graduates. In the unimproved group, 13.6% were uneducated, 31.8% were educated upto primary level, 27.3% upto secondary level, 18.2% upto high school and 9.1% were graduates. The difference was not statistically significant.

FIG. 3 COMPARISON OF THE GROUPS BY EDUCATION

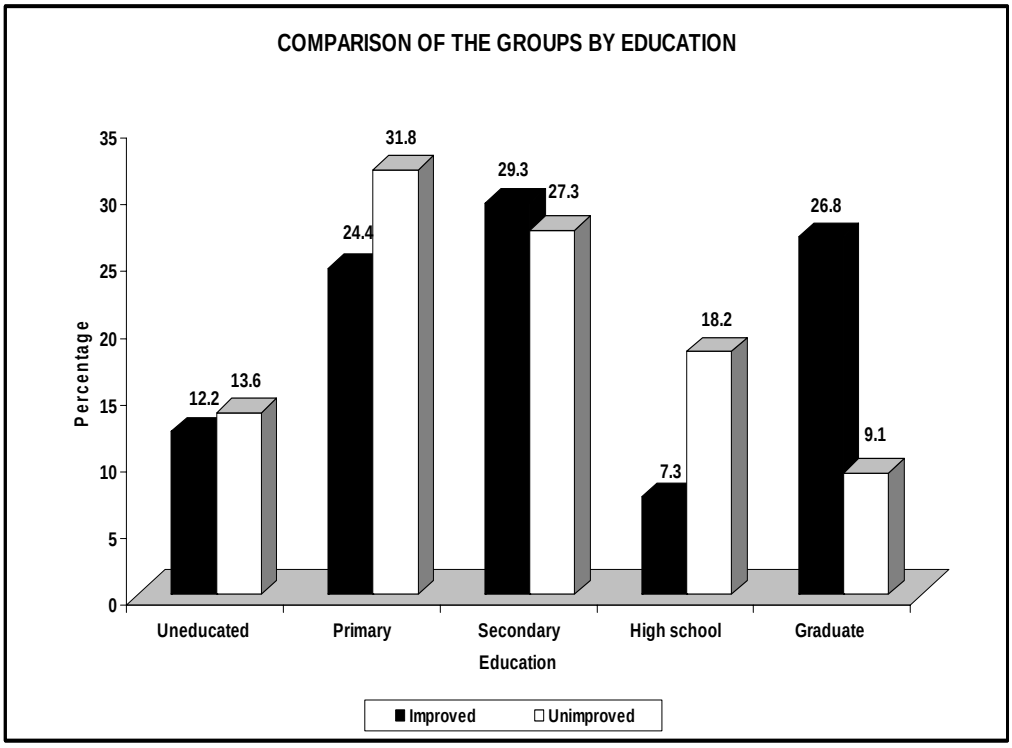


TABLE NO. 7

COMPARISON OF THE GROUPS BY SOCIO ECONOMIC STATUS

SE status	Improved		Unimproved		Total
	n	%	n	%	
Low	34	82.9	16	72.7	50
Middle	6	14.7	5	22.8	11
High	1	2.4	1	4.5	2
Total	41	100	22	100	63

χ^2 1.07 p=0.59

In the improved group 82.9% were from lower socioeconomic group, 14.7% were from middle socio-economic group and 2.4% belonged to higher socio-economic group. In the unimproved group 72.7% were from the lower socio-economic group, 22.8% were from the middle socio-economic group and 4.5% belonged to higher socioeconomic group. The difference was not statistically significant. As our study was done at a government institute, majority of the individual were from the lower socio-economic class.

FIG. 4 COMPARISON OF THE GROUPS BY SOCIO ECONOMIC STATUS

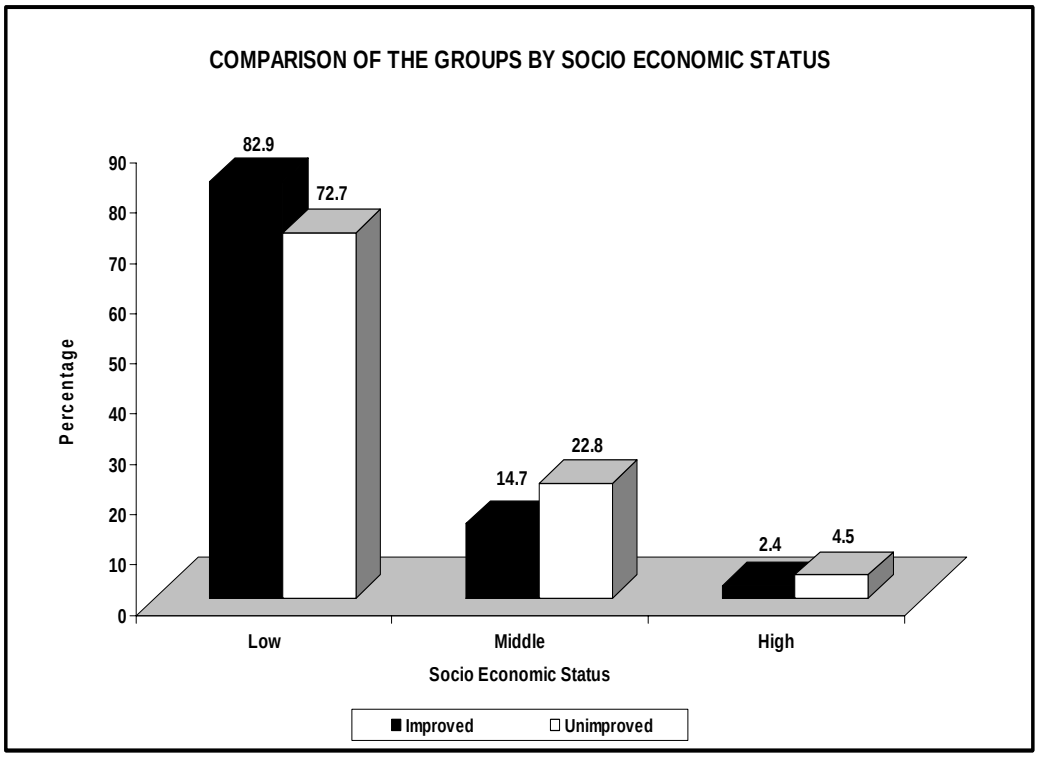


TABLE NO. 8

COMPARISON OF THE GROUPS BY OCCUPATION

Employment	**Improved**		**Unimproved**		**Total**
	n	**%**	**n**	**%**	
Employed	10	24.4	6	27.3	16
Unemployed	31	75.6	16	72.7	47
Total	41	100	22	100	100

$\chi^2 = 0.062$ p=0.802

Out of the improved group, 24.4% were employed and 75.6% were unemployed. In the unimproved group 27.3% were employed and 72.7% were unemployed. The difference was not statistically significant.

FIG. 5 COMPARISON OF THE GROUPS BY OCCUPATION

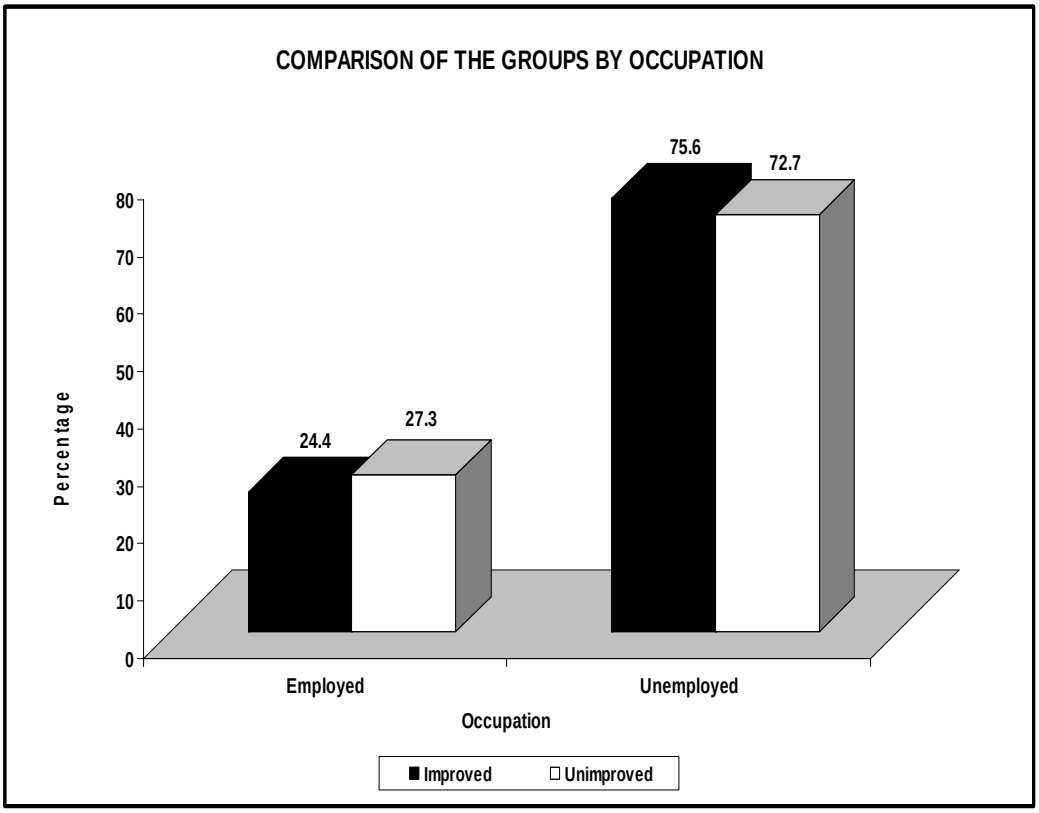


TABLE NO. 9

COMPARISON OF THE GROUPS BY MARITAL STATUS

Marital status	Improved		Unimproved		Total
	n	%	n	%	
Married	16	39.0	9	40.9	25
Married and separated	3	7.3	1	4.5	4
Divorced	0	-	0	-	0
Widow	2	4.9	1	4.5	3
Unmarried	20.	38.8	11	50.0	31
Total	41	100	22	100	63

$\chi^2 = 0.193$ p=0.97

In the improved group 39% were married, 7.3% separated, 4.9% were widowed and 38.8% were unmarried. In the unimproved group 40.9% were married, 4.5% were separated, 4.5% were widowed and 50% were unmarried. The difference was not statistically significant.

FIG.6 COMPARISON OF THE GROUPS BY MARITAL STATUS

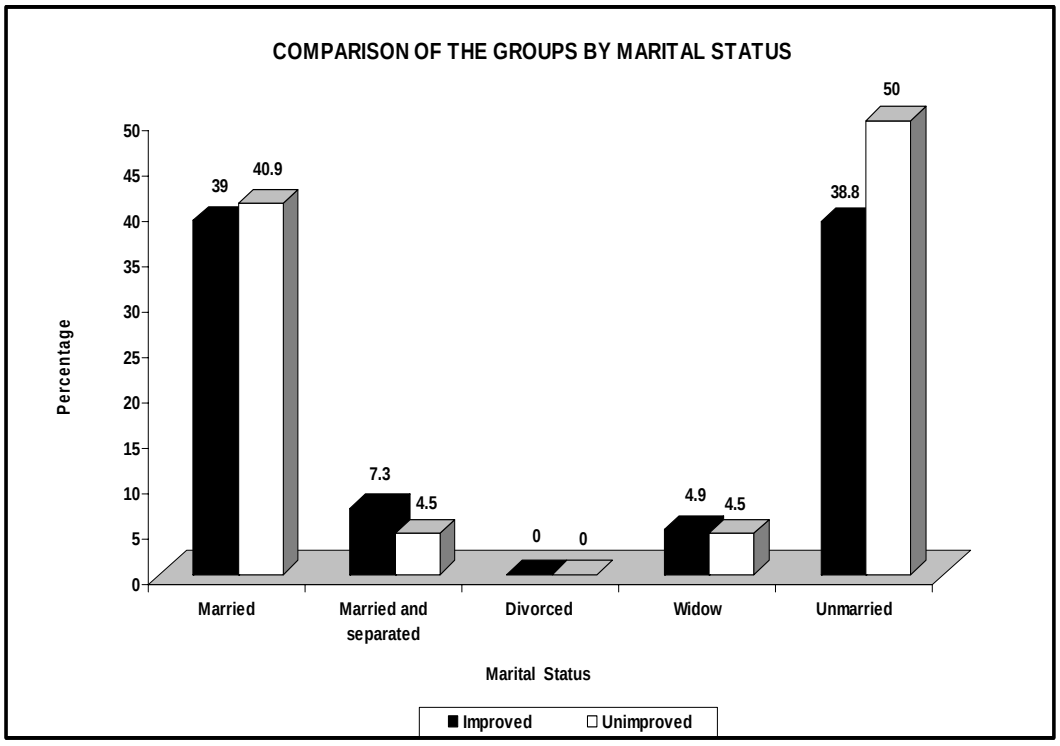


TABLE NO. 10

COMPARISON OF THE GROUPS - TYPE OF FAMILY AND FAMILY HISTORY OF SCHIZOPHRENIA

Variable	Improved (n=41)	Unimproved (n=22)	χ^2	P
Type of family (%)				
Joint	75.6%	72.7%	0.02	0.88
Nuclear	24.47%	27.3%		
Family history of schizophrenia				
Yes	26.8%	27.3%	0.01	0.96
No	73.2%	72.7%		

In the improved group 75.6% belonged to joint family system and 24.4% belonged to nuclear family. In the unimproved group 72.7% belonged to joint family, while 27.3% belonged to nuclear family. The difference was not statistically significant.

Family history suggestive of schizophrenic illness was present in 26.8% among the improved group and in 27.3% among the unimproved group, the difference being statistically insignificant.

TABLE NO. 11

COMPARISON OF GROUPS BY DIAGNOSIS

Diagnosis	Improved		Unimproved		Total
	n	%	n	%	
Paranoid	24	58.5	8	36.4	32
Hebephrenic	1	2.4	1	4.5	2
Catatonic	1	2.4	0	-	1
Undifferentiated	15	36.6	13	59.1	28
Total	41	100	22	100	63

χ^2=3.75 p=0.28

Among the improved group of patients, 58.5% were paranoid subtype, 2.4% were hebephrenic type, 2.4% were catatonic type and 36.6% were of undifferentiated subtype. In the unimproved group 36.4% were paranoid type, 4.5% were hebephrenic type and 59.1% were of undifferentiated subtype. The difference was not statistically significant.

FIG.7 COMPARISON OF GROUPS BY DIAGNOSIS

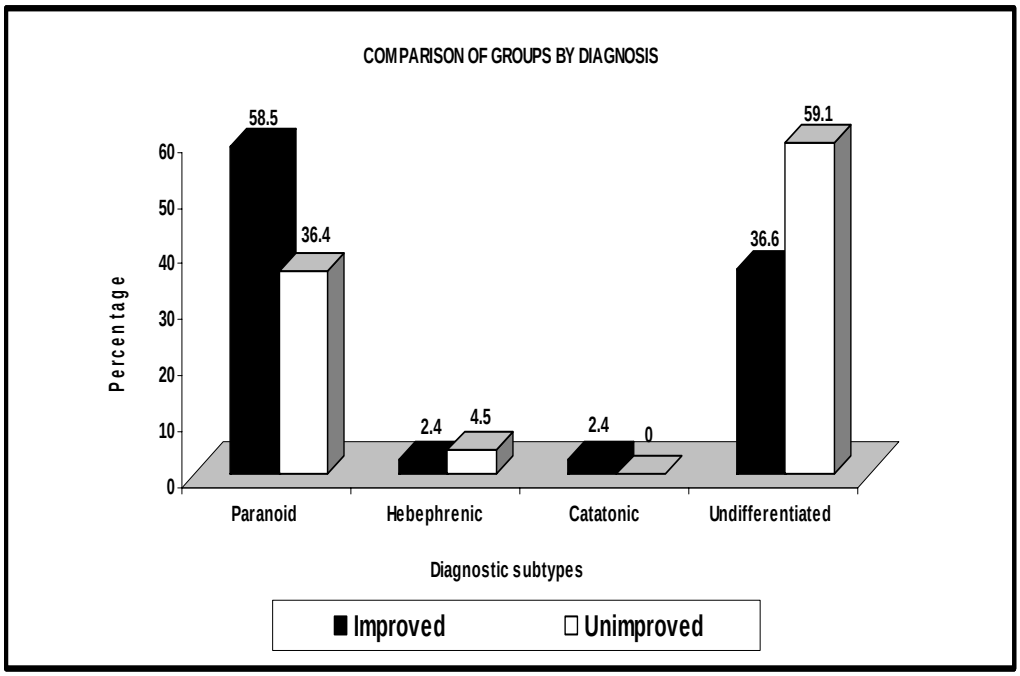


TABLE NO. 12

COMPARISON OF THE GROUPS - HOSPITALIZATION

Hospitalization (days)	Improved		Unimproved		Total
	n	%	n	%	
<7 days	22	53.7	8	36.4	30
8-14 days	17	41.5	8	36.4	25
15-21 days	1	2.4	4	18.2	5
22-28 days	1	2.4	2	9.1	3
Total	41	100	22	100	63

χ^2=6.79 p=0.78

In the improved group 53.7% were hospitalized for less than a week, 41.5% between 8-14 days, 2.4% between 15-21 days and 22-28 days. In the unimproved group 36.4% were hospitalized for less than a week and between 8-14 days, 18.2% between 15-21 days and 9.1% between 22-28 days. The difference between the groups was not statistically significant.

TABLE NO. 13

COMPARISON OF THE GROUPS - AGE AT PRESENTATION AND THE AGE AT ONSET OF ILLNESS

Variable	Improved n=41	Unimproved n=22	t value	P
Age at presentation (months)	29.41 ± 6.4 (Mean ± SD)	31.68 ± 7.3	1.26	0.212
Age at onset (months)	28.02 ± 5.9	28.27 ± 7.1	0.15	0.88

Mean age at first presentation was 29.41 months for the improved group and 31.68 for the unimproved group, the difference being statistically insignificant. Age at onset of illness was 28.02 among the improved group and 28.27 for the unimproved group. The difference was not statistically significant.

TABLE NO. 13

COMPARISON OF THE GROUPS BY SYMPTOM SEVERITY

Symptoms	**Improved (n=41)**	**Unimproved (n=22) Mean ± SD**	**t value**	**p**
Psychoticism	3.92 ± 1.9	3.45 ± 2.5	0.83	0.409
Disorganization	2.85 ± 2.2	3.90 ± 2.6	1.65	0.104
Negative	1.56 ± 2.8	4.31 ± 3.9	3.16	0.002

The score on psychotic symptom domain was 3.92 ±1.9 for the improved group and 3.45± 2.5 for the unimproved group, the score on disorganization domain was 2.85 ±2.2 for the improved group and 3.9 ±2.6 for the unimproved group. The difference was not statistically significant for both the above domains. In the improved group the score on negative symptom domain was 1.56 ±2.8 and 4.31±3.1 for the unimproved group and the difference between the two groups was statistically significant (P< .05).

FIG. 8 COMPARISON OF THE GROUPS BY SYMPTOM SEVERITY

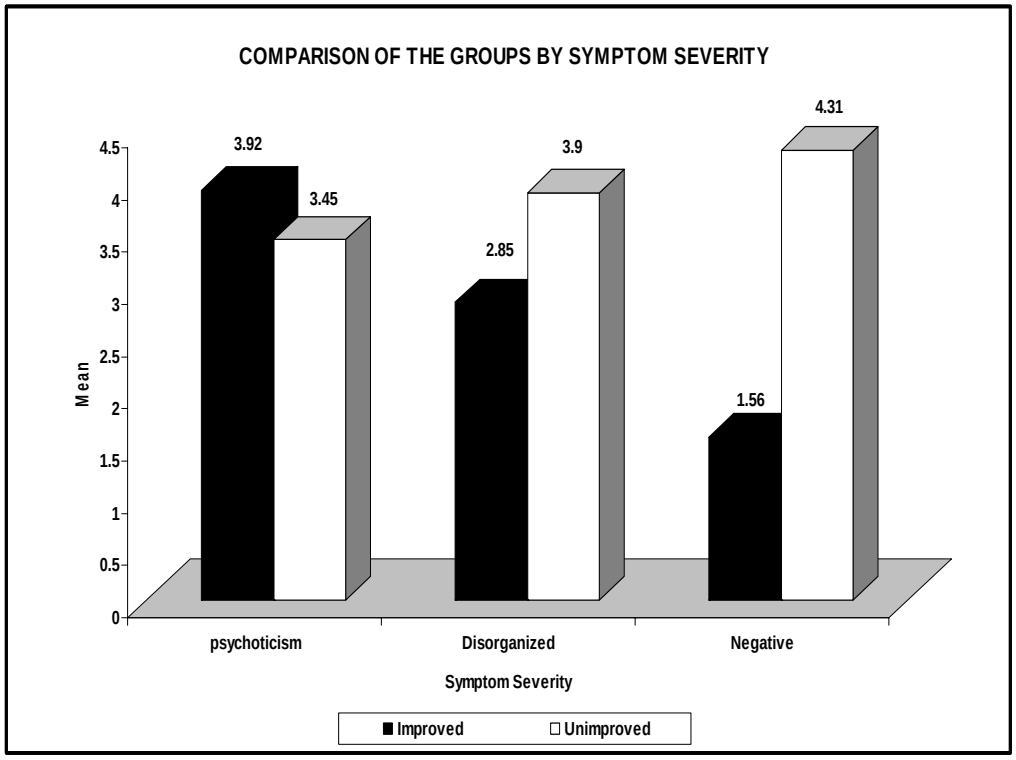


TABLE NO. 14

COMPARISON OF THE TWO GROUPS ON DURATION OF UNTREATED PSYCHOSIS

Variable	**Improved n=41 Mean ± SD**	**Unimproved n=22 Mean ± SD**	**t value**	**P**
Log DUP	0.898 ± 0.5	1.357 ± 0.5	3.41	0.001

In the improved group the duration of untreated psychosis was 0.898±0.5 (logDUP), the corresponding DUP in months being 7.92 months and in the unimproved group the duration of untreated psychosis was 1.36±0.5 (logDUP), the corresponding DUP in months was 22.78. The difference between the two groups was statistically significant.

FIG. 9 COMPARISON OF THE TWO GROUPS ON DURATION OF UNTREATED PSYCHOSIS

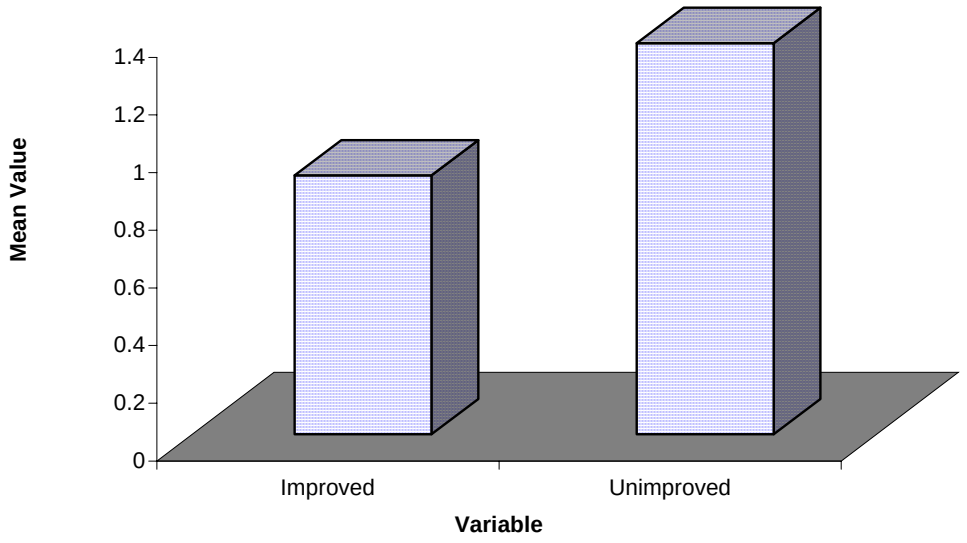


TABLE NO. 15

COMPARISON OF THE GROUPS ON PREMORBID FUNCTIONING

Variable	Improved n = 41	Unimproved n = 22	T value	p
Premorbid social adjustment (Total Score)	25.78 ±6.8	31.81 ±2.5	3.54	0.001

In the improved group the premorbid social adjustment score was 25.78±6.8 and the score in the unimproved group was 31.81±2.5. The difference between the two groups was statistically significant.

TABLE NO. 16

COMPARISON OF THE TWO GROUPS BY MODE OF TREATMENT

Mode of Treatment	Improved		Un Improved		Total
	n	%	n	%	
Typical drugs	2	4.9	-	-	2
Atypical	32	78.0	12	54.5	44
ECT & Drugs	7	17.1	10	45.5	17
Total	41	100	22	100	63

$\chi^2 = 6.44$ p = 0.03

In the improved group 4.9% were treated with typical antipsychotic drugs, 78% with atypical drugs, 17.1% with ECT and drugs. In the unimproved group 54.5% were treated with atypical drugs, 45.5% were treated with ECT and drugs. The difference between the two groups was statistically significant (P< .05).

TABLE NO.17

CORRELATION OF DUP WITH IMPROVEMENT AT 8 WEEKS

Variable	Correlation coefficient	P value
Log DUP	−0.3999	0.001
PSA Total	−0.4132	0.001

The correlation between duration of untreated psychosis and premorbid functioning with improvement at 8 weeks is statistically significant (P<.05).

TABLE NO.18

PARTIAL CORRELATION OF DUP WITH IMPROVEMENT AT 8 WEEKS CONTROLLING FOR THE CONFOUNDING FACTORS SUCH AS AGE, AGE AT ONSET, SYMPTOMS AT BASELINE, AND PREMORBID FUNCTIONING

Improved	Correlation coefficient	P value
LogDUP	−0.1794	.186

The correlation of DUP with improvement after controlling for confounding factors is not significant (P>.05)

TABLE NO.19

PARTIAL CORRELATION OF PREMORBID FUNCTIONING WITH IMPROVEMENT AT WEEKS AFTER CONTROLLING FOR AGE, AGE AT ONSET DUP AND SYMPTOMS AT BASELINE

Improved	Correlation coefficient	P value
PSA Total score	−0.1802	.184

The correlation of premorbid social adjustment with improvement after controlling for confounding factors is not significant (P>.05).

DISCUSSION

Studies state that a long duration of untreated psychosis confers a poor prognosis in schizophrenia.

Socio-demographic variables and DUP:

The mean duration of untreated psychosis for the whole sample is 22.3 months which is longer than the DUP reported in studies done in western countries. But mean DUP in this study is shorter when compared to some of the Indian studies (4 years in a study by Philip et al, 11.64 years in a study by padmavathi et al and more than 5 years by Tirupati et al). Among the whole sample 34% had a DUP greater than two years with 4 patients having a DUP greater than 8 years which again confirms the finding that patients in developing countries come late to treatment (Isaac et al, Thara et al).

The role of socio-demographic variables in determining the duration of untreated psychosis has given contrasting results across various studies. Studies have shown that males have a longer DUP than females but we could not establish any such difference in gender to be associated with DUP. Numerous studies have not reported any relation of DUP with gender.

The finding of a significant positive correlation of DUP with the age at first presentation shows that the duration of untreated psychosis increases as the age at first presentation to treatment increases, the result being similar to

the findings of Padmavathi et al that never treated patients were older in age and ill for a longer duration and were more symptomatic and severely disabled. This finding is in contrary to other studies that have not found a association between age and DUP.

There is no significant correlation of duration of untreated psychosis with the educational level, marital status and socioeconomic status at baseline assessment, a finding which is similar to most other studies. One study in India has reported that untreated patients were most often uneducated and divorced and such a finding is not found in our study. In our study we found no correlation between DUP and employment, a finding contrary to the report of Morgan et al that unemployment has a less strong effect on duration of untreated psychosis.

Some of the Indian studies have reported that a longer duration of untreated illness in schizophrenic patients was due to the larger extended/ joint family, which was able to compensate and cope with the dysfunctional member, concluding that such family system seemed to be a crucial factor related to the delay in treatment. In our study, though 70% of the patients were in the joint family system, there was no significant correlation of family type with DUP. In the West London first-episode study of schizophrenia, most of the patients were living alone or homeless. However, this study carried out in a Government Institute has its limitations regarding demographic variables like educational status, socioeconomic status and employment.

Clinical variables and DUP

There is no significant association between the subtypes of schizophrenia with the duration of untreated psychosis at baseline assessment. Only few studies have studied the relation of diagnostic subtypes with DUP and have not found any significant association.

In our study premorbid functioning is found to have a positive correlation with duration of untreated psychosis, showing that poor premorbid functioning is associated with a longer DUP than those with a better premorbid functioning, This finding is similar to the studies done by Verdoux et al and Malla et al where they have reported that poor premorbid functioning is associated with a long DUP and poor outcome. Some of the studies have not shown any such association between DUP and premorbid functioning.

The correlation of DUP with symptom severity at baseline in this study has found a significant positive correlation with negative symptoms, but not with the disorganization and psychotic symptom domain. This finding is similar to the studies that have found a longer DUP to be associated with higher levels of negative or deficit symptoms at first presentation (Perkins et al). The negative correlation of DUP with psychotic symptom domain in the study, though not significant implies that schizophrenic patients with positive symptoms seek treatment earlier and hence have a shorter duration of untreated psychosis. Drake et al reported that longer DUP was associated with higher

positive symptoms at presentation which is not found in our study. Some of the studies do not find any such association between DUP and baseline symptoms (Loebel et al, Haas et al, Harris et al)

The total number of patients at 8 weeks assessment is 63(65%) and the follow up rate is considerably lower when compared to most other studies, both Indian and studies done in western countries. The poor attrition rate could not be explained by any of the socio-demographic and clinical variables and the duration of untreated psychosis, a finding similar to the study done by Harris where they compared between those who completed follow up and those who did not. Information regarding the reasons for dropout was not available as those patients and their relatives could not be traced by any means.

In the follow up assessment there is no significant difference between the improved and the unimproved group of patients on any of the socio-demographic variables such as education, socio-economic status, marital status, employment and family type. This is in contrary to the studies that have shown that being married has a good outcome.

There is no significant association between the two groups by age, age at onset of illness which is contrary to the finding of Perkins et al that younger age at onset predicts a poor prognosis and is a potential confounding factor of DUP and outcome.

DUP and outcome at 8 weeks

There is a statistically significant difference between the improved and the unimproved groups on the duration of untreated psychosis, as the mean DUP for the improved group is 7.92 months and 22.78 months for the unimproved group of patients. This finding is similar to other studies that shorter DUP is associated with good outcome and treatment response than those with a longer DUP. In a study done by Philip et al, reported that patients with a short DUP have shown improvement at the end of 6 weeks following treatment. There have been contrasting reports that DUP has an influence on the outcome in the short term but not on the long term. Drake et al in his study concluded that DUP's relationship to outcome is strongest in the initial months of psychosis and has implications for targeting early intervention.

The subtype of schizophrenia did not show any significant difference between the improved and the unimproved groups though paranoid schizophrenia is the most common diagnosis in the sample.

In this study there is no difference among the two groups by family history suggestive of schizophrenia in 1st or 2nd degree relatives.

The duration of hospitalization between the two groups was not significant as more than 80% of the patients were hospitalized for less than two weeks. This finding is similar to the report of Haas et al that there is no significant difference in terms of duration of hospitalization between the long and short DUP groups.

Treatment response

The mode of treatment between the two groups is statistically significant as 78% of the improved group were treated with atypical antipsychotics and 54.5% among the unimproved group with atypicals. This difference could be explained by the fact that patients with a shorter DUP would have had a better response to treatment as described by Perkins et al in his study. This result has to be interpreted with caution as the type of drugs, dosage, and adequacy of dose was not included in our study. Few studies differ as Barnes et al found that there was little evidence of any association between dup and the development of resistance to initial drug treatment.

In our study the premorbid social adjustment score is statistically significant between the improved and the unimproved groups, indicating that poor premorbid functioning is associated with poor improvement. This finding is similar to the reports of Verdoux et al that premorbid functioning is an important predictor of outcome. Again the premorbid Social Adjustment scale used in this study assesses premorbid functioning in social and school activities, for which 11.34% of the sample in our study were uneducated making it difficult to assess in these group of patients.

Confounding factors, DUP and outcome

In order to find the relationship of confounding factors associated with DUP and outcome, a partial correlation was done controlling for the

confounding factors such as age, age at onset of illness, symptom domains of psychotic, disorganized and negativism and premorbid functioning. The correlation found that DUP is not statistically significant after controlling for the confounding factors, as unadjusted DUP explained for 39% of variance in the outcome which decreased by 17% after adjusting for the confounding factors. This finding that duration of untreated psychosis is not an independent predictor of outcome is in contrary to most of the studies that reported DUP to be significant predictor of outcome after controlling for the confounding factors.

As premorbid functioning has shown a statistically significant correlation with improvement at 8 weeks, we did a partial correlation controlling for the confounding factors and found that premorbid functioning is not statistically significant. This finding is similar to studies that report premorbid functioning is not a strong predictor of outcome and the observed association between DUP and outcome was not explained by premorbid adjustment.

Thus in our study we found that duration of untreated psychosis is not an independent predictor of outcome and is confounded by variables such as premorbid functioning, mode of treatment and other variables suggesting that duration of untreated psychosis alone is not a predictor of short term outcome.

SUMMARY AND CONCLUSION

The aim of this study is to find the social and clinical determinants of duration of untreated psychosis, the influence of duration of untreated psychosis on short-term outcome and the relationship of premorbid functioning on duration of untreated psychosis and outcome in a sample of drug-naïve schizophrenia patients diagnosed according to the ICD-10. Strict inclusion and exclusion criteria's were used to get a homogenous sample.

100 patients were selected for the study of which 97 were assessed at baseline with SAPS and SANS for psychopathology, PSA scale to assess premorbid functioning, duration of untreated psychosis and a socio-demographic profile were obtained. 63 patients were assessed at 8 weeks of follow up for psychopathology and categorized into improved and unimproved as per CGI-SCH and GAF scale. Correlation of DUP with socio-demographic, clinical and symptoms at baseline was done, comparison between the improved and the unimproved groups was done. The results were analyzed using chi-square test, t-test, Pearson's correlation and partial correlation.

The study showed the following results

1. Significant positive correlation between duration of untreated psychosis and the age at first presentation.

2. Significant positive correlation between duration of untreated psychosis and negative symptoms at baseline.

3. Significant positive correlation between duration of untreated psychosis and premorbid functioning at baseline.

4. Improved group of patients had a short duration of untreated psychosis than the unimproved group.

5. Improved groups of patients had a better premorbid functioning than the unimproved group.

6. Statistically significant difference between the improved and the unimproved groups by the mode of treatment.

7. Statistically significant difference between the improved and the unimproved groups in the negative symptom domain.

8. There is no significant correlation of duration of untreated psychosis and premorbid functioning with improvement after the confounding factors were controlled.

The findings from this study suggest that a longer duration of untreated psychosis is associated with increased age at presentation, higher negative symptoms and poor premorbid functioning. The results show that improved patients have a short duration of untreated psychosis and better premorbid functioning than the unimproved patients but the association is not significant after the confounding factors were controlled. This finding concludes that

duration of untreated psychosis is not an independent predictor of outcome as stated in literature.

It is conceivable that the reported better outcome for schizophrenia in India is unlikely to be because of shorter DUP. However, instituting treatment earlier gives further advantage and can make the outcome in our people even brighter.

LIMITATIONS

1. Assessment of duration of untreated psychosis involves retrospective recall of time of onset of psychosis, which has the usual recall bias from the patient.

2. As short term outcome was measured in this study the change in symptoms after 8 weeks could be more a measure of speed of recovery.

3. Variables related to duration of untreated psychosis such as pathways to care, mode of onset, substance use were not included.

4. Treatment details were not described in detail as it could have a significant influence on outcome.

5. The researcher was not blind to the patients at the time of follow up assessment as literature says that there is a likely chance for bias in assessment.

6. High attrition rate among the sample during follow up.

IMPLICATIONS

Schizophrenia may involve a progressive pathological process that is well developed by the time the frank psychopathology of schizophrenia emerges. An association between duration of untreated psychosis and clinical outcome offers hope that early intervention programs that are effective in reducing the length of the initial psychotic episode may enhance the likelihood of recovery from a first episode of schizophrenia and perhaps reduce cumulative morbidity. Ameliorating the symptoms of initial psychosis may not only lessen the immediate suffering and burden of disease experienced by patients and their families, but it may also improve long-term prognosis by limiting progression of the illness and preserving a person's ability to respond to antipsychotic medication.

In future studies it will be particularly important to evaluate the effect of reduction of the duration of untreated psychosis on initial negative symptom severity and negative symptom response to treatment. From a public health perspective, it is of major importance to further investigate the links between duration of untreated psychosis, premorbid characteristics, outcome in large sample sizes and in studies aimed at assessing the impact of early identification and treatment of schizophrenia.

FUTURE DIRECTIONS

Studies that advance our understanding of the mechanism responsible for the relationship of duration of psychosis and outcome will most likely provide critical information about the neuropathology of schizophrenia. The evidence for clinical deterioration after a prolonged period of initially untreated psychosis, manifested through the development of secondary resistance to antipsychotic treatment and progressive functional impairments, suggests that at least part of the clinical deterioration characteristic of schizophrenia is mediated by a progressive pathophysiological process. Longitudinal studies, especially those that to attempt to look at change in brain structure and function beginning at the premorbid and prodromal stage of illness and extending through the first episode, are likely to increase our understanding of the nature and timing of the neurochemical, neuroanatomical, and clinical pathways that underlie clinical deterioration in schizophrenia.

Another important issue relates to the observation of treatment resistance in individuals with a DUP as short as 4 weeks, as well as preserved responsiveness to antipsychotic treatment with DUP longer than 5 years. Variability in treatment responsiveness may reflect fundamentally different neurobiological process involved in the development and progression of symptoms. The potential protective factors that may contribute to the preservation of treatment responsiveness and to improved clinical outcome in

patients with a long DUP merit further attention, as they may lead to discovery of new therapeutic medications.

At the end of this study we suggest that the future studies include variables such as recognition of illness, access to and availability of care, stigma, perinatal complications and neurological soft signs.

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APPENDIX-I

PROFORMA

Name:

Age:

Sex:

Education: Uneducated/ Primary/ High school/ Secondary/ Graduate

Occupation: Employed/ Unemployed

Socio-economic status: Low/ Middle/ High

Marital status: Married/ Separated/ Divorced/ Widow/ Unmarried

Type of family: Nuclear/ Joint

Family history: Yes/ No

Age at onset:

Diagnosis: Paranoid/ Hebephrenic/ Catatonic/ Undifferentiated/ Simple

Duration of Untreated Psychosis (months):

Duration of Untreated Psychosis: 1-6mon/ 7-12mon/ 13-18mon/ 19-24mon/ >24months

Duration of Hospitalization: <7days/ 8-24days/ 15-21days/ 22-28 days

Mode of treatment: Typical antipsychotics/ Atypicals/ ECT

APPENDIX - II

Scale for Assessment of Positive Symptoms (SAPS)

Hallucinations	
1) Auditory Hallucinations:	0 □ 1 □ 2 □ 3 □ 4 □ 5 □
2) Voices Commenting:	0 □ 1 □ 2 □ 3 □ 4 □ 5 □
3) Voices Conversing:	0 □ 1 □ 2 □ 3 □ 4 □ 5 □
4) Somatic or Tactile Hallucinations:	0 □ 1 □ 2 □ 3 □ 4 □ 5 □
5) Olfactory Hallucinations:	0 □ 1 □ 2 □ 3 □ 4 □ 5 □
6) Visual Hallucinations:	0 □ 1 □ 2 □ 3 □ 4 □ 5 □
7) Global Rating of Hallucinations:	0 □ 1 □ 2 □ 3 □ 4 □ 5 □
Delusions	
8) Persecutory Delusions:	0 □ 1 □ 2 □ 3 □ 4 □ 5 □
9) Delusions of jealousy:	0 □ 1 □ 2 □ 3 □ 4 □ 5 □
10) Delusions of Guilt or Sin:	0 □ 1 □ 2 □ 3 □ 4 □ 5 □
11) Grandiose Delusions:	0 □ 1 □ 2 □ 3 □ 4 □ 5 □
12) Religious Delusions:	0 □ 1 □ 2 □ 3 □ 4 □ 5 □
13) Somatic Delusions:	0 □ 1 □ 2 □ 3 □ 4 □ 5 □
14) Delusions of Reference:	0 □ 1 □ 2 □ 3 □ 4 □ 5 □
15) Delusions of Being Controlled:	0 □ 1 □ 2 □ 3 □ 4 □ 5 □
16) Delusions of Mind Reading:	0 □ 1 □ 2 □ 3 □ 4 □ 5 □
17) Thought Broadcast:	0 □ 1 □ 2 □ 3 □ 4 □ 5 □
18) Thought Insertion:	0 □ 1 □ 2 □ 3 □ 4 □ 5 □
19) Thought Withdrawal:	0 □ 1 □ 2 □ 3 □ 4 □ 5 □
20) Global Rating of Delusions:	0 □ 1 □ 2 □ 3 □ 4 □ 5 □
Bizarre Behavior	
21) Clothing and Appearance:	0 □ 1 □ 2 □ 3 □ 4 □ 5 □
22) Social and Sexual Behavior:	0 □ 1 □ 2 □ 3 □ 4 □ 5 □
23) Aggressive and Agitated Behavior:	0 □ 1 □ 2 □ 3 □ 4 □ 5 □
24) Repetitive or Stereotyped Behavior:	0 □ 1 □ 2 □ 3 □ 4 □ 5 □
25) Global Rating of Bizarre Behavior:	0 □ 1 □ 2 □ 3 □ 4 □ 5 □
Positive Formal Thought Disorder	
26) Derailment:	0 □ 1 □ 2 □ 3 □ 4 □ 5 □
27) Tangentiality:	0 □ 1 □ 2 □ 3 □ 4 □ 5 □
28) Incoherence:	0 □ 1 □ 2 □ 3 □ 4 □ 5 □
29) Illogicality:	0 □ 1 □ 2 □ 3 □ 4 □ 5 □
30) Circumstantiality:	0 □ 1 □ 2 □ 3 □ 4 □ 5 □
31) Pressure of Speech:	0 □ 1 □ 2 □ 3 □ 4 □ 5 □
32) Distractible Speech:	0 □ 1 □ 2 □ 3 □ 4 □ 5 □
33) Clanging:	0 □ 1 □ 2 □ 3 □ 4 □ 5 □
34) Global Rating of Formal Thought Disorder:	0 □ 1 □ 2 □ 3 □ 4 □ 5 □
Inappropriate Affect	
35) Inappropriate Affect:	0 □ 1 □ 2 □ 3 □ 4 □ 5 □

Total Psychoticism Score : _____

Total Disorganization Score: _____

0 = None; 1 = Questionable; 2 = Mild; 3 = Moderate; 4 = Marked; 5 = Severe

APPENDIX - III

Scale for Assessment of Negative Symptoms (SANS)

Affective Flattening or Blunting

1) Unchanging Facial Expression:	0 □ 1 □ 2 □ 3 □ 4 □ 5 □
2) Decreased Spontaneous Movements:	0 □ 1 □ 2 □ 3 □ 4 □ 5 □
3) Paucity of Expressive Gestures:	0 □ 1 □ 2 □ 3 □ 4 □ 5 □
4) Poor Eye Contact:	0 □ 1 □ 2 □ 3 □ 4 □ 5 □
5) Affective Non-responsivity:	0 □ 1 □ 2 □ 3 □ 4 □ 5 □
6) Lack of Vocal Inflections:	0 □ 1 □ 2 □ 3 □ 4 □ 5 □
7) Global Rating of Affective Flattening:	0 □ 1 □ 2 □ 3 □ 4 □ 5 □

Alogia

8) Poverty of Speech:	0 □ 1 □ 2 □ 3 □ 4 □ 5 □
9) Poverty of Content of Thought:	0 □ 1 □ 2 □ 3 □ 4 □ 5 □
10) Blocking:	0 □ 1 □ 2 □ 3 □ 4 □ 5 □
11) Increased Latency of Response:	0 □ 1 □ 2 □ 3 □ 4 □ 5 □
12) Global Rating of Alogia:	0 □ 1 □ 2 □ 3 □ 4 □ 5 □

Avolition – Apathy

13) Grooming and Hygiene:	0 □ 1 □ 2 □ 3 □ 4 □ 5 □
14) Impersistence at Work or School:	0 □ 1 □ 2 □ 3 □ 4 □ 5 □
15) Physical Anergia:	0 □ 1 □ 2 □ 3 □ 4 □ 5 □
16) Global Rating of Avolition – Apathy:	0 □ 1 □ 2 □ 3 □ 4 □ 5 □

Anhedonia – Asociality

17) Recreational Interests and Activities:	0 □ 1 □ 2 □ 3 □ 4 □ 5 □
18) Sexual Activity:	0 □ 1 □ 2 □ 3 □ 4 □ 5 □
19) Ability to Feel Intimacy and Closeness:	0 □ 1 □ 2 □ 3 □ 4 □ 5 □
20) Relationships with Friends and Peers:	0 □ 1 □ 2 □ 3 □ 4 □ 5 □
21) Global rating of Anhedonia – Asociality:	0 □ 1 □ 2 □ 3 □ 4 □ 5 □

Attention

22) Social Inattentiveness:	0 □ 1 □ 2 □ 3 □ 4 □ 5 □
23) Inattentiveness during Mental Testing:	0 □ 1 □ 2 □ 3 □ 4 □ 5 □
24) Global Rating of Attention:	0 □ 1 □ 2 □ 3 □ 4 □ 5 □

TOTAL NEGATIVE SYMPTOM SCORE: _____

0 = None; 1 = Questionable; 2 = Mild; 3 = Moderate; 4 = Marked; 5 = Severe

APPENDIX - IV

CLINICAL GLOBAL IMPRESSION – SCHIZOPHRENIA SCALE

I. Severity of illness

Considering your total clinical experience with patients with schizophrenia, how severely ill has the patient been during the last week?

The following symptoms were assessed.

1. Positive symptoms (e.g. hallucinations, delusions or bizarre behavior)
2. Negative symptoms (e.g. affective flattening, avolition or anhedonia)
3. Depressive symptoms (e.g. . sadness, depressed mood or hopelessness)
4. Cognitive symptoms (e.g. impaired attention, concentration or memory)
5. Overall severity

Rating of severity

1. Normal, not ill
2. Minimally ill
3. Mildly ill
4. Moderately ill
5. Markedly ill
6. Severely ill
7. Among the most severely ill

1I. Degree of change

Compared to the previous evaluation*, how much has the patient changed? Rate improvement whether or not, in your judgement, is due entirely to treatment?

1. Very much improved
2. Much improved
3. Minimally improved
4. No change
5. Minimally worse
6. Much worse
7. Very much worse

APPENDIX - V

PREMORBID SOCIAL ADJUSTMENT SCALE

Standardized entry questions are used for each item. Scoring is on a scale from 1 to 7 for each of the five items. Each item is scored separately for childhood (5-11years) and adolescence (12-16 years) and total score is pbtained by adding the two.

1. Sociability and isolation.

    1. Not withdrawn, active social interaction

    3. Mild withdrawl, enjoyed socialization when involved-occasionally sought opportunities to socialize

    5. Moderately withdrawn, given to daydreaming and excessive fantasy, did not seek contact

    7. Unrelated to others, isolated, avoided contacts

2. Peer relations.

    1. Many friends, close relationships

    3. Casual friends only

    5. Deviant friendship patterns: only friends with children older or younger

    7. Socially isolated, not even superficial relationships

3. Scholastic performance

    1. Excellent student, top of class

    3. Average student

    5. Failing all classes

    7. Required special education

1. Adaptation to school

    1. Good adaptation, enjoyed school, no discipline problems

    3. Fair adaptation, occasional discipline problems, not very interested in school

    5. Poor adaptation, disliked school, frequent truancy and discipline problems

    7. Refused to have anything to do with school- delinquency or vandalism directed against school

2. Interests

    1. Active, involved in a range of school, sporting and social activities and hobbies

    3. Involved in one school, sporting, or social activity with other younger people

    5. Introverted interests- one or a few hobbies which required no contact with others

    7. No interests- withdrawn and indifferent toward interests of the average youngster

APPENDIX - VI

GLOBAL ASSESSMENT OF FUNCTIONING SCALE

Consider psychological, social, and occupational functioning on a hypothetical continuum of mental health illness. Do not include impairment in functioning due to physical or environmental limitations.

91-100 Superior functioning in a wide range of activities, life's problems never seem to get out of hand, is sort out by others because of his or her positive qualities. No symptoms.

81-90 Absence or minimal symptoms, good functioning in all areas, interested and involved in a wide range of activities, socially effective, generally satisfied with life, no more than every day problems or concerns.(e.g., an occasional argument with family members.)

71-80 If symptoms are present they are transient and expectable reactions to psycho social stressors: no more than slight impairment in social, occupational or school functioning. (Temporarily falling behind in school work).

61-70 Some mild symptoms(e.g. depressed mood and mild insomnia) OR some difficulty in social, occupational, school functioning, but generally functioning pretty well, has some meaningful interpersonal relationships.

51-60 Moderate symptoms (e.g. flat affect and circumstantial speech, occasional panic attacks) OR moderate difficulty in school, occupational or social functioning. (e.g. few friends, conflicts with peers or co-workers)

41-50 Serious symptoms (e.g. suicidal ideation, severe obsessional rituals, frequent shop lifting) OR any serious impairment in social, occupational or school functioning (e.g. No friends, unable to keep a job).

31-40 Some impairment in reality testing or communication (e.g. speech is at times illogical, obscure, or irrelevant) OR major impairment in several areas of life such as school, family relations, judgement, thinking or mood(depressed man avoids friends, neglects family and is unable to work; child frequently beats up younger children and is defiant at home, and is failing at school).

21-30 Behavior is considerably influenced by delusions or hallucinations OR serious impairment in communication or judgement (e.g. sometimes incoherent, acts grossly inappropriately, suicidal preoccupation) OR inability to function in almost all areas (stays in bed almost all the day; no job, home or friends).

11-20 Some danger of hurting self or others (suicidal attempts without clear expectation of death, frequently violent, manic excitement) or occasionally fails to maintain personal hygiene OR gross impairment in communication (e.g. largely coherent or mute).

1-10 Persistent danger of severely hurting self or pothers (recurrent violence) OR persistent inability to maintain minimal personal hygiene OR serious suicidal act with clear expectation of death.