

Effect of Duration of Untreated Psychosis on Outcome of Schizophrenia

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Abstract

Duration of untreated psychosis (DUP) as a prognostic indicator of functional outcome is a variable of interest in schizophrenia research. The effect of DUP may be due to the toxic effect of the illness on the brain. Some studies hold that the effect of duration of untreated psychosis on outcome is inconsistent and holds good only for short term outcomes.

AIM: To study the effect of duration of untreated psychosis on the outcome of schizophrenia in short and long term.

Objectives: To study the duration of untreated psychosis (DUP) at the time of first contact with mental health services, total duration of positive and negative symptoms in the illness course, proportional symptom free period (PSFP), proportional period of good functioning (PPGF), average functioning in symptom free period (AFSFP) in a retrospective cohort.

Inclusion Criteria: Patients with ICD 10 diagnosis of schizophrenia. Availability of records from the initial visit. Availability of reliable attendant. Patient on regular medication (defined as no periods without more than 4 weeks of medication) from records and good compliance

Exclusion Criteria: Co morbid Psychiatric/ medical illness, Co morbid substance abuse (cannabis/ alcohol), discontinued drugs for more than 4 weeks currently

Materials And Methods: 100 consecutive patients meeting inclusion and exclusion criteria are assessed with SAPS, SANS and SOFAS (Social and Occupational Functioning assessment Scale)

Results: There was significant difference in the proportional symptom duration between the groups ($p=0.006$), but the < 10 year duration of illness group contributed to the difference ($p=0.010$). The negative symptom severity varied significantly with the duration of untreated psychosis ($p=0.03$), the significant difference being noted in the >10 year group. The Chlorpromazine equivalent needed by the patient to achieve remission was significantly higher with increasing duration of untreated psychosis ($p=0.001$), the difference being significant throughout the illness.

Conclusion: The duration of untreated psychosis influences the outcome of schizophrenia patients. Increasing DUP is directly proportional to the proportional symptomatic period, negative symptoms and Chlorpromazine dosage required for maintaining remission. The effect of DUP on proportional symptomatic period is significant in the short term but

loses its significance in the long term. However, the effect of DUP on negative symptom score, becomes more significant with increasing duration of illness.

Keywords: Duration of untreated psychosis, schizophrenia

Introduction: For decades now, attempts to understand the natural course of schizophrenia and the effect of treatment in altering the natural course of the illness is underway¹. Duration of untreated psychosis (DUP) as a prognostic indicator of functional outcome is a variable of interest in schizophrenia research². The effect of DUP may be due to the toxic effect of the illness on the brain^{3,4}, at a microscopic as well as macroscopic level. There are findings from pathological and neuro imaging studies^{5,6} which corroborate this findings as well. These findings have led to the implementation of early identification programmes in the health initiatives of developed countries^{7,8}. But some studies hold that the effect of duration of untreated psychosis on outcome is inconsistent and holds good only for short term outcomes.

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Materials and Methods: Patients diagnosed with Schizophrenia with duration of treatment greater than one year, attending the OPD consecutively were screened and those meeting inclusion criteria were asked to participate in the study. After obtaining an informed consent, the demographic data (sex, educational status, previous occupation, current occupation). Illness characteristics i.e the age of onset, duration of illness, the number of acute episodes, the course of illness, duration of untreated psychosis, the number of hospitalization, the number of antipsychotics used, the current Chlorpromazine equivalent⁹ patient is getting were collected as well as verified from the records of the patients. The details regarding the current symptomatology and performance in the various walks of life including personal care, communication, employment status, work satisfaction and interpersonal relationship were collected for quantification. The total symptomatic period defined as (sum of duration with positive symptoms and duration with negative symptoms requiring hospitalization) is calculated from records, from which proportional symptomatic period (PSP) is calculated (Total symptomatic period / total duration of illness). The average functioning in symptom free period (AFSFP) is measured in terms of Social and Occupational Functioning Assessment Scale (SOFAS) score, (which measures functioning on a scale from 1-100), and graded (Poor-<50, Moderate- 51-70, Good->71).

The total duration of good functioning (defined as SOFAS scale score >70) is obtained from attender, from which proportional period of good functioning (PPGF) is

calculated (Total duration of good functioning/ total duration of illness).

Tools Used: 1.Scale for assessment of positive symptoms (SAPS) is applied for positive symptom assessment. 2.Scale for assessment of negative symptoms (SANS) is applied for assessment of Negative symptoms, 3.Social and occupational functioning assessment scale (SOFAS) is used to assess the functioning level in the patients.

Statistical Analysis: Statistical analysis is done using SPSS 20 software. Percentages were calculated for categorical variables and mean for continuous variables. The effect of variables on functioning was calculated by independent samples t test and ANOVA. The results are significant at $p < 0.05$.

Results

Table 1:Sociodemographic Characteristics:

Socio Demographic Variables		Proportion (Percentage)
Gender	Male	52.0
	Female	48.0
Age	<30 years	27.0
	31-40 years	39.0
	>40 years	34.0
Education	Uneducated	6.0
	Primary education	25.0
	Secondary education	45.0
	College/ technical education	17.0
	Professional education	7.0
Occupation At onset of illness	Student	25.0
	Housewife / Meaningful Occupation	
	Well employed	36.0
	Unemployed	13.0
		6.0
Socioeconomic status	Low	63.0
	Middle	33.0

Primary Outcome measure: The effect of duration of untreated Psychosis over the proportional symptomatic period, proportional period of good functioning, average functionality of the patient in the symptom free period are analyzed. The effects of Duration of untreated Psychosis on primary outcome measures are dichotomized over the duration of illness to assess if the significance is maintained over years. **Secondary Outcome Measure:** The effect of Duration of untreated psychosis on the current symptom severity as assessed by SAPS and SANS score, The Chlorpromazine equivalent needed for symptom control (in currently asymptomatic patients / currently symptomatic patients), Effect of drug dosage on Average functioning in symptom free period (AFSFP)

	High	4.0
ILLNESS VARIABLES		
Age at onset of illness	<20 years	17.0
	20-30 years	42.0
	30-40 years	33.0
	>40 years	8.0
Duration of illness	1-2 years	15.0
	2-5 years	24.0
	5-10 years	35.0
	10-20 years	19.0
	>20 years	7.0
Duration of untreated psychosis	<1 month	27.0
	1-6 months	46.0
	>6 months-2 years	19.0
	>2 years	8.0
Average SAPS score Average SANS score	Mean (SD)	9.08 (9.5)

43% of the sample had significant positive symptoms currently. The proportion of patients having positive symptoms did not vary across groups. Remission was achieved in 72% of patients in the course of the illness.

Table 2: Outcome measures

Outcome measures		Percentage
Proportional symptomatic period (PSP)	<25%	36.0
	25-50%	28.0
	50-75%	15.0
	75-100%	21.0
Proportional period of good functioning(PPGF)	Nil	28.0
	<25%	23.0
	25-75%	30.0
	>75%	19.0
Average functioning in symptom free period (AFSFP)	Poor	31.0
	Moderate	31.0
	Good	38.0

Analysis:The mean age at onset of the sample was 28.44 years(SD 7.76). The mean duration of illness 14.26 years (SD 27.27).

DUP Vs PPGF: The proportional period of good functioning or the average functioning in symptom free

period was not affected directly by the duration of untreated psychosis.

PPGF	Duration of untreated psychosis				Chisquare
	<1 month	1-6months	>6months-2 year	>2 years	
<25%	18.5	28.2	26.3	62.5	12.912 P=0.167
25-50%	18.5	26.08	26.3	25.0	
51-75%	25.9	30.4	36.8	12.5	
76-100%	37	15.2	10.5	0	

*All measures in percentages

DUP Vs PSP:

Table 3: Proportional symptomatic period Vs Duration of untreated psychosis:

Proportional symptomatic period	Duration of untreated psychosis				Chisquare
	<1 month	>1-6 months	>6 months-2 years	>2 years	
<25%	47.2	36.1	11.1	5.6	Phi==0.479 P=0.006
26-50%	17.9	39.3	32.1	10.7	
51-75%	33.3	46.7	20.0	0.0	
>75%	0.0	71.4	14.3	14.3	

*All measures in percentages

Duration of illness	Proportional symptomatic period	Duration of untreated psychosis				Chisquare
		<1 month	>1-6 months	>6 months-2 years	>2 years	
<10 years	< 25%	66	30.5	14	33.3	<10 years P= .010
	26-50%	11	22.2	50	33.3	
	51-75%	22	16	14.2	0	
	76-100%	0	30.5	21.4	33.3	

*All measures in percentages

There was significant difference in the proportional symptom duration between the groups (p=0.006), but the < 10 year duration of illness group contributed to the difference (p=0.010).

The group with duration of illness >10 years, the difference is not significant (p=0.240)

Duration of illness	Proportional symptomatic period	Duration of untreated psychosis				Chisquare
		<1 month	>1-6 months	>6 months-2 years	>2 years	

>10 years	<25%	55.5	22.2	40.0	20.0	P=0.240
	26-50%	33.3	33.3	40.0	40.0	
	51-75%	11.1	11.1	20.0	0	
	76-100%	0	44.4	0	40.0	

*All measures in percentages

DUP Vs AFSFP:

The average functioning in symptom free period did not vary with the duration of untreated psychosis.

Average functioning in symptom free period	Duration of untreated psychosis				Chisquare
	<1 month	>1-6 months	>6 months-2 years	>2 years	
Poor	22.2	36.9	21.05	50	0.408
Moderate	33.3	23.9	47.3	25	
Good	44.4	39.1	31.5	25	

*All measures in percentages

DUP Vs Negative symptoms: The negative symptom severity varied significantly with the duration of untreated psychosis

Table 4: Duration of untreated psychosis Vs Negative symptom scale score:

SANS score	Duration of untreated psychosis				Chisquare
	<1 month	>1-6 months	>6 months-2 years	>2 years	
Mild	66.6	36.9	26.3	12.5	Phi=0.44 P=0.003
Moderate	33.3	56.5	73.6	62.5	
Severe	0	6.5	0	25.0	

*All measures in percentage

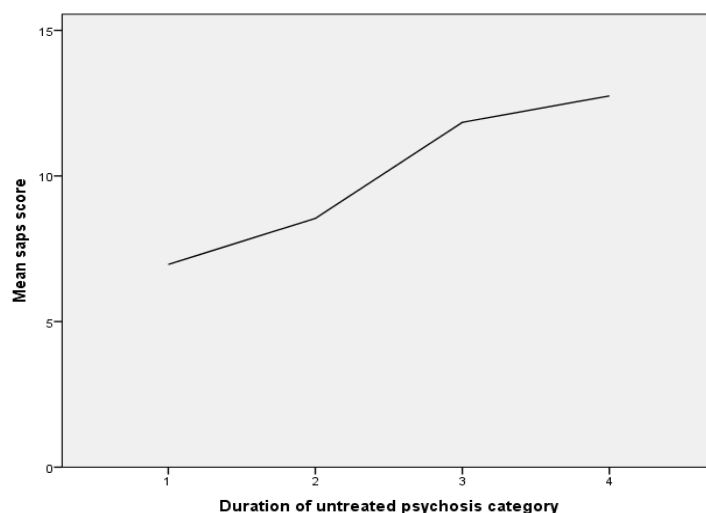
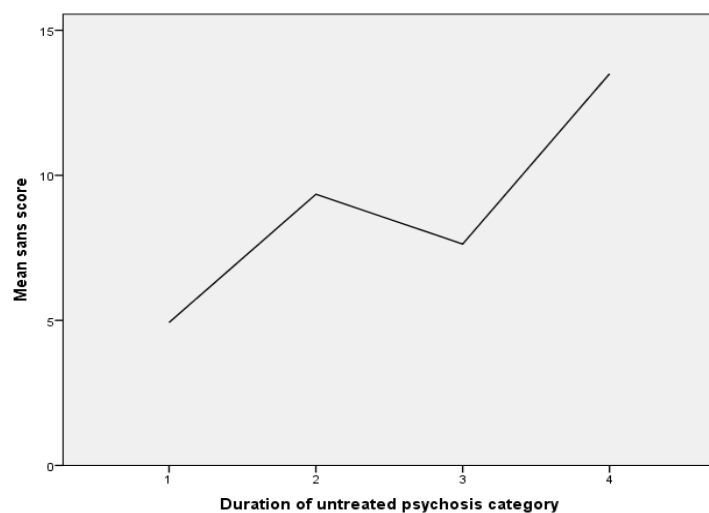


Figure 1: Effect of DUP on current positive (SAPS) and negative symptoms (SANS). *Duration of untreated Psychosis category 1- <1 month, 2- >1-6 months, 3- >6 months – 2 years, 4- > 2 years

Duration of illness	SANS score	Duration of untreated psychosis				Chisquare
		<1 month	>1-6 months	>6 months-2 years	>2 years	
<10 years	Mild	66.6	41.6	35.7	33.3	P=0.073
	Moderate	33.3	52.7	64.2	33.3	
	Severe	0	5.5	0	33.3	

>10 years	Mild	66.6	20	0	0	P=0.021
	Moderate	33.3	70	100	80	
	Severe	0	10	0	20	

*All measures in percentages

DUP Vs Drug dosage:

The Chlorpromazine equivalent needed by the patient to achieve remission was significantly higher with increasing duration of untreated psychosis.

Table 6: DUP Vs Chlorpromazine Equivalent:

Duration of untreated Psychosis	Chlorpromazine Equivalents		ANOVA
	Mean	SD	F=11.64 P=0.01
<1 month	226.85	175.94	
1-6 months	262.47	118.42	
6 months-2 years	383.26	127.12	
>2 years	515.62	180.74	

*All measures in percentages

The increased chlorpromazine equivalent needed for achieving remission, holds significance both in the short term(<10 years) as well as long term (>10 years)

Duration of illness	Duration of untreated psychosis	Chlorpromazine Equivalent (mg)		ANOVA
		Mean	SD	
<10 years	<1 month	237.50	203.32	P=0.018
	1-6 months	268.02	129.66	
	>6 months-2 years	379.71	138.43	
	> 2years	450.00	150.00	

>10 years	<1 month	205.55	109.52	P=0.00
	1-6 months	242.50	64.60	
	>6 months-2 years	393.20	101.33	
	>2 years	555.00	201.86	

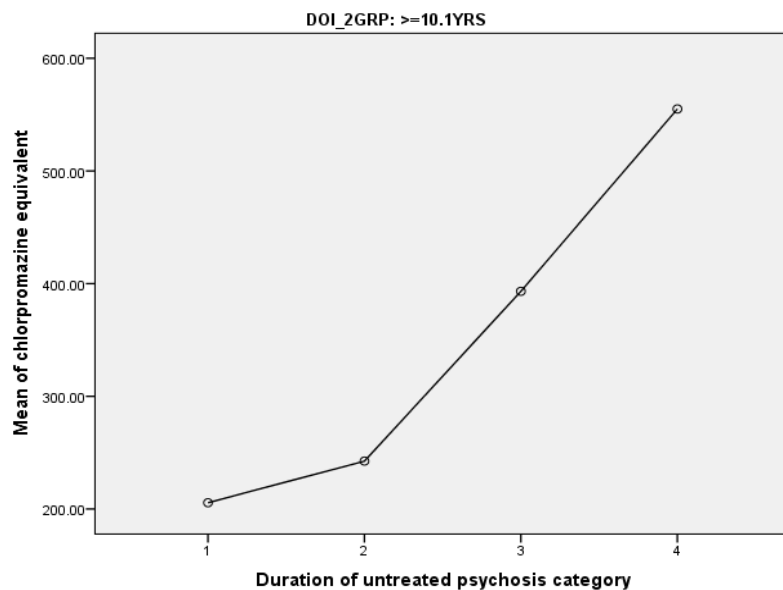
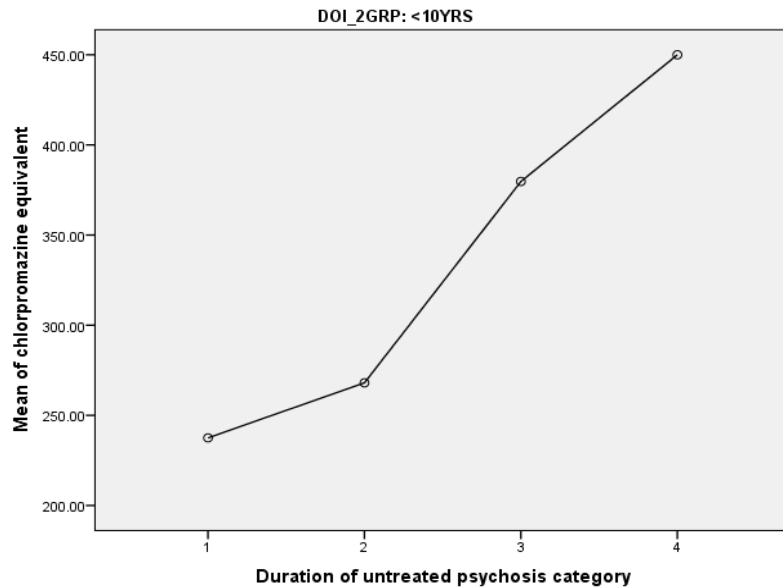


Figure2: Effect of Duration of untreated psychosis on Chlorpromazine Equivalent needed by patient in <10 year (a) and > 10 year(b) groups. *Duration of untreated Psychosis category 1- <1 month, 2- >1-6 months, 3- > 6months – 2 years, 4- > 2 years

AFR Vs Chlorpromazine Equivalent

Average function in remission was inversely related to the Chlorpromazine equivalent needed for remission

Average functioning in remission	Chlorpromazine Equivalents (mg)		ANOVA
	Mean	SD	
Poor	336.51	182.93	F=3.54 P=0.033
Moderate	321.74	130.67	
High	242.10	161.82	

Discussion

Our study results that DUP correlates with proportional symptomatic period(PSP) in the short term, but not in the long term.,correlates closely with the results of Srivatsava et al 2011¹⁰.,which states that the advantageous outcomes provided by Shorter DUP is pronounced for short term outcome, but lost in the long term due to numerous other social factors.

Our study results contrasts the results by Ho B Andreason et al 2001¹¹, that such results are inconsistent.

Strengths And Limitations

Our study measures very salient outcome indicators to study the effect of duration of untreated psychosis. We have removed the effect of irregular medications on severity of illness as a potential confounding factor by retrospective case selection method. We used Duration of untreated psychosis in shorter intervals resulting in observation of finer distinctions between groups.

In 8% cases DUP and DUI could not be delineated and hence an arbitrary assumption was made. Other factors affecting the outcome like family support, supportive psychological treatments and social skills and vocational trainings have not been taken into account.

Conclusion

The duration of untreated psychosis influences the outcome of schizophrenia patients. Increasing DUP is directly proportional to the proportional symptomatic

period , negative symptoms and Chlorpromazine dosage required for maintaining remission. The effect of DUP on proportional symptomatic period is significant in the short term but loses its significance in the long term. However, the effect of DUP on negative symptom score, becomes more significant with increasing duration of illness. The average functioning in remission was inversely proportional to the Chlorpromazine dosage required to achieve remission., and hence is indirectly related to DUP albeit the absence of direct relationship.

Significant benefits were attained when the Duration of untreated psychosis is less than 1 month, and the benefits obtained thereafter are equivocal.

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