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ORIGINAL ARTICLE

A Study of Oxytocin Levels in a Sample of Bipolar Affective Disorder

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Background Bipolar disorder is characterized by mood swings with both manic and depressive symptoms. Social cognitive abnormalities have recently been recognized as a core feature of mood disorders, which persist during remission. The neuropeptide oxytocin may be a trait marker of bipolar disorder, and its dysregulation might be involved in the pathophysiology of bipolar disorder.

Aim To find out and compare oxytocin levels between cases of bipolar I disorder and a control group and to estimate predictors of susceptibility and remission of patients with bipolar I disorder.

Patients and Methods A total of 45 patients with bipolar I disorder and 30 age-matched and sex-matched healthy controls were examined. Structured Clinical Interview for DSM Disorders I was used to rule out any pathology in the control group and to confirm the diagnosis of bipolar I disorder in the cases. Furthermore, Beck depression inventory and Young mania scale were completed by the cases. Salivary oxytocin hormone levels were measured in all participating individuals.

Results Patients with bipolar I disorder, whether in depression, mania, or remission, showed higher significant levels of oxytocin when compared with controls, where manic cases showed significantly higher level of oxytocin when compared with depressive and remittent cases.

Conclusions Higher oxytocin levels were suggested to be a predictor for bipolar disorder or mania development, and lower levels of oxytocin might predict remission but do not predict the severity of the disorder.

Keywords Affective disorder, Beck depression, Biomarker, Bipolar disorder, Oxytocin, Young mania.
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INTRODUCTION

Bipolar disorder is a major health concern, characterized by mood episodes, namely, periods of elevated or irritable mood, referred to as mania, periods of depression, and mixed manic and depressed states (American Psychiatric Association, 2013).

The 1-year prevalence of bipolar disorder in Egypt was 2.7% according to the National Survey for Mental Health in Egypt (2017) (Odejimi *et al.,* 2020).

The neuropeptide oxytocin has attracted great attention among the general public, basic neuroscience researchers, psychologists, and psychiatrists owing to its profound prosocial, anxiolytic, and 'antistress' behavioral and physiological effects and its potential application for treatment of mental disorders associated with altered socioemotional competence. During the last decade, substantial progress has been achieved in understanding the complex neurobiology of the oxytocin system (Grinevich and Neumann, 2021).

By definition, patients with bipolar disorder would ideally be free from interepisode disturbance. However, reduced performance in neuropsychological tests is reported in euthymic patients with bipolar disorder (Kato, 2019).

Social cognitive abnormalities have recently been recognized as a core feature of mood disorders and correlate with illness load (i.e. illness duration and symptom severity), supporting the need for early intervention (Billeke and Aboitiz, 2013). It is also associated with lower

social functioning, higher disability, and poor prognosis. As these deficits are known to persist in the remitted state, patients may still have poor social adjustment owing to impairments in social cognition even during symptomatic remission from affective or psychotic episodes (Mercedes Perez-Rodriguez *et al.,* 2015).

Several lines of evidence suggest that the neuropeptide oxytocin may be a potential treatment for social cognitive deficits across diagnoses (Gumley *et al.,* 2014). Many studies review the evidence for social cognitive abnormalities in mood and psychotic disorders as well as the clinical trials of intranasal oxytocin administration across diagnoses and evaluate the evidence for improvement of social cognition across disorders (Cusi *et al.,* 2013).

Owing to the novelty of the role of oxytocin in bipolar disorder, this research study was conducted to evaluate the level of oxytocin in patients with bipolar disorder and to compare it with the level in normal healthy controls. Moreover, this study aimed to find whether oxytocin could serve as a biomarker for bipolar disorder.

PATIENTS AND METHODS

This was a comparative cross-sectional study conducted on 45 patients with bipolar I disorder, who are divided equally into depressive, manic, and remission cases, and 30 healthy controls who were matched for age, sex, residency, marital status, and occupational state. The recruited patients were selected from two psychiatric hospitals in Benha City (Benha University Hospital and Benha Mental Hospital). A Structured Clinical Interview for DSM Disorders (SCID) I for confirmation of diagnosis of bipolar 1 disorder, for exclusion of comorbidities, and for exclusion of any psychiatric disorders in cases and control groups was used. Further assessment using Beck depression inventory and Young mania scale was also performed. In addition, salivary oxytocin samples were obtained from all participants for assessment. The study subjects were informed of the possibility of using the data obtained for academic purpose.

Inclusion criteria were both sexes, aged 18 years and above, and patients on psychotropic medications provided the dose has not been adjusted in the last week. Exclusion criteria were age less than 18 years; female participants: currently pregnant or lactating, or with menstrual irregularities; patients with comorbid medical disorders (seizures and major head trauma); major illnesses (cancer, IHD, renal failure, or liver cell failure); endocrinal diseases (hypopituitarism, hyperprolactinemia, and thyroid disorders); neurological disorders that may affect mood, for example, DS; other comorbid psychiatric disorders, for example, schizophrenia, anxiety disorders, and history of substance abuse; and patients receiving any hormonal therapy or females using hormonal contraceptives; and patients taking drugs that might affect mood or oxytocin levels, for example, corticosteroids.

Tools

All participants (cases and controls) were subjected to the following:

1. Psychometric test measuring psychiatric disorders SCID-I was used for diagnosing the major Axis I DSM-IV disorders for all participants (First *et al.,* 1995). The Arabic version of the SCID-I was used in this study (El Missiry *et al.,* 2003).

2. Biological investigations included measurement of salivary oxytocin level.

Some participants were subjected to the following:

1. Beck depression inventory II for assessment of depression (Beck *et al.,* 1996) for only depressive patients or cases in remission. The Arabic version of the Beck depression inventory II used in this study was translated and validate d by Abdel-Khalik (2002).

2. Young mania rating scale (Young *et al.,* 1978) for only manic patients or cases in remission. The Arabic version of the Young mania rating scale used in this study was translated and validated by Abdel-Hamid *et al.,* (2018).

Ethical consideration

A consent was obtained from the patients and care givers, including data about the aim of the work, study design, site of the study, and tools used in it. It was explained to both groups that they can withdraw from the study at any time without any consequences and it will not affect the type of care they were receiving at the facility. It was also assured to all participants the confidentiality of results.

Statistical Analysis

The collected data were revised, coded, and tabulated using the Statistical Package for Social Sciences (IBM Corp, Released, 2011). Shapiro test, mean±SD, Student *t* test, Mann–Whitney test (*U* test), Kruskal–Wallis test, χ^2 test, Fisher's exact test, correlation analysis, and regression analysis were used. All reported *P* values were two-tailed, and *P* value less than 0.05 was considered to be significant (Greenberg *et al.,* 1996; Fischer *et al.,* 2003; Khothari, 2004).

RESULTS

Table 1 shows that 42.2% of the sample were males, whereas 57.8% were females, with a mean age of 33 years, ranging from 18 to 65 years. Among all studied cases, 37.5% were single, 55.6% were married, 4.4% were separated, and 2.2% were widowed. Regarding occupations, 17.8% had higher performance jobs, 20% were housewives, 22.2% were students, 8.9% were workers, 17.8% were clerks, 11.1% were unemployed, and 2.2% were retired. Regarding residence, 60% lived in rural areas and 40% lived in urban areas. No significant differences were found between studied cases and controls regarding age, sex,

marital status, and residence (P >0.05 for each). There was significantly higher frequency of smoking in patients with bipolar disorder when compared with the control group (P= 0.029).

Table 2 shows that regarding depression, the median Beck scale score was 34 and ranged from 14 to 51; 6.7% had mild, 13.3% had moderate, 46.7% had severe, 33.3% had extreme depression on the scale. Its median level decreased in remission cases to 6, ranged from 3 to 7. Regarding mania cases, the median young mania scale score was 34 and ranged from 23 to 54; all cases had manic degree. Its median level decreased in remission cases to 2 and ranged from 0 to 2.

From Table 3, it can be deduced that all oxytocin values in the current study were within normal range. However, the total number of bipolar cases, as well as depressive, manic, and remittent cases showed significantly higher levels of oxytocin when compared with the control group (P <0.001, P <0.001, P <0.001, and P= 0.002, respectively). Although manic cases showed significantly higher levels of oxytocin when compared with depressive and remittent cases (P= 0.015 and 0.007, respectively), the levels of oxytocin did not differ significantly between depression and remission cases.

Table 4 shows the logistic regression analysis for prediction of bipolar disorder susceptibility using age, sex, marital status, residence, education, smoking, and oxytocin level. Smoking and higher oxytocin level were associated with a risk of bipolar disorder occurrence in the univariate analysis. However, in the multivariate analysis, only higher oxytocin was suggested to be an independent risk predictor for bipolar disorder development.

In Table 5, linear regression analysis was performed for prediction of factors affecting severity of depression, using age, sex, marital status, residence, education, smoking, attacks, hospitalization, family history, suicidal thoughts, ECT, treatment modalities and oxytocin level as confounders. Younger age, suicidal thoughts, and previous ECT were associated with higher severity of depression in the univariate analysis. However, in the multivariate analysis, none was suggested to be an independent risk predictor for depression severity.

In Table 6, linear regression analysis was conducted for prediction of factors affecting severity of mania, using age, sex, marital status, residence, education, smoking, attacks, hospitalization, family history, suicidal thoughts, ECT, treatment modalities, and oxytocin level as confounders. Hospitalization, suicidal thoughts, and previous ECT were associated with more severe mania cases in the univariate analysis. However, in the multivariate analysis, only hospitalization and previous ECT were suggested to be independent risk predictor for severe mania.

Table 1: Comparison of sociodemographic data among studied bipolar cases and controls:

			Control (N=30)		Bipolar (N=45)		P
Age	Age (years)	Mean±SD	31.6	10.2	33.0	12.1	0.634
	<30	n (%)	15	50.0	25	55.6	0.730
	30–50	n (%)	13	43.3	15	33.3	
	>50	n (%)	2	6.7	5	11.1	
Sex	Males	n (%)	11	36.7	19	42.2	0.630
	Females	n (%)	19	63.3	26	57.8	
Marital status	Single	n (%)	14	46.7	17	37.8	
	Married	n (%)	16	53.3	25	55.6	0.601
	Separated	n (%)	0	0	2	4.4	
	Widow	n (%)	0	0	1	2.2	
Occupation	Higher performance	n (%)	7	23.3	8	17.8	0.666
	House wife	n (%)	5	16.7	9	20.0	
	Student	n (%)	4	13.3	10	22.2	
	Worker	n (%)	5	16.7	4	8.9	
	Clerk	n (%)	3	10.0	8	17.8	
	Unemployed	n (%)	6	20.0	5	11.1	
	Retired	n (%)	0	0.0	1	2.2	
Residence	Rural	n (%)	21	70.0	27	60.0	0.377
	Urban	n (%)	9	30.0	18	40.0	
Smoking		n (%)	2	6.7	12	26.7	0.029*

*: P value less than or equal to 0.05= statistically significant.

Table 2: Beck and Young mania scores of the studied bipolar cases:

	Bipolar (*N*=45)			
	Total (*N*=45)	**Depressive (*N*=15)**	**Manic (*N*=15)**	**Remission (*N*=15)**
Beck scale				
Median	–	34	–	6
Range	–	14–51	–	3–7
Beck scale [*n* (%)]				
Normal	–	0	-	15(100)
Mild	–	1(6.7)	–	–
Moderate	–	2(13.3)	–	–
Severe	–	7(46.7)	–	–
Extreme	–	5(33.3)	–	–
Young mania scale				
Median	–	–	34	2
Range	–	–	23–54	0–2
Young mania scale [*n* (%)]				
No	–	–	–	15(100)
Hypomania	–	–	–	–
Manic	–	–	15(100)	–

*: Significant; less than 0.05; **: High significant; less than 0.01; ***: Very high significant less than 0.001.

Table 3: Comparison of oxytocin level among bipolar studied cases and controls:

		Bipolar (*N*=45)			
	Control (*N*=30)	**Total (*N*=45)**	**Depressive (*N*=15)**	**Manic (*N*=15)**	**Remission (*N*=15)**
Oxytocin					
Median	85.4	139.1	126.9	188.5	135.3
Minimum	30	52.8	110	99.2	52.8
Maximum	116.5	281.6	183.4	281.6	196.8
P values	–	Pct<0.001***	Pcd<0.001***	Pcm<0.001***	Pcr=0.002**
	–	–	Pdm=0.015*	Pmr=0.007**	Pdr=0.443

Pct: comparison between total bipolar and control; Pcd: comparison between depression and control; Pcm: comparison between mania and control; Pcr: comparison between remission and control; Pdm: comparison between depression and mania; Pdr: comparison between depression and remission; Pmr: comparison between mania and remission.

Table 4: Regression analysis for prediction of bipolar I disorder susceptibility:

		Bipolar (*N*=45)			
	Control (*N*=30)	**Total (*N*=45)**	**Depressive (*N*=15)**	**Manic (*N*=15)**	**Remission (*N*=15)**
Oxytocin					
Median	85.4	139.1	126.9	188.5	135.3
Minimum	30	52.8	110	99.2	52.8
Maximum	116.5	281.6	183.4	281.6	196.8
P values	–	Pct<0.001***	Pcd<0.001***	Pcm<0.001***	Pcr=0.002**
	–	–	Pdm=0.015*	Pmr=0.007**	Pdr=0.443

CI: confidence interval; OR: odds ratio.

Table 5: Regression analysis for prediction of factors affecting severity of depression in the studied group:

	Univariate		Multivariate	
	B	***P***	***β***	***P***
Age (numerical)	−0.610	0.020*	−0.467	0.209
Sex: females versus males	1.200	0.151		
Married versus single	2.376	0.186		
Urban versus rural	7.909	0.171		
Higher education versus lower education	−1.667	0.487		
Smoking versus nonsmokers	-6.000	0.357		
Duration (numerical)	−0.546	0.391		
Number of attacks (numerical)	0.583	0.255		
Hospitalization	−3.808	0.624		
FH (positive versus negative)	5.518	0.288		
Suicide	10.977	0.048*	3.850	0.611
ECT	10.977	0.048*	0.941	0.876
Mood stabilizers	-6.643	0.529		
Atypical antipsychotics	−3.692	0.634		
LAP	−10.500	0.313		
Oxytocin (numerical)	0.053	0.612		

FH, family history; *: Significant, less than 0.05; **: High significant, less than 0.01; ***: Very high significant, less than 0.001.

Table 6: Regression analysis for prediction of factors affecting severity of mania in the studied group:

	Univariate		Multivariate	
	β	***P***	***β***	***P***
Age (numerical)	0.110	0.518		
Sex (female versus male)	2.778	0.560		
Married versus single	0.778	0.532		
Urban versus rural	5.535	0.220		
Higher education versus lower education	4.194	0.176		
Smoking	1.111	0.817		
Duration (numerical)	0.117	0.667		
Number of attacks (numerical)	0.262	0.352		
Hospitalization	7.692	0.008**	10.000	0.044*
FH	4.444	0.393		
Suicide	12.083	0.043*	1.667	0.819
ECT	12.083	0.043*	9.667	0.045*
Mood stabilizers	−3.269	0.666		
Atypical antipsychotics	5.227	0.364		
LAP	−0.700	0.898		
Oxytocin (numerical)	0.034	0.439		

FH: family history; *Significant, less than 0.05; **: High significant, less than 0.01; ***: Very high significant, less than 0.001.

In Table 7 logistic regression analysis was conducted for prediction of remission of bipolar disorder using age, gender, marital status, residence, education, smoking, attacks, baseline severity, hospitalization, family history, suicidal thoughts, ECT, treatment modalities and oxytocin level. Lower baseline severity scales, frequency of suicidal thoughts, lower oxytocin levels were associated with prediction of remission in univariate analysis. However, in multivariate analysis, only lower baseline severity scale, lower oxytocin levels were suggested to be independent favorable predictors for remission of bipolar disease.

Table 7: Regression analysis for prediction of bipolar remission in studied group:

	Univariate		Multivariate	
	β	***P***	***β***	***P***
Age (numerical)	0.110	0.518		
Sex (female versus male)	2.778	0.560		
Married versus single	0.778	0.532		
Urban versus rural	5.535	0.220		
Higher education versus lower education	4.194	0.176		
Smoking	1.111	0.817		
Duration (numerical)	0.117	0.667		
Number of attacks (numerical)	0.262	0.352		
Hospitalization	7.692	0.008**	10.000	0.044*
FH	4.444	0.393		
Suicide	12.083	0.043*	1.667	0.819
ECT	12.083	0.043*	9.667	0.045*
Mood stabilizers	−3.269	0.666		
Atypical antipsychotics	5.227	0.364		
LAP	−0.700	0.898		
Oxytocin (numerical)	0.034	0.439		

CI: confidence interval; OR, odds ratio; *:Significant, less than 0.05; **: High significant, less than 0.01; ***: Very high significant, less than 0.001.

DISCUSSION

Bipolar affective disorder is a chronic and complex disorder of mood that is characterized by a combination of manic, hypomanic, and depressive episodes, with substantial subsyndromal social cognitive impairment that commonly presents between major mood episodes (Haggarty *et al.,* 2021).

The neuropeptide oxytocin has attracted great attention of the basic neuroscience researchers, psychologists, and psychiatrists owing to its profound prosocial, anxiolytic, and ‘antistress‘ behavioral and physiological effects and its potential application in the treatment of mental disorders associated with altered socioemotional competence (Grinevich and Neumann, 2021).

A range of studies have shown correlations between basal oxytocin levels and the strength of social and bonding behaviors in both healthy individuals and in those suffering from psychiatric disorders (Striepens *et al.,* 2011). Clinical reports suggest oxytocin to be a promising drug for psychiatric disorders such as anxiety disorders, schizophrenia, and autism. Oxytocin may also have therapeutic potential in the treatment of bipolar affective disorders (Matsuzaki *et al.,* 2011).

So, this study was aimed to calculate oxytocin levels in patients with bipolar disorder and to compare with those of the control group and to investigate whether there is a reliable relation that could serve as a biomarker for bipolar disorder and remission by finding out the level of oxytocin in cases of bipolar disorder, in depressive episodes and manic episodes, and also during remission and comparing them with a control group.

Regarding smoking, bipolar cases had a significantly higher proportion of smokers when compared with the control group (P= 0.029). This was similar to Vermeulen *et al.,* (2021), who found that smoking initiation and lifetime smoking are likely to be a causal risk factor for developing bipolar disorder. Another study also found important clinical correlates of tobacco smoking in patients with bipolar disorder (Medeiros *et al.,* 2018). This may be explained owing to impulsivity, which is a core feature of bipolarity even in females. Moreover, most of the studied control group were females from rural or small towns where it was not common for females to smoke.

Regarding occupation, this study revealed that 44.5% of the cases were employed. Ekinci *et al.,* (2011) obtained

a different finding, as 81.3% of their study cases were employed, which may be explained by higher employment rate among mentally ill patients in developed countries. Occupations also differed significantly between mania and depression (P= 0.001). The highest frequency of those having depression were housewives and students, whereas the highest frequency of those having mania were clerks, higher performance employees, and workers. Otherwise, no significant differences were found regarding occupations between the studied groups. This comes in agreement with Xiang *et al.,* (2013) in their research on a Chinese population. The slightly higher prevalence of females and housewives having bipolar disorder may be a consequence of the social and occupational deterioration associated with the disorder itself, and it is also culturally accepted for females to show slight impairment of functional outcomes, especially in rural areas, and usually they do not seek psychiatric help for the fear of stigma of mental illness. Moreover, students were prevalent, as most of the studied group were of a younger age.

All oxytocin values in the current study were within normal range. However, oxytocin levels showed higher significant levels when comparing patients with bipolar disorder, whether in depression, mania, or remission, with the control group (P <0.001, P <0.001, P <0.001, and P= 0.002, respectively). Manic cases showed significantly higher levels of oxytocin when compared with depressive and remittent cases (P= 0.015 and P= 0.007, respectively). Strikingly, levels of oxytocin did not differ significantly between depression and remission cases. This is in line with the study by Lien *et al.,* (2016), which found that oxytocin levels of patients with BP (42.0±23.7) was significantly higher than those of controls (28.4±14.0, P <0.01). Turan *et al.,* (2013) also stated that serum oxytocin was significantly higher in patients with manic attacks of bipolar disorder and lower in those with depressive attacks in comparison with control. Daban *et al.,* (2007) provided evidence of the association between oxytocin and affective disorders, as oxytocin levels were significantly higher during manic attacks. Eser (2013) revealed elevated serum oxytocin in both manic and depressed patients of bipolar disorders, with no significant difference between both groups. This was also confirmed by Yuen *et al.,* (2014) when comparing patients with bipolar disorder with controls (P= 0.0093 and 0.015, respectively). Another Egyptian study assumed that significant differences between manic patients and control according to serum oxytocin level were present, with P value less than 0.111, being higher in cases with manic symptoms (Bayomy *et al.,* 2016).

From the previous research studies, it may be hypothesized that oxytocin may be a biomarker of BP in either manic or depressive episodes.

In contrast, these studies were not in agreement with Ozsoy *et al.,* (2009), as serum oxytocin levels were decreased in the patients compared with those in the controls. Bao *et al.,* (2008) also found decreased plasma oxytocin levels in patients especially during depressive episodes.

However, early studies speculated no difference between the CSF oxytocin levels of patients and those of the control groups (Marazziti and Dell'Osso, 2008).

With the information in the literature and the findings from this study (namely that oxytocin levels increase during manic episode) when assessed together, it is likely that increased dopamine as well as oxytocin may play a role in the occurrence of euphoria, distractibility, excessive involvement in pleasurable activities that have a high potential for painful consequences, hypersexuality, socially incompatible behavior, and cognitive dysfunction, which are seen during manic episodes in bipolar disorder.

When sex was studied in relation to OXT as one of the most important sociodemographic data, it revealed a nonstatistically significant association, which is similar to Omar *et al.,* (2018), who found no sex or age-related differences in oxytocin levels.

On the contrary, previous studies have shown that depressed women have a lower mean oxytocin concentration (Ozsoy *et al.,* 2009). Moreover; an elevated plasma oxytocin level was noted during relationship distress in women. These different results may be contributed to by the greater variability in pulsatile oxytocin release in depressed women (Yuen *et al.,* 2014).

This may be explained by the hypothesis that women may be more sensitive to the effect of stress on oxytocin, and the variation in women may be sex-specific features such as number of births and lactation history. However, owing to the small numbers of male patients and controls, it would be unwise to draw a conclusion from the result. Nevertheless, this finding may indicate that alterations in oxytocin levels in depression vary between the sexes.

A logistic regression analysis conducted for prediction of bipolar disorder susceptibility whether mania, depression or remission revealed that smoking and high oxytocin levels were associated with the risk of bipolar disorder in general or manic episode occurrence but not depression in univariate analysis. However, in multivariate analysis, only higher oxytocin was suggested to be an independent risk predictor for bipolar disorder whether mania, depression, or remission (0.008).

This agreed with Vermeulen *et al.,* (2021) and Medeiros *et al.,* (2018), who found that smoking initiation and lifetime smoking are likely to be a causal risk factor for developing bipolar disorder. Given that smoking is a modifiable risk factor, these findings further support investment into smoking prevention and treatment to reduce mental health problems in future generations.

Although in this research oxytocin showed no significant change with the severity of Beck and Young mania scales, it could serve as a predictor for the disorder in any of its poles, as it was higher in patients than controls.

From the regression analysis regarding the prediction of severity of depression, it was speculated that the younger the age, suicidal thoughts, and previous ECT were associated with higher severity of depression in univariate analysis. In multivariate analysis, none was suggested to be an independent risk predictor for severity of depression. Moreover, regarding mania, hospitalization, suicidal thoughts, and previous ECT were associated with a higher severity of prediction of mania in univariate analysis, and hospitalization and previous ECT were suggested to be independent risk predictors for the severity of mania in multivariate analysis. This is in line with Parris *et al.,* (2018), who reported that suicide, longer duration of illness, and hospitalization are attributed to a higher frequency of bipolar disorder.

When logistic regression analysis was conducted for prediction of remission of bipolar disease, it revealed that lower baseline severity of the Beck depression inventory and the Young mania scale, frequency of suicidal thoughts (0.006), and lower oxytocin levels (0.043) were associated with prediction of remission in univariate analysis. However, in multivariate analysis, only lower baseline of the severity on both scales (<0.001) and lower oxytocin levels (0.041) were suggested to be independent favorable predictors for remission of bipolar disorder.

Thus, higher level of OXT is considered a predictor for susceptibility of bipolar disorder whether mania, depression, or remission, and lower levels were associated with prediction of remission but does not predict severity of the disorder.

This should be taken in consideration as OXT may act as a biomarker of bipolar disorder and trend toward a potential treatment that may take a place to reduce the prevalence of subsyndromal social cognitive impairment, which has been negatively associated with compliance with therapy, including rehabilitation, functional outcome, resumption of social activities, quality of life, and reduction of economic burden, including hospitalization and rehabilitation. These direct and indirect costs are very high and should not be underestimated.

CONCLUSION

This study revealed that oxytocin levels showed higher significant levels when comparing patients with bipolar disorder, whether totally or in depression, mania, or remission, with the control group (P <0.001, P <0.001, P <0.001, and P= 0.002, respectively). Manic cases showed significantly higher levels of oxytocin when compared with depressive and remittent cases (P= 0.015 and 0.007, respectively). Strikingly, levels of oxytocin did not differ significantly between depression and remission cases.

Smoking and high oxytocin were associated with a risk of bipolar disorder or mania occurrence in univariate analysis. However, in multivariate analysis, only higher oxytocin was suggested to be an independent risk predictor for bipolar disease or mania development and lower levels might predict remission but not predict severity of the disease.

LIMITATIONS

The studied groups were taken from two hospitals that represent only a small social category. All the patients were on psychotropic medications; thus, it was not possible to prevent drug effect on oxytocin levels. We did not experimentally control female menstrual cyclicity in the study, as there is interaction of female reproductive hormones and oxytocin. Only salivary oxytocin was measured, which was not enough as central and peripheral oxytocin can be independently regulated under certain conditions.

RECOMMENDATION

Taking into account all the limitations of the study, further studies with larger study groups are recommended to replicate and extend the current study findings and to achieve more adequate power to test the hypothesis, so that some insignificant correlations may prove to be significant. More participants, especially males, are necessary to bring about a greater clarity on sex effects on OXT biology in bipolar disorder. The relationship between concomitantly collected salivary and CSF samples needs to be assessed to more precisely determine the role of OXT biology in bipolar disorder. Further studies are needed regarding the effect of the different treatment modalities on oxytocin levels and its outcome on bipolar disorder.

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Nil.

CONFLICTS OF INTEREST

There are no conflicts of interest.

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