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FAMILIAL LIABILITY AND AGE OF ONSET AMONG PATIENTS WITH MAJOR MENTAL ILLNESS

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Abstract

Familial liability or susceptibility has been shown to increase the risk for psychotic disorders, however, little is known about familial liability (FL) among patients with major psychiatric disorders in Nigeria. This study aimed to determine the rate of FL and factors influencing the age of onset among patients with schizophrenia and bipolar disorders. This was a cross-sectional survey of patients with either diagnosis of bipolar disorder or schizophrenia based on ICD-10 criteria. Data were collected through a pretested socio-demographic questionnaire, incorporating age, duration of illness, the onset of illness, and family history (FH) of mental illness. Data were presented as tables, charts and bivariate analysis was performed to determine the relationship between variables. The level of significance was set at P < 0.05. Of the 235 participants, 66 (28.1%) had a FH of mental illness. The age of onset ranges from 12-70years with a mean of 30.1years (SD=11.1years) and majority 85 (36.2%), were within the age group 30-39 years and had developed the illness before the age of 30years (54.5%). The males were twice more likely to developed mental illness before the age of 30 compared with their female counterparts [OR=2.42, (CI = 1.40-4.25), (p=0.013)], likewise, the singles compared with the ever-married [OR=4.24, (CI=2.45-7.34), (p=0.000)]. Although nearly a third of the participants had a FL to mental illness, there was no association between age of onset and FH of mental illness. However, the males and the singles were more likely to have developed mental illness at an earlier age compared with their counterparts.

Keywords: Age of onset, bipolar disorder, familial liability, schizophrenia

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1. Introduction

Schizophrenia and bipolar disorder (BD) are major psychiatric disorders with familial disposition. As noted by many researchers, the presence of family history (FP) is a major risk factor for these disorders (Byrne et al., 2002; Kendler et al., 1997; Klein et al., 2003). Several factors increase the risk of mental disorders in the general population. Of these, studies from the western world have repeatedly reported the role of heredity in the risk for mental illness (Jeppesen et al., 2015; Laursen et al., 2005; Mortensen et al., 2010). Familial liability (FL) or predisposition increases the risk of psychotic disorders by about five-fold independent of environmental influence (Mortensen et al., 2010; van Os et al., 2003). However, the additive effect of both environmental and familial predispositions increases the risk of developing psychotic disorders further (van Os et al., 2003).

Although schizophrenia is strongly associated with schizophrenia and related disorders among first-degree relatives, the presence of other psychiatric diagnoses among first-degree relatives increases the individual's risk of schizophrenia (Mortensen et al., 2010). According to Mortensen et al, (2010), the risk due to FH schizophrenia only is 6.0%, however, the population attributable risk due to FH of mental illness, in general, is about six times this value, thus showing the impact of other psychiatric disorders in predisposition to schizophrenia.

The risk of offspring developing schizophrenia increases with increase in the number of parents with the history of mental illness, with both parents with history of schizophrenia, the risk increases to about four folds compared with just one of the parents with such history (Gottesman et al., 2010). Similarly, the risk of bipolar disorders increases to about five folds in offspring of couples with a history of bipolar disorder compared to where only one of the parents is affected (Gottesman et al., 2010). This suggests as FL increases, the risk of developing both schizophrenia and bipolar disorders increases. Nevertheless, the risk of developing schizophrenia due to the presence of family history of psychiatric disorders decreased as the age of onset increases (Byrne et al., 2002), and men were more at risk of both schizophrenia and bipolar disorders compared with women (Aleman et al., 2003; Kennedy et al., 2005; Ochoa et al., 2012).

Studies have shown that positive FH of mental illness is associated with poor prognostic factors including early-onset, increased frequencies of relapse or severity of episodes and substance misuse (Esterberg & Compton, 2012; Kao & Liu, 2010; Nuhu et al., 2016; Post et al., 2015). People with positive FH of bipolar disorder, recurrent depression, substance misuse, and other mental health difficulties are more likely to have an early age of onset of either schizophrenia or bipolar disorders (Esterberg & Compton, 2012). Patients with early-onset, on the other hand, were more likely to present with an increased level of cognitive impairment, impulsivity, and poor outcome (Kao & Liu, 2010; Ochoa et al., 2012). The severity of symptoms of illness may furthermore be influenced by the interaction between FH and gender (Esterberg & Compton, 2012).

In Nigeria, there are limited studies looking at the extent of FH among people with schizophrenia and bipolar disorders, and its relationship with age of onset. We, therefore, sought to determine the rate of occurrence of family liability, and identify factors associated with the age of onset as well as the relationship between positive family history and age of onset among patients with schizophrenia and bipolar disorder.

2. Materials and Methods

2.1. Study setting and design

This cross-sectional survey was carried out at the Psychiatric out-patient of the Ekiti State University Teaching Hospital (EKSUTH), located in Ekiti State, Nigeria. The Hospital provides tertiary health care for people of the State and environs. Besides providing care in various specialties and sub-specialties of Medicine, the hospital also provides mental health care for people of the state and its environs.

2.2. Study population and sampling

Participants were patients with either diagnosis bipolar disorders or schizophrenia based on ICD-10 criteria as evaluated by Consultant Psychiatrists attending the psychiatric out-patients of EKSUTH, Ado-Ekiti. In this study, consecutive patients with the diagnosis of either schizophrenia or bipolar affective disorders were recruited for the study through a convenient sampling technique. Data were collected over 3 months period, with the mind that majority of the patients would have been seen at the out-patient clinic (based on the duration of appointment usually given).

2.3. Instrument

Consecutive patients with the diagnosis of either schizophrenia or bipolar affective disorder were interviewed with pretested socio-demographic questionnaires, that incorporates the age, sex, duration of illness, the onset of illness and duration on medications. A family history of mental illness was also elicited with a pre-tested questionnaire on history of similar illness or other mental illness in the first- or second-degree relatives. Because of the low level of knowledge of mental illness by the participants and record-keeping generally, participants were not asked for specific psychiatric diagnoses, but a history of mental illness in the first- and second-degree relatives.

The functional recovery was assessed by the managing physician who responded to the question "*Considering your total clinical experience with this particular population of patients, how mentally ill is the patient at this time?* to assess extent wellness compared with healthy individuals or someone with mental illness on a 7-point Likert scale based on their experience with this population of patients (7 = among the most extremely ill patients, 6 = Severely ill, 5 = Markedly ill, 4 = Moderately ill, 3 Mildly ill, 2 = Borderline mentally ill, 1 = Normal, not at all ill, 0 = Not assessed).

The age of onset was dichotomized into two, using the mean age of onset as the cut-off. The first group was those who have developed the illness on or before the age of 30 years and those who developed the illness after the age of 30.

Inclusion and exclusion criteria

Patients younger than seventeen years or had not been receiving treatment for up to six months or had co-morbid mental illness were excluded from the study.

2.4. Ethical Considerations

The study protocol was approved by the Research and Ethics Committee of the EKSUTH, Ado-Ekiti. Written informed consent was obtained from all participants before the questionnaires were administered. The confidentiality of information provided by the participants was also ensured. (Number: EKSUTH/A67/2019/09/019 (10 Oct 2019))

2.5. Data analyses

Data were analysed using Statistical Package for Social Sciences (SPSS) version 25 (IBM Inc.). Descriptive statistics including mean, frequency tables, and charts were performed to determine the distribution of characteristics of the variables studied. Chi-square test as well as the odds ratios were performed to determine the relationship between family history of mental illness, socio-demographic variables, and age of onset. A p-value of ≤0.05 was adjudged significant.

3. Results

Table 1: Sociodemographic characteristics of the participants

Variables	Frequency	Percentage
Age group		
<19	2	0.9%
20-29	53	22.6%
30-39	85	36.2%
40-49	53	22.6%
50-59	30	12.8%
60 and above	12	5.1%
Gender		
Male	82	34.9%
Female	153	65.1%
Educational levels		
None	10	4.2%
Primary	26	11.1%
Secondary	70	29.8%
Tertiary	129	54.9%
Marital status		
Single	119	50.6%
Married	84	34.9%
Divorced/separated/widows	34	14.5%
Employment status		
Employed	120	51.1%
Unemployed	90	38.3%
Students	25	10.6%
Age of onset		
< 21	51	21.7%
>21	184	78.3%
< 30	128	54.5%
>30	107	45.5%

3.1. Socio-demographic variables

A total of 235 patients with either schizophrenia or bipolar affective disorders took part in the study. Their ages range between 17-75years with a mean of 38.5 years (SD=11.2years). The age of onset ranges from 12-70years with a mean of 30.1years (SD=11.1years). As shown in Table 1, the majority of participants 85 (36.2%) were within the age group 30-39 years (36.2%), followed by those between 20-29years (22.6%). Majority 128 (54.5%) developed the illness before the age of 30years while 49 (21.4%) on or before the age of 21 years. Most of the participants were females 153(61.5%), had tertiary education 129 (54.9%), single 119 (50.6%), and were employed 120 (51.1%).

3.2. Family history of illness and diagnoses

Table 2 shows the FH of illness and the diagnoses of the participants. A total of 203 (86.4%) had schizophrenia while the rest had Bipolar affective disorder. Sixty-six (28.1%) had a family history of mental illness.

Table 2: Family history and diagnoses

Variables	Frequency	Percentage
Family history		
No	169	71.9%
Yes	66	28.1%
Number of relations		
>1	8	12.1%
One	58	87.9%
Diagnoses		
Schizophrenia	203	86.4%
Bipolar disorders	32	13.6%

3.3. Patterns of family relationship with the probands

Figure 1 shows the pie-chart showing the family relationship with the probands. The majority of the participants 24 (32%) reported siblings as relative with the history of mental illness, followed by mother (18%), and cousins were the least.

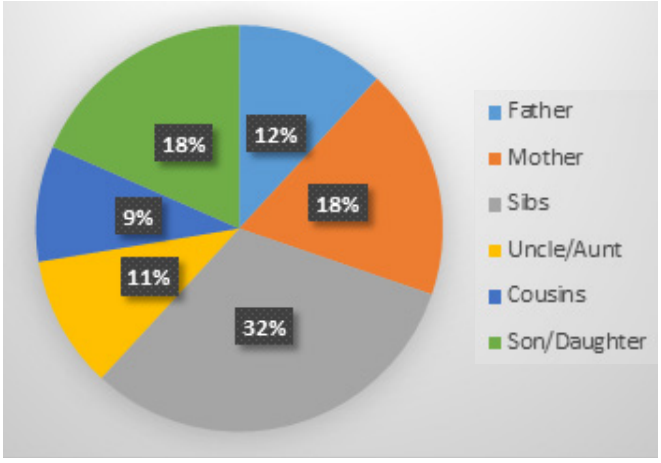

Figure 1: Pie chart showing patterns of family relationship

3.4. Relationships between the age of onset and participants' characteristics

Table 3 shows the relationship between age of onset and participants' characteristics. Compared with the females, the males were more likely to developed mental illness before the age of 30 [OR=2.42, (CI=1.40-4.25), (p=0.013)]. Similarly, the singles were over four times more likely to develop mental illness before the age of 30 compared with those that were ever married [OR=4.24, (CI=2.45-7.34)], (p=0.000)]. There was no statistically significant relationship between levels of education, participants' diagnosis, family history of mental illness, and age of onset of illness.

Table 3: Relationship between the age of onset and participants' characteristics

Variables	Age of onset			
	<30years	>30years	OR (95% CI)	P-value
Gender				
Male	56 (68.3)	26 (31.7)	2.42 (1.40-4.25)	0.013
Female	72 (47.1)	69 (52.9)		
Educational levels				
Primary and below	18 (50.0)	11 (50.0)		0.611
Secondary	36 (51.4)	34 (48.6)		
Tertiary	74 (57.4)	55 (42.6)		
Marital status				
Singles	85 (71.4)	34 (28.6)	4.24 (2.45-7.34)	0.000
Ever Married	43 (37.1)	73 (62.9)		
Family history				
No	94 (55.6)	95 (44.4)	1.18 (0.67-2.09)	0.570
Yes	34 (51.5)	32 (48.5)		
Diagnoses				
Schizophrenia	111 (54.7)	92 (45.3)	1.07 (0.50-2.25)	0.870
Bipolar disorders	17 (53.1)	13 (46.9)		

OR=Odds ratio

3.5. Age of onset and functional recovery/severity of illness

Figure 2 shows the relationship between age of onset and functional recovery/severity of illness. Compared with those with the onset of illness 30years and above, a higher number of those with the onset of illness below 30years were adjudged to be borderline to severely ill at the time of interview while a higher number of those who were rated normal had the onset of illness after the age of 30 years.

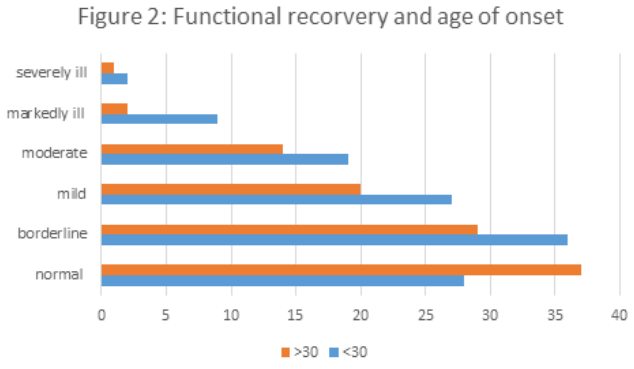

Figure 2: Relationship between functional recovery and age of onset

4. Discussion

Schizophrenia and bipolar disorders occur more frequently in first- and second-degree relatives of people with mental illness (Chou et al., 2017). In this study, nearly a third of the participants reported FH of mental illness suggesting a high genetic predisposition. A FH of schizophrenia for example, had been reported as the strongest single indicator for an individual with schizophrenic risk (Mortensen et al., 2010). The presence of an affected co-twin, first-degree, or second-degree relative increases the relative risk by about 2 to 38 times. (Chou et al., 2017) Similarly, the risks of schizophrenia and BD in offspring of couples with schizophrenia and the other with BD were 15.6% and 11.7% respectively as against 4.4% in offspring where only one of the parents is affected (Gottesman et al., 2010). Familial predisposition has been reported to increase the risk of psychotic disorder by about five-fold independent of environmental influence (Mortensen et al., 2010; van Os et al., 2003). This suggests the effect of heritability in predisposition to schizophrenia and BD.

In this study, participants' age of onset ranges from 12-70years with an average age of about 30 years, indicating most of the participants were relatively young. There was no significant difference in the age of onset of people with the diagnosis of schizophrenia and bipolar disorder. This suggests that both disorders show a relatively young age of onset. Again, over half of the participants had developed mental illness before the age of 30years while about one fifth before the age of 21 years, denoting most had a relatively early age of onset. Similar to other psychiatric illnesses, most individuals with schizophrenia and BD developed these disorders in late adolescence or early twenties, with a slightly later onset in females (Gogtay et al., 2011; Häfner et al., 1994). Several reasons have been deduced to explain this; the early adulthood represents a time of maturation and comes with its peculiar challenges (Pantelis et al., 2007; Wood et al., 2008). Studies have shown that patients with early-onset were more likely to show greater levels of cognitive impairment, a higher level of impulsivity as well as poor outcome (Kao & Liu, 2010; Ochoa et al., 2012). This may explain the lower-level functionality observed with most patients with early onset illness as noticed in this study.

He majority of the participants that were adjudged to have borderline to severe illness were more likely to have developed the illness before the age of 30 whereas those who were normal were more likely to have developed the illness after the age of 30. Studies have shown an association between age at onset and the outcomes (Immonen et al., 2017; Käkelä et al., 2014; Post et al., 2015). Patients who were relatively young at onset were more likely to have more hospitalizations, more negative symptoms, more relapses, and poorer social and occupational functioning (Immonen et al., 2017; Kao & Liu, 2010).

In this study, relative to their female counterparts, the males were more likely to develop a mental illness at an earlier age similar to other findings (Gogtay et al., 2011; Ochoa et al., 2012). This is not limited to schizophrenia alone but to bipolar disorders as well (Aleman et al., 2003; Kennedy et al., 2005; Ochoa et al., 2012). Among patients with schizophrenia on the other hand, a meta-analysis showed that the presence of a FH of psychosis is associated with an earlier age at onset in both sexes, with male gender presenting with early onset in those without FH of mental illness (Esterberg et al., 2010). This is supported by a recent study focusing on illness course that reported no association between gender and age at onset after adjusting for severity of symptoms at presentation (Drake et al., 2016), suggesting early age at illness onset might be a pointer to increased genetic vulnerability with gender as a modifier. Nonetheless, the presence of accumulated trauma, obstetric complications, and cannabis use may explain the relatively lower the age at onset in males (Stepniak et al., 2014).

Among patients with bipolar disorders on the other hand, studies examining the relationship between age at onset and gender have produced varying results (Kawa et al., 2005; Kennedy et al., 2005; Raymont et al., 2003; Viguera et al., 2001). Significantly, men had been reported to present with earlier onset of first-episode mania and bipolar disorder compared to women (Kennedy et al., 2005; Raymont et al., 2003; Viguera et al., 2001) while others had reported men and women had similar age of onset but differ in the type of episode at onset and comorbidity pattern (Kawa et al., 2005).

Oftentimes, the onset symptoms of schizophrenia begin in the 2nd and 3rd decade of life, though the onset may be earlier or later, and may even extend to the 7th decade of life (Gogtay et al., 2011). This may explain the long-range of age-onset noted in the study. However, some authors had raised the possibility of those disorders occurring at the later end of life as other variants (Howard et al., 2000; Maglione et al., 2014).

Varying findings have been reported on the impact of the FL of mental illness (Esterberg & Compton, 2012; Ritsner et al., 2005; Ritsner et al., 2007). Positive first-degree FH of psychosis had been reported to be associated with younger age at onset (Esterberg & Compton, 2012; Hiker et al., 2017). However, there was no significant relationship between familial predisposition and age of onset in this population. Other environmental factors such as trauma, life adversity, obstetric complications which are likely to be more prevalent in this environment may explain this finding. Nevertheless, the risk of developing schizophrenia as a result of familial disposition decreased as the age of onset increases (Byrne et al., 2002). Furthermore, there was no significant difference in the age of onset of both schizophrenia and bipolar disorder, suggesting similar factors may influence the age at onset.

Compared with those that were ever married, participants who were single were more likely to have developed the illness before the age of 30. Marriage has been reported to be associated with reduced risk of early onset of most mental disorders in both males and females (Mojtabai et al., 2017; Scott et al., 2010). Nevertheless, individuals with major mental illness are at higher risk of marital dissolution, or less likely enter into new marriages (Scott et al., 2010). Although marriage acts as a protective factor, it may also act as a predisposing/precipitating factor for most psychiatric disorders (Mina, 2019). Nonetheless, longitudinal studies are needed to provide greater clarity on the temporal association between the age of onset of mental health symptoms and marital status.

A substantial number of participants had a family history of mental illness, mostly as siblings and parents. However, no association was found between age of onset and family history of mental illness, suggesting other factors may contribute to early onset. Males and singles were more likely to develop mental illness earlier compared with their females or ever married counterparts. Similarly, those with early age of onset were more likely to present with more severe form compared with those who developed the illness at an older age.

(Abbreviations: BD: Bipolar Disorder, FH: Family History, FL: Familial Liability, SPSS: Statistical Package for Social Sciences.)

Patient informed consent : Informed consent was obtained.

Ethics committee approval : The ethics committee approval has been obtained from Ekiti State University Teaching Hospital with Ethics and Research committee report number of EKSUTH/A67/2019/09/019 (10 Oct 2019).

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Author contribution subject and rate:

Adetunji Obadeji (%50): conception/design of the work, data acquisition, analysis interpretation and drafting and its critical revision for important intellectual content

Lateef Olutoyin Oluwole (%28): involved in refining the conception of the work, the interpretation of data for the work and revising it critically for important intellectual content.

Christopher Goson Piwuna (%22): involved in refining the conception of the work, the interpretation of data for the work and revising it critically for important intellectual content.

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