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A Comparative Study to Assess the Clinical Association of Nicotine Dependence in Patients with Schizophrenia

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Abstract: ***Background: Schizophrenia is a chronic psychiatric disorder with a high prevalence of nicotine dependence. The co-occurrence of these two conditions poses challenges to prognosis and treatment. Objectives: To compare the severity of positive and negative symptoms of schizophrenia in patients with and without nicotine dependence and assess the relationship between illness duration and nicotine dependence severity. Methods: This cross-sectional, comparative study included 66 patients with schizophrenia (DSM-5 criteria), divided into nicotine-dependent (n=33) and non-dependent (n=33) groups. Assessments included the Positive and Negative Syndrome Scale (PANSS) and Fagerström Test for Nicotine Dependence (FTND/FTND-ST). Results: Both groups were statistically comparable in terms of sociodemographic characteristics. Nicotine-dependent patients had significantly higher PANSS positive (23.5 ± 5.3 vs. 18.6 ± 4.9; p<0.001) and negative scores (20.4 ± 5.5 vs. 16.0 ± 5.2; p=0.001). A significant relationship was found between longer illness duration and greater nicotine dependence (p=0.007). Conclusion: Nicotine dependence is associated with increased symptom severity in schizophrenia and correlates with chronicity of illness, underscoring the need for integrated smoking cessation interventions in schizophrenia care.***

Keywords: schizophrenia symptoms, nicotine dependence, illness duration, PANSS score, smoking cessation strategies

1. Introduction

Schizophrenia is a severe and disabling mental illness that affects approximately 1% of the global population and remains one of the leading causes of long-term disability worldwide [1]. Persons with schizophrenia are at high risk of shorter life expectancy due to the increased mortality related to circulatory and respiratory diseases, with chronic cigarette smoking being a major contributory factor [2], [3]. Smith PH et al. conducted a study to correlate smoking and mental illness in the U.S. population and concluded that compared to the general population, patients with psychiatric disorders are more likely to smoke [4]. The current ratio of smoking prevalence is 5.3 times higher in schizophrenic patients compared to the general population [5]. Several neurobiological hypotheses have attempted to explain this strong association, including the self-medication hypothesis, which posits that nicotine enhances dopaminergic transmission and improves attention, motivation, and working memory, which are commonly impaired in schizophrenia.

Upregulation of nicotinic receptors due to chronic smoking has been linked to lower levels of social withdrawal, motivational responses, blunted emotions, and improved cognitive function [6-7]. Lyons MJ et al, in their study inferred that several characteristics of smoking and schizophrenia relationship indicate a potential dysfunction in the nicotinic acetylcholine receptor system, suggesting that this dysfunction may play a key role in the disease progression. Unaffected relatives of patients with schizophrenia have higher rates of smoking, suggesting that physiological mechanisms driving smoking may also share a hereditary component similar to schizophrenia [8].

It has been observed in multiple studies that higher smoking rates are linked to early disease onset, poorer quality of life, poorer prognosis, increased disease severity, and higher hospital admissions, signalling that the increased desire to smoke may be linked to important regulators of disease onset and progression. [9-13]

Some studies have also inferred that tobacco use is an outcome rather than a cause of schizophrenia. It was observed that nonmedicated patients with schizophrenia who are smokers presented with more severe psychotic symptoms at baseline and showed better improvement after medication than nonsmokers, suggesting patients with worse symptoms tend to smoke to relieve symptoms. [14]

Despite global awareness, there is limited region-specific data from India, where cultural, social, and healthcare dynamics differ substantially. Understanding this relationship in Indian patients is crucial for designing integrated and culturally appropriate interventions that address both psychiatric symptoms and nicotine dependence. This study was conducted to explore the clinical association of nicotine dependence in individuals diagnosed with schizophrenia. The primary goal was to assess the frequency and severity of nicotine dependence in this population. It also aimed to evaluate the relationship between nicotine use and the chronicity of illness and to compare symptom severity—specifically positive and negative symptoms—between patients with and without nicotine dependence.

2. Methodology

This hospital-based, cross-sectional comparative study was carried out in the Department of Psychiatry of a tertiary hospital over a period of 18 months. A total of 66 patients,

diagnosed with schizophrenia as per DSM-5 criteria and aged between 18 and 65 years, were recruited after obtaining informed consent. Patients were evaluated by two qualified psychiatrists to confirm diagnosis. Participants were then divided into two equal groups: those with nicotine dependence (n=33) and those without nicotine dependence (n=33), based on their scores on the Fagerström Test for Nicotine Dependence (FTND for smokers and FTND-ST for smokeless tobacco users). The Positive and Negative Syndrome Scale (PANSS) was used to assess the severity of psychotic symptoms. Demographic data, illness duration, and other clinical parameters were collected using a semi-structured proforma.

Statistical analysis: All the categorical variables will be summarized as frequency with percentage. All the categorical variables will be summarized as mean with standard deviation or median with interquartile range. The normality of the continuous variable will be assessed with the Kolmogorov-Smirnov test. The association of categorical variables across groups will be carried out using the chi-square test/ fisher exact test. The association of nicotine dependence with schizophrenia will be assessed using chi square test/ Fisher's exact test. All the statistical tests will be done at a 5% level of significance, and a p-value of < 0.05 will be considered as statistically significant.

3. Results

The study sample included 66 participants, equally divided between nicotine-dependent and non-dependent groups. The two groups were statistically comparable across demographic variables such as age, gender, marital status, education level, socioeconomic status, and locality, showing no significant differences.

Table 1: Comparison of Sociodemographic and Clinical Characteristics Between Nicotine-Dependent and Non-Dependent Schizophrenia Patients (n = 66; 33 in each group)

Variable	Nicotine-Dependent (n = 33)	Non-Dependent (n = 33)	p-value
Age (Mean ± SD)	36.06 ± 10.47	34.36 ± 9.84	0.486
Gender (Male)	30 (90.9%)	28 (84.8%)	0.713
Marital Status (Married)	20 (60.6%)	19 (57.6%)	1.000
Education (≥10th Pass)	23 (69.7%)	24 (72.7%)	1.000
Locality (Rural)	18 (54.5%)	16 (48.5%)	0.802
Socioeconomic Status (Upper/Upper Middle)	8 (24.2%)	10 (30.3%)	0.781
Duration of Illness (Mean ± SD)	8.94 ± 6.95	7.21 ± 6.55	0.240
Family History of Psychiatric Illness	3 (9.1%)	4 (12.1%)	1.000

As shown in Table 1, no significant differences were observed between groups across sociodemographic and clinical variables. (all $p > 0.05$). This confirms that both groups were comparable at baseline.

Table 2: Distribution of Severity of Nicotine Dependence Among Nicotine-Dependent Schizophrenia Patients (n = 33)

FTND Severity Level	Score Range	Number of Patients (n)	Percentage (%)
Low Dependence	0–3	6	18.2%
Moderate Dependence	4–6	14	42.4%
High Dependence	7–10	13	39.4%
Total	—	33	100%

Table 2: Among the 33 nicotine-dependent schizophrenia patients, the majority had moderate (42.4%) to high (39.4%) levels of dependence. Only 18.2% of patients exhibited low dependence. This suggests that nicotine use in schizophrenia is often not casual but reflects clinically significant dependence, which may require targeted interventions.

Table 3: Comparison of PANSS Scores Between Nicotine-Dependent and Non-Dependent Schizophrenia Patients (n = 66; 33 in each group)

PANSS Domain	Nicotine-Dependent (Mean ± SD)	Non-Dependent (Mean ± SD)	p-value
Positive Symptom Score	23.5 ± 5.3	18.6 ± 4.9	**< 0.001**
Negative Symptom Score	20.4 ± 5.5	16.0 ± 5.2	**0.001**
General Psychopathology	42.2 ± 6.4	40.6 ± 5.3	0.212
Total PANSS Score	86.1 ± 12.3	75.2 ± 10.8	**< 0.001**

Table 3: Nicotine-dependent patients had significantly higher Positive, Negative, and Total PANSS scores compared to non-dependent patients ($p < 0.001$ for positive and total; $p = 0.001$ for negative symptoms). General psychopathology scores were higher in the nicotine-dependent group but did not reach statistical significance ($p = 0.212$). These findings indicate that nicotine dependence is associated with greater severity of schizophrenia symptoms, particularly in the positive and negative domains.

4. Discussion

The present study aimed to examine the clinical association of nicotine dependence among patients with schizophrenia. Both groups were comparable in terms of sociodemographic and clinical characteristics, minimizing confounding bias.

A significant finding of this study was the higher positive, negative, and total PANSS scores in the nicotine-dependent group, suggesting greater symptom severity in these individuals. These findings align with several earlier studies. Patkar et al. observed that smokers had significantly higher PANSS scores, particularly in the positive and negative domains, compared to non-smokers, suggesting a more severe clinical profile in nicotine-dependent patients (15). Similarly, Sagar et al., in an Indian context, reported that nicotine dependence was significantly associated with higher PANSS-positive scores, supporting the self-medication hypothesis that patients may use nicotine to modulate psychotic symptoms (16).

Furthermore, our study found that over 80% of nicotine users had moderate to high dependence as measured by the Fagerström Test. This echoes results from Agarwal et al., who found that more than 75% of schizophrenia patients who

smoked had moderate or high nicotine dependence (17). Another study by Zhang et al. also supports the notion that nicotine dependence is more than a casual behavior among individuals with schizophrenia and is often tied to neurobiological vulnerability (18).

Interestingly, some studies suggest nicotine may transiently improve attention or reduce extrapyramidal side effects (19). However, in our study nicotine use was linked with greater overall severity, raising concerns about its long-term clinical impact.

Thus, the findings of this study not only corroborate past Indian and international research but also emphasize the need for integrated tobacco cessation strategies tailored for patients with schizophrenia.

5. Conclusion

This study highlights a significant clinical association between nicotine dependence and greater severity of schizophrenia symptoms, particularly in the positive and negative symptom domains. Despite both groups being comparable in sociodemographic and clinical variables, nicotine-dependent patients exhibited significantly higher PANSS scores, suggesting a greater overall psychopathological burden.

The majority of nicotine users fell within the moderate to high dependence range, indicating that tobacco use in this population is not merely a lifestyle habit but may be driven by underlying neurobiological mechanisms or serve as maladaptive self-regulation. These findings underscore the need for routine screening and structured tobacco cessation strategies as part of the holistic management of schizophrenia.

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