Original Article

Genealogy Study of Three Generations of Patients with Bipolar Mood Disorder Type I

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ABSTRACT

Introduction: The purpose of this research is genealogy examination of three generation of bipolar mood disorder Type I patients. **Methods:** Patients selected using Poisson sampling method from 100 patients with bipolar mood disorder Type I, referring to a psychiatric center of Amir Kabir Hospital of Arak, Iran. Examine issues such as physical ailments, psychological review of living and deceased family members of each patient, drawn family pedigree using pedigree chart, check the relationship of the different pattern of the autosomal dominant and recessive disease, sex-linked dominant and recessive and linked to Y chromosome have been performed on patients. Different methods used in this study are pedigree chart and young mania rating scale and SPSS and Pearson's correlation test for analyzing the data collected. **Results:** Among the studied inheritance patterns, the most common inheritance pattern was autosomal recessive. There was a significant relationship between age, number of generation, and inheritance patterns with physical ailments in families of patients with bipolar mood disorder ($P < 0.05$), but there was no significant association with mental illness ($P > 0.05$). Furthermore, there was a significant relation between generation and skin, gastrointestinal, ovarian, lung, coronary heart disease, diabetes mellitus, hypertension, Cerebrovascular accident (CVA), hyperlipidemia, cardiomyopathy, hypothyroidism, and kidney disease in patients with bipolar affective disorder Type I ($P < 0.05$). **Conclusion:** The results showed that autosomal recessive was the most pattern of inheritance and there is a significant relationship between generation and some physical disorders in patients with bipolar mood disorder Type I.

Key words: *Bipolar disorder, family characteristics, genealogy, mood disorders, patients*

INTRODUCTION

Bipolar mood disorder Type I is a complex psychiatric disease that characterized by repeated episodes of depression and mania or hypomania. This disorder with its recurrent nature could be recurred or became chronic so that on the basis of some researches, the symptoms of this disorder does not recur in only 7% of cases.[1-3]

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The onset of bipolar mood disorder Type I has been typically reported in late adolescence or early adulthood with a period of depression after one or more cycles of depression with the occurrence of mania.[2,4-6] It is worth noting that not much information available in terms of the prevalence of bipolar mood disorder Type I in Iran, but Mohammadi *et al*.[7] reported the prevalence rates of

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bipolar disorder Type I and Type II about 1.0%–7.0% over the lifetime of Iranian adult population generally. Prevalence of bipolar depression in Iran has been reported 1% during 2011–2012 by Radgoudarzi *et al*.[7-9] Many research linked the causes of bipolar depression to environmental and biological factors; for example, some studies have shown that people with certain genes are more likely to develop bipolar disorder[8-11] and children with a family history of bipolar disorder are more at risk for this disorder than children who do not have this history.[10,12-14] As well as environmental stressors, inflammatory disorders, and immune system changes (the level of preinflammatory cytokines such as interleukin [IL]-1 and tumor necrosis factor alpha and some anti-inflammatory and regulatory cytokines such as IL-4, and 10 in people with bipolar disorder is significantly higher than healthy people), the volume loss of anterior cingulate gyrus, particularly gray matter, and decreased activity of orbitofrontal cortex and anterior cingulate are the other causes besides genetic factors that have been considered by researchers as causal factors for bipolar depression.[12,15-18] Finally, since various studies have been shown the strong genetic influence in the pathophysiology of bipolar disorder, it seems that further research among various races and communities, particularly in genetic relation to other diseases, could considerably help faster and more effective treatment of patients with this disorder, and so, this study aimed to survey the pedigree of three generations of patients with bipolar mood disorder Type I.

MATERIALS AND METHODS

This research is an analytical, observational study and patients selected using Poisson sampling method from 100 patients with bipolar mood disorder Type I referring during April–May 2013 to a psychiatric center of Amir Kabir Hospital of Arak city, Iran. The implementation of this research was conducted in three phases: The first step is to select the participants from patients referring to the psychiatric center of Amir Kabir Hospital of Arak, Iran, who were eligible for inclusion criteria and not eligible for exclusion criteria [Table 1]. In the second step, after obtaining informed consent from patients and their families (at all stages of study moral Declaration of Helsinki and moral decisions of the Ethics Committee of the Arak University of Medical Sciences has been considered), cases such as physical and psychiatric illnesses of living and deceased people in patient's family have been reviewed, and the pedigree for each family was drawn using pedigree chart. In the third step, using the different definitions of dominant and recessive autosomal pattern, sex-linked dominant and recessive and Y chromosome-linked in each pedigree and relation between each pattern that mentioned above along with a variety of mental and physical diseases were reviewed. The required tools to gather data used in this study were as follows.

Table 1: Inclusion and exclusion criteria

Inclusion criteria
Eligible for bipolar Type I disorder according to DSM-IV-TR
A minimum age of 18 and maximum of 65 years
Getting a score of 18 or higher on YMRS
Exclusion criteria
The dependence on drugs, except nicotine and caffeine
IQ below 70 3
Use of medications that have caused symptoms similar to mania such as antidepressant, antituberculosis, or cortisone
The patient or his family's unwillingness to continue participating in the study

YMRS – Young Mania Rating Scale; IQ – Intelligence Quotient; DSM-IV-TR – Diagnostic and Statistical Manual of Mental Disorders-4th Edition-Text Revision

Young mania rating scale

This 11-point scale is to measure the severity of mania designed by Young in 1987. Scoring is based on objective patient report about his medical condition in the last 48 h and objective observations of interviewer during the interview. Completion of this scale takes about 30–15 min. Each article in the scale scores between 0 and 4, expect four articles (irritability, speech, thought content, and aggressive behavior that weigh twice as much as other articles and scores between 0 and 8). In mania tests, the criterion for entry is score 20 or higher; further, score 12 and even score 7 based on some studies would be consider as the eve of the semi-mania.[18] In review of validity and reliability of this scale on Iranian specimens, it is shown that the reliability rate of questions with Cronbach's alpha method was 0.72 for patient group and 0.63 for normal group. Furthermore, the rate of diagnostic validity of the scores and canonical correlation was 0.92, and results of the validity of the questions showed that the accuracy of all questions in the resolution normal from patient group. Concurrent validity scale of young mania scale with a comprehensive diagnostic international questionnaire was 0.87 and for the first evaluation was 0.89 and for the second evaluation was 0.84.

Pedigree chart

Pedigree is a tree diagram of the relationship between the family inheritances that using symbols are able to demonstrate genetically relations between different generations of a family.[19]

In this study, we used SPSS (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, version 20.0. IBM Corp., Armonk, NY, USA) and Pearson's correlation test and a significant level of 0.05 to analyze the data.

RESULTS

The data showed that most patients with bipolar mood disorder Type I were at the age range of 26–35 years and that 60% of them were diagnosed with the disease at the age range of 15–25 years, 42% of the patients were married, and 47% of them had the education level of diploma to bachelor. Most patients had no history of head injury (97%), family marriage (71%), or underlying disease factor (60%). All the basic characteristics of our outpatients are listed in Table 2. The hereditary patterns of bipolar mood disorder have been studied and autosomal recessive inheritance had the most frequency [Table 3]. There was a significant relationship between patient age and number of generation [Table 4]. There was no considerable correlation between hereditary patterns and mental problems such as obsessive–compulsive disorder or paranoid schizophrenia in bipolar mood disorder Type I patients ($P > 0.05$). However, there was a significant relationship between the hereditary patterns and physical ailments in bipolar mood disorder Type I patients ($P < 0.05$) [Table 5]. In addition, the findings showed that relation between generation and skin cancer, gastric, ovarian, and lung in patients with bipolar mood disorder Type I was significant ($P > 0.05$) [Table 6]. There was no significant relation between generation and prostate and hematologic malignancies ($P > 0.05$) [Table 6]. Furthermore, the relation between generation and coronary heart disease, diabetes mellitus, hypertension, CVA, hyperlipidemia, cardiomyopathy, hypothyroidism, and kidney disease was significant in patients with bipolar mood disorder Type I (P value <0.05) but not significant between generation and brain tumor, thalassemia, and rheumatoid arthritis ($P > 0.05$) [Table 7].

Table 2: Frequency and percentile distribution of variables in patients with bipolar mood disorder Type I

	Percentile
Age	
15-25	11
26-35	35
36-45	20
46-55	22
56-65	12
Age at onset of disorder	
15-25	60
26-35	24
36-45	13
46-55	3
Marital state	
Single	36
Married	52
Divorce	12
Education	
Illiterate	9
Under Diploma	39
Diploma to Bachelor	47
Above Bachelor	5
The underlying disease	
Yes	40
No	60
Head trauma	
Yes	3
No	97
Familial marriage	
Yes (3rd generation)	9
Yes (above 3rd generation)	20
No	71
The number of patients with bipolar mood disorder Type I in the family	
1	54
2	36
3	7
4	1
5	1
6	1

DISCUSSION

As the findings of this study showed that the largest number of bipolar mood disorder Type I cases were married and their education level was between diploma to bachelor and disorder was started at early age, these findings are against of the findings of research that says this disorder is more common in single and divorced people with low education but are consistent with evidence that say symptoms of the disorder start

Table 3: Distribution of inherited features in three generations of bipolar mood disorder in patients with bipolar mood disorder Type I

Inheritance features of bipolar disorder	Distribution
Autosomal recessive	64
Autosomal dominant	11
Sex-linked dominant	1
Sex-linked recessive	5
Autosomal recessive + X-linked recessive	16
Autosomal dominant and autosomal recessive + sex-linked dominant	2
Autosomal dominant and autosomal recessive + X-linked recessive	1
Mitochondrial	0
Related to Y	0

Table 4: Distribution of relationship between generation and age of patients with bipolar mood disorder Type I

	15-25	26-35	36-45	46-55	55-65	*P*
No	4	23	11	17	1	0.002
1st generation	0	0	0	0	1	
2nd generation	5	8	3	0	4	
3rd generation	2	4	6	5	6	

Table 5: Comparison of inheritance patterns in families of patients with mental and physical diseases with bipolar mood disorder Type I

	Autosomal recessive	Autosomal dominant	Sex-linked dominant	X-linked recessive	Autosomal recessive + X-linked recessive	Autosomal dominant and autosomal recessive + sex-linked dominant	Autosomal dominant and autosomal recessive + X-linked recessive	Related to Y	Mitochondrial	*P*
Mental illness										
No	39	4	0	2	8	2	1	0	0	0.780
Obsessive–compulsive disorder	2	2	0	0	1	0	0	0	0	
PTSD	2	0	0	0	0	0	0	0	0	
GAD	12	4	1	2	2	0	0	0	0	
Major depression	7	0	0	1	5	0	0	0	0	
Paranoid schizophrenia	2	1	0	0	0	0	0	0	0	
Physical illness										
No	0	0	0	0	15	2	1	0	0	0.001
Malignancy	16	0	0	0	0	0	0	0	0	
Cardiovascular diseases	14	0	0	0	0	0	0	0	0	
Medical diseases	16	0	0	0	0	0	0	0	0	
Endocrine diseases	11		0	0	0	0	0	0	0	
Neurological diseases	7	2	0	0	0	0	0	0	0	
Rheumatoid arthritis	0	1	0	0	0	0	0	0	0	
Thalassemia minor	0	2	0	0	0	0	0	0	0	

PTSD – Posttraumatic stress disorder; GAD – Generalized anxiety disorder

Table 6: Comparison between generations and malignancies in patients with bipolar mood disorder Type I

	No	First	Second	Third	First and second	Second and third	*P*
Prostate							
Yes	0	-	1	-	-	-	0.01
No	99	-	0	-	-	-	
Hematologic							
Yes	0	1	-	-	-	-	0.01
No	99	0	-	-	-	-	
Skin							
Yes	0	1	1	-	-	-	0.001
No	98	0	0	-	-	-	
Gastrointestinal							
Yes	0	3	1	-	1	-	0.001
No	95	0	0	-	0	-	
Ovarian							
Yes	0	-	1	1	-	-	0.001
No	98	-	0	0	-	-	
Lung							
Yes	0	1	2	-	-	1	0.001
No	96	0	0	-	-	0	

before age 20 among the 60%of adult people.[6,20-23] In our study, history of head injury or family marriage had no considerable association with the presence of bipolar mood disorder; on the other hand, the study showed the relationship between the positive family history of bipolar mood disorder and occurrence of it in next generations. These results were against of studies, reporting that bipolar mood disorder are related to head injury during childhood but were consistent with researches that confirm bipolar mood disorder is related with the presence of another bipolar affective disorder patient in family.[22,24-26] There are few studies investigating the pattern of inheritance and locus of bipolar mood disorder gene in chromosomes. Our results are inconsistent with Homer *et al*.'s findings; they studied 52 families and reported that bipolar mood disorder under autosomal dominant model may relate to the chromosome 5 in the subset of families;[25] On the other hand, a trial in 1996 studied the possible role of dopamine transporter (DAT) in bipolar mood disorder. In this study, different polymorphisms of DAT locus were investigated and the highest load score belonged to 5' TaqI RFLP (HDAT-TaqI) under the autosomal recessive model; however, the authors of that article emphasized that the results were unsatisfied and more studies need to be done.[27]

CONCLUSION

Overall, our results indicated that among these study cases, autosomal recessive can be the answer of hereditary pattern for most of our subjects. In addition, there was a significant relationship between the age of the patient and number of generation in family and hereditary models with physical ailments in family of bipolar mood disorder patients but no significant relation with mental

Table 7: Comparison between generations and diseases in patients with bipolar mood disorder Type I

	No	First	Second	Third	First and second	Second and third	First and second and third	*P*
Cardiovascular								
Yes	0	1	4	-	5	-	1	0.001
No	89	0	0	-	0	-	0	
Diabet-melitus								
Yes	0	-	1	-	4	1	2	0.001
No	92	-	0	-	0	0	0	
Brain-tumor								
Yes	0	1	-	-	-	-	-	0.001
No	99	0	-	-	-	-	-	
Hypertension								
Yes	0	-	1	-	3	-	2	0.001
No	94	-	0	-	0	-	0	
CVA								
Yes	0	4	2	-	3	-	-	0.001
No	91	0	0	-	0	-	-	
Hyperlipidemia								
Yes	0	1	2	-	2	1	2	0.001
No	92	0	0	-	0	0	0	
Cardiomyopathy								
Yes	0	1	2	-	-	-	-	0.001
No	97	0	0	-	-	-	-	
Hyperthyroid								
Yes	0	1	2	-	-	-	-	0.001
No	97	0	0	-	-	-	-	
Thalassemia minor								
Yes	0	-	1	-	-	-	-	0.01
No	99	-	0	-	-	-	-	
Rhomatoid-artheraitis								
Yes	0	-	1	-	-	-	-	0.01
No	99	-	0	-	-	-	-	
Kidney diseases								
Yes	0	-	2	-	-	-	-	0.001
No	98	-	0	-	-	-	-	

CVA – Cerebrovascular accident

illness.[28-31] There was a significant relation between generation and skin cancer, gastric, ovarian, lung, coronary heart disease, diabetes mellitus, hypertension, CVA, hyperlipidemia, cardiomyopathy, hypothyroidism, and kidney disease in bipolar mood disorder Type I patients but no significant relation between generation and brain tumor, thalassemia, rheumatoid arthritis, prostate, and hematologic malignancies.[32-34] Finally, since the results of this study as well as the other studies showed that genetic factors play a decisive role in the disorder and physical disorders associated with it, so it is recommended that for drug therapy in the treatment of this disorder, to achieve therapeutic results, it is better to prescribe drugs with better positive influence on the genetic origin of this disorder.

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Conflicts of interest

There are no conflicts of interest.

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