Original paper

Association of family history of bipolar disorder with risk of violence in inpatient mania: A cohort study

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Background

Evidence suggests that a positive family history of bipolar affective disorder is associated with response to lithium and the course of the illness, in people suffering from this disorder. This may indicate a subgroup of patients with unique characteristics and treatment responses.

Aims

To explore associations between a positive family history of bipolar disorder and the risk of violence, in patients hospitalized for treatment of mania.

Methods

Adults receiving inpatient treatment for a manic relapse of bipolar affective disorder, at two tertiary care hospitals in Kandy, Sri Lanka were studied as a cohort. For each participant with a positive family history of bipolar disorder, an age and gender matched adult, also suffering from a manic relapse of bipolar affective disorder but without a family history, was included as a control. A second researcher, who was blind to the participants' family history, assessed the risk of violence among all participants, at baseline, and at weekly intervals thereafter until discharge, using the historical clinical risk management Scale 20 (HCR-20).

Results

A total of 148 participants were included, with 74 each in the study arm and control arm respectively. Of all participants, 57% were females. Significantly higher rates of unemployment, harmful use of alcohol and absence of confiding relationships were found in participants with a positive family history; they also had a significantly higher mean average HCR-20 scores compared to controls.

Conclusion

A positive family history of bipolar affective disorder was associated with a higher risk of violence during hospitalization for a manic relapse, as indicated by the mean average HCR-20 scores. A positive family history may be a potential identifier of those at a higher risk of violence in bipolar mania.

Key words: bipolar affective disorder, violence, risk assessment, family history, Sri Lanka

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Introduction

Bipolar affective disorder has a complex mode of inheritance. The heritability is around 80% (1). Even though family, twin and adoption studies have identified aetiological genetic factors, candidate susceptibility genes have not been conclusively identified (2). Studies report a general recurrence risk of 8.7% among first-degree relatives, indicating a familial aggregation in bipolar disorder (3). A study conducted using the Danish psychiatric registers shows that first-degree relatives of patients with bipolar disorder have a 14-fold higher risk of developing the disorder compared to the general population (4).

Certain identified characteristics of bipolar patients are shown to be associated with presence of a family history of bipolar disorder. A better response to the mood stabiliser lithium is seen among patients with a positive family history compared to patients without a family history (5). In addition a positive family history is also associated with the course of the illness (6). Genetic polymorphisms related to serotonin and dopamine transporters have been associated with subtypes of bipolar disorder such as anxious dysthymic and irritable aggressive types (7). These findings indicate the possibility of a subgroup of patients with unique characteristics.

Bipolar disorder is associated with increased risk of violence not only in patients with the disorder, but also in their unaffected siblings (8). Evidence also suggests that violence in general maybe heritable and a family history of violence predicts aggressive behaviour in affected individuals (9). A high heritability of testosterone levels and its association with violent behaviour has been found in studies on domestic violence (10).

Exploration of associations, if any, between family history of bipolar affective disorder and risk of violence is likely to be useful in predicting and assessing risk of violence in patients during a manic episode. This would aid the clinician in allocating resources more relevantly to safeguard the patient, family members, the wider community and the hospital staff where bipolar patients are managed during manic episodes.

The main objective of this study was to explore the association, if any, between a positive family history of bipolar disorder and the risk of violence during a manic episode, in patients with bipolar affective disorder. Further potential associations between variables such as employment, comorbid harmful use of alcohol, presence of confiding relationships and treatment adherence and a positive family history of bipolar disorder were also examined.

Methods

A cohort study design was used to explore the association between family history and the risk of violence. A retrospective cohort study design was used to assess the secondary objectives mentioned above. Adult patients admitted to psychiatry inpatient units of Peradeniya and Kandy Teaching Hospitals, during a consecutive six-month period, were considered for inclusion in the study. Both hospitals are large tertiary care institutions situated in Kandy, Sri Lanka. The hospitals are situated within five kilometres of each other and receive admissions from the Central Province, as well as neighbouring provinces, including transfers.

The diagnosis of a current manic episode was made according to the international classification of diseases 10th edition (ICD-10) (11). The symptomatology was assessed and diagnosis was made via a clinical interview by a consultant psychiatrist.

For study purposes, a positive family history was defined as the presence of bipolar disorder in a first or second-degree relative of the patient, as determined by clinical records. For each participant with a positive family history of bipolar disorder, an age and gender matched patient with bipolar mania without a positive family history was included as a control. The study group participant and the relevant control were recruited from the same hospital. Patients with a family history of other psychiatric disorders were not excluded from either group.

Any participant found to have an identified organic pathology such as frontal lobe disease or dementia was excluded from the study. In addition, patients who had features of substance intoxication on admission were not included. Patients admitted with a relapse of bipolar mania, who were discharged or transferred to another unit prior to completion of at least one week's observation were also excluded from the analysis.

Assessment of risk of violence was done via the historical clinical risk management scale 20 (HCR-20), which is a validated, structured scale used worldwide (12). This scale employs a structured professional judgement approach for assessment of risk of violence in clinical settings. The HCR-20 was applied by a second researcher, who was blind to the family history status of study participants. The risk of violence to others according to the HCR-20 was assessed within 24 hours of the admission, and weekly thereafter, as well as at the time of discharge, in all participants, by the same clinician in both hospitals. The total duration of admission and management was decided by clinicians independent of the study.

For the purpose of this study, poor treatment adherence was defined as missing at least one dose of medication, on more than three consecutive days, during the preceding one month. This definition was a modification of measurements of adherence from a past study (13). A participant was considered to be employed, if he or she was employed full or part time for at least six months during the previous year. Comorbid harmful use of alcohol was determined based on the ICD-10 criteria (11). The presence of a confiding relationship was decided on clinical judgement, based on assessments of individual patients.

Statistical analysis was done using SPSS software. The average HCR-20 score per each patient and the mean score for the group was calculated. Associations, if any, between family history of bipolar affective disorder and risk of violence were assessed using the independent t test method. Secondary objectives were analysed using chi-square analysis.

Participants who gave written informed consent for participation were included in the study. Ethical approval for the study was obtained from the Ethical Review Committee of the University of Peradeniya.

Results

A total of 157 participants met criteria for inclusion in the study, during the study period, of whom, 80 patients had a family history of bipolar disorder; they were considered as the study group. The research team was able to identify an age and gender matched control (with bipolar mania, but without a family history of the disorder) for 77 of the study group participants. Of these 77 pairs, in two patients the weekly risk assessment could not be completed as they were transferred to other wards for medical evaluation. Further one patient who was assessed regularly had to be discontinued from the study, since the diagnosis in this patient was later changed to schizoaffective disorder. Thus the total number of participants included in the study was 148 persons, which consisted of 74 pairs, with a 1:1 ratio between the study and control groups.

Among the participants, 51% of the study group (n=38) and 50% of the control group (n=37) had psychotic features ($\chi^2 = 0.027$, p =0.869, CI 95%). The duration of the inpatient stay ranged from 8 to 41 days. The mean duration of inpatient treatment was 13.43 days for the study group and 12.57 days for the control group (t =1.643, p= 0.063 at CI 95%).

Significantly higher rates of unemployment ($\chi^2 = 7.043$, p=0.008, CI 95%), comorbid harmful use of alcohol ($\chi^2 = 21.148$, p<0.001, CI 95%) and absence of at least one confiding relationship ($\chi^2 = 8.107$, p = 0.004, CI 95%) was present in the study group compared to the control group (Table 1).

Analysis of the risk of violence to others, as measured by the mean of average HCR-20 scores in each group, showed that participants with a positive family history of bipolar disorder had significantly higher scores compared to participants with a negative family history (t=2.511, p=0.013 at CI 95%).

Discussion

A key finding that emerged from this study is that patients with a positive family history of bipolar affective disorder, had a significantly higher mean of average HCR-20 scores compared to controls without a family history. This finding suggests that a positive family history of bipolar affective disorder, in persons hospitalised for a relapse of bipolar mania, may be a potential identifier of those at higher risk of violence, as measured by the HCR-20.

There are several possible reasons for this association, which need to be considered. On one hand, the positive family history of bipolar affective disorder may indicate a greater genetic loading and a more severe form of the illness; this may have contributed to a worse clinical profile, greater unemployment and higher risk of violence in this group of patients (14). In keeping with this hypothesis, recent research shows that a more severe course of illness in bipolar disorder is seen, in the presence of a positive family history of mood disorder (14). A factor against this explanation in this study is that there was no significant difference in the presence of psychotic symptoms in participants with and without a family history of bipolar affective disorder.

Participants with a positive family history also had significantly higher rates of comorbid alcohol use; this is likely to be another factor contributing to the greater risk of violence among these participants (8); and the higher rates of comorbidity in turn may have been linked to the positive family history in the study group. A

Table 1. Comparison of participants with and without a family history of bipolar affective disorder

	Study group Positive family history of bipolar disorder (n = 74)	Control group Negative family history of bipolar disorder (n = 74)	Statistical significance of difference between the two groups (p value)
Mean age (years)	37.2 (SD 13.1)	37.2 (SD 13.1)	
Gender	Males 43.2%	Males 43.2%	
Percentage of those with psychotic symptoms	51%	50%	p = 0.869
Percentage employed	31.1%	52.7%	p = 0.008
Percentage with comorbid harmful use of alcohol [ICD-10]	48.6%	13.5%	p < 0.001
Percentage with at least one confiding relationship	48.6%	71.6%	p = 0.004
Percentage with poor treatment adherence before admission	75.7%	62.2%	p = 0.076

similar association has been reported by a large study conducted in Sweden, which reported a shared aetiology for bipolar disorder, violence and substance use (8). Another alternative explanation to be considered is whether the positive family history included a direct genetic heritability for increased risk of violent behaviour.

Limitations

All participants in this study were inpatients, and may have represented an extreme subgroup in relation to violence risk compared to outpatients. Furthermore the possibility of a learned behavioural effect, for example due to exposure to violence from other family members who also suffered from bipolar affective disorder, may have contributed to the higher risk of violence in the group with a positive family history. Previous studies have reported increased violence in offspring exposed to violent acts of parents and other adults (15).

Conclusions

The findings of this study indicate that patients experiencing a relapse of bipolar mania with a positive family history of bipolar disorder, had a significantly higher risk of violence, compared to controls who did not have a positive family history. Whether the reason for this association is due to genetic factors, comorbid substance use, poor treatment adherence, a learned behavioural effect or other yet unexplored factors, is not clear. Further multicentre studies are required to explore these hypotheses further. Nevertheless a positive family history of bipolar disorder is likely to be a useful indicator of possible increased risk of violence, in those being admitted to a psychiatric unit for management of a manic relapse of bipolar affective disorder.

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Conflicts of interest

None declared

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