Original Article

Predictors of 6-month follow-up Outcome of Drug Treatment in Schizophrenia in a tertiary hospital of Bangladesh

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Abstract

Background: Schizophrenia may have a better outcome in low- and middle-income countries. In Bangladesh short-term outcome of drug treatment of schizophrenia is also better. It is required to see the predictors of outcome of drug treatment of schizophrenia in Bangladesh. Objectives: General objective of this study is to assess the outcome of 6-month follow-up of patients with schizophrenia. Specific objective of this study is to find out the predictors of 6-month follow-up outcome of drug treatment in schizophrenia. Methods: Patients with a SCID-1/P diagnosis of schizophrenia (n=42) were assessed prospectively at baseline, at 6-week and at 6-month follow-up. Socio-demographic and relevant variables and questionnaire for family support and previous work record for the study were read in front of the patients and guardians and were filled up by the researcher. Psychopathological measurements were applied at base line by researcher and at 6-week and at 6-month by research assistant for the study population. Results: Follow-up data were available for 38 patients at 6-month and among them 86.85% achieved partial remission, 7.89% had not responded and 5.26% had relapsed. In multivariate analysis by General Linear Model Analysis of socio-demographic and relevant variables with the mean BPRS score as outcome in this study we found that age, education, marital status and history of previous work record were significantly associated with the 6-month treatment outcome. Conclusions: Drug treatment outcome of schizophrenia in Bangladesh is better in short-term follow-up. Increase family support and early management by drugs should be a target for intervention.

Introduction: Schizophrenia is a chronic relapsing psychotic disorder that primarily affects thought and behaviour[1]. The world-wide prevalence of schizophrenia is about 1%[2]. In Bangladesh, a recent study was done in collaboration with WHO, the prevalence rate of schizophrenia was to be found 0.6 %[3]. Schizophrenia is often a chronically disabling condition; it is therefore responsible for a great deal of population's morbidity. In social terms chronic illness generally consume much of the total health budget. The outcome of a case of schizophrenia is remarkably heterogeneous and unpredictable [4, 6]. For example, in the International Pilot Study of Schizophrenia [5, 6], tests were made of the predictive value of several sets of criteria based on symptoms. All proved largely unsuccessful at predicting outcome at 2 years or 5 years[6].

Poor outcome in schizophrenia is associated with younger age of onset, male sex, poor pre-morbid functioning and persistence of negative symptoms. There is also evidence that the duration of psychotic symptoms prior to treatment correlates with time to remission and level of remission [6,7].

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Schizophrenia in western world societies as a "chronic debilitating illness" with a poor prognosis and a poor functional outcome. This statement is not true in worldwide.

At least two major international studies, the International Pilot Study of Schizophrenia[9] and the Determinants of Outcome of Severe Mental Disorders[10] have provided convincing evidence for a better outcome in India and other "less developed" countries than in the west. The multi-site study of factors affecting the course and outcomes of schizophrenia in India found that 64% of the participants were in remission at a 2-year follow-up and only 11% continued to be ill[11].

Such numbers are likely to be reversed in United States. Outcome of schizophrenia appears to be better in low- and middle-income countries. Established factors apparently contributing to good prognosis of schizophrenia in low- and middle-income countries are low expressed emotion, good social support, tolerance of odd behaviour by society and family, marriage. Doubtful factors apparently contributing to good prognosis of schizophrenia in low- and middle-income countries are less industrialization and urbanization, early death of those with bad outcome, increased prevalence of acute psychosis11. Patients with schizophrenic illness had the most severe and disruptive psychopathology. The families with schizophrenic patients were most distressed and socially isolated. They had difficulties in the areas of household functioning, financial and community problems[12]. The general objective of this study was to assess the short-term pharmacological treatment outcome of schizophrenia and the specific objective of this study was to assess predictors of the 6-month follow-up outcome of drugs treatment in schizophrenia in a tertiary level hospital. Social support as a predictor of outcome in low- and middle-income countries has attracted considerable attention to minimize the damaging effects of the illness and improves outcome.

Materials and Methods
This was a follow-up study of patients who had been attended in out-patient department and had been hospitalization in in-patient department of Psychiatry, BSMMU, with no prior psychiatric treatment between September 2009 to December 2009 and whose diagnosis met SCID-1/P research criteria for schizophrenia and who met the inclusion and exclusion criteria of the sample. Socio-demographic and relevant variables were applied at baseline and Brief Psychiatric Rating Scale was applied at baseline, at 6-week and at 6-month. Researcher used NICE guideline protocol to treat the schizophrenic patients who were collected as sample.

Untreated cases of schizophrenia irrespective of age and sex were included in this study. Patients of schizophrenia with co-morbid psychiatric disorders and co-occurring general medical condition and with cognitive impairments where the interview was difficult were excluded from the study. The researcher was duly careful about ethical issues related to this study. The clearance of the ethical committee of the Department of Psychiatry, BSMMU was taken. In this study the following research instruments were used:

1. A pre-designed semi-structured questionnaire for the study 'Short-term Treatment Outcome of Schizophrenia in a Tertiary Hospital of Bangladesh' which include data on gender, age, education level, employment status, marital status, monthly family income and relevant information about outcome of schizophrenia.

2. SCID–The Structured Clinical Interview for Diagnosis of DSM-IV Axis-I Disorder (SCID-I) is a structured interview for making the major DSM-IV Axis-I diagnosis8. In this study researcher used SCID-1/P edition, research version, module B and C to diagnose the schizophrenia14.

3. BPRS (Brief Psychiatric Rating Scale) From Ventura, Green, Shaner and Liberman15, This scale consists of 24 symptom constructs, each to be rated in a 7-point scale of severity ranging from 'not present' to 'extremely severe'. It was used to estimate the clinical response or course of the illness. This instrument was applied by researcher at baseline to see the symptoms severity of the disease and was applied by research assistant at 6-week and at 6-month to see the clinical response. Trained researcher applied SCID-1/P edition for the diagnosis of schizophrenia after the clinical diagnosis by consultant psychiatrist and collected as sample who met the inclusion and exclusion criteria.

Informed written consent was taken from the patient, parents or guardian where appropriate and ethical issue was strictly maintained. After taking consent, questionnaire for socio-demographic and relevant variables and questionnaire for family support and previous work record for the study were read in front of the patients and guardians and were filled up by the researcher. The researcher then applied BPRS to the patient to estimate the severity of symptoms at baseline. The researcher was blind to the clinical assessment at 6-week and at 6-month follow-up, which was done by research assistant. The patients or guardians were advised to visit every three weeks initially for four and then monthly for three visits for follow-up up to 6 months. BPRS was applied by trained research assistant at 6-week and at 6-month. Besides these follow-ups, researcher ensured drug compliance of the patients through cell phone communication with the parents or guardians and also by follow-up visits.

Inter-rater reliability test was done between researcher and research assistant at baseline. It was done by BPRS score of the first five patients (applied by the researcher and research assistant at the same day at baseline by two separate interviews) with Pearson's correlation co-efficient test or r test. Data analysis was performed by SPSS, version 15 for Windows. After cleaning the data, it was edited and coded. Tests of significance were applied with the student's t-tests, ANOVA test, F-test at 95% confidence interval level. Results were presented as text, tables and figures.

Results

A total number of 38 patients were included in this study. In order to include 38 patient's researcher had diagnosed 47 consecutive cases of schizophrenia in in-patient and out-patient Department of Psychiatry by using SCID-1/P edition of research version after clinical diagnosis by consultant psychiatrist. Out of 47 cases 44 were matched with the sample criteria. Among the 44 patients 2 were refused to participate in this study, so participation rate was found 95.45%. 42 patients collected as sample and BPRS was applied by researcher at baseline, 3 patients were dropped out at 6-week and 1 patient was at 6-month, so 38 patients came for follow-up at 6-month and BPRS was applied by the trained research assistant at 6-week and at 6-month. Among the 42 patients 4 were dropped out from this study, so drop-out rate was found 9.52%.

The vast majority of patients (n=27) were treated with risperidone (4–10 mg), 7 patients (n=7) with long-acting injection Fluphenazine (25 mg) fortnightly and 4 patients with olanzapine (10 – 20 mg) daily. Two patients relapsed, one treated with risperidone and another treated with injection Fluphenazine Decanoate and possible causes of relapsed were poor family support and non-adherence with the treatment. Three patients were not responding, two of them were treated with long-acting injection Fluphenazine Decanoate and one was treated with risperidone initially. A total 38 patients were followed-up using BPRS. Among the respondents, 86.85% patients were in partial remission, 5.26% patients relapsed and 7.29% patients were not responding 6-month after treatment. After 6 months of appropriate drug intervention a significant improvement on the total BPRS score (p<0.001) was achieved. Inter-rater reliability test between researcher and research assistant done by Pearson's correlation coefficient test (r test) and found that r=0.959 which was strong positive degree correlation. In a multivariate analysis the predictors of outcome were found that age, education, marital status, history of previous work record was significant association with the 6-month outcome of drug treatment in schizophrenia.

Table 1: Socio-demographic characteristics of the patients

Age in years	Frequency	Percent
10-18	7	18.42
19-28	14	36.84
29-38	8	21.05
39-48	7	18.42
>49	2	5.26
Mean (SD)	29.32 (11.407)	
Gender		
Male	17	44.7
Female	21	55.3
Residence		
Urban	12	31.6
Rural	26	68.4

Religion		
Islam	36	94.7
Hindu	2	5.3
Level of education		
Illiterate	3	7.9
Primary	14	36.8
Secondary	7	18.4
SSC	9	23.7
HSC	1	2.6
Graduate	2	5.3
Post graduate	2	5.3
Marital status		
Unmarried	18	47.4
Married	20	52.6
Family type		
Nuclear	13	34.2
Joint	25	65.8
Occupation		
Unemployed	2	5.3
Student	7	18.4
Housewife	13	34.2
Service	3	7.9
Business	1	2.6
Others	12	31.6
Monthly income (TK.)		
< 5000	1	2.6
5000-10000	14	36.8
10000-20000	19	50.0
> 20000	4	10.5

Mean age (standard deviation) =29.32(11.407) years. Data were used for General Linear Model Analysis and ANOVA test.

Table 2: Characteristics of relevant variables of the patients:

Variables	Frequency	Percent
Family history of mental illness		
Present	14	36.8
Absent	24	63.2
Previous history of illness		
Present	2	5.3
Absent	36	94.7
Family Support		
Good	30	78.9
Bad	8	21.1
Onset of disease		
Suddenly	17	44.7
Gradually	21	55.3

History of work record		
Good	25	65.8
Bad	13	34.2
Duration of illness		
< 1 year	19	50.0
>1 year	19	50.0
Family and society tolerance		
Yes	30	78.9
No	7	18.4
Not Applicable	1	2.6
Treatment started		
< 9 months	8	21.1
> 9 months	30	78.9

Data were used for General Linear Model Analysis and ANOVA test.

Outcome at 6-month follow-up

The mean score on the BPRS of 38 subjects at baseline, at 6-week and at 6-month were 60.47 (SD ±7.59), 41.21 (SD ±7.29) and 34.89 (SD ± 8.72) respectively. These findings were shown in Table 3. Among the respondents, partial remission was in 33 patients (86.85%), not responding patients were 3 (7.89%) and relapsed were in 2 patients (5.26 %). These findings were shown in figure 1.

Fig. 1: Distribution of patients on outcome of Schizophrenia
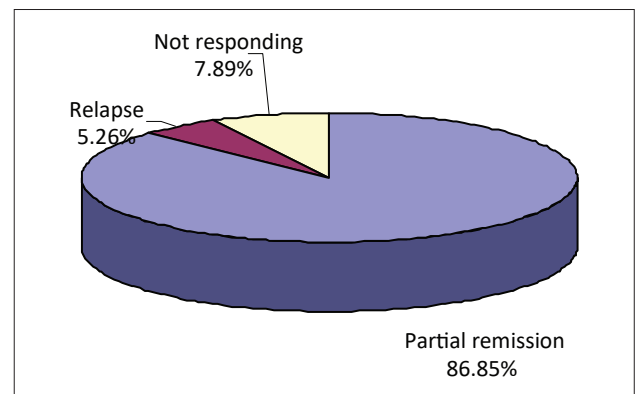

Fig.1: The above pie chart showed that 86.85% patient with schizophrenia had partial remission, 7.89% patient not responding and 5.26% patient had relapsed 6-month after treatment.

Table 3: BPRS score of the patients on clinical measures at the three assessment points

	N	Mean BPRS score	Standard Deviation	P-value
At base line	38	60.47	±7.59	0.001***
At 6 weeks	38	41.21	±7.29	
At 6 weeks	38	41.21	± 7.29	0.001***
At 6 months	38	34.89	±8.72	

The table 3 showed mean BPRS score (60.47 ± 7.59) at baseline is very highly significant improvement to 41.21±7.29 (p value 0.001) at 6-week and very highly significant improvement to 34.89 ±8.72 (p value 0.001) at 6-month.

Fig.2: Plot of psychopathological symptoms (Brief Psychiatric Rating Scale) score from baseline to 6-month follow-up by clinical outcome
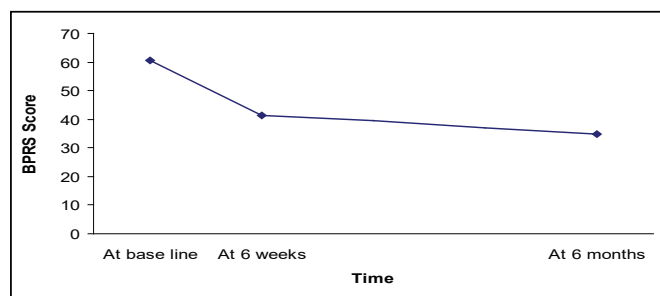
This figure presented graphical presentation of BPRS score and time followed by drug treatment. It showed that within initial 6-weeks BPRS score sharply decline but after 6-week to 6-months, decline is very slow BPRS scores fall as symptoms improve.

Table 4: Predictors of good outcome in schizophrenia after 1st contact with psychiatric services using BPRS score as the outcome: General Linear Model Analysis.

	Model 1ᵃ	Model 2ᵇ	Model 3ᶜ	Model 1 T	Model 1 p-value	Model 2 T	Model 2 p-value	Model 3 T	Model 3 p-value
Age	.731	.617	.674	3.852	.001*	4.376	.000*	5.554	.000*
Sex	-.633	.327	2.946	-.137	.892	.095	.925	.996	.328
Habitat	.347	-.538	-3.809	.070	.945	-.146	.885	-1.202	.240
Education	18.884	20.962	20.676	2.968	.006*	4.436	.000*	5.086	.000*
Marital status	11.201	8.281	9.794	2.251	.033	2.240	.034	3.080	.005*
Persons come with patient	4.744	3.153	1.201	1.629	.115	1.457	.157	.646	.524
Family history	6.465	3.921	2.367	1.496	.147	1.222	.233	.857	.399
Family Support	13.243	11.919	-.436	1.684	.104	2.041	.052	-.087	.932
Work record	-7.756	-11.887	-12.462	-1.553	.132	-3.205	.004*	-3.905	.001*
Duration	6.049	4.120	4.184	1.214	.236	1.113	.276	1.314	.200
Family and society tolerance	-4.475	-10.383	-3.955	-.511	.613	-1.597	.122	-.707	.486
Treatment	-1.009	-4.755	-3.770	-.155	.878	-.982	.335	-.905	.374

a dependent variable baseline BPRS
b dependent variable at 6 weeks BPRS
c dependent variable at 6 months BPRS
Sex: male 0; female 1
Marital status: 1 unmarried; 0 other marital statuses
Education: 1 literate; 0 illiterate
Family history: 1 present; 0 absent
Family support: 1 good; 0 bad
Work record: 1 good; 0 bad

Duration of illness: 0 < 1 year; 1 > 1 year
Family and society tolerance: 1 yes; 0 no
Treatment: 0 < 6 months; 1 > 6 months

Table 5: Test of significance by ANOVA test
Model 1:

ANOVA

Model		Sum of Squares	Df	Mean Square	F	Sig.
1	Regression	125882.358	12	10490.197	94.335	.001***
	Residual	2557.642	23	111.202		
	Total	128440.000	35			

Model 2:

ANOVA

Model		Sum of Squares	Df	Mean Square	F	Sig.
2	Regression	59432.624	12	4952.719	55.747	.001***
	Residual	2043.376	23	88.842		
	Total	61476.000	35			

Model 3:

ANOVA

Model		Sum of Squares	Df	Mean Square	F	Sig.
3	Regression	44664.529	12	3722.044	58.336	.001***
	Residual	1467.471	23	63.803		
	Total	46132.000	35			

Table 5 showed that it was very highly significant in all the three models of ANOVA test and these three models were shown in table no. 4.

Discussion

Schizophrenia is a major psychiatric disorder which is still now burden to the family and also to the country. Due to repeated relapse of schizophrenia, functional, social and occupational activities gradually deteriorate and ultimately lead to defect state. Thus, the schizophrenic patients become burden to the family, society and state as well. The findings of such study will help to determine the disease burden and consequent fiscal requirements. Therefore, it will provide feedback to the family, researchers and finally to the policy makers.

In current study 86.85% of patients with schizophrenia had partial remission, 7.89% had not responding and 5.26% had relapse in short-term treatment outcome. Our findings were not close to the study by Saravanan et al.16 where remission with deficits was 50% (included relapse 10%) and complete remission was 50% because they carried

out 1-year but we carried out 6-month follow-up study. A study in India was conducted by Srinivasan and Tirupati19 was found that 67 percent of 88 patients were employed and that most of them were in full-time employment in mainstream jobs with minimal or no disability or support in the workplace. These findings were nearer to our study.

In this study the mean BPRS score at baseline, at 6-week and at 6-month was found 60.47 (SD ±7.59), 41.21 (SD ±7.29) and 34.89 (SD ±8.72) respectively. Our finding was closely related to the study by Saravanan et al.16 where mean BPRS score at baseline and at 6-month were 56.7 (SD 5.2) and 32.5 (SD 6.9) respectively.

In this study the mean age of the patients was (29.32±11.40) years ranging from 11 to 60 years. Most of the patients were in the age ranges 19-28 years (36.84%) followed by age range 29-38 years (21.05%) and 10-18 years and 39-48 years age range both were 18.42%. A study in India done by Saravanan et al.16 found that the mean age was 29.5 (±7.0). This finding was consistent with our study. Another study in Indonesia conducted by Kurihara et al.18 was found that the mean age was 26.7 years (SD ±7.83) which was a beat below of our result.

In our study 55.3%% patients were female and 44.7% patients were male. In India a study conducted by Saravanan et al.16 found 46% were women and 54% were men. This result was close to our study. In this study 31.6% of the respondents were residing in urban areas and 68.4% were residing in the rural areas. This finding was nearer to the finding of Saravanan et al.16 where they found 80% residing in the rural and 20% residing in the urban areas.

In our study, among the respondent's level of education, very few patients were illiterate (7.9%). Highest percentage patients (36.8%) had Primary level followed by SSC (23.7%), Secondary (18.4%), Graduate (5.3%), Postgraduate (5.3%), and HSC (2.6%). This finding close to the study of Bashar et al.13 where they found illiterate (10.8%), highest percentage patients (23.5%) had Secondary level followed by Primary (19.6%), SSC (15.7%), Graduate (17.6%%), Postgraduate (1%), and HSC (11.8%).

Regarding occupation, in this study we found housewife were more common (34.2%), then others were (31.6%), student were (18.4%), service holder were (7.9%), unemployed were (5.3%), and business man were (2.6%). In this study, among the respondent's marital status, 52.6% were married and 47.4% were unmarried. This finding close to the study of Karim et al.17 where they found 37.12% were married and 54.54% were unmarried, 3.78% were widow, 3% were divorced and 1.51% were separated.

In this prospective study we found that family history of mental illness was present in 36.8% and absent in 63.2% family. This study revels that previous history of mental illness was present only in 5.3% patients and absent in 94.7% patients reflects that majority of the samples were first episode schizophrenia.
In our study we found that 50% patients were more than 1 year and 50% patients were less than 1-year duration of illness. Rabbani, MG12 found that mean duration of illness was 4.90 (SD±5.7) months which was nearer to our study. Marital state can be considered an outcome measure, as its maintenance depends on stability and functioning of both partners.

Conclusions
The current study demonstrates that short-term treatment outcome of schizophrenia in Bangladesh is better. In this study we found that age, education, marital status and history of previous work record were significantly associated with the 6-month treatment outcome. A majority of schizophrenic patients were found in Bangladesh, if these schizophrenic patients treated by early and properly by the antipsychotic drugs, they may be improved as the outcome is better in our country; they would not be disease burden.

Conflict of interest: Authors declare no conflict of interest.

References

1. Green, B, Schizophrenia. Retrieved from October 25, 2009, http:/priory.com/schizo.htm.

2. Davis, LM and Drummned, MF 1990, 'The economic burden of schizophrenia', Psychiat Bulletin, vol. 14, pp. 522-25.

3. Firoz, AHM, Karim, ME, Alam, MF, Rahman, AHM, Zaman, MM et al. 'Prevalence, Medical care, Awareness and Attitude Towards Mental Illness in Bangladesh', Bang J Psychiatry, 2005; vol. 20, no. 1, pp. 9 -36.

4. Hafner, an der Heiden, W, Course and outcome of schizophrenia. In S Hersch and Dweenberger, eds, Schizophrenia, Chapter 8, 2nd edn, 2003; Blackwell. Oxford.

5. World Health Organization. 'Schizophrenia: An International Follow-up Study', New York, Wiley, 1973.

6. Gelder, M, Harrison, P, Cowen, P, Chapter 12, Shorter Oxford Textbook of Psychiatry, 5th edition, 2006; pp. 267-306.

7. Marshall, M, Lockwood, A, Lewis, S et al., 'Association between duration of untreated psychosis and outcome in cohorts of first episode patients, a systemic review', Arch Gen Psychiatry, 2005b; vol. 62, pp. 975-83.

8. American Psychiatric Association (APA) Diagnostic and Statistical Manual of Mental Disorder, 4th edition, 2005,1400K Street N W., Washington DC.

9. World Health Organization. 'Schizophrenia: An International Follow-Up Study', John Wiley & Sons, 1979.

10. Sartorius, N, Jablensky, A, Korlen, A et al. 'Early manifestations and first-contact incidence of schizophrenia in different countries', Psychological Medicine,1986; vol. 16, pp. 909-28 (Medicine).h

11. Verghese, A, John, JK, Rajkumar, S et al. 'Factors associated with course and outcome of schizophrenia in India: results of a two-year multi-centre follow-up study', Br f Psychiatry, 1989; vol.154, pp.499-503.

12. Rabbani, MG. 'Family Burden of a Patient with Schizophrenic Illness', Bang J Medicine, 1992; vol. 3, no. 1, pp. 21-8.

13. Basher, K, Firoz, AHM, Mandal, MC, Hossain, MD, Alam, FM. 'Socio-demographic Parameters and Quality of Life of Schizophrenic Patients', Bang J Psychiatry, 2008; vol. 22, no. 2, pp. 18-27.

14. First, MB, Spitzer, RL, Gibbon, M and Williams, JBW. "Structured Clinical Interview for DSM-IV-TR Axis-1 Disorders-Patient Edition (SCID-1/P, 1/2007 revision)", Biometrics Research Department, New York State Psychiatric Institute, Department of Psychiatry, Columbia University, New York, 10032,2007.

15. Ventura, Green, Shaner & Liberman. 'The drift buster', Internl J Methods Psychiat Researc,1993..

16. Saravanan, B, Jacob, KS, Johnson, S, Prince, M, Bhugra, D, David, AS. 'Outcome of first episode schizophrenia in India: Longitudinal study of effect on insight and psychopathology', Br J Psychiatry,2010; vol. 196, pp. 554-59.

17. Karim, ME, Mullick, MSI, Chowdhury, S, Islam, ME. Epidemiology of Schizophrenia – Study in Two Urban Hospital', Journal of IPGMR, 1994; vol. 9, no. 2, pp. 54-7.

18. Kurihara,T, Kato, M, Reverger, R, et al. 'Eleven-year clinical outcome of schizophrenia in Bali', Acta Psychiat Scandinavica, 2005; vol. 112, pp. 456- 62.

19. Srinivasan, L & Tirupati, S. 'Relationship between cognition and work functioning among patients with schizophrenia in an urban area of India', Psychiat Services, 2005; vol. 56, pp.1423- 28.