Original Article

Evaluation of the Effective Factors on Bipolar I Disorder Frequent Recurrence in a 5 Years Longitudinal Study Using Generalized Estimation Equations Method

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Abstract

Background and Purpose: Patients with Bipolar I Disorder recurrence experiences mood variation between manic and depression during the time. Hence, that is need to the longitudinal study on Bipolar Disorder patients. This study aims to evaluate the effective factors on Bipolar I Disorder frequent recurrence in 5 years longitudinal study using generalized estimation equations (GEE) method.

Materials and Methods: Data were collected with repeated measurements on 255 Bipolar I Disorder patients in mazandaran, Iran, in a longitudinal study between 2007 and 2011. The outcome variable is Bipolar I Disorder recurrence, and the predictor variables are as follows: sex, age of onset, family history (Grade 1), economic status and education level. In this paper, SAS PROC GENMOD was used to apply GEE regression to the assessment of parameters corresponding to the factors causing recurrence.

Results: The age was among 13-55 years and the average of age of onset was 24.1 years. Almost of patients were male and had economic status with (upper/middle) deciles and also had a diploma and under diploma education level. The results of GEE method showed that the covariate of family history (Grade 1) increased the odds of recurrence (odds ratio [OR] >1; P < 0.0500); and age of onset decreased the odds of recurrence in patients with Bipolar I Disorder (OR <1; P < 0.0500).

Conclusion: Predictor variables in recurrence Bipolar I Disorder include first-degree relatives' psychiatric family history and age of onset. Understanding this factors, and educate patients, and their families are valuable for the prevention and planning the treatment.

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Key words: Bipolar I disorder recurrence, Longitudinal study, Generalized estimation equations

1. Introduction

Patients with recurrence Bipolar I Disorder experiences severely and repetitious mood variation between manic and depression or both during the time (1). The Bipolar Disorder is one of the republic hygiene problems. That causes to substantial disability and decreases hope to life in patients (2). The Bipolar patients suffer from social and individual disorders and occupational status. The symptoms of the disorder are such as aggression, irritability, anxiety, sleep reduction, pessimism, suicide and unconscious sexual behaviors; which is different among patients (1). On the basis of research that was done by depression and psychosis national association in 2000, the rate of Bipolar 1 and 2 Disorders was estimated about 3.4% in United States. Many studies have been done for identity effective factors on Bipolar Disorder recurrence (3). The treatments for Bipolar Disorder are such as drug therapy, psychotherapy, educational plans for patients and their family, but almost disorder has recurrence (4).

In a study by Ghoreyshizadeh, et al. in 2009, the results of study on 140 Bipolar I Disorder patients showed that the effective factors on recurrence are as follow: discontinue in mood adjustment drugs, dose reduction, use of unsteady mood drugs, substance abuse and drug dependency, sleep disorder, life events (nice/bad) and unawareness of treatment role (5). In other study on 21 Bipolar patients under prophylaxis therapy during 4 years; the results showed that only social-mental covariates had significant effect on occurrence of recurrence such as: low level of social protection, unsocial personality, type of entertainment in relief times, low family society (6).

Depending on frequent variations in status and severity of emotional symptoms among Bipolar patients, that is need to the longitudinal study about Bipolar disorder recurrence (1). The longitudinal study is repeated measurements of outcome on each patient during the time (7). A few researches have been done about Bipolar Disorder in Iran such as: the study of Molavi et al. in 2011; which employed multivariate regression for prediction of the recurrence rate for 6 months follow-up of patients (8), the study of Amini et al. in 2007; which predicted the Bipolar Disorder outcome on inpatients at the Roozbeh hospital for 1 year follow-up (9), the study of Shabani et al. in 2004 about the recurrence rate among Bipolar I Disorder patients for 17 months follow-up (10), the descriptive – analytical study of Mousavi et al. in 2002 for 1 year follow-up of patients (11).

On the other hand; in a longitudinal study, the observations are correlated because of repeated measurements on patients (7). There are methods that include the within subject correlation structure in data such as marginal models. Generalized estimation equations method (GEE) in Marginal model was introduced by Liang and Zeger in 1981. In this method, the relation between predictor variables and outcome variable is modeling with assumed correlation structure; which illustrates the dependency in data during the time (12). This estimation method provides consistent and unbiased coefficients estimation even if the correlation structure is not choosing accurately (13). This method is applicable for any response variable with distribution of the exponential family such as count, binary, categorical, ordinal and normal (14). GEE method was applied in a few Bipolar Disorder studies such as: a clinical trial study was illustrated about advantages and limitations of GEE method for analysis of Bipolar Disorder data (15). Another study has been done about evaluation of factors associated with irregularity in use of anti-depression drug using GEE method (16). This study aims to evaluate the effective factors on Bipolar I Disorder frequent recurrence in a 5 years longitudinal study using GEE method.

2. Materials and Methods

Totally 255 Bipolar I Disorder patients were included in the study. This longitudinal study with census was done during 5 years follow-up between 2007 and 2011. The patients have at least one recurrence history and have one of clinical symptoms such as anxiety or depression or both on basis of DSM-IV-TR criteria (American psychiatry association, 2000) and also inpatient at Zare hospital in sari, Iran. Patients' biography and recognition of the disorder were done by psychiatrist. Furthermore, that was used of the patients' medical records and interviewed with patients via phone in order to data collection.

The GEE method was employed for analysis of correlated longitudinal data. The analysis was done using SPSS for Windows (version 19, SPSS Inc., Chicago, IL, USA) descriptive analysis and SAS 9.1.3 software for marginal modeling and GEE method. Significance level was defined as P < 0.05.

3. Results

The analysis was performed on 255 Bipolar I Disorder patients. The patients were 114 female (44.7%) and 141 male (55.3%). The mean and standard deviation for age of onset were 24.11 and 8.61, respectively. The age range was from 13 to 55 years old. Almost of patients had diploma and under diploma education level (Table 1). About 28.2 % of patients had recurrence the history in family Grade 1.

The logit link function was used for binary response variable. Hence, the Marginal model is as follow:

Logit p (y = 1|x) = $\beta_0 + \beta_1$ sex + β_2 age of onset + β_3 family history + β_4 economic + β_5 education + β_6 time

The results of GEE in a marginal modeling for occurrence of Bipolar I Disorder recurrence are presented in Table 2. Results showed that the recurrence history in family Grade 1 and age of onset were statistically significant (P < 0.05). The OR of recurrence among patients with family history Grade 1 was 1.16 times of odds in patients without family history Grade 1. Also, with increasing in age of onset, the OR of recurrence was 0.99.

Table 1. The distribution of covariates in basis on some demographic characters (n = 255)

Parameter	Category	n (%)
Education level	Unread	32 (12.5)
	Elementary/middle	89 (34.9)
	High school/diploma	97 (38)
	Collegiate	37 (14.5)
Economic status	Low decile	87 (34.1)
	Decile (middle/upper)	168 (65.9)

Table 2. The regression results of GEE method for Bipolar I Disorder data

Parameter	Category	Estimate	SE	OR (95% CI)	P value
Intercept	-	-0.896	0.1718	0.408 (0.292, 0.572)	0.0001
Sex	Female	0.023	0.0810	1/024 (0.873, 1.200)	0.7730
	Male*	-	-	-	-
Age of onset	-	-0.008	0.004	0.992 (0.984, 1.010)	0.0370**
Education	Unread	0.225	0.1519	1.252 (0.930, 1.686)	0.1390
	Elementary/middle	0.166	0.1122	1.181 (0.948, 1.472)	0.1380
	High school/diploma	0.154	0.1099	1.166 (0.942, 1.444)	0.1590
	Collegiate*	-	-	-	-
Family history (Grade 1)	Yes	0.153	0.0774	1.165 (1.001, 1.356)	0.0480**
	No*	-	-	-	-
Economic status	Lower decile	-0.127	0.0776	0.88 (0.756, 1.025)	0.1010
	Middle/upper*	-	-	-	-
Time	-	0.004	0.0127	1.004 (0.979, 1.029)	0.7710

*Reference group, **It is significant at level of 0.05. SE: Standard error, CI: Confidence interval, OR: Odds ratio, CI: Confidence interval, GEE: Generalized estimation equations

4. Discussion

Mood disorders are the cause of death and the main disorders in childhood and adolescence. The Bipolar Disorder recurrence is common among different types of mood disorders (1). In the present study for evaluation of effective factors on Bipolar I Disorder recurrence using GEE method, the results showed that the covariates of family history (Grade 1) and age of onset had significant effect on disorder recurrence. The OR of disorder recurrence was more among patients with family history (Grade 1). This result was accommodated to results of other studies that indicated the important role of genetic on cause of the disorder (1,17,18). Also, the genetic and other hypertension problems had effected on made of disorder among patients with lower age. Another result of present study using GEE method showed that, the OR of disorder recurrence was more among patients with lower age of onset. This result was accommodated to results of other studies (1,19,20).

In a study about evaluation of factors associated with irregularity in use of anti-depression drug, the results of GEE method were showed that there was not statistical difference in regularity usage among patients with both anti depression and mood adjustment drugs usage; but the depression mood was associated with increase in irregularity (16). In some of study; the results indicated that the rate of disorder was more in male because of the encounter with economic problems and related tensions and also, was more among patients with lower education level (8,14,21,22). In the present study, the results using GEE method showed that there was not statistical difference in recurrence among male and female. Some of the studies was confirmed this results (1,23). On the basis of Kaplan's handbook; the patients with higher economic and social levels were more in risk of Bipolar Disorder and the patients with lower economic and social levels was more in risk of depression. In the present study, the covariates of sex and economic status and education level did not have an effect on disorder recurrence. Difference in results may be related to low number of patients with lower economic level that referred to hospital.

In the end for the future studies that suggest to comparison between statistical methods for analysis of longitudinal data and also doing the multicenter studies in order to precise evaluation of factors associated with disorder frequent recurrence.

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