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Qurat ul ain Khan
Neuro Care Clinic, # 804, AlKhaleej Towers, Shaheed e Millat Rd, Karachi

Sana Younus
Aga Khan University, Stadium Road, Karachi, Pakistan

Hania Hasan
Dow University of Health Sciences, Baba-e-Urdu Road, Karachi, Pakistan

Muhammad Zaman Khan
Aga Khan University Hospital, Stadium Road, Karachi, Pakistan.

ASSOCIATION OF BIPOLAR I DISORDER WITH CONVERSION DISORDER AND SYNCOPE- A RETROSPECTIVE CLINICAL STUDY FROM PAKISTAN

Qurat ul ain Khan[1], Dr Sana Younus[2],Hania Hasan[3], Muhammad Zaman Khan[4]
[1]Consultant Psychiatrist and Neuropsychiatrist, NeuroCare Clinic, # 804, AlKhaleej Towers, Shaheed e Millat Rd, Karachi
[2]Adult & Child and Adolescent Psychiatrist, Insturctor, Department of Psychiatry, Aga Khan University, Stadium Road, Karachi, Pakistan,
[3]Medical student, year 4, Dow University of Health Sciences, Baba-e-Urdu Road, Karachi, Pakistan,
[4]Research coordinator, Department of Psychiatry, Aga Khan University Hospital, Stadium Road, Karachi, Pakistan.

Correspondence to: *Qurat ul ain Khan Consultant Psychiatrist and Neuropsychiatrist, NeuroCare Clinic, # 804, AlKhaleej Towers, Shaheed e Millat Rd, Karachi. Email:qak_pk@hotmail.com*

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ABSTRACT:

Background: Bipolar I disorder (BD I) is a chronic mood disorder that begins in early adulthood. Its association with conversion disorder and syncope has not been widely studied, especially in Pakistani population.

Aims: We aim to study the association of bipolar disorder with conversion and syncope.

Method: Medical records of all consecutive patients diagnosed with bipolar I disorder according to DSM-IV TR in the inpatient and outpatient psychiatric setting at the Agha Khan University Hospital, Karachi from July 2013 to June 2016 were retrieved and those with mood disorder secondary to neurological or medical condition or due to substance abuse were excluded from the study. The diagnosis was made as documented in medical records and the study is retrospective in nature. Details about their demographics and disease characteristics were collected on pre-designed forms and analyzed using chi-square and multivariate analysis.

Results: Of the 469 patients who had BD I, 33 (7%) had conversion symptoms and 6 (1.3 %) had syncope. In both groups, patients were mostly between 16 and 40 years of age and majority of them were females. Loss of consciousness (LOC) was the most frequent symptom in conversion group and 9 of 33 patients first presented with conversion without mood symptoms. 4 of 6 patients in the syncope group had mania and syncope as the initial presentation.

Limitations: Retrospective nature of the study and low prevalence of syncope and conversion patients. For making a diagnosis of BD I, we used the codes in the medical records and there was not a way to double check the diagnosis.

Conclusion: BD I patients can have symptoms of conversion and/ or syncope or atypical presentation which can cause delayed diagnosis and treatment of BD I. Recognizing this association is important to improve management options especially in middle and low-income countries including Pakistan. This has important implications for clinicians in the management of BD I.

Key words: Bipolar disorder, conversion, syncope, dysautonomia, Pakistan, LMIC

INTRODUCTION: Bipolar I disorder is a recurring, chronic, mood disorder that typically presents with episodes of mania/mixed symptoms and depression (Müller and Leweke, 2016) and is the sixth leading cause of disability worldwide(Merikangas et al, 2011). It usually begins in adolescence/early adulthood and adversely affects physical, mental, and emotional wellbeing of patients as well their functioning capacity (Valente & Kennedy, 2010). Association of bipolar disorder has been described with conditions such as obsessive compulsive disorder (OCD), anxiety disorders, and social phobia in different cultures and geographical regions of the world (Khan and Sanober, 2016), (Cederlöf et al, 2014). Association of bipolar I disorder (BD I) with OCD in Pakistani population was also reported by our group with a frequency of 7.5 % (Khan, Younus, Hasan, Khan, 2019). However this was a retrospective study and diagnosis was made based on medical records. Association of mood and bipolar disorder with conversion disorder (Wyllie, Glazer,

Benbadis, Kotagal, Wolgamuth, 1999), dysautonomia (Todder, Bersudsky, Cohen, 2005), and syncope (Hayne, 2002) has been reported in the literature. Low cardiac vagal tone index by heart rate variability (Hage, Britton, Daniels, Heilman, Porges & Halaris 2017) has been reported in bipolar patients in a prospective study. Association of neurally mediated and unexplained syncope in association with anxiety (Lee, Park, Byeon, On, Yim, Kim, 2013) and increased trait anxiety in young women with vasovagal syncope have also been reported in a case control study. Literature also reports a case of severe mixed bipolar disorder in association with syncope and dysautonomia (McMeekin, 2002) and another case with conversion disorder (Skidmore, Anderson, Fram, & Weiner, 2007). However this has not been studied thoroughly like many other conditions and a few studies are found in the literature with scarce indigenous studies. These associations have not been reported in Pakistani population. Pakistan is a low and middle-income South Asian country with 97 % Muslim population (Khan, 2014) and culture that is heavily influenced by religious and social beliefs. The literacy rate of the country is low and awareness about psychological conditions is as low as 36 % (Husain, & Faize2020) which may affect the symptomatology and expression of psychiatric conditions in the society. People may interpret psychiatric symptoms as certain cultural phenomenon prevalent in the society such as Jinn possession (Khan, Sanober, Opel, Zaman, 2016) or as forms of physical/non psychiatric conditions in the form of conversion and syncope. It was noticed that BD I in some cases may present as conversion disorder and may have some association with dysautonomia and syncope in Pakistani population. We aim to study these associations in this clinical study. This is the first study to report this association in Pakistani population.

Materials and Method:

Medical records of all consecutive patients diagnosed with bipolar I disorder according to DSM-IV TR in the inpatient and outpatient psychiatric setting at the Agha Khan University Hospital, Karachi from July 2013 to June 2016 were retrieved. The records were reviewed retrospectively and information was collected by a psychiatry resident using pre designed proformas for the study. These proformas were designed to collect information for this study. In addition to demographic information, data was collected about the presence or absence of conversion disorder (according to DSM-IV TR), syncope of unknown origin and vasovagal syncope, details about features of conversion disorder, medications, family history etc. Exclusion criteria included patients younger than 16 and those with first presentation of bipolar like symptoms at 60 or later as in younger and older age non mood disorder conditions may also present like mood disorders, intellectual or developmental disability, or mood disorder secondary to substance abuse, medical and neurological condition. The Aga Khan Research Ethics Review Committee exempted the study from full approval protocol (3648-Psy-ERC-15) due to no direct human involvement or intervention and the retrospective nature of the study. Statistical Package for the Social Sciences (SPSS) 22.0 was used to calculate frequencies and percentages of demographic variables. Chi square was calculated to check for significant associations between variables, with p value $<= 0.05$ being significant. In case of such associations, multivariable analyses was done using binary logistic regression analysis.

Results:

Total number of patients diagnosed with BD I was 500. 10 were excluded because they were younger than the study age-group or had first presentation later than 60, 8 because of the presence of substance use meeting criteria for substance induced mood disorder, 6 due to other medical/neurological conditions identified as the cause of mood swings, such as brain injury, and 7 due to missing information. The number of BD I patients included in the study was 469 (N = 469) and there was an almost equal distribution of males and females. 33 of 469 (7%) had conversion disorder. Of 469 patients with BD I, 6 (1.3%) had syncope. Demographics of these patients are shown in Table 1. Among those who had conversion disorder more than half were from a younger age and two thirds were females. About half had duration of illness between 1-5 years. Other features and co morbidities of patients with conversion disorder and syncope are shown in Table 2. Loss of consciousness (LOC) was the most common symptom of conversion followed by jerky movements and LOC/pseudo seizures. Most were on combination of psychotropic medications from different classes. 8/33 had OCD, and 1 had conversion and OCD as the initial symptom. In 9/33 cases, conversion without mood symptoms was initial symptom. A few cases had mania and conversion as initial presentation, and few had depression and conversion as initial presentation. 50 % had no psychiatric history in the family and none had history of epilepsy in the family. Among those who had syncope half were from a younger age group and majority were females with duration of illness longer than 10 years. 1/6 had OCD. None of the cases of syncope had OCD as the initial presentation.

Table 1: Demographics of bipolar disorder I patients with conversion and syncope

Variable	BD I with conversion n= 33 n (%)	BD I with Syncope n= 6 n (%)	Total
Age in years			
16-20	4 (12.1)	1 (16.7)	5
21-30	11 (33.3)	1 (16.7)	12
31-40	8 (24.2)	1 (16.7)	9
41-50	4 (66.7)	2 (33.3)	6
51-60	4 (66.7)	0 (33.3)	4
61-70	1 (3.0)	1 (16.7)	2
71 and above	1 (3.0)	0	1
Gender			
Male	12 (36.4)	1 (16.7)	13
Female	21 (63.6)	5 (83.3)	26
Marital Status			
Married	18 (54.5)	4 (66.7)	22
Single	12 (36.4)	2 (33.3)	14
Divorced	1 (3)	0	1
Widower	2 (6.1)	0	2
Separated	0	0	0
Education			
No formal education	1 (3)	0	1
Primary	1 (3)	1 (16.7)	2
Secondary	3 (9.1)	1 (16.7)	4
Matric (10 years)	7 (21.2)	0	7
Intermediate (12 years)	5 (15.2)	0	5
Graduate (14 years)	7 (21.2)	0	7
Post graduate (16 years or more)	4 (12.1)	1 (16.7)	5
Missing	5 (15.2)	3 (50)	8
Occupation			
Unemployed	2 (6.1)	0	2
Homemakers	11 (33.3)	3 (50)	14
Students	4 (12.1)	0	4
Teachers	4 (12.1)	1 (16.7)	5
Businessmen	6 (18.1)	0	6
Professional	2 (6.1)	0	2
Retired	0	0	0
Skilled labor	2 (6.1)	0	2
Landlord	0	0	0
Missing	2 (6.1)	2 (5.7)	4
Family history			
No family history	17 (51.5)	1 (2.9)	18
Bipolar disorder	3 (9.1)	1 (20)	4
Anxiety, GAD, phobia	0	0 (2.9)	0
Schizophrenia, psychosis	1 (3)	0 (5.7)	1
Missing	0	2 (33.3)	2
ID	0	0	0
Substance use	0	0	0
Depression	4 (12.1)	0	4
OCD	0	0	0
Non specific	6 (18.1)	2 (33.3)	8
Suicide	1 (3)	0	1
Epilepsy	0	0	0
Dementia	1 (3)	0	1

BD – Bipolar disorder; OCD – Obsessive compulsive disorder; GAD- Generalized anxiety disorder; ID- Intellectual disability

Table 2: Clinical profile of bipolar disorder I patients with conversion and syncope

Variable	BD I with conversion n= 33 n (%)	BD I with Syncope n= 6 n (%)	Total
Duration of illness			
Less than 1 year	2 (6.1)	0	2
1-5 years	16 (48.5)	2 (33.3)	18
5-10 years	3 (9.1)	0	3
10-15 years	3 (9.1)	2 (33.3)	5
More than 15 years	6 (18.2)	2 (33.3)	8
Missing	3 (9.1)	0	3
Treatment (Medications)			
No medicine	0	0	0
SSRIs only	1 (3.0)	0	1
Mood stabilizer plus anti-psychotic plus anti- depressant/ anxiolytic	9 (27.3)	1 (16.7)	10
Other anti-depressants/ anxiolytics only	0	0	0
Anti-psychotics only	5 (15.2)	1 (16.7)	6
Mood stabilizer only	2 (6.1)	1 (16.7)	3
Mood stabilizer plus antpsychotic	7 (21.2)	1 (16.7)	8
Anti-depressants/ anxiolytic plus antipsychotic	6 (18.2)	2 (33.3)	8
Anti-depressants/ anxiolytic plus mood stabilizer	3 (9.1)	0	3
Missing	0	0	0
Co-morbid conditions			
None	10 (30.3)	1 (16.7)	11
OCD	8 (24.2)	1 (16.7)	9
Cardiovascular conditions	5 (15.2)	0	5
Asthma	0	1 (16.7)	1
Migraine	2 (6.1)	0	2
Thyroid disorder	1 (3.0)	0	1
Seizures	1 (3.0)	0	1
Dementia	1 (3.0)	0	1
Autoimmune disorders	1 (3.0)	0	1
Hepatitis	0	0	0
Lithium toxicity	0	0	0
Missing	12 (36.4)	4 (66.7)	16
Initial presentation			
Syncope	NA	0	0
Conversion	9 (27.3)	NA	9
OCD and conversion	1 (3.0)	NA	1
OCD and syncope	NA	0	0
Mania and conversion	6 (18.2)	NA	6
Mania and syncope	NA	4 (66.7)	4
Depression and conversion	6 (18.2)	NA	6
Most common symptom			
Jerky movements	1 (3.0)		1
LOC	15 (45.5)		15
Jerky movements and LOC	7 (21.2)		7
Catatonia like symptoms	5 (15.2)		5
Others	2 (6.1)		2

SSRI- Selective serotonin reuptake inhibitor; LOC- Loss of Consciousness; NA- Not applicable

Discussion:

Presentation of bipolar disorder may vary in different cultures depending upon the social beliefs of the society (Khan, Sanober, Opel, Zaman, 2016). It is observed that in Pakistan patients with BD I had symptoms of conversion disorder and syncope in some cases and co-existence of these conditions often delayed diagnosis, treatment, and management. In this study 7 % of patients with BD I also had a diagnosis of conversion disorder and majority were females. Association of bipolar disorder with conversion disorder,

female gender, low education, and low socioeconomic status has been reported before (Yayla et al, 2015). Pakistan is a low middle income country (LMIC) with a low literacy rate, very low awareness about psychiatric conditions, very wide mental health gap, and patriarchal patterns of the society (Niaz 2004). Majority of women are home bound with limited access to money, outdoor resources, and social interactions. When such women develop symptoms of BD I, it may not manifest as in western societies and as suggested in DSM criteria such as by impulsive or risk taking behaviours, sexual promiscuity, substance abuse, or increased occupational or social functioning. Symptoms of conversion such as pseudo seizures may be the manifestation of psychomotor agitation or increased energy in these individuals. LOC in conversion in such cases may also be a manifestation of catatonic symptoms in BD I. Incidence of syncope in BD I was 1.3 % in our study and majority were females. Association of dysautonomic features and syncope with psychiatric disorders have been reported in the literature (Leftheriotis et al, 2008). We believe that syncope in our population with BD I may be due to dysautonomia or catatonic features (Komatsu et al, 2016) but the association is not appreciated by the health care providers which alters the course and prognosis of BD I. Course of illness in BD I patients with syncope and conversion was variable but showed a trend towards longer duration and chronic course of illness and patients were on combination of psychotropics, which may point towards increased severity of illness in these variables or presentations of BD I. About a quarter of BD I patients with conversion also had obsessive compulsive order (OCD). Association of BD I with OCD has been reported in the literature (Amerio A, Odone A, Liapis CC, Ghaemi SN. 2014). Among the patients who had conversion, about one quarter had conversion as the presenting and initial feature in BD I patients. This finding is important and needs to be recognized by the clinicians to avoid misdiagnosis and mismanagement of these BD I cases. About one third of those who presented with conversion as the initial feature, had mood symptoms (mania or depression) with conversion. Clinicians may have a tendency to dismiss the presence of psychiatric illness such as BD in patients presenting with conversion. The finding from this study suggests otherwise. The most common symptom of conversion in this study was LOC followed by a combination of LOC and jerky movements of the body. It is important to recognize that conversion disorder may co-exist with BD I as findings from this study suggest. Manic symptoms have also been reported in the literature in association with conversion disorder (Yukawa, Suzuki, Fukui, Otake, Sugai, & Someya. 2013), pseudoseizures (Wyllie, Glazer, Benbadis, Kotagal, & Wolgamuth. 1999), and medically unexplained somatic symptoms (Edgcomb, Tseng, & Kerner, 2016). Further as discussed above psychomotor agitation and catatonic features may present like conversion in certain patients with BD I in Pakistani population where psychiatric conditions often present atypically. Unlike conversion, syncope was not the initial presentation in any of the 6 cases of BD I patients that had syncope and 4 of 6 patients had symptoms of mania with syncope. This may be suggestive of the fact that syncope in BD I is more common in chronic or more severe forms of the disease, and more likely to occur with active mood symptoms. As discussed above dysautonomia or catatonic symptoms in more severe illness may contribute to syncopal episodes in BD I. We suggest screening of patients with conversion, syncope, and dysautonomia for BD I to avoid misdiagnosis.

Conclusion:

BD I may have conversion and syncope as comorbid conditions or atypical presentations in certain cases in Pakistani population. Recognizing and treating these cases as BD I would improve management and treatment outcomes. However this is a retrospective study and conditions were diagnosed as documented in medical records and could not be further verified. However BD I as documented in medical records was diagnosed by professional psychiatrists.

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and unclassified strokes had the highest severity.

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Author's contribution:
Quratul Ain Khan; concept, data collection, data analysis, manuscript writing, manuscript review
Sana Younus; data collection, data analysis, manuscript writing, manuscript review
Hania Hasan; manuscript writing, manuscript review
Mohammad zaman Khan; manuscript writing, manuscript review