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## RESEARCH ARTICLE

# EFFECT OF NICOTINE DEPENDENCE ON PSYCHOPATHOLOGY OF SCHIZOPHRENIA

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**ABSTRACT**

**Background:** Nicotine use is a major public health problem that increases medical morbidity and mortality. Compared to the general healthy population, the prevalence of smoking is found to be much higher among people with psychotic disorders. In Given its effect on modulating dopamine and glutamate, nicotine may have an impact on the negative and positive symptoms of schizophrenia. In fact, schizophrenia patients may use nicotine to self-medicate negative symptoms. Schizophrenia is associated with poor attention to and processing of sensory stimulation. Nicotine transiently improves sensory gating in schizophrenia.

**Aims and Objectives**

- To determine the prevalence of nicotine dependence and
- Investigate the effect of nicotine dependence on psychopathology among schizophrenia patients.

**Study Settings and Design**: Study was carried out in C.U. Shah medical college and hospital, Surendranagar, Gujarat. 50 patients who met DSM-5 criteria for schizophrenia were recruited from the psychiatric OPD. Written informed consent was obtained from patients who chose to participate in the study. The subjects were administered the Positive and Negative Symptom Scale (PANSS) to rate the symptoms of schizophrenia and the Fagerstrom Test for Nicotine Dependence (FTND).

**Result**s: Present study included total 50 patients of schizophrenia. Group comprised predominantly males (72%, $n$ =33) with the mean age of 37.5 years old (SD = 9.01). The current prevalence of nicotine dependence in the study subjects was found to be 80%. (n=40).Multivariate analysis of covariance was used to examine the relationship between nonsmokers ($n$ = 10, 20%), smokers with severe nicotine dependence ($n$= 16, 32%), mild-moderate nicotine dependence ($n$ = 24, 48%), and PANSS scores. We conducted pair wise comparisons of the total and subscale PANSS scores between nonsmokers, those with mild dependence and those with severe dependence, using Z test. Those with severe nicotine dependence scored less in the negative subscale compared to that of the nonsmokers ($P$=0.17).

**Conclusions:** The rate of nicotine use disorder among schizophrenia patients in this study is higher than that of the general population. Our study found a significant association between nicotine dependence and negative psychopathology symptoms.



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## INTRODUCTION

Nicotine use is a major public health problem that increases medical morbidity and mortality. Compared to the general healthy population, the prevalence of smoking is found to be much higher among people with psychotic disorders (Aguilar, 2005; Baker, 2007 and De Leon, 2005) and, among those suffering from schizophrenia, the occurrence of smoking and nicotine dependence is higher than that of both the general population and those with other mental illnesses. Schizophrenic patients who smoke tend to have higher frequency of heavy smoking (Poirier, 2002; De Leon, 2002; de Leon, 2002; Kellyand, 1999; Kellyand, 2000 and Hughes, De Leon, 2005) with rates ranging from 60% to as high as 80% (9,10,11,12,13). Hence, it is not surprising that smokers with psychiatric disorders suffer higher rates of morbidity and mortality secondary to smoking related illnesses (Lawrence, 2009). Many factors contribute to the increased smoking rate among individuals with schizophrenia, including the potential positive effect of nicotine on neurotransmitter systems involved in schizophrenia, nicotine's mitigation of the side effects of psychotropic agents, increased nicotine withdrawal symptoms in patients with schizophrenia, social factors such as lower income and educational attainment (Goff, ?; Lohr, 1992; Pomerleau, 1992; Ziedonis, 1994).

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**The self-medication hypothesis:** In addition to the obvious symptoms of hallucinations and delusions (i.e. positive symptoms), patients with schizophrenia frequently suffer from negative symptoms (E.g. avolition, social withdrawal, anhedonia) and cognitive deficits such as the inability to focus attention or impaired working memory. Negative symptoms and particularly cognitive deficits are important predictive factors in determining a patient's ability to cope successfully with everyday activities (Kellyand, 1999; 2000 and Hughes , 1986).

**Neurobiology of Nicotine and Psychosis:** Nicotine may interact with many of the same central pathways thought to be aberrant in schizophrenia. Dopamine, serotonin, and glutamate are thought to play important roles in the pathophysiology of schizophrenia. Dopaminergichyperactivity has been associated with psychotic symptoms. Mesotelencephalic dopamine pathways include the (1) nigrostriatal dopamine system involved in movement disorders; (2) mesolimbic structures, such as the nucleus accumbens and ventral tegmental area—regions implicated in the regulation of emotional expression, including positive symptoms of psychosis (delusions, hallucinations, and thought disorder) and in drug reinforcement and reward; and (3) the mesocortical system, which includes ventral tegmental projections to the prefrontal cortex, a region thought to be hypo functional in chronic schizophrenia (Satel, 1955 and Karler, ?). Nicotine seems to play an important role in modulating both dopamine and glutamate transmission. Specifically, it modulates the release of dopamine in mesotelencephalic dopaminergic pathways. Activation of nicotinic acetylcholine receptors on dopaminergic neurons stimulates central dopamine release and turnover (Clarke, 1985 and Carr, ?) Nicotine can stimulate glutamatergic neurons in the prefrontal cortex that enhance basal ganglia glutamate and dopamine activity and may doso presynaptically by increasing intracellular calcium (Ca2+) (McGehee, 1995). In addition to nicotine'sinduction of dopamine transmission, other agents in cigarette smoke may synergistically enhance this effect through the inhibition of monoamine oxidase type B (Fowler, 1996). In summary, the mesolimbicdopaminergic pathways are especially important in mediating reward in nicotine dependence.

**Impact of Smoking on Positive and Negative Symptoms of Schizophrenia:** Given its effect on modulating dopamine and glutamate, nicotine may have an impact on the negative and positive symptoms of schizophrenia. In fact, schizophrenia patients may use nicotine to self-medicate negative symptoms. A deficiency of dopamine has been postulated in prefrontal cortical regions of individuals with chronic schizophrenia. This deficiency may underlie the so-called deficit or negative symptoms of schizophrenia, characterized by anergia, a motivation, affective blunting, and dysfunctional social relationships. The positive symptoms of schizophrenia—delusions, hallucinations, and conceptual disorganization—presumably relate to hyper functional mesolimbic dopamine systems. In smokers with schizophrenia one study found decreased negative symptom scores and increased positive symptom scores, and other study found increased positive and negative symptoms (Goff, ? and Ziedonis, 1994).

**Effects on Auditory Physiology:** Schizophrenia is associated with poor attention to and processing of sensory stimulation. This deficit may be the result of reduced sensory gating (habituation) of hippocampal response to repetitive auditory stimulation, which makes filtering out background noise more difficult. Nicotine transiently improves sensory gating in schizophrenia as assessed by normalization of the P50 wave during auditory evoked potentials, implying that smoking may alleviate difficulties with processing of sensory information in schizophrenia (Adler, 1993).

**Aims and Objectives**

- To determine the prevalence of nicotine dependence and
- Investigate the effect of nicotine dependence on psychopathology among schizophrenia patients.

## MATERIAL AND METHOD

**Study setting:** Study was carried out in C.U.Shah medical college and hospital, Surendranagar, Gujarat. 50 patients were recruited from the psychiatric OPD.

**Inclusion criteria**

- Patients who met DSM-5 criteria for schizophrenia.
- Provided informed consent.

**Exclusion criteria**

Those who

- Diagnosis other than schizophrenia.
- Had an organic mental disorder.
- Had a diagnosis of mental retardation.
- Were experiencing unstable general medical conditions.
- Were grossly psychotic and unable to cooperate.

All patients who were identified as having schizophrenia in the clinic were approached. Written informed consent was obtained from patients who chose to participate in the study, after the discussion of study details. A demographic and clinical data sheet was fulfilled. The subjects were administered the Positive and Negative Symptom Scale (PANSS) to rate the symptoms of schizophrenia and the Fagerstrom Test for Nicotine Dependence (FTND).

**Fagerstrom test for nicotine dependence:** The study used the Fagerstrom Test for Nicotine Dependence (FTND) in order to estimate the severity of nicotine dependence. This tool consists of 5 questions concerning factors associated with smoking. The result obtained is in the range of 0-10 points. The 1-4 points result corresponds to a low to moderate degree of dependence, 5 or more indicate severe dependence (Heatherton, 1991).

**PANSS (Positive and Negative Syndrome Scale for Schizophrenia):** The PANSS is a 30 item, 7-point rating instrument. It has adapted 18 items from the Brief Psychiatry Rating Scale (BPRS) and 12 items from the Psychopathology Rating Schedule (PRS). Each item on the PANSS is accompanied by a complete definition as well as detailed anchoring criteria for all seven rating points, which represent increasing level of psychopathology: 1=absent, 2=minimal, 3=mild, 4=moderate, 5=moderate-severe, 6=severe, 7=extreme. Of the 30 psychiatric parameter assessed on the PANSS, seven constitute a positive scale, seven a negative

scale, 16 a general psychopathology scale. The PANSS is scored by summation of rating across items, such that potential ranges are 7-49 for the positive and negative scales and 16-112 for the General psychopathology scale. The composite scale is arrived at by subtracting negative from the positive score thus yielding a bipolar index that ranges from -42 to +42. Reliability as indicated by Pearson correlation for positive, negative and general psychopathology scale was .80, .68 and .60, respectively ($p<.001$). The reliability was not significant in composite scale (.07) (27)

## RESULT AND DISCUSSION

Present study included total 50 patients of schizophrenia. Group comprised predominantly males (72%, $n$ =33) with the mean age of 37.5 years old (SD = 9.01). The current prevalence of nicotine dependence in the study subjects was found to be 80% ($n$ =40). The mean number of cigarettes/bidis smoked in the sample was 16-18 sticks per day. In 40% of the subjects, there was a positive family history of smoking. Socio demographic characteristics and clinical details, according to smoking status, are shown in Table 4. Multivariate analysis of covariance was used to examine the relationship between nonsmokers ($n$ = 10, 20%), smokers with severe nicotine dependence ($n$= 16, 32%), mild-moderate nicotine dependence ($n$ = 24 , 48%), and PANSS scores, while controlling the gender, ethnicity, use of atypical antipsychotic medication, income, and comorbid using illicit drug or alcohol. The nicotine dependence status was significantly associated with the PANSS score.

We conducted pair wise comparisons of the total and subscale PANSS scores between nonsmokers, those with mild dependence and those with severe dependence, using Z test. Those with severe nicotine dependence scored less in the negative subscale compared to that of the nonsmokers ($P$ = 0.17) thatis shown in Table 5. Based on all the literature reviewed, prevalence of smoking is found to be high among people with schizophrenia and our current study found a similar pattern. The prevalence of nicotine dependence found in this study was 80% ($n$ = 40). Men were more likely to smoke. Other studies have shown similar male preponderance (1,28). The literature is divided into smoking and symptoms of schizophrenia. In this present study, subjects who were severely nicotine dependent scored less in the PANSS negative symptoms. This finding seemed to be in agreement with other previous studies which showed that smokers had lower negative symptoms (Zhang, 2012 and Smith, 2001).

By stimulating the release of dopamine in the nucleus accumbens and prefrontal cortex, nicotine reduces the negative symptoms of schizophrenia, explaining its use as a form of self-medication. These positive effects could be an important mechanism that explains the comorbidity of schizophrenia and nicotine dependence (Mackowick, 2014). Smoking alters the level and effectiveness of medications in the blood, as it is hypothesized that nicotine interacts with many of the same central pathways thought to be abnormal in persons with schizophrenia .Smoking also increases the metabolism of neuroleptics, so individuals with schizophrenia and smoking tend to receive consistently higher doses of antipsychotics compared to nonsmokers (Desai, 2001 and Ziedonis, 1994).

**Table 1. Number of patients in each age groups**

| AGE GROUP | Number of Participants | Percentage of Participants |
|---|---|---|
| ≤ 25 | 05 | 10% |
| 26 – 30 | 09 | 18% |
| 31 – 35 | 11 | 22% |
| 36 – 40 | 08 | 16% |
| 41 – 45 | 08 | 16% |
| 46 – 50 | 05 | 10% |
| 51 – 55 | 02 | 04% |
| > 55 | 02 | 04% |
| Total | 50 | 100% |

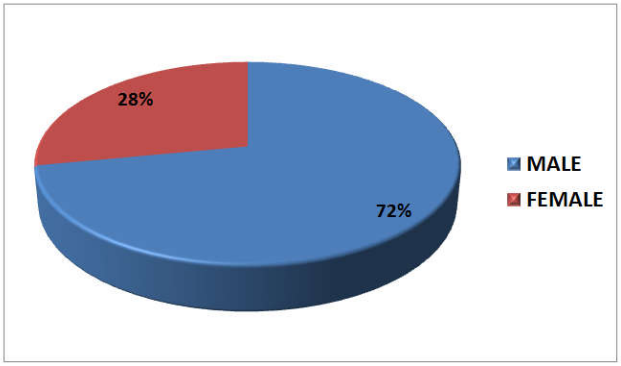


**Figure 1.Sex wise distribution of patients**

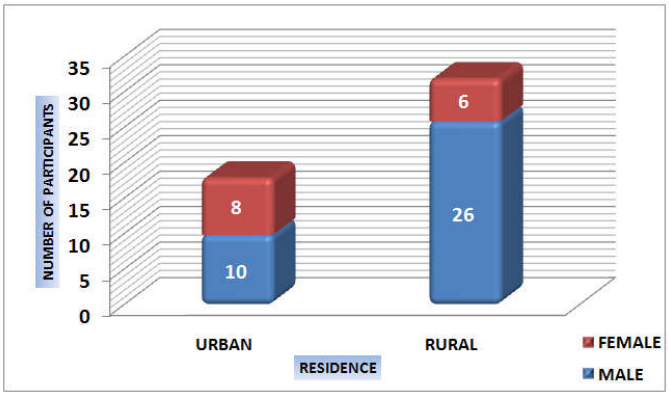


**Figure 2. Residence of patients**

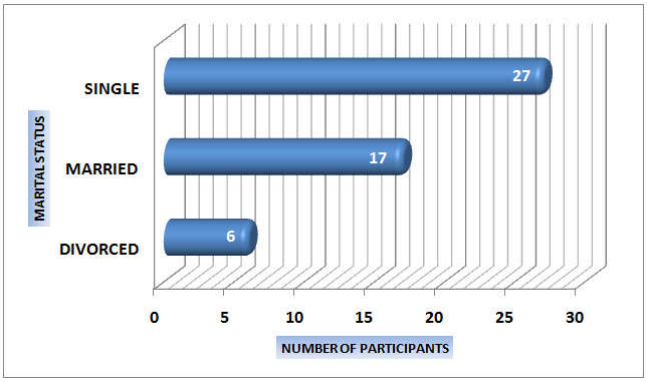


**Figure 3. Marital status of patients**

**Table 2. Duration of illness and number of patients**

| Duration (Years) | Number | Percentage |
|---|---|---|
| 1 – 5 | 06 | 12% |
| 6 – 10 | 24 | 48% |
| 11 – 15 | 15 | 30% |
| 16 – 20 | 04 | 08% |
| 21 – 25 | 01 | 02% |
| Total | 50 | 100% |

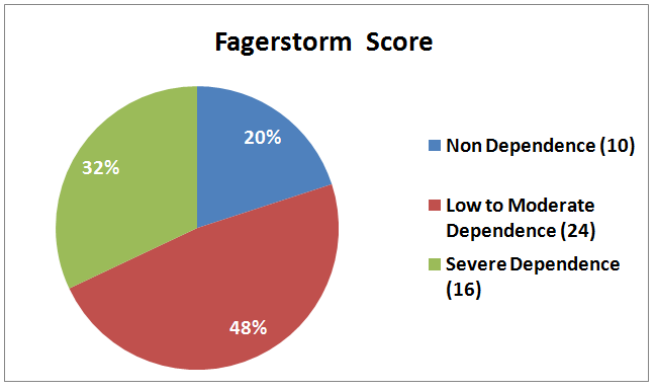


**Figure 4. Nicotine dependence in patients**

**Table 4. Socio-demographic data**

| Characteristics | Nicotine Dependence | Non-nicotine Dependence | Statistic ($\chi 2$) | P Value | OR(95% CI) |
|---|---|---|---|---|---|
| Age, Years: Mean & SD | 37.20 & 9.01 | 35.60 & 8.28 | -- | -- | -- |
| GENDER | | | | | |
| MALE | 33 | 03 | 10.938 | <0.001 (0.00094) | 11.00 |
| FEMALE | 07 | 07 | | | (2.267 – 53.373) |
| RESIDENCE | | | | | |
| RURAL | 25 | 07 | 0.195 | >0.05 | 0.7143 |
| URBAN | 15 | 03 | | (0.659) | (0.160 – 3.189) |
| MARITAL STATUS | | | | | |
| SINGLE | 23 | 04 | 1.437 | >0.05 | -- |
| DIVORCED | 05 | 01 | | (0.487) | |
| MARRIED | 12 | 05 | | | |
| TOTAL | 40 | 10 | -- | -- | -- |

**Table 5. Panss score and nicotine dependance severity**

| | Non smoker | Mild-moderate nicotine dependence | Severe nicotine dependence | N – M Mean difference | N – S Mean difference | M – S Mean difference |
|---|---|---|---|---|---|---|
| Total PANSS | 79.90 (21.158) | 74.33 | 82.88 | 0.67 | 7.476 | 8.435 |
| Mean (SD) | | (15.533) | (7.98) | (0.419) | (0.012) | (0.006) |
| POSITIVE | 13.30 | 19.08 | 19.75 | 4.338 | 0.762 | 1.327 |
| Mean (SD) | (4.218) | (7.430) | (6.382) | (0.045) | (0.391) | (0.256) |
| NEGATIVE | 26.90 | 23.79 | 21.00 | 2.270 | 1.993 | 0.019 |
| Mean (SD) | (9.848) | (6.365) | (5.989) | (0.142) | (0.171) | (0.892) |
| GENERAL | 39.70 | 31.42 | 42.13 | 1.460 | 1.260 | 0.59 |
| Mean (SD) | (8.381) | (10.802) | (9.818) | (0.236) | (0.273) | (0.809) |

## Limitations

- As the information collection was done via self-reporting, it raise the possibility of underestimating the other substances.
- It was not possible to identify a causal relation between the association of smoking and nicotine dependence and other variables because of the cross-sectional design of this study.
- There was no comparison made with a control group.

## Conclusion

The rate of nicotine use disorder among schizophrenia patients in this study is higher than that of the general population. Our study found a significant association between nicotine dependence and negative psychopathology symptoms, which will be an added value for the health care practitioners in their management of nicotine dependence among schizophrenic patients.

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