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Original article

A Study of Risk Factors and its Role in Recurrence in Bipolar Disorder

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Abstract:

Background: Bipolar disorder is a serious condition with bouts of depression, mania or hypomania and there is different risk factors shared in recurrence of the bouts of the disease and there is a trial to always identify importance of each. This study aimed to identify various risk factors that precipitate early recurrence of bipolar episodes and the detection of predictive role of each risk factor in recurrence of bipolar disorder. **Methods:** This Cross-sectional study included fifty patients diagnosed as having bipolar disorder. All studied cases were subjected to the following: semi-structured interview including, Clinical examination, SCID-I, presence or absence of risk factors of recurrence, and pilot. **Results:** There was a highly statistically significant difference regarding occupation among the studied group of bipolar patients (P = 0.024). High statistically significant difference between marital status and bipolar disorder recurrence (P = 0.036). Regarding education there was a statistically significant difference as most of our cases were school students (P = 0. 037). **Conclusion:** A strong prediction was revealed between relapse rates and age which was significant in age group ≥ 40 years and with male gender and occupational status mainly for retired, housewife and employee, sexual satisfaction, current medical comorbidity and positive compliances to medicines and greater associations were revealed for communication problems, premorbid mood swings, also inverted sleep rhythm, also strong prediction was revealed between divorced, postgraduate participants or only once psychiatric admission than multiple (≥3 times).

Keywords: Risk Factors; Recurrence; Bipolar Disorder; Bipolar Episodes

Introduction

Bipolar disorder is a serious condition with bouts of depression, mania or hypomania and there are different risk factors that share in recurrence of the bouts of the disease, and we try to identify importance of each. These different risk factors including; depression during pregnancy, postpartum depression, family history of bipolar disorder, personality disorder, season (spring, summer, autumn and winter), compliance, subsyndromal symptoms (mood swing- behavioral changes), disruption of biological rhythm as (travel- shift work), life stressors (mental, family, work, economic, grief, others), premorbid mood swing, poor social, sleep disturbance, change in mood, behavior, sex, marital status, education, occupation, number of recurrence, type of bipolar, type of treatment and cessation of treatment; psychiatrists try to outline each factor's role in recurrence of bipolar disorder [1, 2].

The idea of a relationship between melancholy and mania can be traced back to the Ancient Greeks, and particularly to Aretaeus of Cappadocia. The modern psychiatric concept of bipolar disorder has its origin in the nineteenth century [3].

The term "bipolar disorder" (or 'bipolar affective disorder') is thought to be less stigmatizing than the older term 'manic-depressive illness', and so the former has largely superseded the latter. However, some psychiatrists and some people with bipolar disorder still prefer the term 'manic-depressive illness' because they feel that it reflects the nature of the disorder more accurately [4].

Bipolar disorder does not appear to have a single cause, but is more likely to result from a range of factors that interact [5].

Some studies have suggested that there may be a genetic component to bipolar disorder. It is more likely to emerge in a person who has a family member with the condition, patients with bipolar disorder often show physical changes in their brains, but the link remains unclear. Neurotransmitter imbalances appear to play a key role in many mood disorders, including bipolar disorder. For adult bipolar disorder, there are now five possible diagnosis including bipolar I disorder, bipolar II disorder, cyclothymic disorder, substance, induced bipolar disorder, bipolar disorder associated with another medical condition and bipolar disorder not elsewhere classified [6].

In bipolar I; patients had at least one manic episode to be diagnosed with bipolar I, and patient may or not have a major depressive episode, while in bipolar II; patient with major depressive episode lasting at least two weeks and at least one hypomanic episode. Patient with bipolar two typically do not experience manic episode intense enough to require hospitalization, but in cyclothymia; it was observed that it is a rare mood disorder, which has similar characteristics of bipolar disorder, just in a milder and chronic form with symptoms of hypomania- a less severe form of mania and symptoms of mild depression- not characterized of full major depression, patient with <2 months free period [7].

Treatment of bipolar disorder aims to minimize the frequency of manic and depressive episodes, and to reduce the severity of symptoms to enable a relatively normal and productive life [8].

Treatment involves a combination of therapies, which may include medications and Electroconvulsive therapy (ECT) and psychological interventions [9]

The purpose of this study was to identify various risk factors that precipitate early recurrence of bipolar episodes and detection of predictive role of each risk factor in recurrence of bipolar disorder.

Patients and methods

This cross-sectional study included fifty patients diagnosed as having bipolar disorder. The study was conducted at Psychiatric outpatient clinic of Benha University Hospital, outpatient clinic and inpatient ward of Benha and Menoufia

Mental Hospitals, during the period from January 2021 to March 2022.

Each patient filled a formed consent to participate in this study. The study was done after being approved by the Research Ethics Committee, Faculty of Medicine, Benha University.

Inclusion criteria were patient diagnosed as a case of bipolar disorder in a recurrent episode according to DSM – IV, who have substance induced mood disorder, age > 18 years old, male or female.

Exclusion criteria were age < 18 years old, patients with comorbid psychiatric condition for example, Schizophrenia, OCD, mental sub normality IQ < 70, medical and neurological disease.

All studied cases were subjected to the following: semi-structured interview including, Clinical examination, SCID-I, presence or absence of risk factors of recurrence, and pilot study.

A semi-structured interview including:

Using full psychiatric sheet of Psychiatric Department in Benha Faculty of Medicine. Occupations were classified according to skill level and International Standard Classification of Occupations that organized jobs into sub-groups according to tasks and duties undertaken into a) Unemployed, b) Employed, which was classified into: 1] Semiskilled that does not require advanced training or specialized skills and 2] Skilled whom is any worker had a special skill, training or knowledge.

SCID-I: Structural clinical interview for DSM-IV axis I disorder (SCID-I); Arabic version was used (El Missiry et al., 2004): for axis I diagnosis of bipolar disorder and exclusion of other comorbid psychiatric disorders. It is administered in a single setting and takes 90-105 minutes to be completed, depending on the psychiatric history, the awareness of the patient to his symptoms and the experience of clinician.

It contains nine diagnostic modules: 1. Mood Episodes, 2. Psychotic and associated symptoms, 3. Psychotic disorders differential, 4. Mood disorders differential, 5. substance use disorders, 6. Anxiety and other disorders, 7. Somatoform disorders, 8. Eating disorders, 9. Adjustment disorders.

Scoring is made on a 3-point rating as follows: (?) = inadequate information, (-) = absent or subthreshold information, (+) = present.

Presence or absence of risk factors of recurrence:

By using a questionnaire which was specially tailored for the study covering all risk factors which will be fulfilled by bipolar disorder patients, informant and psychiatrist, it included the following items:

Depression during pregnancy, postpartum depression. Family history of bipolar disorder. Season (spring, summer, autumn and winter) of last episode. Compliance with medications, or discontinuation of medications. Subsyndromal symptoms (Mood swing- Behavior). Disruption of biological rhythm (Travel- Shift work). Life stressors (Mental, family, work, economic, grief). Premorbid mood swing. Social support. Sleep disturbance. Change in mood, behavior. Substance abuse. Previous suicidal attempt or suicidal ideation. Limited access to support or clinical services.

Pilot study: A pilot study including 10 patients to test the questionnaire took place for three weeks before the actual fieldwork started to assess clarity of questions and semi-structured interview and questionnaires and to exclude any difficulties during the interview. Some adjustments were made in the questionnaire to make it more obvious specially meaning and definition of some questions. This pilot study was done by supervisors of this research.

Approval code: Ms 2-9-2020

Statistical analysis

Statistical analysis was done by SPSS v26 (IBM Inc., Armonk, NY, USA). Categorical data were expressed as number and percentage using 'chi square', Fisher's exact test or 'Z' test for analyzing them. Odds ratios were computed to detect the

risk factors. Continuous variables were presented as mean and standard deviation using the ‘Student t' test for their analyses. The accepted level of significance in this work were 0.05, (P< 0.05) were considered significant).

Results

There was a highly statistically significant difference regarding occupation among studied group of bipolar patients (P = 0.024). High statistically significant difference between marital status and bipolar disorder recurrence (P = 0.036). Regarding education there was a statistically significant difference as most of our cases were school student (P = 0. 037). On the other hand, there was no statistically significant difference regarding other items of socio demographic data and seasonal occurrence. Concerning length of stay, the table shows highly statistically significant differences (P-value = 0.037) more in patients who had previous two weeks extend of their stay in psychiatric department’s ward 16 participants. Regarding types of mood of last bipolar episode, there were highly statistically significant differences (P-value = 0.049) more in patients with mixed episode 22 participants. Regarding the number of recurrence episodes, there were highly statistically significant differences (P-value = 0.047) in patients who had less than three recurrent episodes. Table 1

There were statistically significant differences (P-value= 0.043) regarding current medical comorbidity (hypertension, diabetes mellitus). Regarding sexual satisfaction there were statistically significant differences (P-value = 0.046) in patients who were sexually satisfied. There were statistically significant differences regarding the compliance to psychotropic treatment (Antidepressant, Mood stabilizers, Antipsychotics, Others) (P-value = 0.04).

The table shows statistically significant differences (P-value = 0.044) higher in patients who were not substance abusers 42 participants (84%), where only 8 participants (16%) had reported their substance abuse, which was tramadol and THC addiction only, in the same context no patient reported addiction to amphetamine, barbiturate, benzodiazepines, morphine, cocaine. There were statistically significant differences (P-value = 0.047), where most participants had not recorded previous suicidal ideas and/ or attempts 37 participants (74%). On the other hand, there were no statistically significant differences regarding financial problems and type of treatment (Psychotropic, Electroconvulsive, Both). Table 2

There were statistically significant differences regarding depression during pregnancy (P = 0.006), postpartum depression episodes (P= 0.005), life stressors (P= 0.038). Regarding positive family history of mood disorders, there were statistically significant differences (P-value = 0.042), where in most cases 32 participants (64%) had no family history of any mood disorders. There were statistically significant differences (P-value = 0.045) regarding limited access to clinical support, where in most cases 42 participants (84%) had no restrictions in access to clinical psychiatric services and regarding social environment support (P= 0.056). Table 3

Table 1: Comparison of socio-demographic characteristics and risk factors related to admissions and last episode characteristics of the bipolar disorder patients in remission

Item		Number	Percentage	P-value
Age 'years'				
<40 years		19	38%	0.64
≥40years		31	62%	
Residence	Rural	21	42%	0.61
	Urban	29	58%	
Gender	Female	20	40%	0.63
	Male	30	60%	
Occupation	Non-Employee	9	18%	0.024*
	Employee	41	82%	
Marital Status	Single	17	34%	0.036*
	Married	24	48%	
	Widow	6	12%	
	Divorced	3	6%	
Education	Illiterate	15	30%	0.037*
	Student	16	32%	
	University	13	26%	
	Postgraduate	6	12%	
Number of Previous	None	21	42%	0.052*
Psychiatric	2 times	9	18%	
Admission	Multiple ≥3 times	20	40%	
Length of Stay For 29 participants only (who were admitted to hospitals from whole participants)				
around Two weeks		16	32%	0.037*
Around Eight weeks		13	26%	
Mood Classification	Manic episode	21	42%	0.047*
of last episode	Depressed episode	7	14%	
	Mixed episode	22	44%	
Season of last	Autumn	15	30%	0.47
episode	Winter	10	20%	
	Spring	12	24%	
	Summer	13	26%	

Table 2: Comparison of variables related to bipolar disorder patients in remission, clinical characteristics and subsyndromal symptomatic characteristics.

Item	Number	Percentage	P-value
Current medical comorbidity	18	36%	0.043*
Financial problems	28	56%	0.54
Sexual Satisfaction	33	66%	0.046*
Type of treatment			
Psychotropic	33	66%	0.63
Electroconvulsive	14	28%	
Both	3	6%	
Compliances to Psychotropic Medication	3	6%	0.04*
Smoking	14	28%	0.049*
Substance Abuse	:8	16%	0.044*
Suicidal attempts and ideas	13	26%	0.047*
Subsyndromal symptomatic characteristics			
Mood swings	11	22%	0.054*
Premorbid mood swings	14	28%	0.049*
Sleep disturbances	38	78%	0.043*
Inverted sleep rhythm	15	30%	0.048*
Changes in behavior	13	26%	0.043*

Table 3: Variables related to life events, pregnancy and family characteristics in the bipolar disorder patients in remission and Variables related to social circumstances and limited access to clinical service in the bipolar disorder patients in remission

Item	Number	Percentage	P-value
Depression during pregnancy	1	4%	0.006*
Post-partum depression episodes	1	4%	0.005*
Life Stressors	18	36%	0.038*
Family history of mood disorders	18	36%	0.042*
Social circumstances and limited access			
Limit access to clinical service	8	16%	0.045*
Social Environment support	18	36%	0.054*
Communication Problems with surroundings	30	60%	0.038*

*: statistically significant as P value <0.05

A strong prediction was revealed between age and episode recurrence as the Odds ratio of recurrent bipolar episode were (0.95{95% CI; 1.32; 2.74}), which was significant in age group ≥ 40 years (62%). Besides a strong prediction revealed between gender and occupation and recurrence as the Odds ratio of recurrent bipolar episode were (0.83{95% CI; 1.34; 1.31}) and (0.86{95% IC; 0.41; 0.63}) respectively, which was significant higher in male 60% and Employee 82%. On the other hand, there was poor prediction was revealed between region of residence and episode recurrence as the odds ratio of recurrent bipolar episode were 1.37 (95% CI; 0.36; 0.74) which was non-significant. Table 4

There was a strong statistically significant association revealed between current medical comorbidity and recurrence (0.36{95% CI; 1.34; 2.81}). On the other hand, table shows there was a good prediction correlation in case of sexual satisfaction as the odd ratio was 0.76(95%CI; 0.74; 0.78). As well, table shows a good prediction correlation to treatment by electroconvulsive as the odds ratio was 0.36(0.61; 0.78), which was null in case of both (ECT with Psychotropic) as the odds ratio was 1.96 (0.89; 6.68). There was a strong association determined for participants, who had compliances to psychotropic medication (Antidepressant, Mood stabilizers, Antipsychotics, Others) with bipolar disorder recurrent episodes where odds ratio was 0.27 (95% CI; 0.08; 0.92). There was weak prediction correlation for suicidal ideas and attempts as the association detected with recurrence as the odd ratio was 0.73 (95% CI; 0.46; 1.14). There was poor prediction for financial issues with recurrent episodes as odds ratio recorded was 0.84(95% CI; 0.68; 0.86) which was non-significant. there was good prediction correlation in case of Inverted sleep rhythm as the association detected with recurrence as the odd ratio was 0.71 (95%CI; 0.85; 1.84). Table 5

There was good association detected between life stressors which include (Mental, family, economic, grief, interpersonal separations, loss of self-esteem, afraid of defamation, loss of social prestige and death of loved one) with recurrent episodes of bipolar disorder as the Odds ratio was 0.43 (95%CI; 1.34; 1.85). Good association determined for participants who had positive family history of mood disorders with bipolar disorder in recurrent episodes where Odds ratio was 0.52 (95% CI; 0.63; 1.93). In addition, there was a non-significant association detected between depression during pregnancies and postpartum depression revealed with recurrence episodes of bipolar disorder as the odd ratio was 0.97 (95%CI; 0.09; 0.84) 0.86(95%CI; 0.85; 0.95). There was good significant association determined for participants who had limited access to psychiatric clinic services where odds ratio was 0.73 (95% CI; 0.56; 1.45). Limited

access to clinical service linked to lack of mental healthcare services in rural areas, financial resources, fragmented care, fear of stigma, lack of education and awareness mental healthcare services while social environmental support include patience, love, and understanding bipolar disorder deeply which can play a significant part in treatment and recovery. Also, that there was good prediction correlation between social environment support, odd ratio was 0.42 (95%CI; 0.92; 1.27). Table 6

Table 4: Privilege of socio-demographic characteristics, variables related to admissions and last episode characteristics of the bipolar disorder patients in remission

Item		Number	Percentage	OR (95% IC)
Age 'years'				
<40 years		19	38%	1.00
≥40years		31	62%	0.95(1.32; 2.74)
Residence	Rural	21	42%	1.00
	Urban	29	58%	1.37(0.36;0.74)
Gender	Female	20	40%	1.00
	Male	30	60%	0.83(1.34; 1.31)
Occupation	Non-Employee	9	18%	1.00
	Employee	41	82%	0.86(0.41;0.63)
Marital Status				
Single		17	34%	1.00
Married		24	48%	1.03(0.50; 1.78)
Widowed		6	12%	1.35(0.74; 1.25)
Divorced		3	6%	0.21(0.31; 0.63)
Education				
Illiterate		15	30%	1.00
Primary/ secondary		16	32%	1.03(0.64; 1.72)
University		13	26%	1.01(0.54; 1.94)
Postgraduate		6	12%	0.75(0.24; 1.76)
Number of Previous Psychiatric Admissions				
None		21	42%	1.00
2 times		9	18%	0.17(0.63; 1.49)
Multiple ≥3 times		20	40%	1.00(0.62; 1.74)
Length of Stay				
For 29 participants Only				
Around Two weeks		16	32%	1.00
Around Eight weeks		13	26%	0.73(0.46; 1.48)
Mood Classification of last episode				
Manic episode		21	42%	1.00
Depressed episode		7	14%	1.23(0.76; 1.84)
Mixed episode		22	44%	1.36(0.65; 2.68)
Number of recurrences of bipolar disorder				
< 3 times		21	42%	1.00
3 - 6 times		18	36%	0.19(0.62; 1.48)
> 6 times		11	22%	1.00(0.62; 1.74)
Season of last episode				
Autumn		15	30%	1.00
Winter		10	20%	1.06(0.62; 2.01)
Spring		12	24%	1.09(0.60; 1.91)
Summer		13	26%	1.65(0.36; 1.27)

Table 5: Privilege of variables related to bipolar disorder patients in remission and clinical characteristics and Privilege of variables related to subsyndromal symptomatic characteristics in the bipolar disorder patients in remission

Item	Number	Percentage	OR (95% IC)
Current medical comorbidity	18	36%	036(1.34; 2.81)
Financial problems	28	56%	0.84(0.68; 0.86)
Sexual Satisfaction	33	66%	0.76(0.74; 0.78)
Type of treatment			
Psychotropic	33	66%	1.00
Electroconvulsive	14	28%	0.36(0.61; 0.78)
Both	3	6%	1.96(0.89; 6.68)
Compliances to Psychotropic Medication	3	6%	0.27(0.08; 0.92)
Smoking	14	28%	0.61(0.45; 1.16)
Substance Abuse	8	16%	0.66(0.84; 1.64)
Suicidal ideas and attempts	13	26%	0.73 (0.46; 1.14)
Mood swings	11	22%	1.31(0.84; 2.13)
Inverted sleep rhythm	15	30%	0.71(0.85; 1.84)
Premorbid mood swings	14	28%	0.61(0.45; 1.16)
Sleep disturbances	38	78%	0.91(0.74; 1.82)
Changes in Behavior	13	26%	1.35(0.78; 1.82)

Table 6: Privilege of variables related to life events and family characteristics in the bipolar disorder patients in remission and Privilege of variables related to social circumstances in the bipolar disorder patients in remission

Item	Number	Percentage	OR (95% IC)
Depression during pregnancy	1	4%	0.97(0.09; 0.84)
Post-partum depression	1	4%	0.86(0.85; 0.95)
Life Stressors	18	36%	0.43(1.34; 1.85)
Family history of mood disorders	18	36%	0.52(0.63; 1.93)
Limit access to psychiatric clinic	8	16%	0.73 (0.56; 1.45)
Social Environment Support	18	36%	0.42(0.92; 1.27)
Communication Problems with surrounding	30	60%	0.83(0.67; 0.58)

Discussion

Concerning socio-demographic characteristics of bipolar patient present in our study we found that the mean age was (31.41±5.1) years old, for patients aged less than 40 and (47.7±3.67), for other patients aged equal or more 40 years old, which shows no statistically significant differences regarding the age. Furthermore, we found a strong prediction between age and episode recurrence, with significance of 62% in patients aged ≥ 40 years, which is conflicted with another study recorded that bipolar disorder transcends distinct age boundaries [10, 11].

Most of our patients under the study were males. There were no statistically significant differences regarding gender, while our results had revealed strong prediction to episodes recurrence, and these was significant higher in male gender. However, numerous published trials reported a conflicting gender incidence, where females are at higher risk [12].

Regarding admission, there were highly statistically significant differences more in patients who were never admitted to a psychiatric department ward than the remaining patients where 21 participants were never admitted, 20 participants were admitted more than 3 times, and 9 participants were admitted for 2 times. Concerning length of stay there was a highly statistically significant difference more in patients who had previous two

weeks extend of their stay in psychiatric department's ward than the remaining patients who had previous eight weeks extend of their stay in psychiatric department's ward. On the other hand, patients who had previously been hospitalized for eight weeks played a role in predicting bipolar disorder recurrence.

Our results came in agreement with other recent studies those recorded no-superiority were detected for manic or depressive even mixed episodes with bipolar disorder episode recurrences [13, 14].

Regarding number of recurrence episodes, there were highly statistically significant differences (table 3) more in patients who had less than three recurrent episodes than other patients who had (3-6 times) or (> 6 times). On the other hand, In our study we found strong prediction only with (3-6 times). Regarding seasonal episodes there was no statistical association or prediction revealed for type of season (autumn, winter, spring and summer) with recurrent episodes.

In agreement with our results previous study had recorded no association was found between season, mood classification and disorder prognosis or episodes recurrences [14].

In our study the current medical comorbidity had a strong prediction with recurrence of bipolar disorder. Regarding current medical comorbidity there was statistically significant difference more in patients free of any comorbid medical diseases (hypertension & diabetes mellitus).

Our results came in agreement with another study about the multiple medical comorbidities associated with bipolar disorder episodes recurrences, co-occurrences adding significant complexity to the care of patients with bipolar disorder. This study also found several patterns of associations between bipolar disorder episodes recurrences and medical conditions [15].

There were no associations revealed for mood swing or changes in behavior (impulsive & hyperactive behavior) with recurrent episodes where most of our sample 78% had no mood swing and 74% had no changes in behavior. On the other hand, another study not in agreement with us found that changes in mood or behavior might be premonitory symptoms. As well, those could be clinical features for other psychological or mental disorders thus might be classified as premorbid symptoms [16].

There was good prediction for inverted sleep rhythm with bipolar disorder recurrent episodes and 70% of our cases had no inverted sleep rhythm and this was statistically significant. Regarding sleep disturbances (Insomnia, Hypersomnia) there was statistically significant difference as 78% of bipolar patient recurrent episode had sleep disturbances but there was a weak prediction for sleep disturbances with bipolar disorder recurrent episodes. This finding could be interpreted by chronic unstable circadian rhythm disturbances and continual fluctuations in bipolar patients' energetic levels those influence their episodic recurrences [17].

Regarding Life Stressors 'Mental, family, economic, grief, interpersonal separations, loss of self-esteem, afraid of defamation, loss of social prestige and death of loved one. We found only 36% had reported various sorts of life stressors had been forced.

There was good association detected between various checked life stressors with recurrence episodes of bipolar disorder.

In agreement with our results findings, other study has reported that bipolar adults usually could contribute to worse overall surrounding life stressors those are associated with increased risk of recurrence [18].

There was good prediction as a risk factor between social support with bipolar disorder recurrent episodes as most of our sample 64% had no social support and this

is statistically significant differences while only 36% had social support.

In the UK, numerous groups such as the Manic Depression Fellowship provides both support and educational material to patients and their families [5].

Conclusion

A strong prediction was revealed between relapse rates and age which was significant in age group ≥ 40 years and with male gender and occupational status mainly for retired, housewife and employee, sexual satisfaction, current medical comorbidity and positive compliances to medicines and greater associations were revealed for communication problems, premorbid mood swings, also inverted sleep rhythm, also strong prediction was revealed between divorced, postgraduate participants or only once psychiatric admission than multiple (≥3 times). As well a significant association in detecting episodes recurrence mainly for whom admitted for around eight weeks. On the other hand, a good prediction correlation to positive family history, life stressors, limited access to clinical psychiatric services, social environments and treatment by electroconvulsive or medicines, while moderate associations were revealed for substances abuse with recurrent episodes.

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