Co-morbid anxiety disorders in patients with schizophrenia in a tertiary institution in South East Nigeria: prevalence and correlates.

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Abstract

Background: Anxiety disorders occur commonly in schizophrenia but are often overlooked by psychiatrists. Their presence may compound the challenges faced by these patients and may contribute to poor outcome.

Objectives: The purpose of this study was to determine the prevalence of anxiety disorders among the participants with schizophrenia, and the association between this co-morbidity and disability.

Method: A total of 367 participants were recruited from the out-patient department of Federal neuropsychiatric hospital Enugu, Nigeria. Socio-demographic questionnaire, schedules for clinical assessment in neuropsychiatry, positive and negative syndrome scale and the 12-item version of the World Health Organization disability assessment schedule were administered.

Results: A total of 189 females (51.5%) and 178 (48.5%) males were studied. A lifetime prevalence of 12.3% was reported for anxiety disorder. Anxiety disorder was more likely in females (χ^2=4.93, p<0.03). Specific prevalence for anxiety disorder in schizophrenia was generalized anxiety disorder 6.3%, obsessive compulsive disorder 3.3%, and phobic anxiety disorder 2.7%. Anxiety disorder was associated with increased disability (t=3.50, p<0.001) and psychopathology (t=3.40, p<0.001) among the participants studied. Phobias were associated with prescription of low doses of antipsychotics (χ^2=4.08, p<0.04). There was a low rate of identification of anxiety disorder in routine clinical practice (k=0.08, p<0.001).

Conclusion: Co-morbid anxiety disorders are common in schizophrenia and they are associated with increased disability and psychopathology. The results emphasize the need to screen for anxiety disorders in patients with schizophrenia.

Key words: schizophrenia, anxiety disorder, co-morbidity.

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Introduction

Anxiety disorder is a blanket term covering several different forms of abnormal and pathological fears and anxieties[1]. There are several forms of anxiety disorders which include generalized anxiety disorder, panic disorder, phobias and obsessive compulsive disorder[2]. Anxiety disorders are often co-morbid with other mental disorders[3].

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For over a hundred years now, clinicians and researchers have been challenged by the co- occurrence of anxiety symptoms and psychotic illness[4]. Early clinicians, such as Westphal, Kraepelin, Stengel, and Bleuler considered it either a prodrome or an integral part of the schizophrenic illness[5].

Many studies show that Anxiety disorders co-occur commonly in schizophrenia[6]. Review of literature has reported a wide range of prevalence for anxiety disorder in schizophrenia ranging from 30-85%[7]. A study carried out in Brazil reported that at least 51% of patients with schizophrenia met criteria for at least one form of anxiety disorder[6]. In Turkey, a study that recruited 82 out-patients with schizophrenia diagnosed fifty-five (67.1%) with at least one lifetime co-morbid anxiety disorder[8]. A work that studied racial disparity in the rate of diagnosis of anxiety disorder in Caucasians and African-Americans reported an anxiety disorder di-

agnosis rate of 27% in Caucasians and 13% in African Americans.[9]

A study which was part of Nigerian survey of mental health and wellbeing conducted in 8 out of the 22 states in Nigeria, thus representing about 22% of the national population reported that persons with psychotic experiences were more likely to have experienced other co-morbid disorders like mood disorders, anxiety disorders, substance use disorders[10]. The same study reported a 15% co-morbidity rate for anxiety disorders in patients with non-affective psychosis (including schizophrenia and schizophreniform disorders)[10].

A Turkish study reported the most common anxiety disorder to be obsessive compulsive disorder (39.0%), followed by social phobia with a prevalence rate of 13.4%[8]. Other studies reported specific prevalence of social phobia (17%), obsessive compulsive disorder (15.1%), generalized anxiety disorder (9.4%), panic disorder (5.7%), specific phobia (5.7%) and 1.9% for agoraphobia[11]. A large community-based, controlled, prospective study in in newly diagnosed patients with psychotic disorders found 10 to 20 - percent prevalence rates for co-morbid obsessive compulsive disorder[12].

While anxiety disorder is common in schizophrenia, it is not clear if it affects functioning. Reports about the effects of co-morbid anxiety disorder on function have varied with some studies reporting greater functional impairment[5] while others found no significant difference between the two comparison groups[13]. Rosen and Jahreiss in 1946 concluded that the presence of obsessive compulsive symptoms conferred some protection against cognitive deficits, functional impairment, and negative symptoms associated with schizophrenia[14]. However, more recent studies that used rigorous methods have not replicated these earlier findings[15] but rather have shown poorer outcome[5] and a severe level of disability[16,17]. It has also being associated with a great deal of suffering with increase in hopelessness, suicide risk, higher rates of relapse, re-hospitalization[18] and poorer social functioning[16]. A study conducted in Nigeria reported low quality of life in patients with schizophrenia who had co-morbid anxiety disorder[19]. A study carried out in Israel in 2009 by Mazeh et al reported higher total positive and negative syndrome scale (PANSS) score in in-patients with co-morbid anxiety in schizophrenia but this did not reach statistical significance[20]. A high positive correlation was also reported between the severity of anxiety symptoms and positive symptoms in schizophrenia[21].

However some studies have found patients with a diagnosis of schizophrenia with co-morbid anxiety disorder to have a shorter duration of illness compared to those without such co-morbid condition[8]. Another study by Lysaker et al among patients with obsessive compulsive symptoms found no correlation between the presence of anxiety symptoms and the severity of positive psychotic symptoms in schizophrenia[22]. Emsley in 2001 proposed that anxiety was a core symptom of schizophrenia and that high level of anxiety could possibly predict a favorable outcome in the treatment of schizophrenia, particularly if depressive symptoms are experienced during the acute phase of the schizophrenic episode[21].

Anxiety disorder in schizophrenia remains largely unrecognized by clinicians. A study done in Australia on 100 consecutively admitted in-patients with schizophrenia found that anxiety disorders though common (45% in the patients studied), was unrecognized by clinicians in almost all of the patients[23]. Craig, Hwang and Bromet reported that only about 10 percent of patients with co-morbid obsessive compulsive symptoms were identified by the clinicians.

However, despite the low rate of recognition by clinicians, 20 percent or more of these patients received treatment that was appropriate for co-morbid anxiety disorders[5].

Few studies have been done to ascertain the clinical implications of anxiety disorders on patients with schizophrenia in Nigeria. Considering that it is common and has been associated with significant disability it becomes necessary to study it in this environment.

Therefore this study determined

The prevalence of anxiety disorders among the participants with schizophrenia and the association between co-morbid anxiety disorder and depression with disability.

Method

This was a descriptive cross-sectional study carried out at Federal neuropsychiatric hospital, Enugu, Nigeria between May and December 2011. The sample frame consisted of patients with schizophrenia who attended outpatient clinics on Monday, Tuesday, Thursday and Friday every week. Patients were selected consecutively for the study if they were being managed at the out-patient department of Federal neuropsychiatric hospital Enugu, Nigeria if they had a diagnosis of schizophrenia made by a consultant psychiatrist using ICD-10 criteria and confirmed with present state examination 10 (PSE), and had no other important physical condition or mental disorder besides schizophrenia. A total of 367 patients were recruited.

For the participants with a diagnosis of schizophrenia, schizophrenia section of PSE was administered. Then the socio-demographic questionnaire was administered to all the participants and/or their accompanying relatives. Information about the participants such as age, sex, marital status, level of education, religious affiliation, occupation, age of onset of schizophrenia, use of anticholinergic medication and duration of illness were obtained and coded into a proforma.

Thereafter, anxiety section of PSE was then administered to detect participants with anxiety disorder. Severity of psychotic symptoms was measured and quantified with PANSS in all participants. Finally World Health Organization disability assessment schedule (WHODAS) was administered to measure disability in all the participants.

After the interviews, from the case notes of all the participants the following pieces of information were extracted: current type and dosage of antipsychotic medication, and where applicable, more information about the patient (socio-demographic data).

Antipsychotic medications used by the participants were converted to their chlorpromazine equivalents. Participants who understood English were interviewed with the English language versions of the study instruments while those who did not understand English were administered the Igbo language versions by the researchers who are bilingual in both English and Igbo languages.

Approval was obtained from the ethics committee of the Federal neuropsychiatric hospital Enugu. All participants gave voluntary informed consent before recruitment into the study.

Study instruments

1. Socio-demographic Questionnaire:

This instrument was designed to obtain basic information about a patient's health and biodata. Socio-demographic characteristics such as age, sex, marital status, occupation, employment status, religion, level of education were documented. The age at illness onset and illness duration were also recorded.

2. Present State Examination 10 (PSE 10)

This is a structured diagnostic interview schedule that has been incorporated into the Schedules for clinical assessment in neuropsychiatry (SCAN).

It rates the presence or absence of symptoms and also the severity and frequency of abnormal beliefs and experiences. The presence of each syndrome can be rated from case notes and interviews with the respondent and his informants.

It confirms the presence of schizophrenia using at least one of the following first rank symptoms like voices commenting or discussing the patient in the third person, loud thoughts, thought insertion, thought broadcast or withdrawal, delusions of control, delusional perception and bizarre delusions.

Presence of anxiety is rated on a 2 point scale with 0 indicating that generalized anxiety disorder, panic attacks and phobias were 'absent' and 1 indicating 'present'. The presences of obsession and compulsive symptoms are also rated on a 2 point scale with 0 indicating no evidence of symptoms and I indicating sufficient evidence to proceed. PSE measures clinical severity by the duration and frequency of symptoms and the degree of interference with mental functions (intensity).

Positive and Negative Syndrome Scale (PANSS)

PANSS is a 30-item questionnaire that is used to assess patients' current mental state. It classifies schizophrenia into positive and negative subtypes. It has become one of the standard tools for assessing clinical outcome in treatment studies of schizophrenia. The PANSS includes 30 items on 3 subscales: 7 items covering positive symptoms, 7 covering negative symptoms and 16 covering general psychopathology. Each item is scored on a seven-point item-specific Likert scale ranging from 1 to 7; thus the negative and positive subscales each range from 7 to 49, and the general psychopathology scale from 16 to 112. For the purpose of this study,

scores for the three scales were arrived at by summation of ratings across the component items. The PANSS is interviewer administered and reliability for each scale is fairly high, with excellent internal consistency and inter-rater reliability. Validity also appears good based on correlation with other symptom severity measures and factor analytical validation of subscales.

World Health Organization /Disability Assessment Schedule II (WHODAS) 12 item version

WHODAS is a generic disability measure that is not disorder-specific. It was developed in 1988 by World Health Organization. It was designed to assess disturbance in social adjustment and behavior and the factors that might influence these dysfunctions in persons with mental illness.

The WHODAS II is a self-report questionnaire that assesses activity limitations and disability in the previous month. It was developed to assess six different adult life tasks: Understanding and communication, Self-care, Mobility, Interpersonal relationships, Work and household roles and Community and civic roles. It has been cross-culturally tested in 16 languages in 19 different countries of which Nigeria is one of them (WHO, 2000).

The participants interviewed are asked to indicate the experienced level of difficulty (none 1, mild 2, moderate 3, severe 4, extreme 5), by taking into account the way in which they normally perform a given activity. The sum score for global disability therefore ranges from 12 (no disability) to 60 (complete disability)

The internal consistency and test-retest reliability of the overall WHODAS 2.0 is high. Scoring was done using a simple sum scoring method. It has an administration time of approximately 5 minutes.

Statistical analysis

Data was analyzed using the Personal Computer version of Statistical Package for the Social Sciences (SPSS-PC) Version 15. All tests of significance were two-tailed at the 5% level and confidence interval estimation at 95%.

Results

A total of 367 participants, 189 females (51.5%) and 178 (48.5%) males were studied. The mean age of the participants was 34.1 ± 9.94 (range 18-63 years). The majority of the participants, 266 (72.5%), were less than 40 years. Most of them, 302 (82.3%) had been ill for more than 3 years. Most of the participants, 241 (65.7%), were never married. The majority of the participants, 203 (55.3%), had secondary education and majority were unemployed, 203 (55.3%). Almost all of the participants, 364 (99.2%), were Christians.

A comparison of the socio-demographic characteristics of participants with anxiety disorder and without anxiety disorder (Table 1) showed that more of the participants with anxiety disorder were females and that most of them belonged to the age range 30-49 years. The mean age of the

participants with anxiety disorder was 33.82 ± 8.66 years. There was no significant difference in the rate of marriage, education and employment between the two comparison groups.

Table 1: Comparison of the socio-demographic characteristics of participants with anxiety disorder and without anxiety disorder.

Variables	Anxiety disorder		Test statistic	p-value
	Yes N (%)	No N (%)		
Sex				
Male	19 (42.2)	159 (49.4)	χ^2=0.81	p<0.37
Female	26 (57.8)	163 (50.6)		
Age (years)				
10-29	13 (28.9)	121 (37.6)	t=-0.19	p<0.84
30-49	29 (64.5)	167 (71.9)		
50-69	3 (6.7)	34 (10.6)		
Mean ± S.D	33.82±8.66	34.14±10.12		
Marital status				
Married	10 (22.2)	77 (23.9)	χ^2=0.06	p<0.80
Not married	35 (77.8)	245 (76.1)		
Educational level				
No formal education	2 (4.4)	14 (4.3)	χ^2=0.00	p<0.99
Formal education	43 (95.6)	308 (95.7)		
Employment status				
Employed	24 (53.3)	140 (43.5)	χ^2=1.51	p<0.21
Not employed	21 (46.7)	182 (56.5)		

Forty five (12.3%) of the participants had anxiety disorder. Of all the participants studied, 6.3% had generalized anxiety disorder, 3.3% had obsessive compulsive disorder while 2.7% had phobic anxiety disorder. None of the participants met the diagnosis for panic disorder.

More females (Table 2) had generalized anxiety disorder (χ^2=4.93, p<0.03). There was no significant association between obsessive compulsive disorder (χ^2=0.48, p<0.49), phobia (χ^2=0.54, p<0.46) and gender.

Table 2: Distribution of anxiety disorder by gender.

Variable	Type of anxiety disorder	n	% of anxiety disorder
Male			
	Generalized Anxiety Disorder	6	13.3
	Obsessive Compulsive Disorder	7	15.6
	Phobia	6	13.3
Female			
	Generalized Anxiety Disorder	17	37.8
	Obsessive Compulsive Disorder	5	11.1
	Phobia	4	8.9

It was revealed (Table 3) that among the participants, more of those with generalized anxiety disorder, 16 (69.6%) were on high dosage of antipsychotic compared to 173 (50.3%) without generalized anxiety disorder (χ^2=3.21, p<0.07). The participants with phobic anxiety disorder were significantly more likely to be on low dose compared to those without phobia (χ^2=4.08, p<0.04)

Table 3: Distribution of antipsychotic dosage among participants with anxiety disorder.

	Dosage	Anxiety disorder		Statistics
		Yes n (%)	No n (%)	
GAD				
	High dose	16 (69.6)	173 (50.3)	χ^2=3.21
	Low dose	7 (30.4)	171 (49.7)	p<0.07
OCD				
	High dose	6 (50)	183 (51.5)	χ^2=0.01
	Low dose	6 (50)	172 (48.5)	p<0.92
Phobia				
	High dose	2 (20)	187 (52.4)	χ^2=4.08
	Low dose	8 (80)	170 (47.6)	p<0.04

The participants' WHODAS scores were dichotomized (yes/no) such that participants with a total score of 12 were regarded as having no disability while scores above 12 indicated presence of disability. The participants with anxiety disorder had a mean WHODAS score of 26.0 ± 7.6 compared to 21.5 ± 8.3 for those without anxiety disorder (t= 3.50, p<0.001).

Among the participants studied, Pearson correlation showed no significant correlation between WHODAS scores and dosage of antipsychotics (in chlorpromazine equivalent) among the patients with anxiety disorder (r=0.22, p<0.14).

Among all the participants studied, the mean PANSS score was 45.01 ± 11.89 (range 30-94). The participants with anxiety disorder had a mean PANSS score of 50.6 ± 9.3 compared to 44.2 ± 12.0 for those without anxiety disorder (t= 3.4, p< 0.001).

Forty five participants had any anxiety disorder; the managing psychiatrist identified only 2 (4.4%). There is a poor level of agreement in the rate of identification of anxiety disorders
(kappa= 0.08, p<0.001).

Table 4 Identification of anxiety disorder by managing psychiatrist

		N (%)	Statistics	p-value
Anxiety disorder	**Anxiety disorder identified in folder**	2 (4.4)	kappa=0.08	p<0.001
Anxiety disorder not identified in folder		43 (95.6)		

Table 5 shows the correlates of comorbid anxiety disorder in schizophrenia. None of the variables was a significant predictor of anxiety disorder in schizophrenia.

Table 5: Correlates of comorbid anxiety disorder in schizophrenia.

	S.E.	df	p-value
Gender	.326	1	.363
Age	.167	1	.961
Marital status	.402	1	.631
Education	.799	1	.967
Employment	.330	1	.200
Constant	1.014	1	.024

Discussion

Different studies have reported a wide range of prevalence for anxiety disorder in schizophrenia ranging from 30-85%[7]. The wide variations in the prevalence rate could be due to methodological differences, heterogeneity among definitions of symptoms and rating instruments used for diagnosis. Some of these studies included patients with schizoaffective disorder and schizophreniform disorders and it was difficult to do a direct comparison because the two groups were not analyzed separately.

In this study, a 12.3% prevalence rate of anxiety disorder was found which is comparable to 15% comorbidity rate for anxiety disorders in patients with non-affective psychosis which included schizophrenia and schizophreniform disorders reported in a previous study[24]. A previous work that studied racial disparity in the rate of diagnosis of anxiety disorder in Caucasians and African-Americans with schizophrenia reported 27% anxiety disorder diagnosis rate in Caucasians and 13% in African Americans which they attributed to under-reporting of anxiety symptoms in African-Americans[9]. However it is possible that the difference may be due to racial differences in the rate of anxiety experienced by the two groups. Other studies of anxiety disorder in schizophrenia reported a higher anxiety rate of 43%[23] and 41.5%[22]. These higher rates may be explained by the use of in-patients who may report higher rates of anxiety than the out- patients[23] and the measurement of lifetime rates instead of current rate of anxiety disorder[11].

Differences in the rates of compulsive disorder[13, 14,23,25,26], phobic anxiety disorder[8] and panic disorder[11,23] reported elsewhere and rates revealed in this study may be due to methodological differences.

Participants with co-morbid anxiety disorder had significantly more disability than those without co-morbid anxiety. This may be due to additional burden imposed by anxiety symptoms on a person with schizophrenia. This agrees with what was reported in a previous study which found significantly higher scores in global scale, work subscale, and social life subscale of the Sheehan Disability Scale in schizophrenia subjects with co-morbid anxiety[17,11,27]. This is also in agreement with other studies that found that co-morbid anxiety in schizophrenia was associated with significantly lower level of function[28,29].

The participants in this study who had anxiety disorder had a significantly higher mean PANSS score than those without anxiety disorder. A study carried out in Israel reported higher total PANSS score in in-patients with schizophrenia who also had co-morbid anxiety[20]. This may imply that the presence of anxiety disorder in schizophrenia is a poor prognostic indicator.

There was a low rate of identification of anxiety disorder in the participants by the managing psychiatrists which agrees with a previous Australian study that reported virtually no recognition of anxiety disorder in patients with schizophrenia by the clinicians[30]. The low rate of recognition may be due to more attention being paid to florid psychotic symptoms or the clinicians' inability to recognize the symptoms of anxiety in these patients.

Among the participants, there was an increased rate of generalized anxiety disorder in the females. This agrees with previous studies that report generalized anxiety disorder to be twice as common in females[31].

Conclusion

This study highlights the fact that anxiety disorders are common in patients with schizophrenia and are poorly recognized by psychiatrists. Given that anxiety disorders contribute to significant disability in patients with schizophrenia emphasis should be placed on their recognition and treatment.

Limitations

The results of this study should be interpreted with caution because of several methodological shortcomings. First, it was cross-sectional in nature, thus the causality of relationships between smoking and demographic and clinical variables could not be explored. Second, it was a cross- sectional non-population representative study. Its results cannot be generalized to the entire population. Despite these caveats, findings from this study should serve as a baseline data for comparison in future.

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