Evaluation of Prevalence and Effective Factors on Changing the Diagnosis from Mood Disorders to Schizophrenia after Six Years

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Objective: The purpose of this study was to assess the prevalence and possible variables on changing the diagnosis of mood disorder patients to schizophrenia.
Method: This study was a retrospective and comparative analytic research that was performed in 2006 in Razi psychiatric hospital. The sample consisted of all the 176 patients who were hospitalized in 2000 with the diagnosis of mood disorder. The patients were divided into two subgroups: the stable group with a persistent mood disorder diagnosis and the changed group with a changed mood disorder diagnosis to schizophrenia. Data were analyzed between these groups using chi-square and t student test.
Results: Findings showed that 31.3% of all the patients shifted towards schizophrenia; 23.3% and 32.9% of the patients with major depressive disorder and bipolar disorders shifted towards schizophrenia respectively. No statistical difference was observed between the groups in demographic variables but there was a statistical difference in some of the clinical variables such as psychotic features ($p<0.01$), severe clinical features ($p<0.05$), and the gradual onset of disorder ($p<0.05$) with changing the diagnosis to schizophrenia.
Conclusion: Recognition of clinical variables associated with changing the diagnosis to schizophrenia such as psychotic features, severe clinical features and the gradual onset of disorder will help clinicians to manage these patients better than the past.

Key words
Diagnosis, Mood disorder, Schizophrenia

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Proper diagnosis is the first and most significant principle in psychiatry; and appropriate treatment and clinical interview are the most valuable tools in reaching such a goal as far as psychiatrics are concerned. Non existence of coordination among the clinicians in diagnosis of psychiatric disorders has led to using series of valuable diagnosis criteria in the field of psychiatry; therefore, the application of DSM and ICD criteria has increased the reliability of so many psychiatric diagnoses. Diagnostic stability, declared by Robins and Guze in 1970 for the first time, is one of the reliable criteria for psychiatric diagnoses; therefore, it can be regarded as a considerable factor for suitable planning within the course of time (1).

Diagnostic stability is the rate of the stable diagnosis within time factor. The higher stability of diagnosis can show more psychopathology stability of a disease (2). In Psychiatry, there are numerous factors which are related to diagnostic stability among which the following can be pointed out: changes in symptoms during the course of time, acquiring new information from patients and their families, new interpretation of the previous symptoms and creation and application of new diagnostic tools and entry of revised criteria for clinical diagnoses in the reference books.

Considering the general overlaps in symptoms of psychiatric disorders, specially the mood disorder symptoms, together with the psychotic features and existence of different psychiatric diagnoses between these two groups as well as different mood symptoms in bipolar spectrum disorders, it can be stated that the shifting of diagnosis in patients suffering from mood disorder has a special significance (2-4).

In the study made by Amini and his colleagues in Rouzbeh Hospital of Tehran, 47 patients with the first episode of psychosis were assessed within one year and finally the stable diagnosis of schizophrenia and psychotic mood disorder were reported higher than other diagnoses(5). In that study, diagnostic stability of schizophrenia and psychotic mood disorder were equal to 93% and 91% respectively(6).

Generally schizophrenia and mood psychosis are the most stable diagnoses with psychosis. In psychosis cases shifting to schizophrenia is more than shifting to other major psychiatric disorder diagnoses (7). Bipolar disorders have the least stable diagnosis among the diagnoses of bipolar disorders, schizoaffective and schizophrenia (8). In the study of Enrique Baca-Garcia and his colleagues in Spain, the probability for wrong diagnosis and also diagnosis shifting to bipolar disorder

from psychiatry disorder have been reported at a high rate(9).

In phase of searching the Persian scientific literature in the list of valid internet resources, only one published study was found indicating to study the stable diagnosis of mood disorder and the probability for shifting the diagnosis to schizophrenia. In this study which was conducted by Shabani and his colleagues in Iran Hospital of Tehran, 23 patients with Bipolar I Disorder were followed for two years and one of the patients finally shifted to schizophrenia. The study implemented by Amini and his colleagues was the sole Iranian published study in English resources which studied diagnostic stability in the first phase of psychosis and has some proximity with the present study.

Considering the small number of published Iranian studies dealing with stable psychiatric diagnosis especially in the realm of shifting the mood disorder diagnosis to schizophrenia, it was decided to implement a retrospective study in one of the major psychiatry centers of the country.

Materials and Method

This study was performed in 2006 as a retrospective comparative analysis in Razi hospital. Our study population included all the hospitalized patients in the hospital with the initial diagnosis of mood disorder during 2000.

The criteria for study inclusion were 20-65 age range, first admission in the psychiatry ward of Razi hospital in 2000, the initial diagnosis of major depression disorder and/or bipolar I disorder based on DSM criteria during hospitalization and at least one re-hospitalization after 2000.

The criteria for study exclusion were age under 20 and over 65, proving the previous hospitalization in the psychiatry ward of Razi hospital, doubtful diagnosis of mood disorder, diagnosis of mood disorder based on different criteria of DSM, existence of substance-related disorders, existence of a considerable physical disease causing the mood disorder.

Among all the files of the hospitalized patients with initial diagnosis of mood disorder during 2000, only 176 patients could meet the required criteria to be included in the study. Initially it was decided that only the patients suffering from mood disorder who were hospitalized for the first time in their life to be included in the study. However, considering the fact that only 43 patients were qualified, it was decided that only the evidence for the first admission of the patient in the psychiatry ward of Razi hospital with the initial diagnosis of mood disorder in 2000 would be acceptable. In other words, the other 123 patients had hospitalization records in other hospitals prior to this study.

The assessed variables in this study included age, gender, marital status, educational level, psychotic, atypical, catatonia and melancholia features, positive family history of schizophrenia, severity of disease, pattern of beginning of the illness, improvement status, existence of disorders in Axis II, age at the start of the disease, number of hospitalization and age at first hospitalization.

The final assessment was made based on the study entry and exit criteria during 2000 -2006 by assessing the hospitalized files. Finally the patients were divided in to two qualified groups of: 1) diagnosis shifting from mood disorder to schizophrenia and 2) the group lacking the same and they were compared based on the envisaged variables. For statistical analysis of the quality variables, the Chi-Square test and for the quantity variables the T test were used in the independent samples. The logistic regression was used to determine the relationship between the variables.

Results

We had 176 patients with mood disorders; 30 patients (17%) suffered from major depressive disorder (MDD) and 146 patients (83%) from bipolar I disorder (BID). Of the patients, 59 were male (33.5%) and 117 were female (66.5%). The mean age of the patients was (44.4±12.8) years. Two patients with 65 and 21 years of age were the oldest and the youngest among the subjects.

Considering the marital status, 46% were divorced,

Table 1: comparison and frequency of demographic variables in patients with and without change of diagnosis from mood disorders to schizophrenia

Demographic variables		In patients with change of diagnosis from mood disorders to schizophrenia		In patients without change of diagnosis from mood disorders to schizophrenia		p- value
		Number	Percent	Number	Percent	
Gender	Male	35	29.9	82	70.1	0.590
	Female	20	33.9	39	66.1	
Marital status	Single	20	33.0	40	66.7	0.723
	Married	26	32.1	55	67.9	
	Divorced	9	25.7	26	74.3	
Educational level	Illiterate	14	26.9	38	73.1	0.356
	Primary school	11	34.4	2	65.6	
	Guidance & high school	26	37.7	43	62.3	
	Diploma	3	15	17	85	
	Higher education	1	33.3	2	66.7	

Table 2: comparison and frequency of clinical variables in patients with and without change of diagnosis from mood disorders to schizophrenia

Clinical variables		In patients with change of diagnosis from mood disorders to schizophrenia		In patients without change of diagnosis from mood disorders to schizophrenia		p-value
		Number	Percent	Number	Percent	
Psychotic symptoms	Yes	51	37.5	85	62.5	0.001
	No	4	10	36	90	
Catatonia symptoms	Yes	3	76	1	25	0.056
	No	52	30.2	120	69.8	
Melancholia symptoms	Yes	0	0	1	100	0.499
	No	55	31.4	120	68.6	
Atypical symptoms	Yes	0	0	2	100	0.338
	No	55	31.6	119	68.4	
Clinical severity	Medium	0	0	12	100	0.016
	Severe	53	33.5	105	66.5	
Pattern of beginning of the illness	Acute	17	22.4	59	77.6	0.027
	Gradual	38	38	62	62	
Improvement status	Complete	2	13.3	13	86.7	0.122
	Partial	51	32.7	105	67.3	
Existence of disorders in Axis II	Yes	47	30.9	105	69.1	0.813
	No	8	33.3	16	66.7	

Table 3: Quantitative variables in the patients with and without change of diagnosis from mood disorders to schizophrenia

Quantitative variables	In patients with change of diagnosis from mood disorders to schizophrenia	In patients without change of diagnosis from mood disorders to schizophrenia	p-value
Age	43.45 ± 11.00	44.84 ± 13.51	0.505
Age in beginning of disease	26.96 ± 8.28	28.14 ± 9.74	0.438
Age at first hospitalization	30.31 ± 9.6	31.74 ± 11.4	0.418
Number of hospitalization	6.5 ± 3.01	5.47 ± 3.6	0.052

34.1% single and 19.9% were married ;and in relation to the educational level, 39.2% had junior high school and high school education, 29.5% were illiterate, 18.2% had primary school education, 11.4% held high school diploma and only 1.7% had university level education. Fifty three patients (30.1%) had a positive family history of schizophrenia but the other patients didn't have such a family history.

No psychotic features were observed in 40 patients (22.7%); however,136 patients (77.3%) had psychotic features. Catatonic and melancholic features were observed in 4 patients (2.3%) and 1 patient (0.6%) respectively; and 2 patients (1.1%) suffered from atypical mood disorder.

With regards to severity of disorders, 12 patients (7.1%) had medium severity and 158 (92.9%) had severe symptoms. In 76 patients (43.2%) the start of the disorder was acute (less than two weeks) and in 100 patients (56.8%) was gradual (above two weeks). At the time of discharge from the hospital, complete remission was observed in 15 patients (8.8%) and incomplete remission in 156 patients (91.2%). On the other hand, one of the disorders on axis II was observed in 152 patients (86.4%).

Our findings showed that the mean number of hospitalization in the patients was 5.8±3.3. The minimum and maximum numbers of hospitalization were 1 and 20 times respectively. The mean age for the start of mood disorder was 27.8±9.3 years and the mean age of the first hospitalization was 31.3±10.9 years.

This study showed the change of mood disorders to schizophrenia in 55 patients (31.3%) and the mean age of this variation was 36.1±12.5 years. Among all the patients affected with MDD and BID, changing to schizophrenia occurred only in 7 (23.3%) and 48 patients (32.9%) respectively. The mean time of the diagnosis change to schizophrenia from the start of the illness in patients with BID was 12 years and in the MDD was 11.5 years. In BID the least and the most time of change from the time of the first hospitalization were in order 3 and 34 years and in MDD they were in order 9 and 14 years. Prior to the primary diagnosis of schizophrenia, only 11 patients had had once the other psychiatric diagnosis. 2 and 9 patients with primary diagnosis of OCD and schizoaffective disorder had a change of diagnosis to schizophrenia respectively. All the patients with diagnosis change to schizophrenia preserved this diagnosis until the end of our study.

Table 1 and 2 demonstrate the comparison and frequency of demographic and clinical variables in patients with and without diagnosis change from mood disorders to schizophrenia.

Table 3 illustrates the quantitative variables in patients with and without change of diagnosis from mood disorder to schizophrenia.

Neither of the demographic features in the two groups showed a meaningful statistical difference .However, from the clinical features point of view, more accompaniment with psychotic features (p=0.001), more severity of illness (p=0.016), positive familial history of schizophrenia (p=0.022) and the gradual start of the illness (p= 0.027) had a meaningful statistical relationship with change of clinical diagnosis.

Discussion

This study showed that from the 176 patients, changing from mood disorders to schizophrenia occurred in 55 patients (31.3%). This difference had no meaningful statistical difference (P value: 0.304). A more careful assessment of all the patients affected with MDD and BID, showed a change to schizophrenia in 23.3% and 32.9% of the cases respectively .

The results from this study had a close resemblance to most of the studies in this field. This can be an indication of high probability of the change of mood disorder diagnosis. However, we need a more complete assessment to find the reasons for this phenomenon. We have no special clinical variance to determine or show the change of diagnosis from mood disorders to schizophrenia at the time, however, there are some demographic and clinical variables that may determine the change of clinical course of the illness (10-12).

In our study, no meaningful statistical difference was observed between the demographic features including age, gender, marital status and educational level between the patients with and without change of diagnosis. This result is not in agreement with some other studies .

In one study in Ireland (1995-1999) on the patients affected with schizophrenia and mood disorders, it was showed that diagnosis of the one fourth of these patients changed during the study and the most common new diagnosis was schizophrenia. More diagnostic change was associated with less education, lower level of primary psychopathology and more alcohol and substance abuse (13). Therefore, the symptoms of prodromal phase of schizophrenia could be related to low education level of the patients. On the other hand, the lower level of primary psychopathology might be attributed to difficulty of diagnosis, severity of symptoms at first admission, and difficulties in differential diagnoses which may lead to instability of diagnosis.

It should be noted that we did not study alcohol and substance abuse in this research. The rarity of patients with education levels more than high school diploma in our study makes it difficult to arrive at a precise conclusion.

Kessing showed that female and younger patients may be diagnosed with schizophrenia later (14). Jarbin et al also suggested when the adolescents were diagnosed as schizophrenic or as having psychotic mood disorder, this would be a more stable diagnosis ; and when there is a diagnostic change to schizophrenia, often a history of non-mood psychosis exists in the relatives (15). The existence of atypical psychotic features in adolescents supports the diagnosis of a mood disorder more than a psychotic one (16). For interpreting the role of age and gender a study with larger sample size should be conducted. In addition, adolescence with its special characteristics necessitates a special interpretation different from other age groups .

Using logistic regression to detect and delet confounders have showed that psychotic features, clinical severity of disorder and pattern of beginning were significantly associated with diagnostic change respectively. On the other hand, atypical, melancholic and catatonic features, improvement status, existence of disorders in Axis II and number of hospitalizations were not significantly associated with diagnostic change .

There are few studies dealing with the diagnostic shift from mood disorder to schizophrenia but most of them place great emphasis on more stability of mood psychosis (2, 4, 6, 17). However different statistics have been presented in different studies performed all over the world on stable diagnosis. Lars Vedel Kessing performed a research in Denmark by which he studied all patients who referred to the psychiatry clinic with the initial diagnosis of bipolar disorder during 1994-2004 and finally he observed that diagnoses of 30% of the patients have been shifted to schizophrenia (14). In the same research, Kessing indicated that 16% of the patients suffering from major depressive disorder finally shifted to schizophrenia (18).

In the Veen's study, 49% of the patients suffering from schizophrenia had not received such diagnosis, but they reached schizophrenia diagnosis in time. The stable diagnosis was 91% for schizophrenia and 67% for psychotic mood disorder(19).

Shwartz et al (4) showed that diagnostic stability for schizophrenia, psychotic bipolar disorder, and major depressive disorder were 92%, 83%, and 74%, respectively. Patients with and without diagnostic shift to schizophrenia were not significantly different in their demographic characteristics and family history of schizophrenia. A small percent of shifted patients used antipsychotic drugs prior to their first hospitalization. The group with diagnostic shift had a better function in the year prior to admission, less positive and negative symptoms, less drug abuse in their lifetime, poorer psychosocial adaptation in their adolescence, and longer time from onset of psychosis to hospitalization. The other group, whose diagnoses were not changed stayed longer in the hospital during their first hospitalization, had more provisional diagnosis of schizophrenia, and more severe negative symptoms. Generally, the following factors suggested a shift to schizophrenia: poorer psychosocial adaptation in adolescence, no lifetime drug abuse, more than three months from onset of psychosis to hospitalization,

more provisional diagnosis of schizophrenia, longer hospitalization, anti-psychotics being prescribed at the time of discharge and observing more negative symptoms six months after discharge. Existence of at least five of the above risk factors indicates a shift to schizophrenia in the next 24 months in at least 50% of the cases. Among mood disorders, more diagnostic stability was for psychotic bipolar disorder than major depressive one (4).

Above risk factors along with what was found in our study such as more psychotic features, more clinical severity, and insidious onset of disorder are associated with poorer prognosis of mood disorders. Positive family history of schizophrenia could be an important feature for biologic and genetic factors in diagnosing schizophrenia .

On the severity of the disorder, it should be mentioned that usually patients with more severe disorders are hospitalized. Therefore, any interpretation regarding severity should be made with caution.

Longitudinal studies indicate diagnostic changes and changes in the pattern of manifestation of symptoms with passing the time(20). Diagnostic shift may be a result of the change in the course of disease, increasing the diagnostic information and emergence of new diagnostic tools (4). One of the most important variables for diagnostic stability is the clinical instrument used for diagnosis. Therefore, more study length may lead to more shifts in diagnoses .

Hospitalized patients are those who take more stable diagnoses than outpatients and emergency patients (4). Assessing the patients and their families when they are hospitalized is more convenient and more feasible than when they are in outpatient and emergency facilities(21). On the other hand, when the patient has more severe symptoms, leading them to be hospitalized, making an accurate diagnosis is more convenient and therefore more stable than when he/ she is in outpatient setting. Patients with more unstable symptoms make more contacts with psychiatric clinics and it's more probable for them to receive an incorrect diagnosis which may lead to inappropriate treatments and repeated visits to psychiatric clinics (9, 14). In this regard, the benefit of having hospitalized participants is the strength of our study.

Brief and acute onset psychosis takes more stable diagnoses. In developing countries, these kinds of psychotic disorders seem to be more common than in the developed world. Some of our patients might suffer from these disorders but may have been diagnosed with bipolar disorder in their first admission. They have a better prognosis and less relapse rate (11, 22-25).

Stability of diagnosis may be the result of the time of the next appraisal. In Fragus and his colleagues' study the agreement between initial and the first year diagnoses for schizophrenia and psychotic mood disorder was 95% and between the first and the second year diagnoses was 54% (26).

Conclusion

Diagnostic instability in psychiatry and especially in patients with mood disorders is common. Recognition of clinical variables accompanied by high probability of changing mood disorders to schizophrenia can be effective in the final prognosis of clinical situations .

In spite of all of the limitations in this study, existence of some variables such as more accompaniments with psychotic features, more severity of illness, positive familial history of schizophrenia and gradual start of illness may be accompanied by high probability of changing the diagnosis from mood disorders to schizophrenia .

One of the main limitations of this study was the retrospective evaluation with all of its defects. In spite of careful evaluation of all the files of the hospitalized patients and selection of patients only based on diagnosis criteria of DSM and based on psychiatrists' opinion , some of the acquired information may be insufficient and contradictory or even false. These limitations in retrospective studies can affect the results and conclusion of the study. We hope that the results of the recognition of the variables related to diagnostic stability in this study could be an opening and turning point for more expansive future-oriented studies.

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