DURATION OF UNTREATED PSYCHOSIS (DUP) AND PRE-MORBID FUNCTIONING, MAY PREDICT CLINICAL PRESENTATION IN FIRST EPISODE OF PSYCHOSIS (FEP): NORTH-EAST INDIAN STUDY

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ABSTRACT

BACKGROUND

Duration of untreated psychosis (DUP) is extensively researched in recent years for its effect on first episode of psychosis. We wanted to evaluate as to whether pre-morbid functioning and duration of untreated psychosis (DUP) are related to clinical presentation of first-episode psychosis at first hospitalisation.

METHODS

Forty-four antipsychotic-naïve, first-episode psychosis patients were included with exclusion of organic and substance related psychosis. Patients were assessed with BPRS (Brief Psychiatric Rating Scale), SAPS (Scale for Assessment of Positive Symptoms), SANS (Scale for assessment of Negative Symptoms) and pre-morbid adjustment (PAS) scales on admission. Data was dichotomized into non-affective and affective psychosis. Spearman's correlation and multiple regression analyses were performed using SPSS version 10.

RESULTS

In patients with non-affective psychosis (n=25), DUP was positively correlated to SANS score (r= 0.459, p= 0.021). In affective psychosis patients (n=19), there was positive correlation of DUP with mean PAS scores. Thus when, DUP in months is controlled, there was significant negative correlation among mean PAS score and SAPS scores at admission ($p < 0.05$). Further, regression analysis concluded that pre-morbid functioning in patients with affective psychosis, significantly predict the composite SAPS score (B= -0.642, p= 0.038, and R^2= 0.287). This is a hospital based cross-sectional study was conducted on antipsychotic-naive patients of first episode psychosis in Regional Institute of Medical sciences, Imphal, Manipur. In the present study, 44 patients with diagnosis of first episode psychosis were studied. There were 25 cases of non-affective psychosis and 19 cases of affective psychosis. Number of males with diagnosis of first episode psychosis had been excluded. Schizophrenia was diagnosed in 12 cases and other diagnoses in non-affective group were Brief Psychotic Disorder and Psychosis NOS. In affective psychosis, mania with psychotic features was seen in 14 cases and rest 5 cases were of major depressive disorder with psychotic features.

CONCLUSIONS

Our findings suggest that DUP and pre-morbid functioning may be important predictors of clinical presentation of first-episode psychosis and thus, attempts for early diagnosis may also have effect on treatment response.

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BACKGROUND

Over the last couple of decades, the concept of duration of untreated psychosis (DUP) has been extensively used in research to know its influence on the outcome of first episode psychosis. Psychosis which occurred in a person for the first time in life time period and which is continuous without intervening relapse period is called as first episode of psychosis.[1] Pre-morbid functioning and age at onset are constant and unchangeable determinants of outcome but DUP is modifiable and hence plays important role in overall outcome of patients with first episode of psychosis.

The diagnoses of schizophreniform disorder and brief psychotic disorder in patients presenting with psychotic symptoms for the first time are, by definition, provisional diagnoses, since there is a time limit for the remission of symptoms and consequent diagnostic confirmation.

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Accordingly, the migration to other diagnostic categories is to be expected in a portion of first-episode psychosis patients. The same applies for the diagnosis of major depression in these patients, since this index episode may be the first manifestation of bipolar disorder, whose presence will only be confirmed with the later occurrence of a manic episode.[2]

For this study onset of psychosis is defined as first time when psychotic symptoms were noticed by the patient, family or others in context of a decline in functioning.[3] The start of structured treatment with antipsychotic medications or the start of hospitalisation in highly staffed psychiatric ward[4] is taken as an initiation of adequate treatment.

Duration of Untreated Psychosis (DUP) is defined as the time from manifestation of the first psychotic symptom to initiation of adequate antipsychotic drug treatment. It is to be distinguished from Duration of Untreated Illness (DUI), which has the same end point but begins with the emergence of the first symptom; which is not necessarily a psychotic symptom by its nature.[5] Studies directly comparing the pre-morbid functioning of schizophrenic patients and patients with affective psychosis have shown greater impairment in the schizophrenic subjects.[6] Untreated psychosis may itself be toxic, contributing to a neurodegenerative process, thus DUP is a potentially malleable prognostic factor.[7] The DUP may be influenced by factors closely related to the underlying pathology of the disease, including poor pre-morbid function and insidious onset. At the same time, factors unrelated to disease pathology, such as socioeconomic status, access to and availability of care, recognition of illness, and stigma, also may contribute to duration of untreated psychosis.[8-12] This study therefore had been undertaken as an attempt to investigate the relationship between age at onset, pre-morbid status, duration of untreated psychosis (DUP) and the clinical manifestations of the first psychotic episode. This study will also help us understand socio-demographic variables associated with and influencing on duration of untreated psychosis.

METHODS

A hospital based cross sectional study was conducted in the Department of Psychiatry, Regional Institute of Medical Sciences, Imphal, Manipur from September 2010 to February 2012 (One and half year). Confirmed cases of first episode of psychosis of both sexes between the age group of 14-45 years and hospitalised in psychiatry ward were included. Patients with current/past history of head injury, seizure disorder, medical and/or neurological illness, patients with substance use related psychiatric manifestations (except Tobacco) and patients with no legal guardian to give an informed consent were excluded. Study variables include socio-demographic variables like age, sex, and location etc., pre-morbid adjustment of a patient in life periods up to one year prior to the onset of psychotic illness that is assessed by using Pre-morbid Adjustment Scale (PAS) at admission.[13] Other study variables are age at onset, Duration of Untreated Psychosis (DUP) and clinical symptoms of psychosis. Age at onset is taken as age in completed years, first time when psychotic symptoms were noticed by the patient, family or other in context of a decline in functioning. Duration of Untreated Psychosis (DUP) is the time period from manifestation of the first psychotic symptom to initiation of adequate antipsychotic drug treatment. Clinical features of psychosis viz. Psychiatric symptoms, Positive symptoms and Negative symptoms were assessed with BPRS, SAPS and SANS scales.

Socio-demographic proforma includes socio-demographic details of the individual patient. Pre-morbid adjustment scale (PAS)[14] is used to determine the pre-morbid functioning. The Cannon-Spoor Pre-morbid Adjustment Scale includes rating scales about 5 domains of functioning and a general section of items about quality of life. The 5 domains are: (a) Sociability and withdrawal; (b) Peer relationships; (c) Scholastic performance; (d) Adaptation to school; and (e) Social-sexual aspects of life. The PAS covers 4 life periods: (a) Childhood (up to age 11), (b) Early adolescence (12 to 15), (c) Late adolescence (17 to 18), (d) Adulthood (19 and above) . The structured interview is used to score the PAS items. The PAS is scored under each life period as PAS subscales viz. PAS 1 (Childhood), PAS 2 (Early adolescence), PAS 3 (Late adolescence), PAS 4 (Adulthood). Mean score of PAS is mean of all subscale scores. Worst possible adjustment score would be 1.

The Brief Psychiatric Rating Scale (BPRS)[15] has been in use since 1962 for rating patient behaviours and symptoms. It was developed by Overall and Gorham and it is probably the most widely used rating scale in psychiatric practice. The BPRS is comprised of 24 items that can be rated from 'not present' (1) to 'extremely severe'.[7] A total pathology score can be obtained by adding the scores from each item and sub-scores can be derived by adding scores on specific items together. Subscales are calculated under four domains as a) thinking disturbance b) Withdrawal/Retardation c) Hostile/ Suspiciousness d) Anxious/Depression.

The Scale for the Assessment of Positive Symptoms (SAPS)[16] is a rating scale to measure positive symptoms in schizophrenia. The scale was developed by Nancy Andreasen and was first published in 1984. A SAPS scale is split into 4 domains (subscales) of positive symptoms which includes hallucinations, delusions, bizarre behavior, and positive formal thought disorder. And within each domain (subscales), separate symptoms are rated from 0 to 5 (0= none; 1= questionable; 2= mild; 3= moderate; 4= marked; 5= severe). In addition to using a clinical interview, the investigator should also draw on other sources of information, such as direct observation, reports from the subject's family, reports from nurses, and reports from subject himself. The last item describing each major type of positive symptoms is an overall global rating. This take into account both the nature and the severity of the various types of symptoms observed. In some cases, a single symptom (e.g., extremely severe persecutory delusions) may lead to a very high global rating, even if other symptoms of this type are not present. Summary score for SAPS is sum of the 4

global domain scores (0-20). SAPS composite score is sum of the 30 individual items (0-150). Summary score is a measure of overall severity of positive/negative symptoms.

The Scale for the Assessment of Negative Symptoms (SANS)[17] is a rating scale to measure negative symptoms in schizophrenia. It is intended to serve as a complementary instrument to the Scale for the Assessment of Positive Symptoms (SAPS). SANS is split into 5 domains (subscales) of negative symptoms which assess Affective Flattening or Blunting, Alogia, Apathy, Anhedonia-Asociality and Attention. And within each domain separate symptoms are rated from 0 to 5 (0= none; 1= questionable; 2= mild; 3= moderate; 4= marked; 5= severe). Summary score for SANS is sum of the 5 global domain scores (0-25). SANS composite score is sum of the 20 individual items (0-100).

Diagnosis		Frequency		Percent	
Non-Affective Psychosis	Schizophrenia	25	12	56.8	27.3
	Psychosis NOS		6		13.6
	Brief Psychotic Disorder (with Stressor)		5		11.4
	Brief Psychotic Disorder (without Stressor)		2		4.5
Affective Psychosis	BPAD (Mania) with Psychotic Features	19	14	43.2	31.8
	MDD with Psychotic Features		5		11.4
Total		**44**		**100.0**	

Table. 1. Different Diagnosis in Non-Affective and Affective Group of Psychosis

Variables		Non-Affective Psychosis N (%)	Affective Psychosis N (%)	X2	p
Gender	Male	12 (48)	4 (21)	3.38	0.062
	Female	13 (52)	15 (79)		
Religion	Hinduism	15 (60)	13 (68)	5.69	0.059
	Islam	1 (4)	4 (21)		
	Christianity	9 (36)	2 (11)		
Marital Status	Married	8 (32)	9 (47)	1.06	0.300
	Single/ Divorcee/ Separated	17 (68)	10 (53)		
Socio-Economic Status	Below 15000	13 (52)	12 (63)	4.34	0.114
	15000-30000	8 (32)	7 (37)		
	30000 & Above	4 (16)	0 (0)		
Habitat	Urban	4 (16)	4 (21)	0.19	0.667
	Rural	21 (84)	15 (79)		

Table. 2a. Chi-Square Test for Sociodemographic Characteristics- (Discrete Variables)

Variables	Group	Mean ± S.D.	t	p
Age (in Years)	Non-Affective Psychosis	27.48 ± 7.98	0.676	0.709
	Affective Psychosis	25.84 ± 7.93		
Education (in Years)	Non-Affective Psychosis	5.68 ± 3.79	1.274	0.210
	Affective Psychosis	7.16 ± 3.83		

Table. 2b. Unpaired t Test for Socio-Demographic Characteristics- (Continuous Variables)

Variables	Non-Affective Psychosis (N=25) Mean ± SD	Affective Psychosis (N=19) Mean ± SD	t	df	p
Mean PAS Score[#]	0.27 ± 0.13	0.19 ± 0.07	+2.447	42	0.019*
Age at Onset	23.24 ± 6.35	23.63 ± 6.86	-0.196	42	0.846

Table. 3. Pre-Morbid Functioning and Age at Onset (Yrs.)

Variable	Non-Affective Psychosis (N=25) Mean ± SD	Affective Psychosis (N=19) Mean ± SD	U value, Z	df	p
DUP[#] (Months)	43.51 ± 66.64	26.13 ± 62.65	221.5, -0.38	1	0.7

Table. 4. Duration of Untreated Psychosis (DUP) (Months)

Nonparametric Spearman's correlation (Non-affective Psychosis)		R	p-Value
Mean PAS Score	Age at Onset	-0.300	0.145
Mean PAS Score	DUP (Months)	0.395	0.051
Age at Onset	DUP (Months)	-0.002	0.993

Table. 5a. Non-Affective Psychosis- Correlation: Mean PAS, Age at Onset and DUP

Nonparametric Spearman's correlation (Affective Psychosis)		R	p-value
Mean PAS Score	Age at Onset	-0.131	0.592
Mean PAS Score	DUP (Months)	0.646	0.003**
Age at Onset	DUP (Months)	0.165	0.500

Table. 5b. Affective Psychosis- Correlation: Mean PAS, Age at Onset and DUP

Variables	Non-Affective Psychosis (N=25) Mean ± SD	Affective Psychosis (N=19) Mean ± SD	t	df	p
BPRS Total	77.52 ± 17.88	83.05 ± 12.25	-1.157	42	0.254
SAPS Composite	42.84 ± 17.21	48.63 ± 18.26	-1.077	42	0.288
SANS Composite	39.00 ± 16.68	21.00 ± 23.36	2.984	42	0.005**

Table. 6. Clinical Presentation of First Episode of Psychosis

Variables- Non-affective Psychosis (n=25)		R	p-Value
Mean PAS Score	Total BPRS Score	-0.088	0.675
	SAPS Composite Score	0.234	0.261
	SANS Composite Score	0.306	0.137
Age at Onset	Total BPRS Score	0.022	0.916
	SAPS Composite Score	-0.109	0.605
	SANS Composite Score	-0.027	0.900
DUP (Months)	Total BPRS Score	0.117	0.578
	SAPS Composite Score	0.298	0.148
	SANS Composite Score	0.459	0.021*

Table. 7a. Non-Affective Psychosis: Correlation- Mean PAS Scores, Age at Onset, DUP and BPRS, SAPS and SANS Scores

Partial Correlation- (Affective Psychosis)		R	p-Value
Age at Onset	Total BPRS Score	-0.144	0.569
	SAPS Composite Score	-0.259	0.299
	SANS Composite Score	0.313	0.207
DUP (Months)	Total BPRS Score	0.190	0.449
	SAPS Composite Score	0.253	0.311
	SANS Composite Score	-0.366	0.136

Table. 7b. Affective Psychosis: Partial Correlation- Age at Onset, DUP and BPRS, SAPS, SANS Scores (Control Variable- Mean PAS Scores)

Partial Correlation (Affective Psychosis)		R	p-Value
Mean PAS Score	Total BPRS Score	-0.417	0.085
	SAPS Composite Score	-0.474	0.047*
	SANS Composite Score	0.399	0.101
Age at Onset	Total BPRS Score	-0.083	0.742
	SAPS Composite Score	-0.179	0.477
	SANS Composite Score	0.261	0.295

Table. 7c. Affective Psychosis: Partial Correlation- Pre-Morbid Functioning, Age at Onset and BPRS, SAPS, SANS Scores (Control Variable- DUP in Months)

Dependent Variables	Independent Variables						R^2
	Mean PAS Score		Age at Onset		DUP (months)		
	Beta	p	Beta	p	Beta	p	
Total BPRS	-32.809	0.333	-0.577	0.369	-0.004	0.951	0.068
SAPS Composite	31.810	0.309	-0.198	0.735	0.050	0.385	0.148
SANS Composite	27.725	0.357	0.002	0.997	0.066	0.238	0.034

Table. 8a. Non-Affective Psychosis: Multiple Regression Analysis

Dependent Variables	Independent Variables						R^2
	Mean PAS score		Age at Onset		DUP (Months)		
	Beta	p	Beta	p	Beta	p	
Total BPRS	-96.639	0.084	-0.243	0.569	0.044	0.456	0.201
SAPS Composite	-167.648	0.038*	-0.640	0.293	0.087	0.304	0.287
SANS Composite	184.930	0.070	1.064	0.182	-0.172	0.123	0.271

Table. 8b. Affective Psychosis: Multiple Regression Analysis

RESULTS

Sociodemographic Details and Psychiatric Diagnosis

In the present study, 44 patients with diagnosis of first episode psychosis were studied. There were 25 cases of non-affective psychosis and 19 cases of affective psychosis (Table. 1). Number of males with diagnosis of first episode psychosis had been excluded. Schizophrenia was diagnosed in 12 cases and other diagnoses in non-affective group were Brief Psychotic Disorder and Psychosis NOS. In affective psychosis, mania with psychotic features was seen in 14 cases and rest 5 cases were of major depressive disorder with psychotic features.

All the patients of the first episode psychosis were studied with socio-demographic variables. Female to male ratio was 1.78:1. Discrete sociodemographic variables were analysed using chi-square test, and continuous variables with unpaired t test. Both these tests showed that there is no significant difference of sociodemographic characteristics in non-affective and affective group of psychosis (Table. 2a and 2b).

Age at Onset, DUP and Premorbid Functioning

Age at onset of psychosis and mean PAS scores were normally distributed (Table. 3). In our study, DUP was not normally distributed. Mean DUP was 36 months with standard deviation of 64.78 months which ranges from minimum of 0.17 months (5 days) to maximum of 276 months (23 years) (Table. 4).

In our study, mean PAS score in affective psychosis and non-affective psychosis significantly differ (Table. 3). Age at onset of psychosis in non-affective psychosis does not differ significantly from that of affective psychosis. In non-affective psychosis, mean age of onset was 23.24 years with standard deviation of 6.35 years (minimum- 15 years, maximum- 41 years), while in affective psychosis, mean age of onset was 23.63 years with standard deviation of 6.86 years (minimum- 16 years, maximum – 39 years). (Table. 3) In our study, maximum DUP for untreated schizophrenia was 20 years and maximum duration of untreated bipolar disorder with psychotic features was 23 years.

Also, when mean PAS scores were compared to DUP, it is observed that in case of non-affective psychosis r= 0.395, p= 0.051 (Table. 5a) and in affective psychosis r= 0.646, p= 0.003(Table. 5b). According PAS scale, worst possible mean PAS score is 1 and there is positive correlation between PAS scores and DUP, so poor pre-morbid functioning (mean PAS scores approaching 1) increases duration of untreated psychosis in affective psychosis. This was not seen in non-affective psychosis.

Clinical Presentation

Clinical presentation of first episode of psychosis when correlated between affective and non-affective group of psychosis, it was observed that SANS composite scores differ significantly in these groups (p= 0.005). Negative symptoms were more prominent in non-affective group than affective group of psychosis. (Table. 6)

Effect of Age at Onset, DUP and Pre-Morbid Functioning on Clinical Presentation

Spearman's correlation was performed in non-affective and affective psychosis showed that DUP was positive correlated with SANS composite score in non-affective group of psychosis (p=0.021) (Table. 7a). In case of affective psychosis, mean PAS score and DUP were positively correlated (Table. 5b), so partial correlation was performed keeping DUP and Mean PAS score as control variable. It was observed that in patients with affective psychosis, when mean PAS score is controlled, there was no significant correlation among age at onset, DUP and BPRS, SAPS, SANS scores at admission (Table. 7b) but when DUP in months is controlled, there was significant negative correlation among mean PAS score and SAPS scores at admission ($p < 0.05$) (Table. 7c).

Effect of pre-morbid functioning, age at onset and DUP on clinical presentation of first episode psychosis is assessed by multiple regression analysis done on following variables. Independent variables are Mean PAS score, Age at onset and DUP (in months). Dependent variables are BPRS total score, SAPS composite score and SANS composite score (Table. 8a and 8b). Mean PAS scores in patients with affective psychosis, significantly predicted the composite SAPS score, B= -0.642, p= 0.038, and R2= 0.287 (Table. 8b).

DISCUSSION

In the present study, 44 patients with diagnosis of first episode psychosis were studied. As substance use is more common among males and as per exclusion criteria, females were more as compared to males with first episode of psychosis. Out of 44 patients, non-affective psychosis was diagnosed in 25 patients and affective psychosis was diagnosed in 19 patients. Mean age at onset was 23 years with standard deviation of 6.5 years. In a Monte et al study on pre-morbid functioning; the mean age at onset of psychotic symptoms was 21.6±4.9 years.[18] This is also in accordance with various other literatures on age at onset of psychosis.[19,20]

Since 13 of the patients were 15–18 years old on admission, we did not apply the related part of the PAS to these patients. PAS was scored by converting raw scores into the proportion of a potential total score so that the worst possible adjustment score would be 1. Mean PAS score and PAS childhood subscale score (PAS 1), PAS early adolescence subscale score (PAS 2) as well as PAS general subscale score (PAS G) were positively correlated with each other at very high significance level ($p < 0.01$). So, for further calculation, mean PAS score was taken as representative of pre-morbid functioning. Similar procedure was carried out in a study done in Turkey on first episode of schizophrenia.[21]

Age of Onset, DUP and Premorbid Functioning

There was significant difference in PAS mean scores of patients with non-affective psychosis (0.27 ± 0.13) and patients with affective psychosis (0.19 ± 0.07), $p < 0.05$) (Table. 3). In Cannon et al study, the schizophrenic subjects

exhibited a greater deterioration in functioning than the bipolar subjects which is similar to finding in our study.[22] This study also confirmed that deteriorating pre-morbid function is not seen bipolar patients.[23]

In case of DUP in first episode of psychosis, Craig TJ et al's[24] first episode psychosis study in New York gives similar results. Their findings suggest that duration of untreated psychosis was longest for individuals with schizophrenia and briefest for the patients with bipolar disorder where median DUP was 98 days for schizophrenia, 9 days for psychotic bipolar disorder, and 22 days for psychotic depression. In a Turkish study, for the affective psychosis group; mean DUP was 1.9 ± 1.2 weeks and for the non-affective psychosis group; mean DUP was 9.8 ± 15.5 weeks.[25] A nation-wide register based study in Denmark concluded that DUP is related to a number of demographic(age, sex, ethnicity, marital status, and geographic area), premorbid and healthcare factors(referral source and first FEP contact).[26] Economic conditions, racial and sociocultural factors, and public awareness on psychosis in developing countries also affect DUP.[27] Thus, DUP is a complex and multifaceted phenomenon that is associated with early-course illness development.[28]

There is significant positive correlation between mean PAS scores and duration of untreated psychosis in affective psychosis (r= 0.646, p= 0.003) and there is no significant correlation between mean PAS scores and DUP in non-affective psychosis (r= 0.395, p= 0.051) (Table. 5a and 5b). Pre-morbid adjustment scale denotes that when mean PAS score is worst and approaching 1 there is worst possible pre-morbid adjustment. Thus, these findings of positive correlation between mean PAS score and DUP suggest that poor pre-morbid functioning in first episode patient increases the duration of untreated psychosis. Larsen TK et al[29] suggest that poor pre-morbid functioning could result in late detection and treatment. In a recent cross-sectional study on 110 patients with non-affective psychosis, at least 75% had long DUP, which was associated with lower level of education, poor insight, younger age at onset, and at least one parent deceased.[30] In principle, it means that a significant correlation between DUP and outcome would disappear if pre-morbid functioning is controlled variable.

We didn't find any correlation between pre-morbid functioning and age at onset or in between DUP and age at onset in both the groups of first episode psychosis. But in another study, bi-variate correlations showed age at onset of the illness to be significantly related to mean PAS score (r= -0.318, P=0.04), PAS-2 (r= -0.383, P=0.007), and PAS-3 (r= -0.465, P=0.02), but not to PAS-1.[21]

Clinical Presentation of First Episode of Psychosis

Clinical presentation of FEP is assessed by BPRS, SAPS and SANS scores at admission in non-affective and affective psychosis. In our study there was no significant difference between mean SAPS composite and mean BPRS scores at admission in non-affective and affective psychosis. But there was significant difference between mean SANS composite ($p < 0.01$) in non-affective and affective group of first episode of psychosis (Table. 6) This suggests that negative symptoms were predominantly present in non-affective psychosis as compared to affective psychosis.

Effect of Pre-Morbid Functioning, Age at Onset and DUP on Clinical Presentation of First Episode of Psychosis

As DUP is not normally distributed and as there was no significant correlation between PAS scores, age at onset and DUP in non-affective psychosis, non-parametric Spearman's correlation of pre-morbid functioning, age at onset and DUP with BPRS, SAPS and SANS scores at admission was done. Amongst mean PAS score, age at onset and DUP, the DUP only has significant positive correlation with SANS composite (r= 0.459, p= 0.021) at admission in non-affective psychosis (Table. 7a). This suggests that in non-affective schizophrenia spectrum psychosis, long DUP is associated with more negative symptoms at presentation of first episode. Negative symptoms and cognitive deficits of schizophrenia are correlated in their severity also share many features.[31] It is also demonstrated that longer DUP in FEP patients is associated with worse cognitive scores, and that this association is more pronounced in a subgroup of patients who have lower premorbid intelligence.[32] A meta-analysis suggests a very small but significant association between longer DUP and reduced performance in planning/problem-solving ability.[33] These findings are in accordance with various other studies provided stronger evidence for a relationship between poor pre-morbid adjustment and negative symptoms and not with positive symptoms.[34,35,36,37] In a study on south American first episode psychosis cohort, patients with shorter DUP achieved three times more likely negative symptom remission.[38] In a recent 2 year follow-up study, duration of active psychosis (DAP) was found as a better predictor of negative symptoms than DUP at 2-year follow up.[39] However, in a Indian study, there was no association seen between DUP and outcome of psychosis.[40]

Partial correlation was performed in patients with affective psychosis as DUP and PAS mean scores were positively correlated. When DUP is controlled there was significant negative correlation in SAPS scores at admission and mean PAS scores (Table. 7c). This reveals that when modifiable factor like DUP is controlled, patients with poor pre-morbid functioning (high mean PAS scores) show predominantly fewer positive symptoms. Malla et al suggest that continuous poor social adjustment during childhood and adolescence may be a vulnerability marker for greater propensity toward negative symptoms, while lower academic performance during childhood and early adolescence is likely to be a marker for poor cognitive functions.[41] Pre-morbid adjustment scale also gives insight into academic performance as it has subscales of education and scholastic performance.

On multiple regression analysis, in patients with non-affective psychosis, DUP in months, mean PAS score and age at onset were not significant predictors of clinical presentation at admission (Table. 8a). Norman and Malla

reported that patients with schizophrenia have a longer DUP which is associated with social withdrawal, poor functioning and prominent negative symptoms.[5]

Regression analysis in patients with affective psychosis reveals that mean PAS scores significantly predict SAPS composite score at admission (p= 0.038, $R^{2=}$ 0.29) (Table. 8b). This finding suggests that in case mood disorders with psychotic symptoms, individuals with poor pre-morbid adjustment (negative correlation between mean PAS and SAPS scores in affective psychosis) may have fewer positive symptoms.

Limitations

In this study, sample size was less, and study was conducted only on hospitalised patients of first episode of psychosis. Patients with substance use disorders (other than Nicotine) and psychosis are also excluded. Scales were applied at the time of admission and in highly un-cooperative patients as late as 48 hrs of admission. Caregiver's recall bias is expected in patients with early onset and long duration of untreated psychosis (DUP).

CONCLUSIONS

Our findings suggest that DUP and pre-morbid functioning are important predictors of clinical presentation of first-episode psychosis. This result is echoed by other studies[21,29,41] on untreated psychosis although definitions of onset, first episode and DUP vary greatly in these studies. Attempts at early diagnosis of first-episode psychosis should be made which might have significant effect on treatment response.

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