ORIGINAL ARTICLE

Age-at-onset and association with clinical features in bipolar inpatients: A case-records-based study from a tertiary hospital in eastern part of Nepal

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Abstract

Introduction: *There are suggestions that age-at-onset (AAO) of bipolar disorder may differ geographically and (AAO) may influence the clinical characteristics. Lack of any published data from eastern part of Nepal prompted this study*

Objective: *The aim of the study was to find the mean AAO in admitted patients in a tertiary care hospital from eastern part of Nepal and to study the association of clinical variables with AAO.*

Method: *Retrospective analysis was done of bipolar in-patients' case-records (N=229) who were discharged from 2012 to 2014. Diagnosis was based on International Classification of Diseases, Clinical Descriptions and Diagnostic Guidelines, tenth version (ICD-10). All variables from files were noted in a Performa prepared by the department for the purpose. Mean AAO was determined. The association of early-onset (below or equal to 18 years of age) and late-onset (later than 18 years) with clinical variables (comorbidity, family history, lifetime presence of psychosis and suicidal attempts) was assessed with Chi-Square test (0.05).*

Result: *Mean AAO was 23.97 (SD 8.7) years. AAO was significantly associated with comorbidity and not significantly associated with family history of bipolar disorder, lifetime presence of psychotic symptoms or suicidal attempt(s).*

Conclusion: *AAO and comorbidity are associated. Present findings need to be seen with the limitation of the study.*

Keywords: Age-at-Onset, Bipolar Disorder, Nepal

INTRODUCTION

The lifetime prevalence rate of bipolar I disorder may range from 0-2.4% with onset ranging five years to 50 years or more. It is a heritable disorder and one or more co-morbidities are often present.[1] The estimated lifetime risk of suicide in bipolar disorders is 15 times more than in general population and one fourth of all suicides may be accounted by bipolar disorder.[2]

The age-at-onset (AAO) is a method to look for homogeneous group within the phenotypic heterogeneity of bipolar disorders. There were significant differences between early AAO and late AAO in terms of poor clinical outcome[3,4] and significant association of cortical thickness.[5] David et al. in 2009 reported that late AAO bipolar patients were more likely to present with psychosis compared with early AAO[6]; however, McElroy et al. and Kennedy et al. demonstrated more likelihood of psychotic

features in early AAO bipolar patients.[7,8] Similarly, some of the studies showed higher rates of family history in early AAO[9-11] and others did not find the significant difference.[6,11] Co-morbidity was significantly associated in some studies[12,13] but there was no significant association in other studies.[6,11]

There are also conflicting results that geographical situation might affect the AAO. For example, one study conducted in 1665 bipolar patients across different countries (Italy, Argentina, Unites States of America, Spain, Turkey etc) concluded that AAO in these countries were comparable.[3] However, a recent review has mentioned that AAO in 'North American samples was earlier than European samples and 10 years earlier than South American samples'.[14]

Considering the lack of published data from this geographical area, this article is an attempt to report the mean AAO in admitted patients in a tertiary care hospital from eastern part of Nepal and to study the association of clinical variables with AAO.

MATERIAL AND METHOD

This was a part of the project to study bipolar disorders in Psychiatry ward of B.P. Koirala Institute of Health Sciences (BPKIHS), Sunsari, Nepal. The case records of 229 in-patients discharged with the diagnosis of bipolar affective disorder (any index episode) from 2012 to 2014 were analyzed. The diagnoses in this centre were based on International Classification of Disease-Clinical Descriptions and Diagnostic Guidelines, tenth version (ICD-10)[15] - by World Health Organization for psychiatric disorders and is verified by at least one consultant psychiatrist. The sociodemographic and clinical variables were recorded on a structured Performa prepared for the purpose by the department. The information was based on the case-records. The study was approved by the Institutional Review Board (IRB) of the BPKIHS.

McElroy et al. and Patel et al. had conducted a study in admitted patients with the early-onset bipolar disorder with the cut-off point of 18 years of age.[7,16] Recent studies have described three distributions of AAO; during childhood (less than 12 years), adolescence (12-18 years), and adult onset (more than 18 years).[3,12] However, in these studies also, childhood and adolescent group have been grouped together and compared with late-onset group with the cut-off age of 18 years. Based on this, early-onset was defined as the first hypomanic, manic, depressive or mixed episode before or at 18 years of age and late-onset after 18 years of age. Age-at-onset was based on the report by family members and/or patient during admission. Family history was defined as the report of any diagnosis of hypomania, mania, depression or mixed episode in any blood-related family members. Psychotic symptom was defined as any reported hallucinations or delusions during lifetime in depressive, manic or mixed episodes. Suicidal attempt was defined as any attempt of suicide during lifetime irrespective of during any mood episodes or remission. Co-morbidity was defined as any major psychiatric disorders or physical illness.

The association of AAO with gender, occupation, education, family history of mental illness, presence of psychotic symptoms ever, presence of suicidal attempts ever, presence of any co-morbidity, and course of illness were done with Statistical Package for Social Sciences (SPSS 10.0) using Chi-Square test at the significance level of p-value less than 0.05.

RESULT

The mean ages for total patients (N=229), patients with manic episode (n=194), with depressive episode (n=26), and with mixed episodes (n=9) were 32.13 years (SD 12.3), 32.27 years (SD 12.4), 32.77 years (SD 13.3), and 27.11 years (SD 6.1) respectively. Similarly, the mean AAO for total patients, manic episodes, depressive episodes, and mixed episodes were 23.92 years (SD 8.7), 23.85 years (SD 8.6), 24.42 years (SD 9.7), and 23.89 years (SD 7.4) respectively. There were no patients from upper socio-economic status. There were 78 (34%) and 151 (66%) patients in early-onset and late-onset groups respectively. Association of AAO with socio-demographic variables are shown in Table 1 where occupational status was significantly associated and association of AAO with clinical variables are depicted in Table 2 where co-morbidity was significantly Associated .

Table no. 1: Association of age-at-onset of bipolar disorder with socio-demographic variables (N=229)

Socio-demographic variable	Category	Onset		P-value
		Early-onset n=78 (34%)	Late-onset n=151 (66%)	
Gender	Male	40 (32.3)	84 (67.7)	0.532
	Female	38 (36.2)	67 (63.8)	
Socio-economic status	Middle	15 (33.3)	30 (66.7)	0.909
	Less than Middle	63 (34.2)	121 (65.8)	
Occupation	Employed	22 (22.9)	74 (77.1)	**<0.001***
	Unemployed	38 (62.3)	23 (37.7)	
	Home-making	18 (25.0)	54 (75.0)	
Education	Less than primary	40 (33.9)	78 (66.1)	0.957
	More than primary	38 (34.2)	73 (65.8)	

*significant Difference

Table no. 2: Association of age-at-onset of bipolar disorder with clinical characteristics (N=229)

Clinical characteristic	Category	Onset		P-value
		Early-onset n=78 (34%)	Late-onset n=151 (66%)	
Family history of mental illness	Yes	19 (30.2)	44 (69.8)	0.443
	No	59 (35.5)	107 (64.5)	
Presence of psychotic symptoms ever	Yes	40 (35.1)	74 (64.9)	0.744
	No	38 (33.0)	77 (67.0)	
Presence of suicidal attempt ever	Yes	9 (45.0)	11 (55.0)	0.280
	No	69 (33.0)	140 (67.0)	
Presence of comorbidity	Yes	30 (25.9)	86 (74.1)	**0.008***
	No	66 (32.4)	138 (67.6)	

*significant Difference

There was no association between AAO and precipitating factor for first episode (p=0.20), premorbid adjustment (p=0.34), life-time presence of catatonic symptoms (p=0.28), outcome of hospital stays (no or some improvement versus significant improvement or remission) (p=0.12), and course of illness (episodic with full inter-episodic remission versus episodic with partial inter-episodic remission) (p=0.62).

DISCUSSION:

The mean age at admission was 32.1 years (SD 12.3) for the total sample and 32.2 years (SD 12.4) for manic episodes. The mean AAO was 23.9 years (SD 8.7) for the total sample. The mean AAO and occupational status was significantly associated. Similarly, it was also associated with the presence of co-morbidity, however, it was not associated with family history of mood disorder, presence of psychotic symptoms, life-time presence of suicidal attempt(s).

The mean AAO for bipolar disorder I and II are reported to be 18 years of age and mid-twenties respectively.[2] In paediatric population, study by Faedda et al., as cited by Kowatch et al., has reported the age of first manic episode in 2.8 years of age (SD 3.9)[17] and in geriatric population, it has been mentioned that it can occur for the first time in 60s or 70s years of age.[2] In a review done for AAO with both bipolar I and bipolar II disorders, AAO ranged from around 18 years to 30 years.[14] Studies done in India to study co-morbidity or phenomenology, course and outcome in bipolar disorder reported the mean AAO of around 27 years.[13,18] The median AAO was reported as 24 years (IQR 19-32) by Tondo et al.[19] and 24 years (13.1) by another study.[3]In a review done to compare the difference between bipolar I and II disorders , the AAO of bipolar I disorder patients in studies from United States ranged from 18-21 years in most studies, around 24 years in United Kingdom or Canada, and around 28 years in China.[14] Our mean AAO of around 24 years seems to fall within the range, however, slightly earlier than as reported in Indian studies and later than American studies.

Among 1368 bipolar patients, early-onset (less than or equal to 18 years) when compared to late onset showed significant association with functional outcome, employment and marital status, however co-morbidities or psychotic features were not significant. Family history was highest in less than 12 years of age group, seemed to decrease after 40 years of age, and was in-between in 12-39 years.[3] Another study comparing childhood-and adolescent-onset group with adult group (cut off at 18 years) showed that early-group had higher rates of lifetime co-morbidities (life-time anxiety disorder and alcohol use disorders) and suicide attempt but not for substance use disorder and family history in first degree relative.[12] The strong association of AAO and co-morbidities in the present study is similar to other studies.[9,12,13,20-23] Two studies did not show significant association of AAO and co-morbidities.[6,11] Both studies showed no association of AAO with family history of bipolar disorder. Ernst et al. study additionally did not show significant association of AAO with suicidal attempts.[11] Present study also did not show significant association of AAO with positive family history, lifetime psychosis, lifetime suicidal attempt or psychosis. Nevertheless, many studies have shown the significant association of AAO with positive family history,[9,10,12,22] with psychosis[8,9,23,24] and with suicidal attempts.[12,21,25-28]

Strong association with co-morbidities could be a true picture as most of the studies has shown, however, our definition was broad to include any diagnosable psychiatric or physical illness. For lifetime psychosis, lifetime suicidal attempt or family history, it is likely that this information might have been missed without focused questioning even though they are routinely screened clinically. Different definition of AAO and other methodological difference may have a role as well. The difference in the finding could be due to limitations of the present study. Being a retrospective study, recall bias is inevitable and as it was a case-records-based study, further information was limited. Objective instruments were not used. Additionally this study did not look for the relative contribution of clinical variables, for example, there is a possibility of influence of substance-use-disorder in bipolar patients to set the AAO early.[29]

CONCLUSION:

Conclusion: Age-at-onset may be different for different geographical area. AAO seems to have significant association with employment and psychiatric co-morbidities. Further prospective studies are needed in the community to determine the geographical difference and other associations.

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