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Original Article

Psychiatry/Mental Health Section

A Case-control Study of Sexual Dysfunction and Serum Prolactin Levels in Patients with Psychotic Disorders

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ABSTRACT

Introduction: Sexual functioning has remained widely neglected aspect of patient care for those suffering from severe mental disorders and has received little attention. Yet, it has been construed as one of the major factors contributing to non-adherence with antipsychotic medications.

Aim: To study sexual dysfunction in patients with psychotic disorders and its clinical association with serum prolactin levels.

Materials and Methods: This case-control study was conducted in the Department of Psychiatry at MGM Medical College and associated Mental Hospital, Indore, Madhya Pradesh, India, from 13th February 2020 to 21st January 2021. The study sample consisted of 200 subjects including 100 cases and 100 controls. The case group included patients with a diagnosis of psychotic disorders currently in remission for atleast one month. Remission of the patients was ensured by Brief Psychiatric Rating Scale (BPRS) with a score of <4 on all items and <28 total score. Assessment of sexual dysfunction was done using Arizona Sexual Experience Scale (ASEX). The control group included healthy subjects aged between 18-65 years, either sex having active sexual partners with a score of <3 on all the items of the General Health Questionnaire (GHQ-12). Collection of blood sample was done and serum was analysed for prolactin levels using the Chemiluminescent Microparticle Immunoassay (CMIA) method. Statistical analysis was done using Statistical Package for the Social Sciences (SPSS) version 28.0 for windows.

Results: The mean age of the case group was 39.9±7.457 years while that of the control group was 35.60±9.37 years. The number of male patients (71% and 73%) was higher than females (29% and 27%) in the control group and case group respectively. The difference between the two were statistically significant. The total number of cases who experienced sexual dysfunction came out to be 59 out of 100. Total 55.93% of those having sexual dysfunction were suffering from difficulty in sexual arousal, followed by difficulty with penile erection/vaginal lubrication (49.15%), orgasmic dysfunction (34.48%), and reduced sexual drive (23.72%). Among the cases, the mean serum prolactin level (14.14±10.60 ng/mL) was seen to be significantly higher (p-value <0.001) than the control group (9.46±6.05 ng/mL). Maximum serum prolactin level (29.00±9.95 ng/mL) was seen to be associated with usage of a combination of both 1st and 2nd generation antipsychotics.

Conclusion: There was a significant prevalence of sexual dysfunction in psychotic patients and is associated significantly with elevated serum prolactin levels.

Keywords: Antipsychotics, Arousal, Hyperprolactinaemia, Schizophrenia

INTRODUCTION

Psychotic disorders comprise of a variety of clinical diagnosis including schizophrenia, schizoaffective disorder, other functional psychoses and schizotypal personality disorder. Psychotic disorders are associated with significant morbidity, disability and impaired quality of life [1]. Sexual dysfunction among patients with psychosis could be a symptom of the psychiatric disorder, side effect of psychotropic medication, or can be related to psychiatric co-morbidities, especially depression and substance abuse [2]. In particular, sexual dysfunction affects 30-80% of patients with schizophrenia and is much more prevalent in comparison to the general population [3].

Treatment related sexual adverse effects in psychotic disorders are partially mediated by antagonism of pituitary D2 receptors thereby increasing secretion of prolactin. Hyperprolactinaemia can lead to reduced testosterone levels, in turn causing disruption of the normal functioning of the hypothalamic-pituitary-gonadal axis. This may further manifest as amenorrhea, infertility, gynaecomastia, galactorrhea, decreased libido, erectile dysfunction and anorgasmia [4]. Though, sexual dysfunction can happen with any antipsychotic, significant differences exist amid different drugs [5,6].

Sexual functioning has received little consideration as an important aspect of patient care for those suffering from severe mental disorders. Yet, it has been implicated as one of the major factors contributing to non compliance with antipsychotic medications. Also, people with schizophrenia recognise management of sexual dysfunction to be a major unmet need [6].

Only a few of the studies. have tried to address sexual dysfunction associated with antipsychotic use, however biological parameter like serum prolactin was not included in them [7-10]. Hence, the present study was conducted with an aim to study sexual dysfunction in patients with psychotic disorders and its clinical association with serum prolactin levels.

MATERIALS AND METHODS

This case-control study was conducted in the Department of Psychiatry at MGM Medical College and associated Mental Hospital, Indore, Madhya Pradesh, India, from 13th February 2020 to 21st January 2021. Ethics Committee (IEC approval number-EC/MGM/Feb-20/62) approval was obtained.

Sample size calculation: The study sample consisted of 200 subjects including 100 cases and 100 controls calculated as per the prevalence of psychotic disorders in India (3/1000 individuals) [11].

Sample size was calculated using the formula

$n=4\ pq/d^2$,

where confidence interval=95%; Margin of error=1.

Inclusion criteria:

For cases:

- Patients aged between 18-65 years, with the diagnosis of psychotic disorders currently in remission for at least one month which included schizophrenia, psychosis not otherwise specified, acute transient psychotic disorders, persistent

delusional disorder as per International Classification of Diseases 10th revision [12].

- Patients were on continuous antipsychotic treatment (1st generation/2nd generation/combination) for at least last three months.
- Remission of patient was defined using Brief Psychiatric Rating Scale (BPRS) with a score <4 on all items and <28 total score [13].

For controls:

- Controls were healthy subjects free of any psychiatric illness, general medical condition, or a history of a surgical procedure known to cause sexual dysfunction.
- Subjects were aged between 18-65 years, either sex having active sexual partners and a score of <3 on all the items of General Health Questionnaire-12 [14].

Exclusion criteria for cases and controls:

- Menopausal, pregnant and lactating women were excluded from the study.
- Patients were excluded if they had other co-morbid psychiatric illness, substance abuse, a general medical condition or a history of a surgical procedure known to cause sexual dysfunction.
- Other exclusions were patients taking medications known to affect sexuality and patients with primary sexual dysfunction prior to the onset of psychotic disorders.

Study Procedure

After a complete description of study to the subjects, a detailed physical examination was done to rule out major medical or neurological illnesses. Socio-demographic data was collected. After that clinical assessment of case group was done using BPRS [13]. to ensure remission and sexual functioning was assessed using Arizona Sexual Experience Scale (ASEX) [15]. Assessment of the control group was done by GHQ-12 questionnaire to rule out any mental disorder [14].

Brief Psychiatric Rating Scale (BPRS): The BPRS was used for ensuring remission in cases of psychosis. BPRS is a clinician-administered rating scale for assessing the positive, negative and affective symptoms of individuals having psychotic disorders. The BPRS includes the 18 items associated with positive symptoms, negative symptoms and mood. For each item, the rater enters a number ranging from 1 (not present) to 7 (extremely severe). The BPRS is scored by adding together the scores from the individual items, with higher scores indicating more severe pathology. In the present study, all the cases had a score of <4 on all items and <28 total score [13,16].

General Health Questionnaire-12 (GHQ): The GHQ-12 was used to rule out any psychiatric disorder in control group. The GHQ-12 is a self-administered screening questionnaire, designed for detecting individuals with a diagnosable psychiatric disorder [14]. The positive items were corrected from 0 (always) to 3 (never) and the negative ones from 3 (always) to 0 (never). The total score ranges from 0-36 and higher scores indicate worse health. A score of 2 or less indicates an absence of a mental disorder and a score of 3 or more indicates the presence of disorder [14].

Arizona Sexual Experience Scale (ASEX): The ASEX scale designed to measure five item identified as core elements of sexual function:

- Sexual drive
- Arousal
- Penile erection/vaginal lubrication
- Ability to reach orgasm
- Satisfaction from the orgasm

The items are rated on a 6 point scale ranging from 1 (hyperfunction) to 6 (hypofunction), possible total scores range from 5-30 with higher scores indicating more sexual dysfunction. The scale has two versions, one for males and one for females, with a difference in question three that references penile erections versus vaginal lubrication [15].

A 5 mL blood samples of all groups were drawn after explaining the procedure and were collected in a clot activator (red top) tube. Post which serum was processed from the sample via centrifuge machine and the serum was analysed for prolactin levels using the Chemiluminescent Microparticle Immunoassay (CMIA) method. Reference range was 2.1-17.7 ng/mL for male and 2.8-29.2 ng/mL for female.

STATISTICAL ANALYSIS

Student's t-test was applied to compare mean age and serum prolactin values between case and control group, Chi-square test to compare gender, marital status and locality between case and control group. Pearson's correlation test was used for assessment of correlation between serum prolactin values and total ASEX score. Analysis of Variance (ANOVA) was used to see association between class of drugs and serum prolactin values. Results were analysed using SPSS version 28.0.

RESULTS

The mean age of the case group was 39.9±7.457 years while that of the control group was 35.60±9.37 years. The number of male patients (71% and 73%) was higher than females (29% and 27%) in the control group and case group respectively [Table/Fig-1].

Variables	Case	Control	p-value
Mean age (year)	39.9±7.457	35.60±9.37	0.294*
Gender			
Male	73 (73%)	71 (71%)	0.752#
Female	27 (27%)	29 (29%)	
Marital status			
Married	90 (90%)	85 (75%)	0.219#
Unmarried	10 (10%)	15 (15%)	
Locality			
Rural	35 (35%)	41 (41%)	0.382#
Urban	65 (65%)	59 (59%)	

[Table/Fig-1]: Socio-demographic distribution.
*p-value calculated by student's t-test
#p-value calculated from chi-square test

Total number of cases who experienced sexual dysfunction as per specified criteria of ASEX scale were 59 (59%). It was observed that 55.93% of those having sexual dysfunction were suffering from difficulty in sexual arousal [Table/Fig-2].

Specific dysfunctions	Cases n (%)
Reduced sexual drive	14 (23.72%)
Arousal dysfunction	33 (55.93%)
Difficulty with penile erection/vaginal lubrication	29 (49.15%)
Orgasmic dysfunction	20 (34.48%)

[Table/Fig-2]: Distribution of specific sexual dysfunction in case group as per specified criteria of ASEX scale (n=59).

Among the cases, the mean serum prolactin level (14.14±10.60 ng/mL) was seen to be significantly higher than control group (9.46±6.05 ng/mL) [Table/Fig-3]. Serum prolactin values were significantly higher (18.71±11.45 ng/mL) in patients with sexual dysfunction as compared to those without sexual dysfunction (7.57±3.60 ng/mL) [Table/Fig-4].

On applying pearson correlation for the total ASEX score and serum prolactin values, there was moderate correlation between the two,

Serum prolactin	Cases	Control
Mean±SD (ng/mL)	14.14±10.60	9.46±6.05
t-value	23.64	
p-value (student's t-test)	<0.001	

[Table/Fig-3]: Comparison of Serum Prolactin values between case and control groups.

Serum prolactin in cases (ng/mL)	Mean±SD
Cases without sexual dysfunction (n=41)	7.57±3.60
Cases with sexual dysfunction (n=59)	18.71±11.45
t-value	6.018
p-value	<0.001

[Table/Fig-4]: Comparison of serum prolactin values among cases with and without sexual dysfunction.

with an r-value of 0.4 which was statistically significant (p-value <0.05) [Table/Fig-5].

Maximum serum prolactin level was seen to be associated with usage of combination of both 1st and 2nd generation of drugs (29.00±9.95 ng/mL). This was followed by 1st generation (13.54±10.34 ng/mL) and 2nd generation (9.19±3.32 ng/mL) of drugs respectively. The difference in means was seen to be highly statistically significant with p-value of <0.001 [Table/Fig-6].

Serum prolactin	Total ASEX score
Pearson correlation (r)	0.408**
p-value	<0.001
N	100

[Table/Fig-5]: Correlation of serum prolactin level with total ASEX score.

Class of drug	No. of cases	Serum prolactin level (ng/mL) (Mean±SD)	ANOVA test (F-value)	p-value
1st generation	18	13.54±10.34	13.715	<0.001
2nd generation	73	9.19±3.32		
Both	9	29.00±9.95		
Total	100	14.15±10.61		

[Table/Fig-6]: Class of drug and serum prolactin level.

DISCUSSION

In present study, the mean age of the case group was 39.9±7.45 years while that of the control group was 35.60±9.37 years which is in concordance of Rosenberg KP et al., who found the mean age in psychotic cases to be 36 years and Montejo A et al., who found the mean age to be 34.6 years for males and 33.5 for females [8,9].

The number of male subjects was higher in both case and control groups (73% and 71% respectively) which is in agreement with Montejo A et al., but higher than that in Rosenberg KP et al., [8,9]. The current trend is due to differences in health-seeking patterns among the male and female population of India, where males reach out for help easily as compared to females and also in a developing country like India, females are mostly unaware of sexual issues and are hesitant to speak out owing to the stigma surrounding sexual health.

Most participants in both the case (90%) and control (85%) groups were married. The proportion of married participants was higher than in most of the previous studies [9,10,12]. The finding is consistent with the fact that only subjects having sexual partners were included in the study group which usually corresponds to a married status concerning the socio-cultural background of India. Apart from this, the mean age of study participants was 39.9 and 35.6 (years) in the case and control group respectively which explains the married status of the majority of participants.

It was found that 59% of cases had sexual dysfunction of some kind, similar results were found by Kelly DL and Conley RR, with sexual dysfunction ranging from 50-80% in the psychotic population [17]. The total number of cases with sexual dysfunction was 59, few patients had more than one type of sexual dysfunction together. About 55.93% of those having sexual dysfunction were suffering from difficulty in sexual arousal. This was followed by difficulty with penile erection/vaginal lubrication (49.15%), orgasmic dysfunction (34.48%) and reduced sexual drive (23.72%). The present study findings were consistent with Ravichandran D et al., Kantipudi SJ et al., and Ucok A et al., who also observed difficulty in sexual arousal and erectile dysfunction to be in the greater majority [18-20].

On further evaluation within the case group, we found higher mean serum prolactin values in patients with psychosis having sexual dysfunction (18.7 ng/mL) than those without sexual dysfunction (7.5 ng/mL) and was statistically significant (p-value <0.001). This finding is corroborated by Düring SW et al., in patients with schizophrenia [21].

On applying the Pearson's correlation between serum prolactin and ASEX score, we found a moderate correlation (r-value=0.4) between the two which was statistically significant (p-value=0.001). This finding is corroborated by various studies like Wu TH et al., and can be explained by the physiological antagonism of dopamine and prolactin [22]. The secretion of prolactin is under direct inhibitory control of dopamine neurons located in the tuberoinfundibular region of the hypothalamus and is, therefore, increased by the dopamine blocking action of antipsychotic medications, causing hyperprolactinaemia and in turn sexual dysfunctions [3,10,23].

Maximum serum prolactin level was seen to be associated with the usage of a combination of both 1st and 2nd generation of drugs (29.00±9.95 ng/mL), followed by 1st generation (13.54±10.34 ng/mL) and 2nd generation (9.19±3.32 ng/mL) of drugs respectively. The difference in means was seen to be highly statistically significant with a p-value <0.001. The higher serum prolactin level and greater ASEX score in patients taking FGA and combination drugs of FGA and SGA can be explained by strong D2 blockade and rise of prolactin levels leading to greater dysfunction. Secondarily, the low sexual desire could be due to the negative symptoms of psychosis which are not that efficiently targeted by FGAs [24].

Limitation(s)

The topic of the study was sensitive and some respondents may have been reluctant to discuss their true concerns. Also, this was not a longitudinal study, and there were no measurements of the effects of illness on sexual functioning before medication treatment.

CONCLUSION(S)

In the present study there was a significant prevalence of sexual dysfunction in psychotic patients with difficulty in sexual arousal and erectile dysfunction being most common. Also, raised serum prolactin levels were found to be significantly associated with sexual dysfunction.

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