Clinical Presentation and Course of Persistent Delusional Disorder:

Data From a Tertiary Care Center in India

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ABSTRACT

Objective: Despite its long history as a psychiatric diagnosis, little is known about the sociodemographic and clinical profile of persistent delusional disorder (PDD) or its subtypes, treatment response, and outcomes, particularly in India. We examined the clinical characteristics and course of PDD in patients presenting to a tertiary neuropsychiatry center in India.

Method: A retrospective chart review of patients diagnosed with PDD (*ICD-10*) between January 2000 and May 2014 was conducted. Sociodemographic and clinical data including age at onset, total duration of the illness, clinical symptoms and treatment, hospitalizations, occupational functioning, and follow-up were extracted from the files. The study was approved by the institute ethics committee.

Results: The sample (N = 455) consisted of 236 men and 219 women. The mean age at onset was 32.36 ± 10.47 years. The most common delusion was infidelity (n = 203, 44.6%) followed by persecution (n = 149, 32.7%). Hallucinations were present in 78 (17.1%), depressive symptoms in 187 (41.1%), and comorbid substance dependence in 61 (13.4%) subjects; 141 subjects (31.0%) had a family history of mental illness. Follow-up data were available for 308 subjects, of whom 285 (92.5%) reported good compliance with medication. Of the subjects, 163 (52.9%) showed a good response to treatment. The diagnosis of PDD remained unchanged in 274 of 308 subjects (88.9%).

Conclusion: In our center, PDD appears to be uncommon and has a near-equal gender representation. Infidelity was the most common delusion, which is in contrast to the reported literature. The diagnosis of PDD appears to be stable with good response to atypical antipsychotics if compliance can be ensured.

Prim Care Companion CNS Disord
2016;18(1):doi:10.4088/PCC.15m01883

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Persistent delusional disorder (PDD) has been variously conceptualized but has remained underresearched, despite being categorized as a separate disorder in both diagnostic classification systems (*ICD-10* and *DSM-5*). Most of the available research is descriptive, with little empirical evidence.[1]

The prevalence and sociodemographic profile of PDD has been investigated in a few studies. A meta-analysis of 17 studies reported that the prevalence of PDD was approximately 24–30/100,000 of the population and constituted 1 to 4 of every 100 psychiatric inpatient admissions, concluding that it was "neither a very rare nor a very common psychiatric condition."[2(898)] A subsequent report by de Portugal et al[3] set the figure higher at 60/100,000 individuals in the population.[3] A recent Indian study by Jadhav et al[4] found the prevalence rate to be 1.88%.

The mean age at onset reported by most studies[5–10] appears to be around 35 to 55 years of age, while an Indian study by Grover et al[11] reported the age at onset to be slightly higher (38 years). The age at onset of PDD appears to be higher than that of other psychotic illnesses.[2] In terms of gender distribution, there is a higher prevalence among women than men, with a female to male ratio of 1.29:3.[2]

The most common type of delusion reported in descriptive studies is persecution (58%–64%) followed by infidelity.[5,7,9] A chart review[11] of 88 Indian patients found that the sociodemographic and clinical profile of patients was consistent with findings from western literature, with persecution being the most common theme. PDD has been found to have significant comorbidity with affective disorders, depression in particular being the most common.[3,6,7,12]

Treatment of PDD is a major challenge as medication adherence is an issue. Munro and Mok[13] reported in their review that PDD had a good prognosis when adequately treated. A treatment review[12] found that at least 50% of the patients in the sample had good response to treatment with first-generation and second-generation antipsychotics. Mews and Quante[14] reported that second-generation antipsychotics like risperidone and olanzapine have good response and greater acceptability in treatment. In a study from India,[11] the authors reported good response to both typical and atypical antipsychotics, particularly risperidone. A more recent study[5] found no differences between long-acting risperidone, oral risperidone, and other atypical antipsychotics in treating PDD; however, compliance was understandably better in the long-acting risperidone group.

Given the long history of PDD as a psychiatric diagnosis, very few studies have specifically researched this condition, with most of the available information being retrospective. Further, relatively little is known about the demographic and clinical profile of patients, the frequencies of PDD subtypes, or treatment response and outcomes, particularly in India—there is only 1 other published study on this topic from North India.[11] We conducted a chart review to understand the clinical presentation and course of PDD in a tertiary care center in

Clinical Points

- Delusions of infidelity and persecution are the common clinical manifestations of persistent delusional disorder (PDD), irrespective of gender.
- Patients with PDD respond well to treatment with atypical antipsychotics, particularly risperidone and olanzapine.
- Nearly 50% of patients with PDD also have depressive symptoms and may benefit from antidepressant treatment in addition to antipsychotics.
- The challenge of treating patients with PDD lies in ensuring compliance and retaining them in long-term follow-up; PDD has a good prognosis provided adherence to the treatment regimen can be ensured.

South India, which is culturally and linguistically distinct from North India.

METHOD

We conducted a retrospective chart review at the National Institute of Mental Health and Neuro Sciences (NIMHANS), Bangalore, India. Records of 455 patients who received a diagnosis of PDD (*ICD-10*)[15] between January 2000 and May 2014 were reviewed. It must be noted that all patients presenting to our center are evaluated by at least 2 clinicians independently and prescribed appropriate investigations and treatment. Data from the case records were extracted using a semistructured form designed by the investigators.

The form was used to extract information from the case records including sociodemographic and clinical details such as age, gender, education history, occupational and marital status, age at onset of illness and age at first contact with the hospital, duration of illness, details of symptoms, family history of psychiatric illness in first- and second-degree relatives, treatment details, occupational functioning, number of outpatient follow-up visits, and number of inpatient hospitalizations. Details regarding hospitalization and follow-up were also extracted. Onset was defined as the time interval from asymptomatic status to onset of delusions: acute (< 3 weeks), subacute (3 weeks–3 months), and insidious (> 3 months).

Medication doses were calculated in terms of chlorpromazine equivalents to ensure comparability. Treatment outcomes as documented in the records were coded as follows: < 50% improvement was considered poor, between 50% and 75% was considered partial response, and > 75% was considered good response to treatment.

The data were analyzed using the Statistical Package for Social Sciences (SPSS, version 16.0). Descriptive statistics were used for the analysis of sociodemographic and clinical data. The study was approved by the institute ethics committee. No patients were contacted.

RESULTS

Sociodemographic Profile

A total of 455 case records were reviewed. The sample consisted of 236 men (51.9%) and 219 women (48.1%), of whom 361 (79.3%) were married. Only 20 (4.4%) were illiterate, while the rest had received at least primary school education; 55 (12.1%) were unemployed at the time of first evaluation. Of the subjects, 306 (67.3%) were from a lower socioeconomic status and 274 (60.2%) were from an urban background. The sociodemographic results are provided in Table 1.

Table 1. Sociodemographic Details of Patients Diagnosed With Persistent Delusional Disorder (N = 455)[a]

Variable	Patients
Gender	
Male	236 (51.9)
Female	219 (48.1)
Marital status	
Single	79 (17.4)
Married	361 (79.3)
Separated	6 (1.3)
Divorced	2 (0.4)
Widowed	7 (1.5)
Education	
Illiterate	20 (4.4)
School education	300 (65.9)
Graduation	99 (21.8)
Postgraduation	36 (7.9)
Occupation	
Student	12 (2.6)
Housewife	141 (31.0)
Regular employment	111 (24.4)
Daily wage worker	86 (18.9)
Self-employed	50 (11.0)
Unemployed	55 (12.1)
Socioeconomic status	
Lower socioeconomic status	306 (67.3)
Middle and upper socioeconomic status	149 (32.7)
Residence	
Urban	274 (60.2)
Rural	181 (39.8)

[a]Data are presented as n (%).

Clinical Features

The onset of illness was insidious in 432 (94.9%) subjects, acute in 15 (3.3%), and subacute in 7 (1.5%). Mean age at onset was 32.36 ± 10.47 years. The mean duration of illness at the time of first contact was 44.15 ± 66.66 months, with a minimum of 3 months and a maximum of 448 months. Of the 455 subjects, only 26 (5.7%) had been referred to NIMHANS by a health care professional; 186 (40.9%) had been hospitalized at least once.

Of the sample, 141 (31.0%) had a family history of psychiatric illness in their first-degree relatives and 74 (16.2%) in their second-degree relatives. Family history in first-degree relatives of schizophrenia was reported in 39 (8.6%) subjects, substance dependence in 37 (8.1%), PDD in 21 (4.6%), recurrent depressive disorder in 15 (3.3%), other psychotic disorders in 14 (3.1%), bipolar affective disorder in 12 (2.6%), and anxiety disorders in 4 (0.8%).

Delusions

The main delusion was infidelity (n = 203, 44.6%) followed by persecution (149, 32.7%). Other delusions included hypochondriacal delusions (n = 29, 6.4%), body

Prim Care Companion CNS Disord
2016;18(1):doi:10.4088/PCC.15m01883

dysmorphophobic delusions (n = 24, 5.3%), erotomanic delusions (n = 18, 4.0%), somatic delusions (n = 15, 3.3%), delusions of reference (n = 5, 1.1%), and delusions of grandiosity (n = 5, 1.1%). Seven subjects (1.5%) had more than 1 delusion. Also, 157 patients (34.5%) had delusions secondary to the main theme—delusion of persecution was the most common (n = 72, 15.8%) followed by reference (n = 57, 12.5%) and infidelity (n = 10, 2.1%).

Other Symptoms

Seventy-eight subjects (17.1%) reported hallucinations, with auditory (n = 47, 10.3%) being the most common, followed by tactile (n = 16, 3.5%), olfactory (n = 9, 2%), and visual (n = 6, 1.3%).

Comorbidity

Sixty-one subjects (13.4%) had a comorbid diagnosis of substance dependence, with alcohol dependence alone in 28 (6.2%), nicotine dependence alone in 13 (2.9%), both alcohol and nicotine dependence in 15 (3.3%), and 4 subjects with cannabis dependence.

Since delusion of infidelity is commonly reported among subjects with alcohol dependence, we excluded these 43 subjects and repeated the analysis. The delusion of infidelity remained the most common delusion (177/412, 42.9%) followed by the delusion of persecution (135/412, 32.7%), even after excluding subjects with comorbid alcohol dependence.

Of the subjects, 187 (41.1%) were recorded to have depressive symptoms, while 41 (9.0%) also had anxiety symptoms. Eighteen (3.9%) subjects were diagnosed with syndromal depressive episodes. Paranoid personality traits were documented in 47 (10.3%) subjects.

Treatment

At the time of first contact, 281 (61.9%) subjects were drug-naive, 116 (25.6%) were on treatment with atypical antipsychotics, and 33 (7.3%) were on a combination of atypical antipsychotics with mood stabilizers or antidepressants. Twenty-two (4.8%) subjects were only taking other psychotropic medications (mood stabilizers or antidepressants), while 2 (0.4%) were taking typical antipsychotics. Of the subjects, 436 (95.8%) received only pharmacotherapy and 12 (2.6%) received both pharmacotherapy and electroconvulsive therapy (ECT), while 6 (1.3%) received pharmacotherapy plus psychotherapy. During the treatment period, the most commonly prescribed drug was risperidone (n = 280, 61%), followed by olanzapine (n = 86, 19%) (mean drug dose = 430 ± 166.49 chlorpromazine equivalents). Of the 187 subjects who had depressive symptoms, 50 (10.9%) received treatment with antidepressants along with antipsychotics—fluoxetine in 36 (7.9%), escitalopram in 9 (2.0%), and sertraline in 5 (1.1%).

Response to Treatment

A minimum of 1 outpatient visit after initial evaluation was considered as a requisite for including the subject in the follow-up data. Follow-up data were available for 308 of 455 subjects. The mean ± SD number of follow-up visits was 6.6 ± 10.22, and the mean period of follow-up was 26 ± 31 months. Of the subjects, 147 (32.3%) were lost to follow-up after the initial evaluation.

Of the 308 subjects, 163 (52.9%) had a good response, 90 (29.2%) had a partial response, and 55 (17.8%) had a poor response to treatment. Also, 285 (92.5%) subjects were recorded to have had good compliance with treatment.

Diagnostic Stability

The diagnosis of PDD remained stable in 274 of 308 (88.9%) subjects. The diagnosis was revised in 34 subjects (11.1%)—schizophrenia in 15 (4.8%), bipolar disorder in 7 (2.3%), other psychotic illnesses in 7 (2.3%), obsessive-compulsive disorder in 3 (1%), and recurrent depressive disorder in 2 (0.7%). The results are provided in Table 2.

CONCLUSION

We studied the clinical presentation of PDD using a retrospective chart review method. The fact that we could identify only 455 records of patients with PDD in our center over a 14-year period (where an average of 8,000 to 10,000 new patients are registered each year) indicates that patients with this disorder are not common at our center and possibly do not come into contact with specialized psychiatry services regularly.

The mean age at illness onset was about 32 years, which is much earlier compared to the age at onset of 46–51 years reported in the literature.[6,10,16] The mean duration of illness at first treatment contact was about 44 months, which is considerably less than the approximately 5 years reported in the literature.[3,17]

While our review found a near-equal representation of men and women in the sample, the aforementioned studies[6,10,16] reported a female preponderance. Furthermore, almost 80% of the patients in our study were currently married, which is similar to the findings reported by Wustmann et al[10] and de Portugal et al[16] but is considerably more than the rate of 24%–30% reported by González-Rodríguez et al.[6]

Infidelity was the most common delusion (44.6%), followed by persecution (32.7%). This finding is markedly different from other studies that reported persecution and reference as most common.[6,10,16] While González-Rodríguez et al[6] reported delusion of infidelity in only 5.1% of their sample and Wustmann et al[10] reported delusional jealousy in 7% of their sample, de Portugal et al[16] reported it in 31% of their patients—all of which are considerably lower than our finding. We can only speculate that since our sample was much younger and most of the subjects were currently married, infidelity was most likely the main delusion. It is also likely that with increasing age or a later age at onset, persecution may be the more commonly experienced delusion. However, prospective studies are needed to investigate these hypotheses further. A study by Yamada et al[18] attempted to correlate differences in age at

Table 2. Clinical and Treatment Details of Patients Diagnosed With Persistent Delusional Disorder (N = 455)[a]

Variable	Patients
Clinical features	
Age at onset of illness, mean ± SD, y	32.36 ± 10.47
Duration of illness at first contact, mean ± SD, y	44.15 ± 66.66
Main delusion	
Infidelity	203 (44.6)
Persecution	149 (32.7)
Hypochondriacal	29 (6.4)
Body dysmorphophobic	24 (5.3)
Erotomania	18 (4.0)
Somatic	15 (3.3)
Referential	5 (1.1)
Grandiose	5 (1.1)
Mixed (more than 1 type)	7 (1.5)
Secondary delusion	157/455 (34.5)
Persecution	72 (15.8)
Reference	57 (12.7)
Infidelity	10 (2.1)
Mixed (more than 1 type)	18 (3.9)
Other clinical features	
Hallucinations	78/455 (17.1)
Auditory	47 (10.3)
Tactile	16 (3.5)
Olfactory	9 (2.0)
Visual	6 (1.3)
Comorbidity	
Substance dependence	61/455 (13.4)
Alcohol	28 (6.2)
Nicotine	13 (2.9)
Alcohol and nicotine	15 (3.3)
Cannabis	4 (1.0)
Depressive symptoms	187 (41.1)
Syndromal depression	18 (3.9)
Anxiety symptoms	41 (9.0)
Paranoid personality traits	47 (10.3)
Family history of psychiatric illness	141/455 (31.0)
Schizophrenia	39 (8.6)
Substance dependence	37 (8.1)
Persistent delusional disorder	21 (4.6)
Bipolar affective disorder	12 (2.6)
Recurrent depressive disorder	15 (3.3)
Other psychotic disorders	14 (3.1)
Anxiety disorders	4 (0.8)
Treatment at first contact	
Drug naive	281 (61.9)
Atypical antipsychotics only	116 (25.6)
Atypical antipsychotics plus mood stabilizer/ antidepressant	33 (7.3)
Typical antipsychotics only	2 (0.4)
Mood stabilizer/antidepressant only	22 (4.8)
Treatment received	
Pharmacotherapy alone	436 (95.8)
Pharmacotherapy plus electroconvulsive therapy	12 (2.6)
Pharmacotherapy plus psychotherapy	6 (1.3)
Psychotherapy alone	1 (0.2)
Most common antipsychotics	
Risperidone	280 (61.5)
Olanzapine	86 (19.0)
Antidepressants	50/455 (11.0)
Escitalopram	9 (2.0)
Fluoxetine	36 (7.9)
Sertraline	5 (1.1)
Response to treatment	308/455 (67.7)
Good	163 (52.9)
Partial	90 (29.2)
Poor	55 (17.8)
Good compliance	285/308 (92.5)
Diagnostic stability	
Stable	274/308 (88.9)
Revised	34 (11.1)
Schizophrenia	15 (4.8)
Bipolar disorder	7 (2.3)
Other psychotic illness	7 (2.3)
Obsessive-compulsive disorder	3 (1.0)
Recurrent depressive disorder	2 (0.7)

[a]Data are presented as n (%) unless otherwise specified.

onset of delusions with commonly associated subtypes of delusional disorder and reported that persecutory delusions were associated with the oldest age at onset and somatic delusions were associated with the youngest.

It is interesting to note that almost 35% of the patients also had another delusion related to the main delusion, with persecution being the most common secondary delusion. Delusion of infidelity was reported in a further 2% of the subjects secondary to the main delusion. Hallucinations were reported in only 17% of the subjects, which is much less than the 35% reported by de Portugal et al.[16] However, auditory hallucinations were the most common (10%), and this finding is on par with other reports of 7%–15%. The findings are also similar to those of the Halle Delusional Syndromes (HADES) study that found hallucinations in 18.7% of patients.[6,10,16] Family history of schizophrenia was noted in 8.6% of the subjects, and 15 of the subjects (4.8%) were later diagnosed with schizophrenia. Given the presence of more than 1 delusion, auditory hallucinations, and family history of schizophrenia in some patients, it is very likely that a small minority of patients diagnosed with PDD may actually represent a prodrome of schizophrenia. This finding is also consistent with the report of the HADES study, which suggested that the diagnosis of PDD was stable and only a small minority of patients (16%) with PDD had a revised diagnosis of schizophrenia over a longitudinal follow-up period of 14 years.[17] In our sample, 88.9% of patients retained their diagnosis of PDD during follow-up, which is comparable to findings reported by Grover et al[11] (91%) in the only other study from India. Despite the presence of auditory hallucinations and depressive symptoms in some patients, it appears that PDD is a stable diagnosis.

Depressive symptoms were reported in 41.1% of the subjects, although only 10.9% received antidepressant treatment and only 3.9% were diagnosed with syndromic depression. This is consistent with findings reported by Wustmann et al[10] in which 55.8% of patients had depressive symptoms, not amounting to a major affective disorder, and 39.5% of patients were treated with antidepressants in addition to antipsychotic medication. A more recent study[6] reported that patients receiving selective serotonin reuptake inhibitors (33.3%) along with antipsychotics had higher follow-up rates (75%) and maintained treatment longer. It can be speculated that the follow-up rates in our study may have been boosted had more patients received antidepressants in addition to antipsychotics. It may be useful to consider antidepressants in patients with PDD reporting depressive symptoms.

Substance dependence was the most common comorbid condition, with 15 (3.3%) of the subjects dependent on both alcohol and nicotine, which is similar to other reports.[16]

All 455 patients received treatment with antipsychotics, with risperidone and olanzapine accounting for 80% of the prescriptions. Of the 308 patients for whom follow-up data were available, 285 were reportedly

adherent to treatment and 253 (>80%) of those patients had a good response to treatment. This bodes well as PDD has traditionally been considered difficult to treat. Previous reports[5,11] have suggested that patients with PDD respond well to antipsychotics, particularly to risperidone. An earlier systematic review[12] suggested that there are no significant differences in the response to treatment with different antipsychotics, while a more recent review[14] suggests that risperidone and olanzapine are associated with good response. One previous review[13] of PDD from 1961 onward, with most studies from the 1980s, reported that pimozide was the antipsychotic associated with the best response in PDD. However, very few of our patients received pimozide, so it is not possible for us to make a comparison with their results. Since our review period was from 2000 to 2014 when second-generation antipsychotics were available, it is likely that pimozide was not prescribed as frequently as it was in the earlier decades. Furthermore, the response to treatment in our patients was good, as the mean duration of illness was less than 4 years (44 months) at the time of contact at our center and could have had a favorable impact on the outcome.

Some limitations have to be mentioned. Since this was a chart review, we did not interview any of the included patients for the study, so we are unable to comment on their current clinical status or earlier diagnosis. We did not attempt to confirm a diagnosis of PDD for our study and accepted the diagnosis made by the treating clinicians. It is likely that some of the patients may have received a different diagnosis had we attempted to do so, given that 11% had a change in diagnosis during follow-up. We also did not analyze the data of patients who were lost to follow-up separately. Our data are from a tertiary care center that treats severe mental disorders, and it is likely that our patients have more severe forms of PDD with more comorbidity than what is encountered in community and general hospital–based samples.

It can be surmised that if compliance to treatment with second-generation antipsychotics, particularly risperidone, can be ensured, patients with PDD are likely to respond well to treatment. However, almost one-third of the patients were lost to follow-up, which again highlights the difficulty of retaining them in the treatment process. Compliance with treatment appears to be the most important determinant of outcome.

Submitted: September 9, 2015; accepted October 27, 2015.

Published online: February 4, 2016.

Drug names: escitalopram (Lexapro and others), fluoxetine (Prozac and others), olanzapine (Zyprexa and others), pimozide (Orap), risperidone (Risperdal and others), sertraline (Zoloft and others).

Potential conflicts of interest: None reported.

Funding/support: None reported.

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