Correlates and management of comorbid anxiety disorders in schizophrenia

Chandra Kiran,
Suprakash Chaudhury¹
Department of Psychiatry,
Ranchi Institute of Neuropsychiatry and Allied Sciences, Ranchi, Jharkhand,
¹Department of Psychiatry,
Dr. D. Y. Patil Medical College,
Pune, Maharashtra, India

Address for correspondence:
Dr. Suprakash Chaudhury,
Department of Psychiatry,
Dr. D. Y. Patil Medical College,
Pimpri, Pune - 411 018,
Maharashtra, India.
E-mail: suprakashch@email.com

ABSTRACT

Background: Only a few studies have examined the treatability of anxiety disorders in schizophrenia, even though it is generally accepted that in the absence of schizophrenia, the anxiety disorders are safely and effectively treatable. Aim: The aim of this study was to study the relation of anxiety disorders with the positive and negative symptoms of schizophrenia and the effect of treatment of different anxiety disorders in schizophrenia patients. Materials and Methods: The study was carried out on inpatients of a tertiary care psychiatric hospital using a purposive sampling technique. The schizophrenia patients were evaluated for psychopathology and the presence of anxiety disorder at baseline. After being prescribed with antipsychotic medication in a suitable dose for 8 weeks, they were followed up at monthly intervals for the course of both schizophrenia and anxiety disorders. Thereafter, an selective serotonin reuptake inhibitor (SSRI) was also prescribed to the schizophrenia patients with comorbid anxiety disorder, and the patients were again followed up for a period of 8 weeks to assess the progress of schizophrenia and anxiety disorder. Results: The prevalence of anxiety disorder in 93 schizophrenia patients included in the present study was 45.16%. The most common comorbid anxiety disorders in schizophrenia patients were panic disorder (18.27%), social anxiety disorder (9.68%), obsessive-compulsive disorder (8.60%), and agoraphobia (6.45%). Schizophrenia patients with anxiety disorder had a significantly higher positive score of the Positive and Negative Symptom Scale for Schizophrenia (PANSS) and a significantly lower score on the negative scale and the general psychopathology scale of the PANSS, as compared to the scores of the schizophrenia group without anxiety disorders. Schizophrenia patients with anxiety disorders responded well to the combination of SSRIs and antipsychotics but not antipsychotics alone. Conclusions: Comorbid anxiety disorders are common in schizophrenia. Schizophrenia patients with anxiety disorders differ significantly from those without anxiety disorders in their basic psychopathology. These anxiety disorders are quite responsive to the SSRIs but not to antipsychotics alone. Further, there is a shorter duration of illness in schizophrenia patients with anxiety disorders as compared to schizophrenia patients without anxiety disorders assigning a prognostic significance to the presence of comorbid anxiety disorders in schizophrenia.

Keywords: Anxiety disorders, clinical correlates, comorbidity, schizophrenia, treatment

In psychiatry, the conventional systems of diagnosis with their hierarchical assumptions have played a role in diverting attention from assigning dual diagnosis for co-occurring syndromes. The basic assumption shared by hierarchical system of classification is that there is a hierarchy of diagnoses and that diagnoses that are higher on the hierarchy subsume diagnosis lower on the hierarchy. Therefore, it was assumed that the diagnosis of schizophrenia could somehow explain or account for the presence of lower diagnosis such as anxiety disorders in patients diagnosed with schizophrenia. This assumption is connected to diagnostic reductionism, that is, the
tendency to reduce all of the signs and symptoms shown by persons with schizophrenia to schizophrenia alone. Such reductionism undoubtedly contributes to the widespread tendency to treat schizophrenia as if it were a single unitary disorder and thus prevent clinicians and researchers from paying adequate attention to the accessory symptomatology shown by these patients outside of the core symptoms. The newer editions of classificatory systems have made some progress in recognizing these comorbid syndromes, but remnants of the old thinking persist. These remnants may continue to interfere with the recognition of comorbid anxiety disorders in schizophrenia and their therapeutic implications.11–32

As a result of these advances in recent years, there have been consistent reports of increased prevalence of comorbid anxiety disorders in schizophrenia.33–38 Despite this, little work has been done to establish the clinical validity and practical utility of this phenomenon. Of special concern is that only a few studies have examined the treatability of anxiety disorders in schizophrenia, even though it is generally accepted that in the absence of schizophrenia, the anxiety disorders are safely and effectively treatable. Findings from small preliminary case studies suggest that panic attacks, obsessive-compulsive disorder (OCD), and posttraumatic stress disorder (PTSD) in the presence of schizophrenia may be treatable as well. In view of the paucity of studies in this area, the present study was undertaken to assess the relation between anxiety disorders and the symptomatology of schizophrenia, that is, relation with the positive and negative symptoms. In addition, the response of anxiety disorders to medication (antipsychotics and selective serotonin reuptake inhibitors [SSRIs]) was also evaluated.

**MATERIALS AND METHODS**

This prospective, hospital-based study conducted at Ranchi Institute of Neuropsychiatry and Allied Sciences (RINPAS), Kanke, Ranchi, a 500-bedded postgraduate teaching psychiatric hospital and tertiary referral center for the patients with psychiatric disorders from the states of Jharkhand and Bihar. The study sample was selected using purposive sampling technique and comprised 93 consecutively admitted inpatients fulfilling ICD-10 DCR criteria for schizophrenia.39 The study was conducted with the approval of the Ethics Committee of the Institute. The inclusion and exclusion criteria for the study group are given below.

**Inclusion criteria for the study group**

- Inpatients of RINPAS Meeting ICD-10 DCR criteria for schizophrenia

- Patients in the age range of 18–55 years

- Patients who are drug naïve or off drugs for a period of 1 month or off depot preparation for at least 3 months

- Cooperative for the interview.

**Exclusion criteria for the study group**

- Patients not willing to give informed consent

- History of mental retardation

- History of substance abuse/neurological disorder/ head injury/major physical illness.

After explaining the purpose of the study and obtaining informed consent from the schizophrenia patients, their sociodemographic characteristics were recorded on a specially prepared pro forma. The participants were then assessed using the Mini-International Neuropsychiatry Interview,39 Brief Psychiatric Rating Scale (BPRS),40 and Positive and Negative Symptom Scale for Schizophrenia (PANSS)41 for a baseline assessment of psychopathology. Thereafter, the schizophrenia patients were divided into two groups: schizophrenia with anxiety disorder and schizophrenia without anxiety disorder. The schizophrenia patients with various anxiety disorders were assessed using the appropriate anxiety scales: Acute Panic Inventory,42 Mobile Inventory for Agoraphobia,43 Yale–Brown Obsessive-Compulsive Scale (YBOCS),44 Liebowitz Social Anxiety Disorder Scale (LSADS),45 Generalized Anxiety Disorder-7 Scale (GAD-7),46 and Impact of Event Scale.47

All the schizophrenia patients were prescribed with appropriate antipsychotic medications (haloperidol, trifluoperazine, olanzapine, risperidone, and clozapine) in an adequate dose. They were then evaluated monthly using the above-mentioned scales for psychopathology and appropriate anxiety disorder scale as well as the objective and subjective observations of the patients for the course of both schizophrenia as well as the anxiety disorders symptoms. At the end of 8 weeks, an SSRI (fluoxetine) was prescribed in addition only to schizophrenia patients with anxiety disorders, while the schizophrenia patients without anxiety disorders were continued on their antipsychotic medications. Again, the course of the anxiety disorder and the effect of the same on the schizophrenia symptoms were evaluated for 8 weeks.

The obtained results were then tabulated for evaluation using the aid of computer program SPSS 17 (IBM, ISA). Analysis of general sociodemographic variables, clinical characteristics, and scores on psychopathology scales (BPRS scale and PANSS scale) were done using the t-test, Chi-square test, and Mann–Whitney U-test to identify significant differences between schizophrenia patients with and without anxiety disorders. The association
between the different anxiety disorder scores at baseline and psychopathology scales (BPRS scale and PANSS scale) was obtained using Spearman’s bivariate correlation. Comparison of psychopathology scores before and after treatment was assessed using the Wilcoxon test. In this study, a level of significance of <0.05 (two-tailed) was taken to consider a result statistically significant.

**RESULTS**

The study group of 93 schizophrenia patients consisted of 79 male patients and 14 female patients with a mean age of 31.30 (±8.27) years. There was no significant difference between schizophrenia patients with anxiety disorders and schizophrenia patients without anxiety disorders with respect to the sociodemographic variables [Table 1]. Comparison of the clinical characteristics of schizophrenia patients with and without anxiety disorders showed that the two groups differed significantly on duration of illness, the type of schizophrenia, and the drug status [Table 2]. There were no significant differences between the two groups on age of onset, mode of onset, precipitating factors, past history, and family history of psychiatric illness [Table 2].

The prevalence of anxiety disorder was 45.16% (n = 42) in the schizophrenia patients. Further analysis revealed that the prevalences of various types of anxiety disorders in schizophrenia patients were as follows: panic disorder 18.28% (n = 17), social anxiety disorder 9.68% (n = 9), OCD 8.60% (n = 8), agoraphobia 6.50% (n = 6), PTSD 1.08% (n = 1), and GAD 1.08% (n = 1).

Overall, the schizophrenia group with anxiety disorder had a significantly higher positive score of the PANSS, a significantly lower negative score on PANSS, and a significantly lower score on the general psychopathology scale of the PANSS, as compared to the scores of the schizophrenia group without anxiety disorders. In contrast, the values obtained for the BPRS for the two groups were not significantly different [Table 2]. Distribution of psychopathology scores among various anxiety disorders is summarized in Table 3. There was a significant correlation between positive scores on PANSS and Liebowitz Social Anxiety Scale (LSAS) scores in social anxiety disorder. In agoraphobia patients, a significant correlation was noted between scores on mobility inventory and positive, negative, and general psychopathology of PANSS and the BPRS.

After the baseline evaluation, the schizophrenia patients were given antipsychotics both from the first generation as well as the second generation (haloperidol, trifluoperazine, olanzapine, risperidone, and clozapine) in an adequate dose and their effect on the schizophrenia as well as the anxiety disorder was assessed. There was a significant decrease in

| Table 1: Comparison of sociodemographic characteristics of schizophrenia patients with and without anxiety disorders |
|-----------------|-----------------|-----------------|-----------------|-----------------|
| Variables       | Category        | Schizophrenia with anxiety disorder (n=42), n (%) | Schizophrenia without anxiety disorders (n=51), n (%) | t/χ² |
| Age (years)     |                 |                 |                 |                 |
| Gender          | Male            | 32 (76.2)       | 39 (76.5)       | 3.911           |
|                 | Female          | 10 (23.8)       | 12 (23.5)       |                 |
| Education       | Matric and below| 35 (83.3)       | 43 (84.3)       | 0.650           |
|                 | Above matric    | 7 (16.7)        | 8 (15.7)        |                 |
| Occupation      | Farmer          | 18 (42.9)       | 19 (37.2)       | 1.263           |
|                 | Employed        | 6 (14.3)        | 9 (17.7)        |                 |
|                 | Homemaker       | 7 (16.7)        | 6 (11.8)        |                 |
|                 | Unemployed      | 11 (26.1)       | 17 (33.3)       |                 |
| Marital status  | Unmarried       | 14 (33.3)       | 16 (31.4)       | 0.841           |
|                 | Married         | 22 (52.4)       | 28 (54.9)       |                 |
|                 | Others          | 6 (14.3)        | 7 (13.7)        |                 |
| Religion        | Hindu           | 33 (78.6)       | 38 (74.5)       | 0.850           |
|                 | Others          | 9 (21.4)        | 13 (25.5)       |                 |
| Mother tongue   | Hindi           | 29 (69.4)       | 36 (70.6)       | 1.738           |
|                 | Others          | 13 (30.6)       | 15 (29.4)       |                 |
| Income          | <3000           | 26 (61.9)       | 34 (66.7)       | 5.811           |
|                 | 3001-7000       | 7 (16.7)        | 13 (25.5)       |                 |
|                 | >7000           | 9 (21.4)        | 4 (7.8)         |                 |
| Residence       | Rural           | 31 (73.8)       | 40 (78.4)       | 2.994           |
|                 | Urban           | 11 (26.2)       | 11 (21.6)       |                 |
| Family type     | Nuclear         | 13 (31.0)       | 18 (35.3)       | 0.700           |
|                 | Joint           | 29 (69.0)       | 33 (64.7)       |                 |
the severity of the panic disorder after the administration of antipsychotic drugs but not in the severity of OCD, social anxiety disorder, or agoraphobia. After a period of 8 weeks, the patients were prescribed fluoxetine in addition and the progress of anxiety disorder assessed. It was seen that in all the cases, the severity of the anxiety disorder had decreased in a significant manner [Table 4].

**DISCUSSION**

The current study has attempted to improve over the methodological limitations of the previous studies. These studies had included a small number of patients in the clinical samples and concentrating on a one or few of the anxiety disorders, namely, panic disorder and OCD. Hence, increasing the sample size as well as including all the anxiety disorders with specific treatments for anxiety disorders is a methodological improvement over earlier studies.

**Characteristics of schizophrenia patients with and without anxiety disorder**

In the present study, no significant differences were found in the sociodemographic variables of schizophrenia patients without anxiety disorders and schizophrenia patients with anxiety disorders [Table 1]. This is similar to the findings of many other studies.[5,18-22]

There was a significant difference between the duration of schizophrenic illness in schizophrenics with anxiety disorder and schizophrenics without anxiety disorder [Table 2], as the duration of illness was longer in cases of schizophrenia patients without anxiety disorders as compared to schizophrenia patients with anxiety disorders, which is a

| Variables                                      | Schizophrenia with anxiety disorders (n=42) | Schizophrenia without anxiety disorders (n=51) | t/χ²   | P    |
|------------------------------------------------|--------------------------------------------|-----------------------------------------------|-------|------|
| Illness duration (years), mean±SD              | 5.14±5.25                                  | 9.22±5.38                                    | t=26.903 | 0.01** |
| Age at onset (years), mean±SD                  | 27.28±7.97                                 | 25.16±8.36                                   | t=4.216 | 0.98  |
| BPRS scores, mean±SD                           | 45.25±3.69                                 | 46.57±53.59                                  | t=1.723 | 0.10  |
| Positive subscale of PANSS, mean±SD            | 24.86±3.54                                 | 21.20±5.24                                   | t=4.001 | 0.01** |
| Negative subscale of PANSS, mean±SD            | 21.69±4.01                                 | 26.03±4.39                                   | t=4.976 | 0.01** |
| General psychopathology scale of PANSS, mean±SD| 43.06±3.75                                 | 45.38±5.59                                   | t=3.027 | 0.01** |
| Diagnosis, n (%)                               |                                            |                                               |       |      |
| Paranoid                                       | 36 (85.7)                                  | 24 (47.1)                                    | χ²=24.502 | 0.01** |
| Others                                         | 6 (14.3)                                   | 27 (52.9)                                    |       |      |
| Mode of onset, n (%)                           |                                            |                                               |       |      |
| Abrupt                                         | 1 (2.4)                                    | 1 (2.0)                                      | χ²=3.012 | 0.99  |
| Acute                                          | 4 (9.5)                                    | 3 (5.9)                                      |       |      |
| Insidious                                       | 37 (88.1)                                  | 47 (92.4)                                    |       |      |
| Precipitating factor, n (%)                    |                                            |                                               |       |      |
| Present                                        | 7 (16.7)                                   | 7 (13.7)                                     | χ²=7.393 | 0.764 |
| Absent                                         | 35 (83.3)                                  | 44 (86.3)                                    |       |      |
| Drug status, n (%)                             |                                            |                                               |       |      |
| Drug naive                                     | 19 (45.2)                                  | 14 (27.5)                                    | χ²=7.839 | 0.005** |
| Drug free                                      | 22 (54.8)                                  | 37 (72.5)                                    |       |      |
| Past history of psychiatric illness, n (%)     |                                            |                                               |       |      |
| Present                                        | 3 (7.1)                                    | 5 (9.8)                                      | χ²=4.377 | 0.931 |
| Absent                                         | 39 (92.6)                                  | 46 (90.2)                                    |       |      |
| Family history of psychiatric illness, n (%)   |                                            |                                               |       |      |
| Present                                        | 12 (28.6)                                  | 15 (23.5)                                    | χ²=11.442 | 0.30  |
| Absent                                         | 30 (71.4)                                  | 38 (76.5)                                    |       |      |
| Comorbid anxiety disorder, n (%)               |                                            |                                               |       |      |
| Panic disorder                                 | 17 (40.47)                                 | -                                            | -     |      |
| Social anxiety disorder                        | 9 (21.42)                                  | -                                            | -     |      |
| OCD                                            | 8 (19.04)                                  | -                                            | -     |      |
| Agoraphobia                                    | 6 (14.28)                                  | -                                            | -     |      |
| PTSD                                           | 1 (2.38)                                   | -                                            | -     |      |
| GAD                                            | 1 (2.38)                                   | -                                            | -     |      |

**Statistically significant at 0.01 level. SD ‑ Standard deviation; BPRS ‑ Brief Psychiatric Rating Scale; PANSS ‑ Positive and Negative Symptom Scale for Schizophrenia; OCD ‑ Obsessive-compulsive disorder; PTSD ‑ Posttraumatic stress disorder; GAD ‑ Generalized anxiety disorder
However, a significant difference was found in terms of the other clinical variables between schizophrenia patients with anxiety disorders and schizophrenia patients without anxiety disorders and schizophrenia patients without anxiety disorders, which is similar to the other studies done in this regard.

**Comparison between the scores obtained on various psychopathology scales of schizophrenia with and without anxiety disorders**

There was no significant difference between the two groups on BPRS for schizophrenia with anxiety disorders and schizophrenia without anxiety disorders, which were similar to the other studies. However, a significant difference was found between the two groups on positive, negative, and general psychopathology scale of PANSS. These findings were similar to the previous studies with different studies showing different results. Emsley et al. found a significant difference for the positive subscale of PANSS between the two groups which was also replicated later, which is in agreement with our findings. In contrast to the above findings, Tibbo et al. found a significant difference on the general psychopathology scores of the two groups reflecting the link between the general psychopathology scale and the anxiety disorders as the general psychopathology scale includes anxiety or anxiety-related symptoms (e.g., anxiety, tension, and active social avoidance).

**Psychopathology scores of schizophrenia and anxiety disorder scales**

The mean values obtained on negative, positive, and general psychopathology scale of PANSS as well as the BPRS scores were much higher than the corresponding studies done in the West, which is probably due to the long duration of untreated illness in Indian schizophrenic population, especially belonging to the rural population. The values for the psychopathology scales for panic disorder are in close agreement as those found by the other researchers.

### Table 3: Correlation of psychopathology scores and various anxiety disorder scores in schizophrenia patients with comorbid anxiety disorders

| Type of anxiety disorder | PANSS | BPRS | Spearman correlation of anxiety scores with |  |
|--------------------------|-------|------|---------------------------------------------|--|
|                          | Positive score | Negative score | General psychopathology scale (name in parentheses) | Positive score | Negative score | General psychopathology scale | BPRS |
| Panic disorder (n=17)    | 40.8±14.14 (Acute Panic Inventory) | 39.2±19.25 (Acute Panic Inventory) | 29.2±13.56 (Acute Panic Inventory) | 0.238 | 0.289 | 0.041 | 0.281 |
| Social anxiety disorder (n=9) | 67.4±15.73 (Liebowitz Social Anxiety Score) | 66.8±15.25 (Liebowitz Social Anxiety Score) | 57.4±14.88 (Liebowitz Social Anxiety Score) | 0.807** | 0.435 | 0.009 | 0.160 |
| OCD (n=8)                | 32.8±3.5 (YBOCS) | 32.6±3.2 (YBOCS) | 23.1±2.17 (YBOCS) | 0.780 | 0.570 | 0.551 | 0.405 |
| Agoraphobia (n=6)        | 4.3±1.03 (Mobility Inventory) | 4.1±0.41 (Mobility Inventory) | 3.6±0.52 (Mobility Inventory) | 0.896* | 0.955** | 0.893* | 0.941** |

*Significant at 0.05; **Statistically significant at 0.01; NS - Not significant; S - Significant; BPRS - Brief Psychiatric Rating Scale; PANSS - Positive and Negative Symptom Scale for Schizophrenia; OCD - Obsessive-compulsive disorder; YBOCS - Yale-Brown Obsessive-Compulsive Scale

### Table 4: Comparison of scores on anxiety scale at baseline, after antipsychotics, and after antipsychotics and fluoxetine treatment in schizophrenia patients with comorbid anxiety disorders

| Type of anxiety disorder | 1. At baseline | 2. After antipsychotics | 3. After antipsychotics and fluoxetine | Wilcoxon test comparing 1 and 2 | Wilcoxon test comparing 2 and 3 |
|--------------------------|----------------|------------------------|--------------------------------------|-------------------------------|-------------------------------|
| Panic disorder (n=17)    | 26.1±2.55      | 22.8±2.78              | 23.1±2.17                            | -2.95                         | -3.54                         |
| Social anxiety disorder (n=9) | 24.5±2.74      | 22.2±2.78              | 23.6±2.47                            | -1.732                        | -2.68                         |
| OCD (n=8)                | 23.1±4.57      | 23.6±5.85              | 23.6±4.57                            | -1.414                        | -2.54                         |
| Agoraphobia (n=6)        | 26.4±2.31      | 20.2±2.47              | 20.2±2.47                            | -2.95                         | -3.54                         |

OCD - Obsessive-compulsive disorder; YBOCS - Yale-Brown Obsessive-Compulsive Scale; NS - Not significant; S - Significant

A greater association of anxiety disorder was found with the paranoid subtype of schizophrenia (P ≤ 0.01), which had been shown by the previous studies as well. There was a higher rate of treatment received by patients having schizophrenia only as compared to the other group reported by others also. No significant difference was found in terms of the other clinical variables between schizophrenia patients without anxiety disorders and schizophrenia patients with anxiety disorders, which is similar to the other studies done in this regard.

These findings were similar to the previous studies with different studies showing different results. Emsley et al. found a significant difference for the positive subscale of PANSS between the two groups which was also replicated later, which is in agreement with our findings. In contrast to the above findings, Tibbo et al. found a significant difference on the general psychopathology scores of the two groups reflecting the link between the general psychopathology scale and the anxiety disorders as the general psychopathology scale includes anxiety or anxiety-related symptoms (e.g., anxiety, tension, and active social avoidance).
In addition, the values obtained on positive, negative, and general psychopathology scale of PANSS and BPRS and on LSAS are in accordance with the Western population\(^{[27,28]}\) whereas that for OCD is lower than that reported earlier, which might be because of the inclusion of only acute schizophrenics in the earlier study.\(^{[27,28]}\) The scores on the positive, negative, and general psychopathology scale of PANSS, BPRS scores, and GAD-7 scores are similar to that reported by other researchers\(^{[5,18]}\) and also for PTSD.\(^{[20,30]}\)

**Correlation between anxiety disorder scores and psychopathology scores**

There was no significant correlation between acute panic inventory scores and PANSS scores, that is, positive scores, negative scores, and general psychopathology scores. This is in agreement with an earlier study\(^{[20]}\) but is in contrast with a few related studies which have found a significant correlation between the positive scale of PANSS and panic disorder severity scales.\(^{[21,26,27]}\) The acute panic inventory score was not correlated significantly with the BPRS score either, which again is in agreement with other studies.\(^{[19]}\)

Some researchers have found a higher level of psychopathology in schizophrenia patients with a comorbid diagnosis of panic disorder,\(^{[21,28,31-34]}\) but this was not observed in the present study.

The current study showed no significant correlation between the LSADS scores and PANSS positive subscale score, which is in close agreement with a few studies,\(^{[19,27]}\) whereas a few reported a positive correlation between social anxiety score and PANSS negative score;\(^{[35]}\) while another study found no correlation between LSADS scores with BPRS and PANSS scores.\(^{[6]}\)

There was no significant correlation between obsessive-compulsive symptoms and schizophrenia symptoms as reflected by the YBOCS scores and the BPRS and PANSS scores. Similar to this, a few studies have also found no significant correlation between the YBOCS scores and psychopathology scales.\(^{[21,26,37]}\) A few have found a positive correlation between YBOCS scores and positive scores of PANSS\(^{[27,38,39]}\) or negative score of PANSS.\(^{[21,40]}\) In contrast, some have found a negative correlation between YBOCS scores and negative scores of PANSS.\(^{[41]}\) As there was a single schizophrenia patient with PTSD as well as GAD, statistical analysis could not be done. In earlier studies, a significant correlation between PTSD scores and psychopathology scores for schizophrenia was found reflecting a higher severity of psychopathology in schizophrenic patients with comorbid PTSD.\(^{[40,42-45]}\) Similarly, a significant correlation was found between the GAD-7 scores and the general psychopathology scale of PANSS.\(^{[5]}\) As in the current study, majority of the study sample belonged to the group of chronic schizophrenics, which is different from the other studies with patients mostly belonging to acute schizophrenia and may explain the differences in the results with the other studies.

**Effect of treatment on schizophrenia and the comorbid anxiety disorders**

There was a significant difference in the treatment outcome after the administration of olanzapine and fluoxetine, which has also been reported by other researchers.\(^{[17,19,46-48]}\) Although reports of improvement of panic disorder and agoraphobia with cognitive behavior therapy have been reported by a few of the researchers,\(^{[49,50]}\) this could not be corroborated because of the less number of patients as well as their limited hospital stay. There was a significant difference between the pre- and post-treatment YBOCS scores after the administration of fluoxetine \((P \leq 0.01)\) but not after the administration of olanzapine. These findings are similar to the findings of the previous studies, with no improvement in the OCD after the administration of antipsychotics\(^{[51]}\) but a good improvement after the administration of anti-obsessional agents.\(^{[48,49,52]}\) For social anxiety disorder as well, there was a significant difference between the pre- and post-treatment values after the administration of fluoxetine \((P \leq 0.01)\), but not after the administration of olanzapine which is similar to the findings of a previous study.\(^{[53,54]}\) Given that anxiety disorders are relatively responsive to treatment, greater awareness of their comorbidity with schizophrenia should yield worthwhile clinical benefits to the patient.

**Limitations**

Limitations of the study include possible selection bias being a tertiary care hospital-based study where patients with more severe illness are more likely to be included. No distinction was made between the clinical correlates of patients with acute schizophrenia and chronic schizophrenia. Moreover, the sample consisted mostly of men (81%), thus the findings of the study cannot be generalized. In the treatment aspect also, the effect of only one SSRI was studied.

**CONCLUSIONS**

Comorbid anxiety disorders are quite common in schizophrenia. Schizophrenia patients with anxiety disorders differ significantly from those without anxiety disorders in their basic psychopathology, that is, positive, negative, and cognitive domains. Further, there is a shorter duration of illness in schizophrenia patients with anxiety disorders as compared to schizophrenia patients without anxiety disorders assigning a prognostic significance to the presence of anxiety disorders. Moreover, these
anxiety disorders are quite responsive to the SSRIs but not responsive to the antipsychotics alone. Hence, SSRIs may be tried in such cases for the effective treatment of the anxiety disorders with schizophrenia, leading to the effective relief of distress of such patients.

### Financial support and sponsorship
Nil.

### Conflicts of interest
There are no conflicts of interest.

### REFERENCES

1. Pincus HA, Tew JD, First MB. Psychiatric comorbidity: Is more less? World Psychiatry 2004;3:18-23.
2. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. DSM 5. 5th ed. Arlington, VA: American Psychiatric Association; 2013.
3. World Health Organization. The ICD-10 Classification of Mental and Behavioral disorders (Tenth Revision): Diagnostic Criteria for Research. Geneva: World Health Organization; 1992.
4. Braga RJ, Reynolds GP, Siris SG. Anxiety comorbidity in schizophrenia. Psychiatry Res 2013;210:1-7.
5. Buckley PF, Miller BJ, Lehrer DS, Castle DJ. Psychiatric comorbidities and schizophrenia. Schizophr Bull 2009;35:383-402.
6. McMillan KA, Enns MW, Cox BJ, Sareen J. Comorbidity of axis I and II mental disorders with schizophrenia and psychotic disorders: Findings from the national epidemiologic survey on alcohol and related conditions. Can J Psychiatry 2009;54:477-86.
7. Kiran C, Chaudhury S. Prevalence of comorbid anxiety disorders in schizophrenia. Ind Psychiatry J 2016;25:35-40.
8. Achim AM, Maziaide M, Raymond E, Olivier D, Mérette C, Roy MA, et al. How prevalent are anxiety disorders in schizophrenia? A meta-analysis and critical review on a significant association. Schizophr Bull 2011;37:811-21.
9. Sheehan DV, Lecrubier Y, Sheehan KH, Amorim P, Janavs J, Weiller E, et al. The mini-international neuropsychiatric interview (M.I.N.I.): The development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. J Clin Psychiatry 1998;59 Suppl 20:22-33.
10. Overall J, Gorham D. The brief psychiatric rating scale. Psychol Rep 1962;10:799-812.
11. Kay SR, Fiszbein A, Opler LA. The positive and negative syndrome scale (PANSS) for schizophrenia. Schizophr Bull 1987;13:261-76.
12. Liebowitz MR, Fyer AJ, Gorman JM, Dillon D, Appleby IL, Levy G, et al. Lactate provocation of panic attacks. I. Clinical and behavioral findings. Arch Gen Psychiatry 1984;41:764-70.
13. Chamberless DL, Caputo GC, Jasim SE, Gracely EJ, Williams C. The mobility inventory for agoraphobia. Behav Res Ther 1985;23:35-44.
14. Goodman WK, Price LH, Rasmussen SA, Masure C, Fleischmann RL, Hill CL, et al. The Yale-Brown obsessive compulsive scale. I. Development, use, and reliability. Arch Gen Psychiatry 1989;46:1006-11.
15. Liebowitz MR. Social phobia. Mod Probl Pharmacopsychiatry 1987;22:141-73.
16. Spitzer RL, Kroenke K, Williams JB, Löwe B. A brief measure for assessing generalized anxiety disorder: The GAD-7. Arch Intern Med 2006;166:1092-7.
17. Horowitz M, Wilner N, Alvarez W. Impact of event scale: A measure of subjective stress. Psychosom Med 1979;41:209-18.
18. Tibbo P, Swanison J, Chue P, LeMalleda JM. Prevalence and relationship to delusions and hallucinations of anxiety disorders in schizophrenia. Depress Anxiety 2003;17:65-72.
19. Ulas H, Alptekin K, Akdede BB, Tumuklu M, Akvardar Y, Kitis A, et al. Panic symptoms in schizophrenia: Comorbidity and clinical correlates. Psychiatry Clin Neurosci 2007;61:678-80.
20. Fenton WS, McGlashan TH. The prognostic significance of obsessive-compulsive symptoms in schizophrenia. Am J Psychiatry 1986;143:437-41.
21. Kayahan B, Ozurt O, Veznedaroglu B, Eraslan D. Obsessive-compulsive symptoms in schizophrenia: Prevalence and clinical correlates. Psychiatry Clin Neurosci 2005;59:291-5.
22. Karatzias T, Gumley A, Power K, O'Grady M. Illness appraisals and self-esteem as correlates of anxiety and affective comorbid disorders in schizophrenia. Compr Psychiatry 2007;48:371-5.
23. Yung AR, McGorry PD. The initial prodrome in psychosis: Descriptive and qualitative aspects. Aust N Z J Psychiatry 1996;30:587-99.
24. Mazeh D, Bodner E, Weizman R, Delayahu Y, Cholostoy A, Martin T, et al. Co-morbid social phobia in schizophrenia. Int J Soc Psychiatry 2009;55:198-202.
25. Devulapalli KK, Kelge JA, Nasrallah HA. Temporal sequence of clinical manifestation in schizophrenia with co-morbid OCD: Review and meta-analysis. Psychiatry Res 2008;161:105-8.
26. Emsley RA, Oosthuizen PP, Joubert AF, Roberts MC, Stenf D. Depressive and anxiety symptoms in patients with schizophrenia and schizopreniform disorder. J Clin Psychiatry 1999;60:747-51.
27. Argyle N. Panic attacks in chronic schizophrenia. Br J Psychiatry 1990;157:430-3.
28. Huppert JD, Smith TE. Anxiety and schizophrenia: The interaction of subtype symptoms and psychotic symptoms. CNS Spectr 2005;10:721-31.
29. Lommen MJ, Restifo K. Trauma and posttraumatic stress disorder (PTSD) in patients with schizophrenia or schizoaffective disorder. Community Ment Health J 2009;45:485-96.
30. Lysaker PH, Whitney KA, Davis LW. Obsessive-compulsive and negative symptoms in schizophrenia: Associations with coping preference and hope. Psychiatry Res 2006;141:253-9.
31. Goodwin RD, Amador XF, Malaspina D, Yale SA, Goetz RR, Gorman JM, et al. Anxiety and substance use comorbidity among inpatients with schizophrenia. Schizophr Res 2003;61:89-95.
32. Pallanti S, Quercioli L, Holland E. Social anxiety in outpatients with schizophrenia: A relevant cause of disability. Am J Psychiatry 2004;161:53-8.
33. Tibbo P, Kootsche M, Chue P, Warneke L. Obsessive-compulsive disorder in schizophrenia. J Psychiatr Res 2000;34:139-46.
34. Hwang M, Bermanzohn PC, editors. Schizophrenia and Comorbid Conditions: Diagnosis and Treatment. Washington, DC: American Psychiatric Publishing, Inc.; 2001.
35. Poyurovsky M, Fuchs K, Weizman A. Obsessive-compulsive symptoms in patients with first episode schizophrenia. Am J Psychiatry 1999;156:1998-2000.
36. McGorry PD, Chanen A, McCarthy E, Van Riel R, McKenzie D, Singh BS, et al. Posttraumatic stress disorder following recent-onset psychosis. An unrecognized postsychotic syndrome. J Nerv Ment Dis 1991;179:253-8.
37. Rajkumar RP, Reddy YC, Kandavel T. Clinical profile of “schizo-obessive” disorder: A comparative study. Compr Psychiatry 2008;49:262-8.
38. Scheller-Gilkey G, Moynes K, Cooper I, Kant C, Miller AH. Early life stress and PTSD symptoms in patients with...
comorbid schizophrenia and substance abuse. Schizophr Res 2004;69:167-74.
39. Kilcommons AM, Morrison AP. Relationships between trauma and psychosis: An exploration of cognitive and dissociative factors. Acta Psychiatr Scand 2005;112:351-9.
40. Seedat S, Frithelli V, Oosthuizen P, Emsley RA, Stein DJ. Measuring anxiety in patients with schizophrenia. J Nerv Ment Dis 2007;195:320-4.
41. Mueser KT, Rosenberg SD. Treating the trauma of first episode psychosis: A PTSD perspective. J Ment Health 2003;12:103-8.
42. Shioiri T, Shinada K, Kuwabara H, Someya T. Early prodromal symptoms and diagnoses before first psychotic episode in 219 inpatients with schizophrenia. Psychiatry Clin Neurosci 2007;61:348-54.
43. Siris SG, Mason SE, Shuwall MA. Histories of substance abuse, panic and suicidal ideation in schizophrenic patients with histories of post-psychotic depressions. Prog Neuropsychopharmacol Biol Psychiatry 1993;17:609-17.
44. Kahn JP, Puertollano MA, Schane MD, Klein DF. Adjunctive alprazolam for schizophrenia with panic anxiety: Clinical observation and pathogenetic implications. Am J Psychiatry 1988;145:742-4.
45. Takahashi H, Sugita T, Yoshida K, Higuchi H, Shimizu T. Effect of quetiapine in the treatment of panic attacks in patients with schizophrenia: 3 case reports. J Neuropsychiatry Clin Neurosci 2004;16:113-5.
46. Arlow PB, Moran ME, Bermanzohn PC, Stronger R, Siris SG. Cognitive-behavioral treatment of panic attacks in chronic schizophrenia. J Psychother Pract Res 1997;6:145-50.
47. Hofmann SG, Bufka LF, Brady SM, Rand CD, Goff DC. Cognitive-behavioral treatment of panic in patients with schizophrenia: Preliminary findings. J Cognitive Psychother 2000;14:381-92.
48. Rahman MS, Grace JJ, Pato MT, Priest B. Sertraline in the treatment of clozapine-induced obsessive-compulsive behavior. Am J Psychiatry 1998;155:1629-30.
49. Dwivedi S, Pavuluri M, Heidenreich J, Wright T. Response to fluvoxamine augmentation for obsessive and compulsive symptoms in schizophrenia. J Child Adolesc Psychopharmacol 2002;12:69-70.
50. Goodwin R, Davidson L. Panic attacks in psychosis. Acta Psychiatr Scand 2002;105:14-9.
51. de Haan L, Beuk N, Hoogenboom B, Dingemans P, Linszen D. Obsessive-compulsive symptoms during treatment with olanzapine and risperidone: A prospective study of 113 patients with recent-onset schizophrenia or related disorders. J Clin Psychiatry 2002;63:104-7.
52. Poyurovsky M, Faragian S, Shabeta A, Kosov A. Comparison of clinical characteristics, co-morbidity and pharmacotherapy in adolescent schizophrenia patients with and without obsessive-compulsive disorder. Psychiatry Res 2008;159:133-9.
53. Pallanti S, Quercioli L, Pazzaglia A. Social anxiety and premorbid personality disorders in paranoid schizophrenic patients treated with clozapine. CNS Spectr 2000;5:29-43.
54. Pallanti S, Quercioli L, Rossi A, Pazzaglia A. The emergence of social phobia during clozapine treatment and its response to fluoxetine augmentation. J Clin Psychiatry 1999;60:819-23.