Research Report

RELATION BETWEEN CLINICAL AND SOCIAL VARIABLES AND DURATION OF UNTREATED PSYCHOSIS IN FIRST EPISODE PSYCHOSIS

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ABSTRACT

Background: Several studies have shown that if untreated, psychosis can cause significant reduction in brain volume and worsening of disease outcome. Reducing Duration of Untreated Psychosis (DUP) is an important early intervention strategy. Factors associated with longer DUP remain poorly understood and there is a paucity of Indian studies in this regard.
Methods: We compared sociodemographic data, premorbid functioning and psychopathology of patients of first episode psychosis with brief (six months or less) or long (more than six months) DUP. Premorbid Adjustment Scale and PANSS were used to assess the premorbid functioning and psychopathology respectively.
Results: Lower age, higher educational status of the patient, acute onset, and higher scores for negative symptom or general psychopathology in PANSS were associated with brief DUP.
Conclusions: Certain sociodemographic and clinical features are associated with brief DUP, and there is a need for more, especially longitudinal, studies on this topic.

Keywords: Duration of untreated psychosis, First episode psychosis, Premorbid functioning

INTRODUCTION

Psychotic illnesses cause immense suffering for patients and their families and are among the top 10 causes of disability worldwide as measured using DALY (Disability Adjusted Life Years).[1] Kraepelin had suggested a uniformly deteriorating and degenerative course for psychoses. But, following the work of Bleuler,[2] evidence is accumulating against a uniform progressive decline during the course of schizophrenia. Suggestion by Wyatt[3] that "While psychosis is undoubtedly demoralizing and stigmatizing, it may also be biologically toxic" has led to emergence of the concept of Duration of Untreated Psychosis (DUP). The hypothesis that psychosis is biologically toxic is supported by studies which point to progressive brain changes in ultra-high risk individuals who went on to develop psychosis as compared to those who had not become psychotic.[4] The hope is that, by intervening early and reducing the DUP, one can minimize the brain changes and improve the outcome. For example, in a naturalistic follow-up study on patients with first episode schizophrenia done in Mumbai, Shrivastava

et al. had found that the group with longer DUP had slower clinical recovery.[5]

Most studies of DUP are done on patients with First Episode Psychosis (FEP), as there is advantage of reduced bias of retrospective assessment. Effects of medications and long-term institutionalization are also reduced. FEP studies often include affective psychoses in addition to non-affective psychosis, as there is diagnostic instability and a sharing of many characteristics, including symptomatology.[6]

Defining the onset of psychosis has been difficult due to the subjective and private nature of psychotic symptoms. Also, there have been disagreements regarding as to what constitutes treatment of psychosis. Some researchers believe DUP ends with initiation of treatment with antipsychotics, whereas some say it ends only with 'adequate treatment'. Defining 'adequate treatment' also poses further difficulties — For example, Loebel et al.[7] and Larsen et al.[8] defined 'adequate treatment' as 12 weeks and three weeks of antipsychotic treatment respectively.

If we can modify determinants of DUP, we may be able to reduce delay in treatment and improve the outcome. There is a paucity of Indian studies about the determinants of DUP. Hence this study was undertaken to assess the association of DUP with sociodemographic and clinical variables in patients experiencing FEP.

MATERIALS AND METHODS

This study was conducted from June 2012 to March 2013. Consecutive patients attending the outpatient clinics of Department of Psychiatry, Government Medical College, Kozhikode with a diagnosis of FEP constituted the study population.

Patients aged 18-65 years, able to provide a written informed consent, presenting with FEP conforming to ICD-10[9] codes F20-F29, F30.2 or F32.3, irrespective of whether drug naive or already on psychotropics, were included. Diagnosis was based on clinical interview using MINI (The Mini International Neuropsychiatric Interview English Version 5.0.0).[10] Patients with history of medical illnesses that may significantly influence CNS function or structure (like mental retardation, significant head injury, seizure disorder, etc.), as judged by clinical evidence, were excluded. Patients with comorbid psychoactive substance dependence (except nicotine) as per ICD 10 diagnostic guidelines were also excluded.

Written informed consent was obtained from a relative or friend if the patient was unable to give the consent due to illness. Approvals from the Institutional Research Committee and Institutional Ethics Committee were obtained.

Assessment Tools

Sociodemographic and clinical data, including pathway to care, distance from the patient's home to the nearest mental health centre and actual centre where treatment was sought, etc. were collected with a specifically designed data sheet.

The Cannon Spoor Premorbid Adjustment Scale (PAS)[11] was used to evaluate the level of functioning in the one year before the onset of psychosis. The reason for studying premorbid functioning was that there is previous evidence linking higher premorbid functioning to shorter treatment delays.[12] The tool assesses four domains of functioning in each of the four major life periods (Childhood, Early and Late Adolescence and Adulthood). The scale also has a General section meant to estimate the highest level of functioning the patient achieved premorbidly. After discussion among the research team and other local psychiatrists, socio-sexual domain of the tool was deemed culturally invalid for our population and it was decided not to score that domain. (For example, it had questions pertaining to dating which is not yet seen in the local culture.) As most patients were accompanied by the spouse or children who were not able to provide detailed history regarding the patient's childhood or adolescence, the Childhood, and Early and Late Adolescence life periods of most patients could not be scored, and only the Adulthood could be scored. Scores for only the following domains were used in

Table 1: Sociodemographic and clinical variables of patients (n=45)

Variable	Categories	n(%)
Sex	Female	20(44.44)
	Male	25(55.55)
Education	<7th Standard	16(35.55)
	>7th Standard	29(64.44)
Residence	Rural	35(77.77)
	Urban	10(22.23)
Occupation	Unemployed	22(48.88)
	Unskilled	13(28.88)
	Semiskilled	3(6.66)
	Skilled	7(15.55)
Marital status	Unmarried	8(17.77)
	Married	34(75.55)
	Divorced/Separated	3(6.66)
Socioeconomic status	Above poverty line	10(22.22)
	Below poverty line	35(77.77)
Family history	Absent	25(55.55)
	Present	20(44.44)
Diagnosis	Schizophrenia	7(15.6)
	Persistent Delusional Disorder	7(15.6)
	Acute and Transient Psychotic Disorder	11(24.4)
	Unspecified Nonorganic Psychosis	8(17.8)
	Mania with Psychotic Symptoms	4(8.9)
	Severe Depressive Episode with Psychotic Symptoms	8(17.8)
Pathway to care	Doctor	17(37.77)
	Psychologist	1(2.22)
	Magico-religious	8(17.77)
	Psychiatrist	19(42.22)
Mode of Onset	Acute	30(66.66)
	Insidious	15(33.33)

the final statistical analysis: Sociability and withdrawal in Adulthood, Peer relationships in Adulthood, and the General section. Two patients were 18-year-old and hence the first two of the above domains could not be scored in them.

The Mini International Neuropsychiatric Interview (MINI)[10] was used to diagnose psychotic disorders and mood disorder with psychotic features, and The Positive and Negative Symptom Scale (PANSS)[13] was used to assess psychopathology.

Definitions

As per the definition proposed by Morgan et al., we defined "DUP" as the interval between first noted psychotic symptom(s) and contact with mental health services.[14] Duration of Untreated Illness (DUI) was defined as the interval between first noted nonspecific symptom(s) and contact with mental health services. Following Craig et al., we defined onset of psychosis as one week or more of one of the following symptoms: delusions, hallucinations, grossly disorganized or catatonic behaviour or disorganized speech.[15]

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Table 2: Comparison of sociodemographic profiles of patients with Brief or Long DUP – categorical variables

VARIABLE	BRIEF DUP (<6 MONTHS) n(%)	LONG DUP (>6 MONTHS) n(%)	TEST	SIGNIFICANCE
Sex			$\chi^2=0.18$	p=0.75
Female	14(31.11)	6(13.33)		
Male	16(35.55)	9(20)		
Education			$\chi^2=5.87$	p=0.01[*]
< 7th Standard	7(15.55)	9(20)		
>7th Standard	23(51.11)	6(13.33)		
Residence			$\chi^2=0.06$	p=1.00
Rural	23(51.11)	12(26.66)		
Urban	7(15.55)	3(6.66)		
Occupation			$\chi^2=4.40$	p=0.20
Unemployed	16(35.55)	6(13.33)		
Unskilled	6(13.33)	7(15.55)		
Semiskilled	3(6.66)	0		
Skilled	5(11.11)	2(4.44)		
Marital status			Fisher's exact test	p=0.03[*]
Unmarried	8(17.77)	0		
Married	21(46.66)	13(28.88)		
Divorced/ Separated	1(2.22)	2(4.44)		
Socioeconomic status			$\chi^2=1.03$	p=0.45
APL	8(17.77)	2(4.44)		
BPL	22(48.88)	13(28.88)		

APL-Above Poverty Line; BPL-Below Poverty Line; *P<0.05

As per the definition proposed by Naqvi et al., we divided DUP into: Brief DUP (six months or less) and Long DUP (greater than six months).[16] As done by Harrison et al., mode of onset was operationalized and rated as: acute (psychotic symptoms appeared within a period of one month of first noticeable change) and insidious (psychotic symptoms appeared incrementally over a period of more than one month since the first noticeable change).[17]

Procedure

After getting informed consent, the sociodemographic details, pathways to seeking care, and the distances from the nearest as well as the actual centre which they consulted were collected. If a diagnosis of psychosis was made during the subsequent MINI interview, each patient or relative was asked to date their first experience of onset of both the nonspecific symptom(s) and the psychotic symptom(s). Details of all previous contacts with health services were also collected. Severity of psychopathology was assessed using PANSS, and insight was measured with the scale's Insight subscale. Then the PAS was applied. Information collected at the interview was supplemented with information from other sources like hospital records, family members and school records. If discrepancy was found or if reliable relatives were not available to provide information, consensus about the duration was assigned using all available sources of information.

Table 3: Comparison of clinical variables of patients with Brief or Long DUP: categorical variables

VARIABLE	BRIEF DUP (<6 MONTHS) N(%)	LONG DUP (>6 MONTHS) N(%)	TEST AND STATISTIC	SIGNIFICANCE
Family history			$\chi^2=1.13$	p=0.35
Absent	15(33.33)	10(22.22)		
Present	15(33.33)	5(11.11)		
Pathway to care			$\chi^2=2.61$	p=0.50
Doctor	9(20)	8(17.77)		
Psychologist	1(2.22)	0		
Magico-religious	6(13.33)	2(4.44)		
Psychiatrist	14(31.11)	5(11.11)		
Mode of onset			$\chi^2=36.45$	p<0.001[*]
Acute	29(64.44)	1(2.22)		
Insidious	1(2.22)	14(31.11)		

*p<0.05

Statistical analysis

Statistical analysis was done using SPSS software 16.0. Fisher's exact test and/or Pearson Chi square and T tests were the tests used.

RESULTS

45 first episode psychosis patients were included. Details of the sociodemographic and clinical variables are given in Table 1.

Clinical and social variables of DUP

There was a statistically significant association between brief DUP and married status (p=0.01); higher educational status of the patient (p=0.04); acute mode of onset (p<0.001); lower age (p=0.03); higher PANSS Negative Symptom Score (p=0.003) and higher PANSS General Psychopathology Score (p=0.007) (Tables 2-4).

DUP had no relationship with the following variables: Sex, residence, educational status of caregiver, occupation of patient, socioeconomic status, past history of physical illness, family history of mental illness, pathways to seeking care (Table 3), diagnosis, distance to nearest mental health center, distance to actual mental health center were

treatment was taken, duration of untreated illness, PANSS Positive Symptom score, score in Insight subscale, or the following scores in PAS: Sociability and withdrawal, Peer relationships, or general section (Table 4).

DISCUSSION

Significant association was found between increasing age and longer DUP. The West London first episode study of schizophrenia too had found that patients with higher age at first consultation had a longer DUP.[18] Significant association was found between patients who had an education above 7th standard and DUP. Higher literacy might lead to reduced stigma towards seeking mental health care and this may have contributed to brief DUP. Acute onset had significant association with brief DUP. Any sudden change in the behavior of the patient is more likely to be noticed by family and hence reduce treatment delays. Acute onset has been found to be significant predictor of shorter DUP in the study by Thomas et al. too.[19] A study from Pakistan reported that patients with positive symptoms have a shorter DUP and that patients with more negative symptoms have longer DUP.[16] However, in our study patients with brief DUP had higher PANSS

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Table 4: Comparison of clinical variables of patients with Brief or Long DUP: continuous variables

VARIABLE	BRIEF DUP (Mean±SD)	LONG DUP (Mean±SD)	T VALUE	DF	P VALUE
Age	35±12.73	45.53±11.00	-2.73	43	0.009*
PANSS					
Positive	22.50±5.46	19.07±6.16	1.91	43	0.06
Negative	21.03±10.29	13.80±6.60	2.47	43	0.01*
General	43.53±12.03	32.33±10.66	3.05	43	0.004*
Insight Subscale	6.33±0.76	5.87±0.92	1.82	43	0.07
PAS					
SW	0.79±1.48	1.20±1.82	-0.81	41	0.42
PR	1.25±1.48	2.00±2.10	-1.36	41	0.18
GS	10.07±8.32	14.87±8.72	-1.80	43	0.07

*PANSS: Positive and Negative Symptom Scale; PAS: Premorbid adjustment scale; SW: Sociability and withdrawal; PR: Peer relationships; GS: General scores; *p<0.05.*

negative symptom and general psychopathology scores.

LIMITATIONS

Our sample size was relatively small. A structured tool was not used to assess the DUP. (There is lack of a uniform definition of DUP, and lot of disagreement is there between various researchers in this regard.) Some domains of the PAS were not used in our population. Data regarding various premorbid characteristics in childhood and adolescence were not available for many patients. Only certain factors thought to influence the DUP were assessed, and variables like coping skills and health beliefs of the patient were beyond the scope of this study. Factors determining DUP were estimated retrospectively and there is a chance of recall bias.

CONCLUSIONS

This study suggests that certain sociodemographic and clinical features may be associated with brief DUP. Several previous studies on determinants of DUP have revealed conflicting results. At present, it is difficult to interpret the available data and say which factors cause a delay in seeking help from mental health services. More, especially longitudinal, studies are required, not only to analyze the course of psychotic illnesses, but also to get a better idea about the factors influencing their outcomes.

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