Association of Tobacco Smoking with Psychiatric Co-morbidities among Patients with Chronic Obstructive Pulmonary Disease (COPD)

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Certificate

This is to certify that MD thesis entitled **"Association of Tobacco Smoking with Psychiatric Co-morbidities among Patients with Chronic Obstructive Pulmonary Disease (COPD)"** is the original work carried out by **DR. MAHENDRA SINGH UIKEY** in the Department of Psychiatry, All India Institute of Medical Sciences, New Delhi, under our supervision and guidance.

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Dedicated to

my Family,

my Teachers

&

all Patients

ABBREVIATIONS

- **COPD** Chronic Obstructive Pulmonary Disease
- **OPD** Out-patient Department
- **MINI** Mini International Neuropsychiatric Interview
- **PHQ-9** Patient Health Questionnaire- 9
- **AIR** Anxiety Inventory for Respiratory Diseases
- **AUDIT** Alcohol Use Disorder Identification Test
- **FTND** Fagerstrom Test for Nicotine Dependence
- **RCQ** Readiness to Change Questionnaire
- **ICD** International Statistical Classification of Diseases and Related Health Problems
- **DSM** Diagnostic and Statistical Manual of Mental Disorders
- **OR** Odds Ratio
- **UV** Univariate
- **MV** Multivariate

CONTENTS

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Introduction

INTRODUCTION

Tobacco use is a major preventable cause of premature deaths and diseases worldwide. It is a major risk factor of cardiovascular and respiratory disease, and more than twenty different types of cancer. In 2016, over 1.1 billion people aged 15 years or older were estimated to be smoking tobacco out of which 80% of smokers belonged to low- and middle- income countries. According to Global Adult Tobacco Survey (GATS) 2- India 2016-17, there are 10.7% of the Indian population currently smokes tobacco. Among men, the prevalence of smoking tobacco was 19% and among female population, prevalence was 2% (1).

Every year, 8 million people all over the world lose their lives because of tobacco use.

Most of these deaths are accounted in low- and middle- income countries. Cigarette smoking is the most common form of tobacco consumption. All the forms of tobacco consumption are harmful and any level of exposure to tobacco smoke is unsafe (2). 11.5% of the global deaths in the year 2015 were attributable to tobacco smoking. Out of these deaths, 52.2% deaths occurred in China, India, the USA and Russia(3).The inhalation of complex chemical mixture of combustion compounds present in tobacco smoke causes adverse health outcomes, mainly cancer, pulmonary and cardiovascular diseases through multiple mechanisms including DNA damage, direct endothelial damage and inflammation, and oxidative stress. There is no risk-free level of exposure to tobacco smoke. Chronic Obstructive Pulmonary Disease (COPD) is a preventable and treatable respiratory disease which is characterised by airflow limitations. This limitation is usually progressive and is caused by inflammatory response when the lungs get exposed to obnoxious and toxic gases, mainly caused by the tobacco smoke exposure. Tobacco smoke contains components like Acrolein, Formaldehyde, Cadmium, Hydrogen Cyanide, Nitrogen Oxides, etc., which injure lungs through variety of mechanisms oxidative injury, impairing defence mechanisms, injuring cilia and irritant effects. As the COPD progresses, apart from the lungs it also goes on to affect other systems(4).

According to the current understanding of the pathogenesis of COPD, the chronic exposure of tobacco smoke leads to inflammatory changes and immune cell recruitment in the terminal airspaces of the lung.

The endothelial cells then undergo apoptosis due to the oxidative stress from the toxic chemical compounds of tobacco smoke and due to weakening of matrix-cell attachment. Repeated damage renders repair of elastin and other extracellular matrix components ineffective, finally causing airspace enlargement(5).

In India, there have been a number of studies in different regions reporting prevalence varying from 1.9% to 11.1%(6). The pathogenesis of COPD not only affects lungs but also causes systemic inflammation which explains high frequency of comorbidities such as cardiovascular, nutritional, skeletal and psychiatric disorders. Most common comorbidities are cardiovascular comorbidities, probably because of shared pathophysiological mechanisms like endothelial damage and coagulopathies. Most commonly occurring psychiatric disorders with COPD are depressive and anxiety disorders. Anxiety disorders and COPD have common symptom of dyspnoea and co-occurrence of both illnesses have been linked to early hospital admission during the course of COPD. The depressive disorder is seen more frequently in COPD as compared to other chronic illnesses(7).

Smoking cessation is the single most effective treatment for COPD. Smoking cessation is associated with a reduction in the risk of developing stroke, coronary heart disease, several types of cancer, and it is associated to an increased life expectancy(8).Global Adult Tobacco Survey-India 2016-2017 shows that, 55.4% of current smokers are planning or thinking of quitting smoking. 48.8% of current smokers were advised by health care provider to quit smoking. 38.5% of them made quit attempts in last 12 months. 1.8% of all adults were former daily smokers(1).

Approximately 40% of the COPD patients continue to smoke tobacco. It is also reported that higher nicotine dependency is related to higher probability of developing COPD. The motivation to quit is similar between smokers with COPD and without COPD, but smokers with COPD have lower self-efficacy and self-esteem(9). Moreover, a case control study in hospitalised COPD patients reported that 44% smokers with COPD had coexistent depression(10). The tobacco withdrawal produces anxiety amongst several symptoms which is common to psychiatric disorder. Coexistence of psychiatric disorders intensifies the anxiety symptoms thus making it more difficult for the smokers with COPD to quit.

As opposed to smokers with COPD with coexistent depression, non-depressed ones are twice more likely to quit smoking. So, if psychiatric disorders are treated simultaneously, it is likely to increase the success rates of smoking cessation efforts. It is important to screen the patients with COPD for psychiatric disorders, particularly for anxiety and depressive disorders, so that it could be treated and subsequently improve the smoking cessation and in turn, improve the management of COPD. Hence, this study aims to find the association of tobacco smoking status and psychiatric comorbidities in patients with COPD and further evaluate the relation between severity of nicotine dependence and severity of anxiety and depressive disorder.

Review of Literature

REVIEW OF LITERATURE

Chronic Obstructive Pulmonary Disease (COPD)

Chronic Obstructive Pulmonary Disease (COPD) is not just one disease but an umbrella term that encompasses the chronic lung diseases that cause limitation in the lung's airflow. It is a chronic progressive respiratory condition characterised by incompletely reversible airflow obstruction associated with persistent respiratory symptoms like dyspnoea, cough and excessive sputum production(11).COPD ranked eight most common cause of disease burden when measured by disability-adjusted life years (DALY) in 2015 (12). The prevalence as well as death rates due to COPD increases with the age. COPD is commonly diagnosed after the age of 45 years. The prevalence of COPD is highest in the age group of 75-84 years, followed by age groups of 65-74 years, 55-64 year & 85 years and older, and 45-54 years age-group, in the decreasing order (13). The prevalence of COPD globally was 251 million cases according to Global Burden of Disease Study(14). It is estimated to be 30 million COPD patients in India (15).90% of the COPD related deaths occur in low and middle- income countries. In India, a significant proportion of mortality occurs due to COPD, which is 556,000 (>20%) deaths out of 2,748,000 global deaths (16). It is predicted to be the fourth leading cause of deaths globally (17).

The most important risk factor for COPD is smoking. The 1984 US General Surgeon's report states that 80-90% of the COPD in USA is attributable to tobacco smoking (5). Apart of smoking there are certain other non-smoking risk factors. For genetic risk factors for COPD, there have been limited familial aggregation for pulmonary functions of non-smoker COPD patients. Among these studies α-antitrypsin deficiency and cutis laxa are more clear risk factors in non-smokers COPD concluded with causal relationship. Other risk factors that have been strongly suggested for causing COPD are chronic asthma, air pollution, occupational exposure, biomass smoke and second-hand smoke. On the other hand, some dietary factors such as high uptake of vitamin C and other antioxidants are suggested to be protective factor for COPD(18).

In recent years, numerous large - scale studies have been conducted that examine the effect of inhaled pharmacotherapy on the current control of COPD in terms of the impact

on the symptoms and quality of life of patients, but also the potential of minimizing future risk of exacerbations, death and progression of disease(19). The pharmacological management depends on the stages and the medical comorbidities along with COPD, consisting of Short Acting Beta- Agonist (SABA) with or without additional drugs which are added with the increasing severity of COPD. These classes of drugs are Long Acting Beta-Agonist (LABA), Short Acting Muscarinic-Antagonists (SAMA), Long Acting Muscarinic-Antagonists (LAMA) and Corticosteroids (19,20).

In spite of enhancing importance of pharmacological management in the NICE guidelines, greater emphasis is given to the non-pharmacological management. The foremost step in the non-pharmacological management is removal of the single most important risk factor, i.e., smoking. Cessation of smoking remains an essential goal to prevent disease and stop the progression of disease. Pulmonary rehabilitation has proven to not just be of benefit to patients with a stable illness (improving health, reducing hospital length of stay), but also to reduce the risk of readmission into hospital in patients with an acute exacerbation of COPD recently discharged from hospitals(19).

Tobacco Smoking and COPD

Tobacco use is a leading preventable cause of deaths in United States. It kills 3 times more men and women than their non-smoker counterparts. Major causes of these deaths are cancer, respiratory and cardiovascular diseases (5). Tobacco smoking causes premature deaths. It decreases the survival by 11 years in men and 12 years in women. On the other hand, if a smoker stops smoking before age of 44, one's survival curve will be identical to the survival curve of a non-smoker (21).

A systematic analysis was conducted from the Global Burden of Diseases Study 2015 which synthesized 2818 data sources with Gaussian spatiotemporal process regression and produced estimates of the prevalence of daily smoking by sex, age group and year of 195 countries and territories from 1990 to 2015. This data was used to estimate the smoking attributable mortality and disease burden. This study states that tobacco smoking is the leading risk factor to its attributable diseases in 24 countries as opposed to 16 countries in 1990. Worldwide, cardiovascular diseases (41.2%), cancers (27.6%) and chronic respiratory diseases (20.5%) were the three leading causes of age standardized

DALYs attributable to smoking for both sexes. For cancers and respiratory diseases, smoking is the leading risk factor (3).

It has been well established that smoking is the single most important leading cause for COPD. Despite a mountain of unequivocal evidence of the effects of tobacco smoking that has been gathered and published over past 50 years, in 2015, 1 in every 4 men was a daily smoker (3). It remains to be the leading cause of premature deaths in more than 100 countries. For cancers and the chronic respiratory diseases, tobacco smoking remain to be the leading risk factor (3).

The tobacco smoking is undoubtedly the most important risk factor in causing COPD. According to the data of 2011 Behavioural Risk Factor Surveillance System (BRFSS) analysed by Centres of Disease Control and Prevention (CDC), 6.3% of the US adult population had reported to be suffering from COPD. BRFSS is an annual random telephonic survey conducted by state in collaboration of CDC among the US adult population. Of this people suffering from COPD, 36.4% were former smokers and 38.7% were current smokers, whereas ~25% had no history of tobacco smoking (22).Among the current smoker population, 15.2 % had COPD. This figure has been estimated much higher in several other studies. In 1996, a sample of 1500 from Obstructive Lung Disease in Northern Sweden (OLIN) Study were assessed with structured interview and lung function test. The study suggested that up to 50% of the smokers could develop COPD as opposed to 15-20% as published in many studies(23).

In Health Survey of England, which is an annual household survey that assesses the health of the population of England, it was found that out of 8215 subjects with valid spirometry data, 1093(13.3%) had COPD. Current cigarette smoking was significantly higher in the population with COPD when compared to non-COPD population. 34.9% of the current cigarette smoker had COPD. Smokers with COPD demonstrate a higher dependence on cigarette smoking when compared to non-COPD smokers. Smokers with COPD are less likely to quit smoking than non-COPD smokers(24).

A field survey done in rural and urban population in India in 2001, which included 18217 males and 17078 females found that 5% men and 3.2% women had COPD. 68% of men and 7% of women had history of ever-smoking(25). A meta-analysis of 14 Indian studies to estimate the burden of COPD, reported that 82.3% of COPD was associated with history of ever smoking. Prevalence of COPD in smokers and non-smokers were

7.7% and 2.9%, respectively. In this study, the odds ratio was ranging from 2 to 3.5 for different types of smoking (cigarette, bidi, hookah). Odds ratio for hookah smoking was highest, 3.5(26).

Second-hand Smoke (SHS) and COPD

Second-hand smoke is the smoke produced from burning of tobacco products like cigarettes, beedis, cigars, pipes, etc. The air/smoke exhaled by person while smoking is also considered second-hand smoke. This tobacco smoke contains hundreds of chemicals of which 70 have been proven to cause cancers (5). There is no safe level of tobacco smoke exposure, that is, that any level of second-hand smoke is harmful for health.10-15% of COPD cases were stated to be due to risk factors like exposure to SHS, occupational and genetic exposure(27,28).

GATS 2 shows that 35% of the non-smokers are exposed to SHS at home and 26.2% of the non-smokers are exposed to SHS at their workplace. About 25.7% of all adults get exposed to SHS at public places (1).

Throughout epidemiological studies up until now, there has been limited focus on the causal association between SHS and COPD(29).There might be several reasons behind it. Firstly, several studies are based on self-reports and, secondly, different definitions have been used to describe COPD. Therefore, there are inconsistent reports on the effects of passive smoking on lung functions (29).In meta-analysis of 5 studies, including 28965 participants, association between SHS and COPD. Among both sexes (n=21558), there was a risk ratio (RR) of 1.66 (95% CI: 1.38-2.00).In one men only study,RR was 1.50 (95% CI: 0.96-2-28) whereas in two female only studies, a much higher RR of 2.17 (95% CI: 1.48-3.18) was identified. These studies suggest a positive association between SHS and COPD (29).

Psychiatric Co-morbidities in COPD patients

The term co-morbidity was coined in 1970 by Alvan Feinstein, and described it as, the presence of ‘a distinct additional clinical entity(30).The patient with medical illness often has co-morbid psychiatric illness. It is estimated that 40% of the patients admitted with a general medical illness also have a co-morbid psychiatric illness(31).

In a systematic review of 42 studies, there was increased length of stay (LOS) at hospitals in patients with medical and psychiatric co-morbidities when compared with inpatients without a psychiatric co-morbidity (in 40 out of 42 studies). This finding was statistically significant in 33 studies. The presence of medical-psychiatric co-morbidities also leads to an increased medical cost and an increase in number of re-hospitalisations. Out of six studies which examined the population with co-morbid depressive disorder, five of them had found statistically significant association between higher medical cost and co-morbid depression(31).In a cohort study of 144 adults, depression was estimated to be a significant risk factor for hospital re-admissions with OR= 3.3 (95% CI = 1.20 to 9.25) within 90 days of discharge (32).

A 2016 systematic review and meta-analysis by *Pederson et al., 2016*aimed to evaluate the association between depression and rehospitalisation or mortality in patients with medical illnesses. In 8 studies analysed for rehospitalisation, in 30 days, 395 of 2433 patients (16.2%) were readmitted. In hospital patients with depressive symptoms, re-admission was more common after 30 days compared to patients without depression(20.4% vs 13.7%, RR: 1.73, 95% CI: 1.16-2.58) which was statistically significant (33).Results were similar with readmissions within 90-days (n= 1543) in six studies, (39.8% vs31.0%, RR: 1.68, 95% CI: 1.13-2.50)(33).Among the nine studies evaluated for mortality data, medically ill patients with depression symptoms had a greater risk of dying (2.8% vs 1.5%, RR: 2.13, 95% CI: 1.31-3.44), when compared to those patients without depressive symptoms. These findings were consistent in mortality after 90-days of discharge(33).

The burden of chronic physical diseases and mental disorders is increasing worldwide(34).We now have clear information on the global massive burden of psychiatric illnesses (23 per cent of the total GBD), estimated at 600 million people and most people living with mental disorders (85 per cent) in low- and middle - income countries(34).Less than 20% of people with mental disorders are treated worldwide, even though cost-effective treatments are available (35).Stigma and human rights' violation are faced by most of the people with mental illness.

The existence of a chronic medical condition can reduce the chance of doctors or other professionals noticing or treating depression. The medical illness being the priority, several symptoms like, fatiguability, difficulty in concentration, sleep and appetite

disturbance, etc., might be overlooked. Even if the symptoms are recognised, they might not be taken care, assuming the "depressive symptoms" to be a part of the medical illness.

As COPD is also a chronic medical illness, it is necessary to diagnose and manage the co-morbid psychiatric illnesses in order to improve overall quality of life of the patient.

Prevalence of psychiatric comorbidities in COPD

In a cross-sectional study including 18588 persons, 1736 people had COPD. Out of 1,736 participants with COPD, 40% had ≥3 depressive symptoms. Depressive symptoms are more common in COPD than in coronary heart, stroke , diabetes, asthma, high blood pressure and cancer (36).Several studies have shown the association of psychiatric co-morbidities with COPD. A meta-analysis of 11 studies reported an increased risk of psychiatric disorders in COPD patients (OR 1.78, 95% CI 1.48–2.14; $P<.00001$) (37).

A meta-analysis was done by *Zhang et al., 2011* which included 8 studies. Total sample size was 39587 individuals with COPD compared to 39431 controls. It was found that the prevalence of depression in COPD patients was 24.6% and in controls was 11.7%. This difference was statistically significant(38).

A study in Nigeria compared the mental status of 30 COPD patients with 30 patients with uncomplicated hypertension (HTN), using the 30-item General Health Questionnaire (GHQ-30) and Present State Examination (PSE). It was found that the group of COPD patients had significantly higher prevalence of psychiatric co-morbidity when compared with the group of patients with uncomplicated HTN (30% vs 13.3%, $p<0.05$). Among the COPD patients, 16.7% had depressive disorders, 10% had anxiety disorders and 3.3% had delirium (39).

In a study by *Frei et al., 2014* to develop a co-morbidity index for COPD, depression and anxiety were among the five major co-morbidities that impacted the management and outcome in COPD(40).

There are large variations in the prevalence of psychiatric comorbidities in COPD according to the results of various studies. Dowson et al. studied the prevalence rates of anxiety and depression in 72 COPD inpatients using Hospital Anxiety and Depression

Scale (HADS). The prevalence was found to be 50% for anxiety and 28% for depression(41).

In a Chinese case-control study, 1100 COPD patients and 1100 controls participated. The participants were assessed with HADS-A for anxiety and HADS-D for depression. The COPD patients had significantly higher prevalence of anxiety and depression when compared to controls, with anxiety in 18.3% vs 5.3% and depression in 35.7% vs 7.2%. Study also reported the co-occurrence of anxiety and depression in COPD patients. According to this study, 42% COPD patients with depression also had concomitant anxiety symptoms and 72.1% of COPD patient with a diagnosis of anxiety showed concomitant depressive symptoms. There is significantly higher prevalence of depression and anxiety in severe COPD when compared to mild or moderate COPD(42).

A number of factors are found to be associated with psychiatric co-morbidities in COPD patients. In a cross-sectional study, 53 COPD patients who were admitted in a hospital of China with no previous diagnosis of psychiatric co-morbidities participated to get assessed for depression using Hamilton Depression Rating Scale (HADRS). It was found that 40 out of 53 patients (75.47%) were suffering from depression. 86% of males and 50% of females were diagnosed with depression using HDRS(43).

Among the COPD patients, anxiety prevalence varies from 6-74% (44). According to a meta-analysis of 10 studies to find the prevalence of psychiatric illnesses in COPD patients, the prevalence of clinical anxiety was 10-55% among the in-patients and 13-46% among the out-patients (45).The prevalence of depression ranges from 8-80% among COPD patients (44). Another review by *Maurer et al., 2008*, reported that about 2/3 of COPD patients with depression have moderate to severe depression, which implicates even higher prevalence of mild and subclinical depression (46).

A cross-sectional study was done in Texas, USA in 2005 by *Kunik et al.*, to assess the prevalence of anxiety and depression in people with COPD by using Structured Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (SCID). SCID was used in evaluation of 204 patients with COPD, out of them, 11.7% were suffering from only depressive disorder, 23% people had anxiety disorder only, and 26% patients were suffering from both anxiety and depression at the same time. 91 out of 204 patients were found to be suffering from severe levels of anxiety and/or depression

when measured using Beck Anxiety Inventory(BAI) and Beck Depression Inventory(BDI), respectively(47).

There is enough evidence about presence of psychiatric co-morbidities in COPD. Enough data is available to suggest that predominant psychiatric illnesses which are diagnosed in patients suffering from COPD are depressive and anxiety disorder. The symptoms of anxiety and depression can easily be confused with that of COPD, making diagnosis difficult. Up to 10-80% of the COPD patients have such symptoms, whereas 19-42% of COPD patients have major depressive episode (48,49).

Possible Aetiology of Psychiatric Comorbidity in COPD

Depression had the largest impact on the self-reported health status of COPD patients, followed by anxiety, peripheral artery disease, cerebrovascular disease and symptomatic heart disease(40).

Though the aetiology of psychiatric illness in COPD is unknown, it is thought to be multifactorial. Depression could precede the development of COPD, and genetic factors could be common, but in people with anxiety and depression history of smoking is seen more frequently.

Smoking, ageing, and hypoxaemia are likely to affect to brain function and contribute to the development of psychiatric illnesses in COPD. Other risk factors suggested are, especially for anxiety and depression, are physical disability, dyspnoea, number of co-morbidities, female sex, living alone and quality of life(44).

Hypoxia may also be responsible in developing depression in COPD, apart from inflammatory processes. The presence of low arterial oxygen saturation was associated with periventricular white matter lesions which is also seen in depression(50).

Regarding anxiety, physical factors such as low resistance, incontinence, fear of having an episode of dyspnoeaand constant pharmacological needs can have an impact on social phobias, as well as generalized anxiety disordersand panic attack disorder(45). However, physiological factors such as dynamic hyperinflation and hyperventilation related to dyspnoea may also be part of the pathogenesis(44).COPD negatively affects daily activities that would require exertion- ambulation, social activities, household roles and

functions and recreational activities. In turn, also causes significant reduction in quality of life and increased propensity for development of depressive symptoms(38,51).

Plasma of COPD patients has been demonstrated to also contain elevated levels of pro-inflammatory cytokines such as C- Reactive Protein (CRP), IL-6, fibrinogen, activated leukocytes, and tumor necrosis factor- α (TNF-α)(52,53). In Bergen COPD cohort study, systemic levels of inflammatory markers were assessed. The serum levels of soluble tumour necrosis factor receptor (sTNFR)- 1 were significantly associated with the diagnosis of depression in COPD patients.

The C-reactive protein (CRP) levels were investigated in COPD patients to find an association with comorbid psychiatric illness. It was found that CRP levels were significantly increased in COPD patients with depression when compared to COPD patients without depression. Similarly, duration of cough was significantly higher and FEV_1 was significantly lower in the COPD patients with depression. In the univariate regression analysis, it was found that there was significant association of level of education, duration of cough, gender, history of smoking, FEV_1 and CRP levels. Though, the multivariate regression model revealed high serum CRP level and low FEV_1 as the strongest risk factor for depression in COPD.(43)

There is widespread evidence that systemic inflammation can contribute to psychiatric illnesses and among the inflammatory markers, interleukin- 6 (IL-6) is found to be especially important in humans and animal depressive models for causation of depression(54,55).

Impact of Psychiatric Comorbidity on COPD

According to an Indian cross-sectional study including 124 COPD patients, COPD is associated with significantly lower health-related quality of life (HRQOL). Increase in severity and duration of COPD symptoms negatively impacts HRQOL in COPD (51).

Similar to other chronic illnesses, anxiety or depression in patients with COPD may lead to reduced quality of life, increased LOS, and increased mortality. This outcome is further worsened by the difficulty in smoking cessation and poor compliance with the treatment (44). The psychiatric illness like anxiety and depression significantly impact the functional status of COPD patients (56).

There is evidence to support the fact the concurrent treatment of psychiatric comorbidities is important for the better management of COPD patients. The psychiatric comorbidities may impact the compliance as well as outcome of the management of COPD. When COPD patients with panic disorder were treated with Sertraline over 6 weeks, majority of the patients reported improvement in daily activities as well as in the general well-being(57).

Treatment and Management of Psychiatric Comorbidity in COPD

In a cross-sectional study by *Kunik et al., 2005,* out of the patients with COPD who were diagnoses with depressive and/or anxiety disorder using Structured Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (SCID), it was found that only 31% received treatment for their psychiatric illnesses. The untreated psychiatric comorbidities may negatively impact treatment outcomes of COPD and vice versa(47).

In a randomized controlled trial to evaluate the response of antidepressants on depression in COPD and its impact on patient's functional capacity, a 12-week trial of Nortriptyline was given to 30 patients of COPD with depression. There was significant improvement in the nortriptyline group in terms of mood and anxiolytic effect when compared with the placebo group. There was 60% improvement in Hamilton- Depression Rating Scale (HAM-D) scores of nortriptyline group versus 17% improvement in the placebo group. There was significant relief in anxiety in nortriptyline group by 45% versus only 4% in the placebo group, when measured on Patient-Rated Anxiety Scale (PRAS). Overall, functional impairment, physical disability and psychosocial disability were improved significantly. The greatest improvements were observed for general impairment (almost 9%) and psychosocial impairment (more than 10%), with a smaller increase in physical function (4%)(58).

The COPD patients with anxiety and depression largely remain under diagnosed as well as undertreated, leading to significant impact in overall management, increased health costs and reduction in quality of life.

Tobacco Smoking and Psychiatric Co-morbidities in COPD

In the study by *Xu K & Xiu Li, 2008*, 87.5% of the COPD patients with depression were heavy smokers. Heavy smoking was defined as the number of smoking years × the number of cigarettes smoked per day >400. In univariate regression analysis, smoking history was associated with depression in COPD (OR=5.25, 95% CI: 1.35-20.42, p=0.017) (43).

In a study by *Lou et al., 2014*,more than one third (35.2%) of smokers with COPD reported significant symptoms of depression, and one fifth (19.8%) reported serious symptoms of anxiety(59).

Martinez et al. performed a 2-year cohort study on 328 COPD patients with active smoking history. Depression and anxiety were assessed using HADS at three visits, baseline, at the end of 1 year and at the end of 2 year. The patients who stopped smoking at visit-2 and abstained till visit-3 were compared with patients who continued to smoke till visit-3. At visit-1, prevalence of anxiety and depression in the respective groups was 5.6% vs 5% and 7.6% vs 5.2% respectively. At visit 3, the prevalence of anxiety and depression in the respective groups were 5.5% vs 6.1% and 6.3% vs 6.3%, respectively. The association between the smoking cessation and anxiety symptoms measured through HADS was statistically significant. In addition to this association, there can be impact on the management of COPD.(60)

Relationship of smoking with psychiatric comorbidity in COPD

Several studies have evaluated the association between COPD, psychiatric co-morbidities, and tobacco smoking. A cross-sectional study examined 7482 Dutch employees for respiratory complaints and assessed for depression and anxiety using Hamilton Anxiety and Depression Scale (HADS) and asked questions to assess the smoking status. There was two-fold increased risk of anxiety and depression in patients with COPD when compared with healthy employees. The risk of having anxiety and depression further increased to up to four-fold in patients with current or past history of smoking (61). For anxiety alone, current smoking increased the risk by eight-times in COPD when compared to healthy employees. For depression alone, current smoking had an OR=7.56 in patients with COPD when compared to healthy employees(62).

The multivariate logistic model in a case-controlled study by *Lou et al., 2012* revealed that the history of smoking significantly increased the risk of anxiety (OR=1.27) and depression (OR=1.26). Other factors significantly increasing the risk of anxiety and depression in COPD patients are higher severity of COPD, low household income and concomitant anxiety or depression. These results emphasise on the importance of screening for anxiety and depression in COPD patients, especially with higher severity or with history of smoking, so as to provide a better health care.(42)

In the study by *Goodwin et al., 2012*, any anxiety disorder, GAD, social phobia, and PTSD were associated with significantly increased odds of COPD compared with those without anxiety disorders. However, after adjusting for smoking and nicotine dependence and demographic differences, only social phobia was significantly associated with COPD (63).

A 5-year follow up study was done in Finland to study the effect of co-morbidities on smoking cessation in 739 COPD patients. This study had 58.6% of patients who had quit smoking at the time of enrolment. 28% patients quitted smoking before diagnosis of COPD whereas 30.6% patients quitted after diagnosis of COPD. When compared with non-quitters, quitters were suffering from more advanced COPD. The severity of disease could be acting as a motivational factor in the quitters. The most significant risk factors associated with the failure of smoking cessation were alcohol abuse (OR=2.12) and psychiatric co-morbidities (OR=1.83). The prevalence of psychiatric co-morbidities in non-quitters and quitters was 33.6% vs 17.5% and prevalence of alcohol abuse in non-quitters and quitters was 26.6% vs 11.5%. This again implies that successful treatment of COPD requires combined efforts from pulmonologist and psychiatrist in order to increase the quit rate for tobacco smoking and management of psychiatric co-morbidities simultaneously.(64)

Smoking cessation is significantly impacted by concurrent psychiatric comorbidity. The 2006 Behavioral Risk Factor Surveillance System data(n=248,800) was used to compare the rates of depression, anxiety and depressive symptoms among non-quitters, successful quitters and unsuccessful- quitters. The unsuccessful quitters had 1.2 times more chances of having lifetime anxiety or depression, whereas the quitters had an OR= 0.7. The successful quitters had much lower proportion of current depression when compared to

non-quitters and unsuccessful quitters (8% vs >14%) (65). This result suggests an association between depression and unsuccessful quitting.

Possible Aetiology of co-existing smoking and psychiatric comorbidity in COPD

Many studies have shown that cigarette smoking can increase the risk of anxiety, although it has yet to be confirmed. Evidence of anxiety disorder pathogenesis and increasing signs of anxiety may be due to different neurotransmitter pathway, immune system, mitochondrial activity, and epigenetic modulation, however the literature is heterogeneous and sparse in some fields. Cigarette smoke products, including nicotine and other toxic substances, have an effect on all these pathways, thus affecting anxiety disorders(66).

Fluharty et al., 2017 in a systematic review included 148 studies and found that nearly half of the studies reported that baseline depression or anxiety was associated with some type of later smoking behaviour. These findings support a self-medication model, suggesting that individuals smoke to alleviate psychiatric symptoms. Over a third of the studies found that smoking exposure at baseline was associated with later depression or anxiety, supporting the alternative hypothesis that prolonged smoking increases susceptibility to depression and anxiety(67).

Few studies reporting evidence for a bidirectional model relationship between smoking and depression and anxiety. The affective disturbance in depression may play a role in the depression- nicotine dependence comorbidity. High negative affect (NA- the experience of subjective distress) and low positive affect (PA- engagement with the environment) were associated with the nicotine dependence severity and relapse risk of smoking. Low PA depicts appetitive emotions such as anhedonia, diminished motivation and reinforcement learning. Nicotine positively modifies low PA and reward responsivity. Acute withdrawal from nicotine leads to reduction in the PA, consequently developing further urges to enhance PA. Therefore, the smokers with depression having low PA have increased smoking behaviour to enhance PA. Thus, low PA increases the reinforcement value of smoking. The NA spectrum includes aversive emotions such as sadness, irritability, anxiety and low distress tolerance. Similar to low PA, high NA acts as a motivation to continue the behaviour of smoking. The avoidance of NA inclines the depressed smoker to continue smoking. The individual may not distinguish between the

NA developed by nicotine- withdrawal and the NA developed by other factors. This further affects the maintenance of smoking behaviour in the depressed individual (68).

In a cross-sectional survey done in USA in 2006, 89337 people with COPD were assessed for their mental health using the Veterans Short Form-36. It was found that former smokers had a better mental health when compared to current smokers. The study also observed that the former smoker more actively participated in the study and had a better patient-healthcare provider relationship. The former smokers have better perceptions regarding provider-patient relationship than current smokers.(69)

Smoking cessation is the mainstay for the treatment of COPD. Patients suffering from COPD may even have knowledge about the same but still a large proportion continue to smoke. It is important to identify the factors which may act as a barrier in smoking cessation which may co-occur with COPD.

Tobacco smoking status and alcohol use in COPD

The cornerstone of management of COPD is smoking cessation but it is not easy to achieve. There are several risk factors and effects of co-morbidities that hinders with the cessation and maintenance of the cessation.

In a cohort study of 4-year follow up of 739 patients with COPD, the prevalence of alcohol abuse was 26.6% in non-quitters versus 11.5% in in quitters ($p < 0.001$). The prevalence of psychiatric disorders was 33.6% in non-quitters versus 17.5% in quitters. The cohort was assessed at 0, 1, 2, and 4 years. In multivariate logistic regression for smoking cessation, psychiatric disorders (OR=1.83, 95% CI: 1.23-2.71) and alcohol abuse (OR=2.12, 95% CI:1.35-3.34) were independent risk factors for the failure of smoking cessation. Chronic alcoholism, alcohol use disorder, and treatment of alcohol-use-related disorders were all categorized as “alcohol abuse” in this study. Alcohol abuse also played an independent role in mortality of the patients with COPD (OR= 2.03, 95% CI: 1.14-3.61). Co-existent substance abuse decreases success of smoking cessation and increased the mortality by two-fold(70).

In a cross-sectional study (*Mowls et al., 2014*), 4965 white adults and 380 black adults with COPD participated. 64% of subjects reported of having attempted to quit smoking. It was found that white females were 1.3 times more likely to make quit attempts in past

12 months. The people who reported of doing exercise in past 30 days were 2 times more likely to make quit attempts than those who didn't report any exercise in past 3 days. White smokers who were light and non-drinkers were 1.7 times more likely to make quit attempts when compared to white smokers who were moderate and heavy drinkers. Black smokers who had partners were 4.5 times more likely to make quit attempts than those who didn't have partner. The family dynamics may play a factor in developing motivation in smokers. The heavier the alcohol consumption the lesser will be motivation to quit smoking.(71)

In a cohort study to examine the association between alcohol consumption and 20-year mortality from COPD, 2953 adult males were followed up. Among the never smokers, past smokers and current smokers at the baseline, the mortality rates were 0.6, 1.7 and 2.2 per 1000- person years, respectively. The average number of pack years was positively associated with the alcohol consumption. Average number of pack-years for non- alcohol drinkers was 14.7 whereas in those consuming >9 drinks per day, the number of pack-years was 22.1(72).

In a prospective cohort (*Greene et al., 2008*), 30503 COPD patients participated, and they were assessed using AUDIT-C, CAGE questionnaire and were also asked questions about binge drinking. The group with AUDIT-C score >8 had highest number of current smokers (51%) and heavy smokers smoking >1.5 pack daily (24%). The alcohol consumption was associated with tobacco smoking but it was not found to be directly associated with COPD exacerbation when tobacco smoking as a variable was removed.(73)

COPD patients who are heavy drinkers are less likely to make quit attempts in last 1 year (OR=0.66) when compared to abstainers. This was reported by *Schiller and Ni, 2006.* It included National Health Interview Survey (NHIS) data of 175631 adults of age 25 year or older out of which 11238 had COPD. Most of the COPD patients have the knowledge about the positive effects of smoking cessation and approx. 52% make quit attempts in past 1 year as compared to 45% non-COPD patients, but about 85% are unsuccessful attempts. Only 14.6% of smokers with COPD had successful cessation. This study also reported difference in smoking habits of COPD and non-COPD adults. 36.2% of adults with COPD were currently smoking as opposed to 22% in adults without COPD. 90% of smokers with COPD were having history of smoking every day.(74)

Smoking Cessation Interventions and COPD

In a randomised controlled study done in China (*Chen et al., 2014),* COPD smokers and asymptomatic smokers were randomly sampled into intervention group and control group. Out of 85 COPD smokers, 42 were in intervention group and 43 were in control group. Out of 105 non-symptomatic smokers, 52 were in intervention group and 53 were in control group. Intervention included a cognitive counselling at the baseline visit and self-help material. This was followed by 9 phone calls, each at 1^{st}, 2^{nd}, 3^{rd}, 4^{th}, 6^{th} and 8^{th} week and then 3^{rd}, 4^{th} and 5^{th} month. Main assessments were performed at 4^{th} week and 6^{th} month. The study reported that the abstinence rates of intervention and control groups of COPD smokers were 40.5% vs 18.6%, and this difference was significant. Whereas in the intervention group and control group of non-symptomatic smokers, there was no significant difference in the abstinence rates. The abstinence rates in COPD smokers was 29.4% whereas in non-symptomatic smokers, abstinence rates were significantly lower (6.7%). It was found that individual counselling (OR=3.1), quitting motivation (OR=3.15) and COPD (OR=4.2) were independent predictors of abstinence with COPD being the strongest predictors. So, it can be inferred that COPD plays as one of the most important motivational factors for quitting smoking.(75)

The smoking cessation treatment is necessary in COPD patients with history of current smoking. A descriptive study of 472 patients with severe or very severe COPD with current smoking consisted of mean Fagerström test for nicotine dependence score was 7.4. Continuous abstinence rates of 9-24 weeks were 48.5%. The treatment with Varenicline was more effective than Nicotine Replacement Therapy (NRT)(76).

In a network meta-analysis including 10 RCTs to compare the effectiveness of different smoking cessation treatment for COPD patients. Smoking cessation counselling (SCC) in combination with nicotine replacement therapy (NRT) had the greatest effect on prolonged abstinence rates. It had five times greater efficacy when compared with no intervention, three times more effective than SCC alone and 1.5 times more effective than SCC in combination with an antidepressant. The second most effective smoking cessation treatment was SCC combined with an antidepressant, which had OR= 3.32 when compared with no intervention and OR=1.83 when compared with SCC alone. There was no difference between nortriptyline and bupropion with SCC. Only SCC alone is only slightly superior to no intervention/ usual care (OR=1.82, 95% CI: 0.96-3.44).

The smoking counselling cessation treatment was not helpful in smoking cessation treatment in COPD patients and there is a need to combine SCC with NRT or an antidepressant (77). Another systematic review of nine studies compared usual care, minimal counselling, intensive counselling and intensive counselling combined with the pharmacotherapy, for 12-month continuous abstinence rates and costs per quality-adjusted life year. The smoking cessation with intensive counselling and pharmacotherapy had highest 12-month continuous abstinence rates (13.2%) followed by intensive counselling (6%), minimal counselling (2.6%) and usual care (1.4%). Compared with others, the pharmacotherapy was more cost efficient (78).

Psychiatric co-morbidities in COPD: Indian Scenario

Most of the Indian studies are primarily done to find the prevalence of psychiatric comorbidities in COPD patients. In the Global Burden of Diseases Study 1990-2016, it was reported that COPD was responsible for 75.6% of the DALYs due to chronic respiratory diseases, which was much higher than the second most disabling chronic respiratory illness, i.e., asthma (20%). The number of cases of COPD in India had increased from 28.1 million in 1990 to 55.3 million in 2016. The prevalence increased from 3.3% in 1990 to 4.2% in 2016.

In a home-based survey in Delhi, the prevalence of COPD was 10.1% (95% CI: 8.5-11.9). 24.9% of smokers had COPD. In regression analysis, strongest risk factor was smoking with aOR= 9.48 (95% CI: 4.2-14.1). Other risk factors were environmental tobacco smoke (ETS) exposure (aOR=7.97, 95% CI: 3.3-13.2), occupational exposure (aOR= 6.2, 95% CI: 3.3-10.2), age >50yrs (aOR= 4.2, 95%CI: 2.82-7.84) and past smoker (aOR= 4.1, 95% CI:2-9.45). The current and ex-smokers with >20 pack- years had higher risk of developing COPD when compared to their counterparts with <10 pack-years. The risk of COPD increased by 15% with increase by one pack-year (aOR= 1.15, 95% CI: 1.09-1.22). The ex-smokers have 63% lesser risk of developing COPD (aOR=0.37). Only 48% of the COPD patients were receiving treatment(79).

A recent cross-sectional study was done in 128 COPD patients and they were assessed using Hospital Anxiety Depression Scale (HADS). The study reported the depression in 22.7%, anxiety in 3.1% and both in 5.5% of COPD patients.(80)

Another cross-sectional study assessed 120 COPD pts for depression using Beck's Depression Invetory-2. It was found that 55% of them had depression. Smoking was reported to be associated with 35.48% without depression and 64.52% with depression. Mean score of depression increased with the grade of COPD(81).In a cross-sectional study including 360 COPD patients, majority of non-smokers were diagnosed with GOLD severity grade II whereas majority of smokers were diagnosed with GOLD severity grade III and IV(82).

A pilot study was conducted in South Indian population to find association between inflammatory markers and COPD. It was found that the serum levels of TNF-α, IFN-γ, IL-4 and GM-CSF were significantly elevated in tobacco smokers with COPD when compared with tobacco smoker without COPD(83). This suggest that the tobacco smoking causes COPD through inflammatory mechanisms.

A case control study was done with 74 COPD patients and 74 controls. The psychiatric comorbidities were assessed using Mini International Neuropsychiatric Interview questionnaire version 6.0 (MINI 6.0). History of smoking was present in 71.6% of cases versus 8.1% of controls. 28.4% of COPD patients screened positive for depression whereas only 2.7% of controls were found to have depression.(84)

In a cross-sectional study, 126 COPD patients were assessed for depression using Patient Health Questionnaire (PHQ-9). 49.2% of them were found to have depression and 20.6% had severe depression.(85)

DEFINITIONS OF SMOKING STATUS

As there are no standard definitions for smoking status followed in India. We have reviewed some of the definitions which have been used worldwide.

a. National Health Interview Survey (NHIS):

i. **Current smoker:** An adult who has smoked 100 cigarettes in his or her lifetime and who currently smokes cigarettes.

- **Everyday smoker:** An adult who has smoked at least 100 cigarettes in his or her lifetime, and who now smokes every day. Previously called a "regular smoker".
- **Someday smoker:** An adult who has smoked at least 100 cigarettes in his or her lifetime, who smokes now, but does not smoke every day. Previously called an "occasional smoker".

ii. **Former smoker:** An adult who has smoked at least 100 cigarettes in his or her lifetime but who had quit smoking at the time of interview.

iii. **Never smoker:** An adult who has never smoked, or who has smoked less than 100 cigarettes in his or her lifetime.(86)

b. National Survey on Drug Use and Health (NSDUH):

The NSDUH-S definition uses two questions

i. "Have you ever smoked part or all of a cigarette?" Respondents answering "Yes" are classified as ever smokers, and

ii. Those who answer "No" are classified as never smokers.

iii. Ever smokers are then asked a second question: "During the past 30 days, have you smoked part or all of a cigarette?" Respondents who answer "Yes" are classified as current smokers.(87)

c. **Ministry of Health, New Zealand:**

i. **Current smoker**- Individuals who have smoked greater than 100 cigarettes/ bidis (or any other form) in their lifetime and has smoked in the last 28 days

ii. **Ex-Smoker**- Individuals who have smoked greater than 100 cigarettes in their lifetime but has not smoked in the last 28 days.

iii. **Never Smoker**- Individuals who have not smoked greater than 100 cigarettes in their lifetime and do not currently smoke.(88)

Rationale of Study

RATIONALE OF STUDY

- Tobacco smoking is a leading preventable cause of morbidity and mortality and a major cause of COPD
- Despite the knowledge that quitting would have important long-term benefits, many patients continued to smoke
- This may not be simply due to the lack of motivation to stop smoking, but rather might be associated with other co-morbidities
- Studies have not measure psychiatric co-morbidities and other factors between those who continued to smoke and those who are able to stop smoking/non smokers
- The management of psychiatric co- morbidities may play an important role in the success of smoking cessation programs
- Hence further research needs to be done to evaluate the association of smoking status with psychiatric co- morbidities in patients with COPD for successful smoking cessation

Hypothesis

HYPOTHESIS

- Current tobacco smokers with COPD have higher rates of psychiatric co-morbidities as compared to current non-smokers with COPD

Aims & Objectives

AIMS AND OBJECTIVES

Aim

To examine the association between tobacco smoking status and psychiatric co-morbidities among treatment seeking patients with COPD.

Objectives

Primary objective

To study the association between tobacco smoking statusand psychiatric co-morbidities among treatment seeking patients with COPD

Secondary objectives

A. To assess the relation of tobacco smoking status with various socio-demographic & clinical variables among treatment seeking patients with COPD

B. To study the relation of severity of nicotine dependence with severity of depression and anxiety among current smokers with COPD

Materials & Methods

MATERIALS AND METHODS

Type of study

Cross-sectional study

Sampling frame

Patients with COPD seeking treatment in Outpatient Department (OPD) of Department of Pulmonary, Critical Care and Sleep Medicine, AIIMS New Delhi

Setting of the study

OPD of Department of Pulmonary, Critical Care and Sleep Medicine Department, AIIMS, New Delhi

Inclusion criteria (for both groups)

1. Age >30yr
2. Males
3. Patients with COPD registered at OPD of Department of Pulmonary, Critical Care and Sleep Medicine at least 3 months back or more

Exclusion criteria (for both groups)

1. Individuals who have comorbid medical condition (congestive heart failure, diabetes mellitus, and cerebrovascular accident)
2. Those taking oral corticosteroids
3. Patients who present with an acute exacerbation and clinically unstable
4. Patients who are receiving any treatment for psychiatric disorders or antidepressant for tobacco cessation
5. Patients who not willing to participate

Sample size

In this study, 100 patients with COPD were included with 50 being current smokers and 50 being current non- smokers

Sampling method

Purposive sampling

Operational definition of tobacco smoking status

- **Current smoker-**
- Individuals who have smoked greater than 100 cigarettes/ bidis (or any other form) in their lifetime and have smoked during the past 30 days
- **Current Non-smoker** (former pus Never smokers)
- **Former Smoker**-Individuals who have smoked greater than 100 cigarettes in their lifetime but have not smoked during the past 30 days
- **Never Smoker**-Individuals who have never smoked or who have smoked less than 100 cigarettes in their lifetime.
- They were combined, creating a group of current non-smokers.

Instruments used

Semi- structured Proforma

It included socio-demographic history comprising of age, religion, occupation, education, family income per month, marital status, residence. The treatment details included duration of symptoms of COPD, duration since registration at OPD of Department of Pulmonary, Critical Care and Sleep Medicine, AIIMS Delhi, current stage of COPD. Details of tobacco use included smoking status at the time of diagnosis of COPD and during registration at OPD of Department of Pulmonary, Critical Care and Sleep Medicine, AIIMS Delhi, type of smoking (cigarette, beedi, hukkah, etc.), age of onset of smoking, duration of tobacco use in smoking form, maximum dose of smoking form of tobacco in lifetime, current dose, other forms of tobacco use, total number of

abstinence attempts in lifetime and total number of abstinence attempts in past one year. Treatment details specific to tobacco use included tobacco cessation treatment advised by any doctor while seeking treatment for COPD and any tobacco cessation treatment received. Details of substance use other than tobacco use and details of any medical or surgical co-morbidity was also collected.

Mini International Neuropsychiatric Interview (MINI) with Tobacco Use Disorder Module 7.0.2

The MINI International Neuropsychiatric Interview was developed by Sheehan and Lecrubier in 1990. MINI was developed to meet the need for a brief, reliable and valid structured diagnostic interview that screens many disorders. It is organized in diagnostic sections and uses branching tree logic; it has two to four screening questions per disorder. Additional symptom questions are asked only if the screen questions are positively endorsed. The composition of MINI makes it easier to be used also by non-academics.

MINI with Tobacco Use Disorder Module is a more elaborate version of MINI 7.0.2 for DSM-5. The following disorders are screened in this version: Major Depressive Episode, Suicidality, Mania and Hypomanic Episodes, Panic Disorder, Agoraphobia, Social Anxiety Disorder, Obsessive-Compulsive Disorder, Posttraumatic Stress Disorder, Alcohol Use Disorder, Non-Alcohol Substance Use Disorder, Psychotic Disorders and Mood Disorders with Psychotic Symptoms, Anorexia Nervosa, Bulimia Nervosa, Binge Eating Disorder, Generalized Anxiety Disorder, Antisocial Personality Disorder. It takes 15 minutes to administer this instrument. When MINI and Composite International Diagnostic Interview (CIDI) were administered with CIDI as gold standard, the specificity of the MINI was good for all diagnoses (range: 0.72 to 0.97). Inter-rater reliability was very high, the kappa coefficients ranging from 0.88 to 1.0. Non-cases were identified with high specificity, resulting in high negative predictive values. Sensitivity and positive predictive values were acceptable(89).

Patient Health Questionnaire-9 (PHQ-9)

Patient Health Questionnaire (PHQ) is a self-administered questionnaire which contains 8 diagnoses. PHQ-9 is a 9-item depression module taken from PHQ which is a widely used and is a validated brief measure for assessing depression severity. In this study,

PHQ-9 has been used as a severity measure. It has scoring from 0 to 27. Each of the 9 items are scored from 0 (not at all) to 3 (nearly every day).The total scores ⩾5 are clinically significant, with scores 5–9, 10–14, 15–19, and 20 and above reflecting mild, moderate, moderately severe, and severe depression, respectively. Cronbach's alpha is 0.81. PHQ-9 score ≥10 has a sensitivity of 88% and a specificity of 88% for major depression(90). It is public domain and it can be used free of cost. It takes 3 minutes to administer it. It is available in Hindi.

Anxiety Inventory for Respiratory (AIR) Disease

AIRis a brief scale developed to measure the anxiety in patients suffering from COPD. It was developed by Professor Yohannes and his team in 2013.It contains 10 items with 4-point response options from 0 (no anxiety symptom at all) to 3 (almost all the time). The score range is from 0 to 30, and the high score is correlated to elevated symptoms of anxiety in patients with COPD. It contains non-somatic anxiety symptoms. The Anxiety Inventory for Respiratory disease (AIR) had high internal consistency (Cronbach's α=0.92) and test-retest reliability (ICC=0.81), and excellent convergent validity, correlating with the Hospital Anxiety and Depression, HAD-Anxiety subscale (r=0.91, p<0.001). The scale also discriminated between patients with clinical anxiety (measured using the PHQ) and those without (U=9, p<0.001). A cut-off score of 14.5 yielded a sensitivity of 0.93 and specificity of 0.98 for detection of clinical anxiety(91). In a study by *Yohannes & Willgoss, 2015,* cut-off score of ≥8 on the AIR (based on psychiatric diagnosis of an anxiety disorder) yielded a sensitivity of 0.80, a specificity of 0.75, a positive predictive value of 67% and a negative predictive value of 81% (92).

Alcohol use disorders Identification Test (AUDIT)

AUDIT is an assessment tool developed by World Health Organisation (WHO) to assess alcohol consumption and alcohol related problems. It assesses alcohol use in the domains of harmful use, hazardous use and dependence. It consists of 10 questions about recent alcohol use, alcohol dependence symptoms, and alcohol-related problems. Each question is scored from 0-4, Q9 & Q10 are scored as 0,2,4. Q2 and Q3 assess for hazardous use, Q4 and Q6 for dependence and Q7 & Q10 assess for harmful use. Score 8-15 implies medium alcohol problems and score of >15 implies high level of alcohol problems. The test development samples across countries haveyieldedacceptable sensitivities of 0.90s

and specificities of 0.80s at cut-off score of 8(93).It takes 5 minutes to administer it and is available in Hindi language in public domain.

Fagerstrom Test for Nicotine Dependence (FTND)

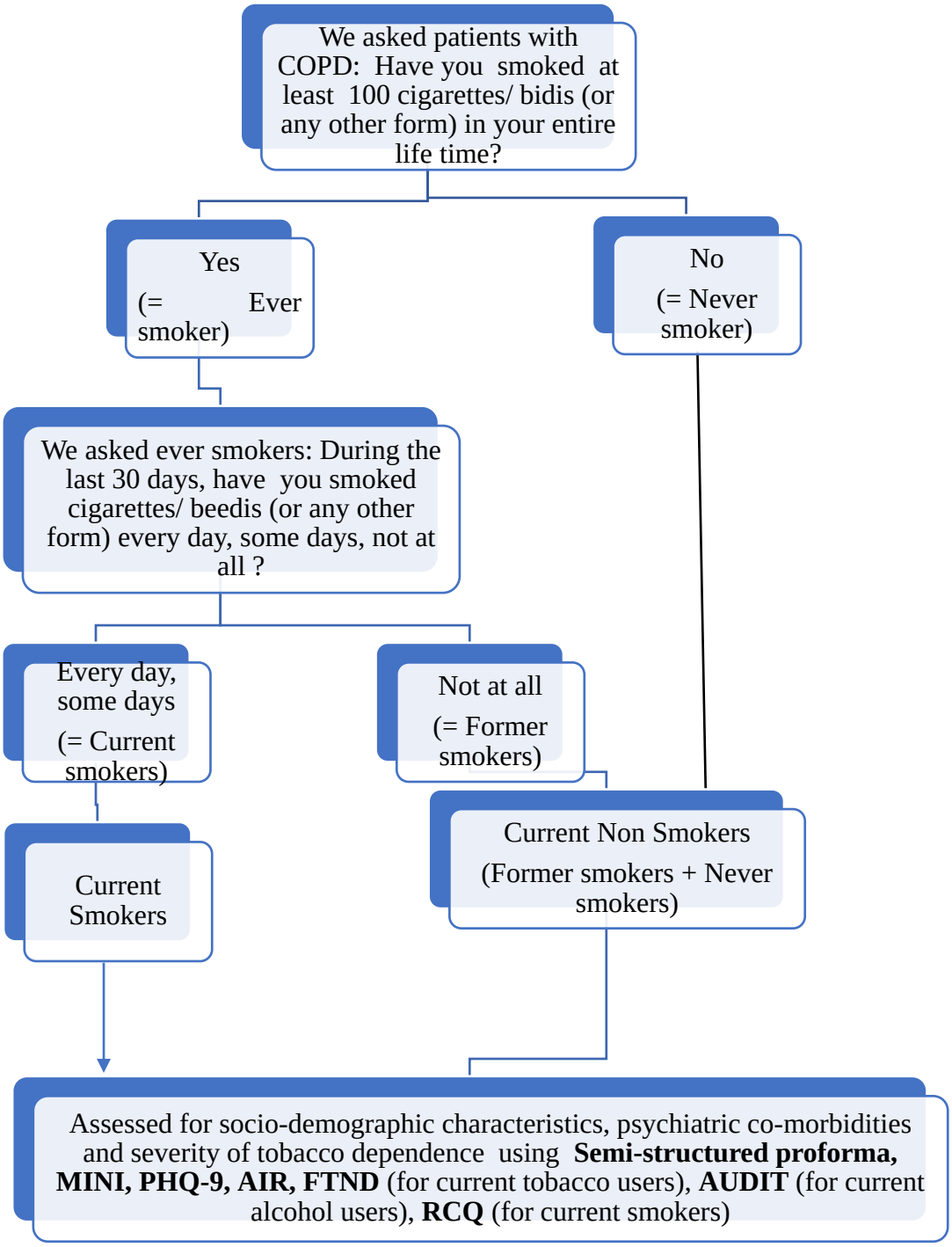
FTND is a standard instrument for assessing the intensity of physical addiction to nicotine. It contains six items that evaluate the quantity of tobacco consumption, the compulsion to use, and dependence. Three items are yes/no items with scores 0 to 1, rest of the three have more than two options with scores ranging from 0 to 3. Minimum total score from the scale is 1 and maximum total score is 10. If total score is 1-2, it equals to low dependence, 3-4 equals low to moderate, 5-7 equals moderate and 8+ score equals high nicotine dependence. Cronbach's α coefficient ranged from 0.55 to 0.74, indicating moderate internal consistency. Correlation between the FTND score and CO levels ranged from 0.19 to 0.59. It is available in public domain(94).

Readiness to Change Questionnaire (RCQ)

RCQ was developed by Heather et al in 1993; in order to assess the level of motivation to quit smoking/tobacco. It is a self-administered 12 item questionnaire. Scoring is done on a Likert scale from -2 to +2 for each response. Four questions have been set for 3 stages of quit Precontemplation (P), Contemplation(C) & Action (A) stage. The Cronbach`s alpha of this scale is 0.85. The time required to administer this scale is about 4 to 5 minutes. Highest score for one of the stages shows the patient to be in that stage of quitting(95).

Study flow

Figure 1: Study flow



Study procedure

The study was started after the approval from Institutional Ethics Committee. The investigator conducted the study at the OPD of Department of Department of Pulmonary, Critical Care and Sleep Medicine. The patients were first screened for their smoking status with questions as mentioned in the Figure 1. Subjects fulfilling the inclusion criteria were approached for the study. 50 current smokers and 50 current non-smokers (former smokers & never smokers) were recruited in the study after obtaining written informed consent. All the subjects were subjected using Semi-structured proforma, MINI with Tobacco Use Disorder Module 7.0.2, PHQ-9, AIR. The subjects with alcohol use were assessed using AUDIT. The current smokers were assessed for nicotine dependence using FTND and for motivation to quit using RCQ. Those who were found to be suffering from any psychiatric comorbidity were psycho-educated about the illness and treatment along with their attending family members and then they were referred to the Department of Psychiatry, AIIMS Delhi. Those with positive history of current alcohol and tobacco use were also psycho-educated about the illness and the treatment along with their family members and were subsequently referred for treatment from Department of Psychiatry, AIIMS Delhi.

Analysis

The quantitative variables were summarized through the descriptive statistics Mean (SD) for the normal distributed data and Median (Inter Quartile Range) for the non-normally distributed data. The categorical variables were summarized through the frequency and percentages. The association of categorical variables between two groups (Current smokers and Current non- smokers) were assessed by Chi-Square test/Fisher's Exact Test. The association of quantitative variables between two groups (Current smokers and Current non- smokers) were assessed by Independent t-test. The association of non-normally distributed variables between two groups were assessed by Mann-Whitney Test. The Karl Pearson's Correlation Coefficient was estimated between score of FTND & score of Anxiety (AIR) and score of FTND & score of Depression (PHQ-9). The two tailed $p<0.05$ was considered statistically significant.

The association of categorical variables between three groups (Current smokers, ex-smokers & non- smokers) was assessed by Chi-Square test/Fisher's Exact Test. The

association of quantitative variables between three groups (Current smokers, Past smokers &Never smokers) was assessed by One-way ANOVA. The association of non-normally distributed variables between three groups was assessed by Kruskal-Wallis Test. The variables for which the difference will found to be statistically significant ($p< 0.05$) will be entered in a logistic regression analysis to compute the odds ratio with 95% confidence interval.

The data was analysed by the licensed SPSS software.

Ethical issue

Ethical clearance was obtained from the Institute Ethics Committee before the commencement of the study. Informed consent was obtained interviewing the participants, and subjects had the right to withdraw consent any time after inclusion in the study. Participants were explained that non-participation will not affect the treatment/service provided to the individual. All the information regarding the subjects was kept strictly confidential during study. Participants were referred to Department of Psychiatry for treatment of psychiatric comorbidities and were motivated for treatment of substance use disorder. Subjects were provided correct knowledge regarding management at the end of the interview.

Results

RESULTS

A total of 50 patients of COPD who are current smokers and another 50 patients of COPD who are current non-smokers were recruited for the study. Table 1 shows distribution of patients according to their smoking status as per the operational definitions of the current study.

Table 1: Tobacco Smoking Status among current smokers and current non-smokers

Group	Frequency	Percentage (%)
Current Smoker	50	50
Current Non-Smoker	50	50
Former smokers	37	37
Never smokers	13	13
Total	100	100

There were 50 current smokers and 50 current non-smokers. Out of 50 current non-smokers, 37 patients were former smokers and 13 patients were never smokers (Table 1).

Socio-Demographic Variables

Table 2 shows mean age of patients in both the groups. All the patients included in the study were males. The mean age of total sample was 59.97 (SD=10.161). The mean age of current smokers' group was 60.1 years (SD= 10.74) and mean age of the current non-smokers' group was 59.84 (SD= 9.66). There was no statistically significant difference between the age of current smokers' group and current non- smokers' group (t= -0.127, p= 0.89) (Table 2).

Table 2: Age distribution of current smokers and current non-smokers

Variable	Current Smoker (n= 50)	Current Non-Smoker (n=50)	Total (N=100)	Statistic
	Mean (SD)	Mean (SD)	Mean (SD)	
Age	60.10(10.739)	59.84(9.656)	59.97(10.161)	t (98)= -0.127, p= 0.899

The marital status and education of both groups are shown in Table 3. 86% of the current smokers' group (n=43) and 96% of the current non-smokers' group (n=48) were married. The current smokers did not differ from current non-smokers in marital status (p= 0.16). 22% of the patients in current smokers' group (n=11) were illiterate whereas 8% of the patients in the current non- smokers' group (n=4) were illiterate. 16% (n=8) were educated up to primary and middle school, 44% (n=22) were educated up to high school and intermediate, and 18% (n=9) were graduate and above in the current smokers' group. Similarly, 36% (n=18) were educated up to primary and middle school, 34% (n=17) up to high school and intermediate, 22% (n=11) were graduate or above in the current non-smokers' group. This difference in education was statistically significant in the two groups (χ^2=7.954, p<0.05). The post-hoc analysis showed that the primary and middle education was significantly higher in current non-smokers when compared to that of current smokers. The proportion of illiterate was higher in current smokers when compared to current non-smokers.

Table 3: Marital Status and Education in current smokers and current non-smokers

Variable		**Current Smoker (n = 50)**	**Current Non-Smoker (n=50)**	**Total (N=100)**	**Statistic**	
Marital status	Married	43 (86%)	48 (96%)	91	Fisher's Exact Test (p= 0.160)	
	Others	7 (14%)	2 (4%)	9		
Education	Illiterate	11 (22%) Adj. residual= 1.96	4 (8%)	15	Post hoc analysis p=0.049*	χ^2=7.954 (p=0.046)*
	Primary and middle	8 (16%)	18 (36%) Adj. residual value= 2.27	26	p= 0.02*	
	Higher and intermediate	22 (44%)	17 (34%)	39	Z= 1.02, p=0.3	
	Graduate and above	9 (18%)	11 (22%)	20	Z= -0.5, p=0.62	

*significant at p<0.05

The Table 4 shows the area of residence and occupation of the two groups. In the total sample, 34% of the patients (n=34) came from rural area and 66% other patients (n=66) resided in urban area. Among the current smokers' group, 30% of the patients (n=15) hailed from rural area and 70% of the patients (n=35) were residing in urban area. Among the current non-smokers' group, 38% of the patients (n=19) were from rural area and 62% of the patients (n=31) were from urban area. There was no statistically significant difference in residence in the two groups (χ^2=0.713, p= 0.398).

Out of the total sample, 10% patients (n=10) were professional, 65% (n=65) had skilled occupation, 21% (n=21) had unskilled occupation and 4% (n=4) were unemployed. 6% of the current smokers (n=3) were professional by occupation whereas 14% of the current non-smokers (n=7) were professionals. Among the current smokers 66% of patients (n=33) had skilled occupation, 26% (n=13) had unskilled occupation and 2% (n=1) were unemployed. Among the current non-smokers' group, 64% population (n=32) had skilled occupation, 16% (n=8) had unskilled occupation and 6% population (n=3) were unemployed. There was no statistically significant difference in occupation of the two groups (Fisher's exact test value= 3.656, p=0.322) (Table 4).

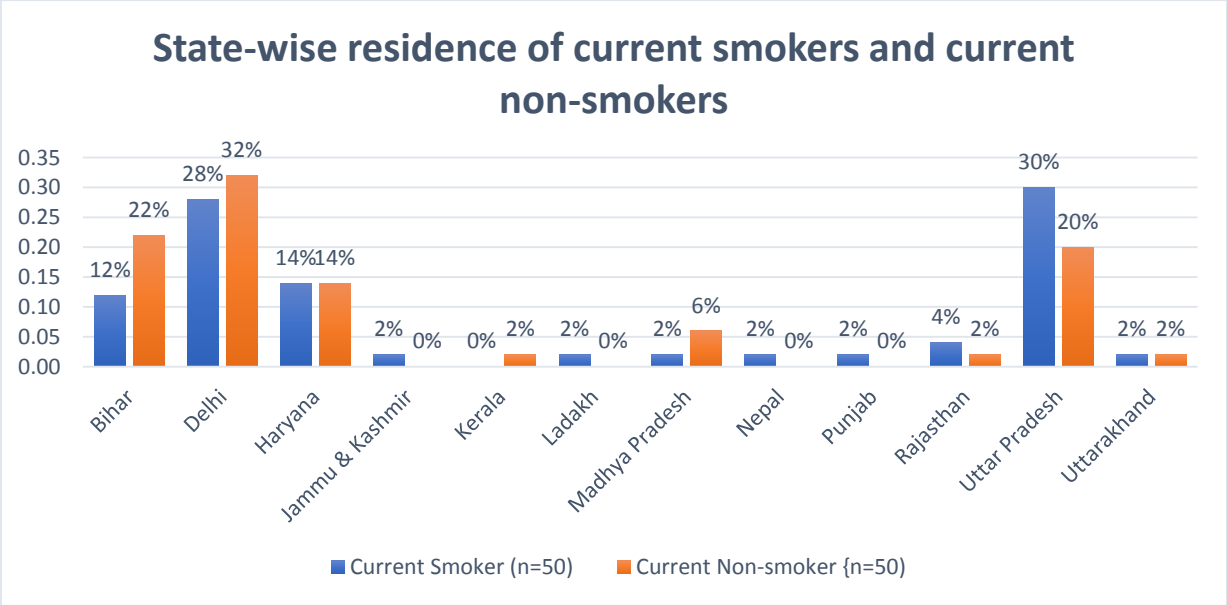
Table 4: Area of residence and Occupation of current smokers and current non-smokers

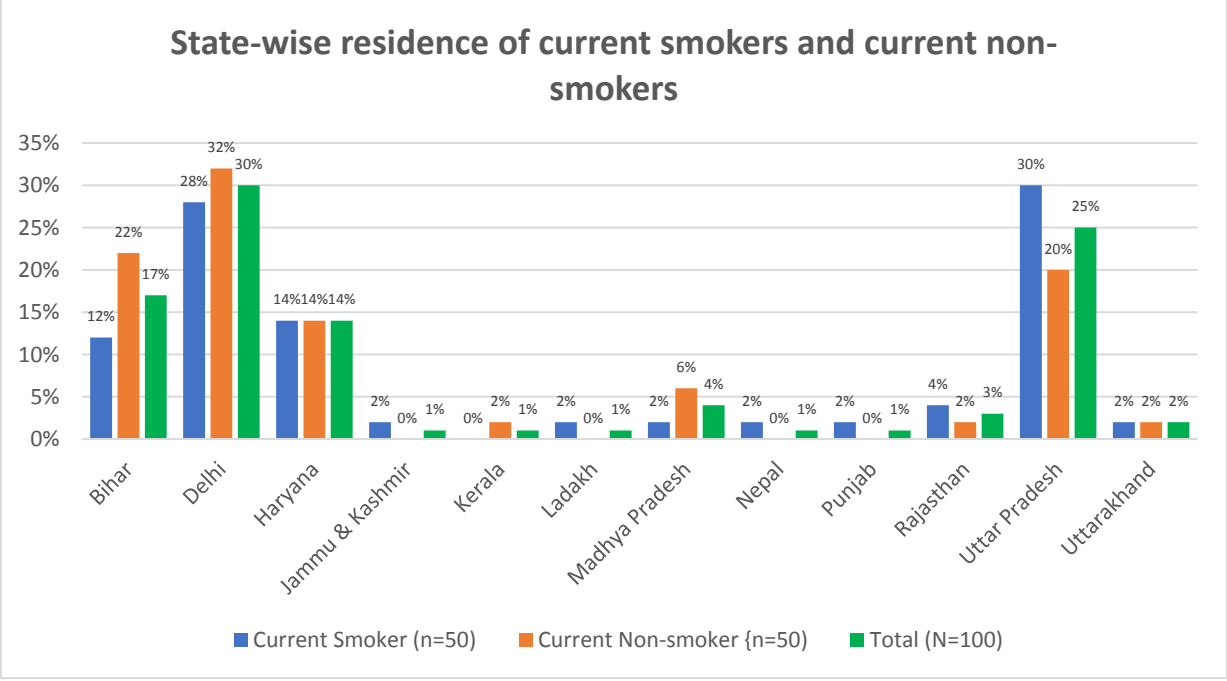
Variable		**Current Smoker (n = 50)**	**Current Non-Smoker (n=50)**	**Total (N=100)**	**Statistic (p value)**
Area of Residence	Rural	15 (30%)	19 (38%)	34	χ^2=0.713 (p= 0.398)
	Urban	35 (70%)	31 (62%)	66	
Occupation	Professional	3 (6%)	7 (14%)	10	Fisher's Exact Test value= 3.656(p=0.322)
	Skilled	33 (66%)	32 (64%)	65	
	Unskilled	13 (26%)	8 (16%)	21	
	Unemployed	1 (2%)	3 (6%)	4	

Figure 1 shows the State-wise residence of current smokers and current non-smokers. 30% of the patients (n=30) among the total sample belonged to Delhi, 25% of the total sample population (n=25) belonged to Uttar Pradesh, 17% and 14% total sample population came from Bihar and Haryana, respectively. 32% of current non-smokers

(n=16) and 28% of current non-smokers (n=28) belonged to Delhi, 20% of current non-smokers (n=10) and 30% of the current non-smokers (n=15) belonged to Uttar Pradesh, 22% of current non-smokers (n=11) and 12% of current smokers (n=6) belonged to Bihar and 14% of each group belonged to Haryana. There was no significant difference between the two groups. Both the groups had higher proportion of patients belonging to Delhi and Uttar Pradesh. One patient from the current smokers' group belong to Nepal, a neighbouring country of India.

Fig 2: State-wise residence of current smokers and current non-smokers





Characteristics of COPD among current smokers and current non-smokers

Table 5 shows duration of COPD symptoms and duration of treatment at OPD of Pulmonary medicine for COPD, in current smokers and current non-smokers. The mean duration of COPD symptoms in the total sample population (n=100) was 4.75 years (SD= 5.38, Median= 3, IQR= 1,6). The mean duration of COPD symptoms in the current smokers' group (n=50) was 3.11 years (SD= 3.64, Median= 2, IQR= 1,4). The mean duration of COPD symptoms in the current non-smokers' group (n=50) was 6.38 years (SD= 6.31, Median= 4.5, IQR= 2,10). There was statistically significant difference between current smokers and current non-smokers (p=0.0004).

The mean duration of treatment of total sample (n=100) for COPD in the OPD of Pulmonary Medicine is 15.5 months (SD=16.64, Median=12, IQR=5,24). Among the current smokers' group (n=50), the mean duration of treatment for COPD at OPD of Pulmonary Medicine was 11.66 months (SD=11.03, Median=6, IQR=4,15) which was lower than the mean duration of treatment for COPD in current non-smokers' group (n=50) which was 19.34 (SD=20.19, Median=12, IQR=6.75,24). This difference was statistically significant (U=869, p=0.008).

Table 5: Duration of symptoms of COPD and duration of treatment in Pulmonary Medicine OPD in current smokers and current non- smokers

Variable	Current Smoker (n=50)	Current Non-Smoker (n=50)	Total (N=100)	Statistic
	Mean (SD) Median (IQR)	Mean (SD) Median (IQR)	Mean (SD) Median (IQR)	
Duration of COPD symptoms (in years)	3.11(3.64) 2(1,4)	6.38(6.31) 4.5(2,10)	4.75(5.38) 3(1,6)	U= 746.5, p= 0.0004***
Duration of treatment (months) at Pulmonary Medicine OPD	11.66 (11.03) 6(4,15)	19.34 (20.19) 12(6.75,24)	15.5(16.64) 12(5,24)	U=869, P=0.008*

*significant at p<0.05

***significant at p<0.001

Table 6 shows severity of COPD according to Global Initiative for Obstructive Lung Disease (GOLD) criteria in current smokers and current non-smokers. The lung function of the patients with COPD is routinely done in OPD of Department of Pulmonary, Critical Care and Sleep Medicine. Based on FEV_1/FVC ratio and FEV_1, the GOLD criteria classify COPD based on the severity of airflow obstruction into mild, moderate, severe, and very severe. Among the total sample (n=100), 31% had mild COPD, 47% had moderate COPD, 19% had severe and 3% had very severe COPD. In current smokers' group, 24% of patients (n=12) had mild COPD, 48% (n=24) had moderate COPD, 26% (n=13) had severe COPD and 2% (n=1) had very severe COPD. Among the current non-smokers' group, 38% (n=19) had mild COPD, 46% (n=23) had moderate COPD, 12% (n=6) had severe COPD and 4% (n=2) had very severe COPD. The current smokers did not differ from current non-smokers in severity of COPD. However, there were more current smokers suffering from severe COPD as compared to current non-smokers [26% (n=13) vs 12% (n=6), Fisher's exact test value= 4.524, p=0.193].

Table 6: Severity of COPD in current smokers and current non-smokers

Variable		**Current Smoker (n=50)**	**Current Non-Smoker (n=50)**	**Total N=100**	**Statistic**
Stage of COPD	Mild	12 (24%)	19 (38%)	31	Fisher's Exact Test value= 4.524, p=0.193
	Moderate	24 (48%)	23 (46%)	47	
	Severe	13 (26%)	6 (12%)	19	
	Very Severe	1 (2%)	2 (4%)	3	

Characteristics of Smoking status in current smokers and current non-smokers (former smokers)

Table 7 shows the type of smoking preferred by the current smokers and current non-smokers (former smokers). The current non-smokers' group consisted of 37 former smokers who were compared with the current smokers' group for characteristic of smoking status. Out of the total sample who were current or past smokers (n=87), 23% of the patients (n=20) smoked cigarettes and 77% (n=67) smoked bidi and other forms of smoking tobacco. 32% of the patients of current smokers' group (n=16) smoked

cigarettes as compared to only 10.8% (n=4) of current non-smokers' group. 68% of the current smokers' group (n=34) and 89.2% of the current non-smokers' group (n=33) smoked bidi or any other forms of smoking tobacco. The current smokers had significantly higher proportion of patients (32%) with history of cigarette smoking as compared to current non-smokers (10.8%) with past history of cigarette smoking (p=0.023).

Table 7: Type of smoking in current smokers and current non-smokers (former smokers)

Variable		**Current Smokers (n= 50)**	**Current Non-smokers (Former Smokers) (n=37)**	**Total (N=87)**	**Statistic**
Type of Smoking	Cigarette	16 (32%)	4 (10.8%)	20 (23%)	Fisher's Exact Test, p= 0.023*
	Bidi and others	34 (68%)	33 (89.2%)	67 (77%)	

*significant at p<0.05

Table 8 shows the duration and dose of smoking in current smokers and current non-smokers (former smokers). In the total sample (n=87), mean age of onset of smoking was 21.83 years (SD=6.92, Median=20, IQR=18, 25). Mean age of smoking in the current smoker group was 21.4 years (SD=7.26, Median=20, IQR=16.75, 25) whereas the mean age of smoking in the former smokers was 22.41 (SD=6.49, Median=20, IQR=19.5, 25). There was no difference between the two groups in mean age of onset of tobacco smoking (U=778.5, p=0.2).

In the total sample (n=87), the mean duration of smoking was 33.84 years (SD=12.75). The mean duration of smoking in the current smokers' group was 38.88 years (SD=11.3) whereas the mean duration of smoking in former smoker was 27.03 years (SD=11.47). The mean duration of smoking in the current smokers was significantly higher than the mean duration of smoking in current non-smokers (former smokers) (t=-4.81, p<0.001).

In the total sample (n=87), the mean maximum number of bidis/ cigarettes smoked per day was 16.02 (SD=14.95, Median=12, IQR=6, 20). The mean maximum number of

cigarettes or bidis smoked per day in the current smokers' group was 17.88 (SD=13.27, Median=15, IQR=9.5, 22.5). The mean maximum number of bidis or cigarettes smoked per day in the current non-smokers' (former smoker) group was 13.51 (SD=16.82, Median=6, IQR=5, 15). The mean maximum number of cigarette/ bidis smoked per day was statistically significantly higher in current smokers than current non-smokers (former smokers) (U=618.5, p=0.008).

The mean total number of abstinences attempts in total sample (n=87) was 1.83 (SD=1.56, Median=1, IQR= 1, 3). The mean total number of abstinences attempts in the current smokers group was 1.92 (SD=1.72, Median=1.5, IQR=0.75, 3) and the mean total number of abstinences attempts in current non-smokers' group was 1.83 (SD=1.56, Median=1, IQR=1, 3). There was no statistically significant difference in the mean total number of abstinences attempts between the two groups (U=895.5, p=0.795).

Table 8: Duration and dose of tobacco smoking in current smokers and current non-smokers (former smokers)

Variable	**Current Smoker (n=50)**	**Former Smoker (n=37)**	**Total (N=87)**	**Statistic**
	Mean (SD) Median (IQR)	**Mean (SD) Median (IQR)**	**Mean (SD) Median (IQR)**	
Age of onset of smoking (in years)	21.4 (7.26) 20 (16.75, 25)	22.41 (6.49) 20 (19.5, 25)	21.83 (6.92) 20 (18, 25)	U= 778.5, p=0.2
Duration of use (in years)	38.88 (11.3)	27.03 (11.47)	33.84 (12.75)	t= -4.805 (p<0.001)***
Maximum Dose (No. of cigarette/bidi per day)	17.88 (13.27) 15 (9.5, 22.5)	13.51 (16.82) 6 (5, 15)	16.02 (14.95) 12 (6, 20)	U= 618.5, p=0.008*
Total Abstinence attempts	1.92 (1.72) 1.5 (0.75,3)	1.7 (1.31) 1 (1,2)	1.83 (1.56) 1 (1,3)	U=895.5, p=0.795

*significant at p<0.05

***significant at p<0.001

The current smokers were assessed for nicotine dependence with FTND scale. The mean FTND score of current smokers was 3.94 (2.38).

Smokeless Tobacco use in current smokers and current non-smokers

Table 9 shows smokeless tobacco use in current smokers and current non-smokers. 20% of the total sample population (n=100) consumed tobacco in smokeless form. 24% of the current smokers' group (n=12) and 16% of the current non-smokers' group (n=8) used smokeless tobacco. The current smokers did not differ from current non-smokers in smokeless tobacco use (p=0.454).

Table 9: Smokeless Tobacco use in current smokers and current non-smokers

Variable		**Current Smoker (n = 50)**	**Current Non-Smoker (n=50)**	**Total (N=100)**	**Statistic**
Smokeless Tobacco Use	Yes	12 (24%)	8 (16%)	20	Fisher's Exact Test (p= 0.454)
	No	38 (76%)	42 (84%)	80	

All the subjects were assessed for tobacco use (both smoking form and smokeless form) in last one-year duration using MINI with Tobacco Use Disorder Module 7.0.2. Out of 50 current smokers, 43 patients (86%) screened positive for Tobacco Use Disorder in past 12 months. 10 out of 50 current non-smokers (20%) also screened positive for Tobacco Use Disorder in past 12 months.

Characteristics of Alcohol use in current smokers and current non-smokers

Table 10 shows the alcohol use in past 1 year in current smokers and current non-smokers. Out of the total sample (n=100), 20% of the patients (n=20) had consumed alcohol in past one year. 26% of the current smokers' group (n=13) and 14% of the current non-smokers' group (n=7) had consumed alcohol in past one year. There was no difference between the two groups (χ^2=2.25, p=0.134).

Table 10: Alcohol use in past 1 year in current smokers and current non- smokers

Variable		Current Smoker		Current Non-Smoker		Total	Statistic
		n = 50	%	n=50	%	N=100	
Alcohol Use in Last 1 year	Yes	13	26	7	14	20	χ^2=2.25, p=0.134
	No	37	74	43	86	80	

Table 11 shows the AUDIT scores of the patients who consumed alcohol in past 1 year among current smokers and current non-smokers (n=50). 6% (n=6) of them had AUDIT score >8. AUDIT score >8 indicated harmful or dependent use of alcohol in past one year. 12% of the current smokers' group (n=6) had AUDIT score >8 and none of the patients in current non-smokers' group had AUDIT score >8. 14% of the current smokers' group and 14% of the current non-smokers' group had AUDIT score <8. 74% of the current smoker and 86% of the current non-smoker did not use alcohol. There was statistically significant difference in AUDIT scores of the two groups (p=0.04) and there was a trend towards higher harmful or dependent use of alcohol in current smoker as compared to current non-smoker with COPD.

Table 11:AUDIT Scores in current smokers and current non-smokers

Variable		Current Smoker		Current Non-Smoker		Total	Statistic
		N=50	%	n=50	%	N=100	
AUDIT Grade	No harmful use (<8)	7	14	7	14	14	Fisher's Exact Test value= 6.556, p=0.040*
	Harmful/ Dependent use (>8)	6	12	0	0	6	
	No alcohol use	37	74	43	86	80	

Medical Comorbidities in current smokers and current non-smokers

Table 12 represents the medical comorbidities in current smokers and current non-smokers. 40% of the total sample (n=40) had medical comorbidities. 50% of the current smoker group (n=25) and 30% of the current non-smoker (n=15) had medical comorbidities. A significantly higher proportion of current smokers had been diagnosed with medical comorbidities when compared to the current non-smokers (p=0.041).

Table 12: Medical comorbidities in current smokers and current non-smokers

Variable		Current Smoker		Current Non-Smoker		Total	Statistic
		n= 50	%	n=50	%	N=100	
Medical Co-morbidities	Yes	25	50	15	30	40	χ^2=4.166 (p=0.041)*
	No	25	50	35	70	60	

*significant at p<0.05

Psychiatric comorbidities in current smokers and current non-smokers

Table 13 shows lifetime prevalence of psychiatric comorbidities in current smokers and current non-smokers. All the patients were first screened and assessed for psychiatric illness using MINI with Tobacco Use Disorder Module 7.0.2. Psychiatric diagnoses were generated using diagnostic criteria from International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD 10).

42% of the current smokers' group (n= 21) and 24% of the current non-smokers' group (n=12) had suffered from depressive disorder in their lifetime. There was no statistically significant difference between two groups (χ^2=3.664, p=0.056). But results showed a trend for higher proportion of lifetime depressive disorder in current smokers as compared to current non-smokers with COPD.

12% of the current smokers' group (n=6) had suffered from panic disorder whereas none of the patients from the current non-smokers' group ever had panic disorder. There was statistically significant difference in proportion of panic disorder in the two groups (χ^2=6.383, p=0.012). 5% of the total sample had agoraphobia (n=5). 6% of the current smoker group (n=3) and 4% of the current non-smoker (n=2) had agoraphobia. There was no statistically significant difference in proportion of agoraphobia between two

groups (χ^2=0.211, p=0.65). 2% of the current non-smoker group (n=1) had social anxiety disorder. There was no statistically significant difference in the proportion of social anxiety disorder between the two groups (χ^2=1.01, p=0.315). 6% of the current smoker group (n=3) have suffered from generalized anxiety disorder (GAD) in their lifetime whereas none of the current non-smoker ever suffered from GAD. There was no statistically significant difference in the proportion of GAD between the two groups (χ^2=3.093, p=0.079). 7% of the total sample (n=7) had alcohol use disorder (DSM-V). 12% of the current smoker group (n=6) and 2% of the current non-smoker group (n=1) had alcohol use disorder. There was statistically no significant difference in the proportion of alcohol use disorder between the two groups (χ^2=3.84, p=0.05).

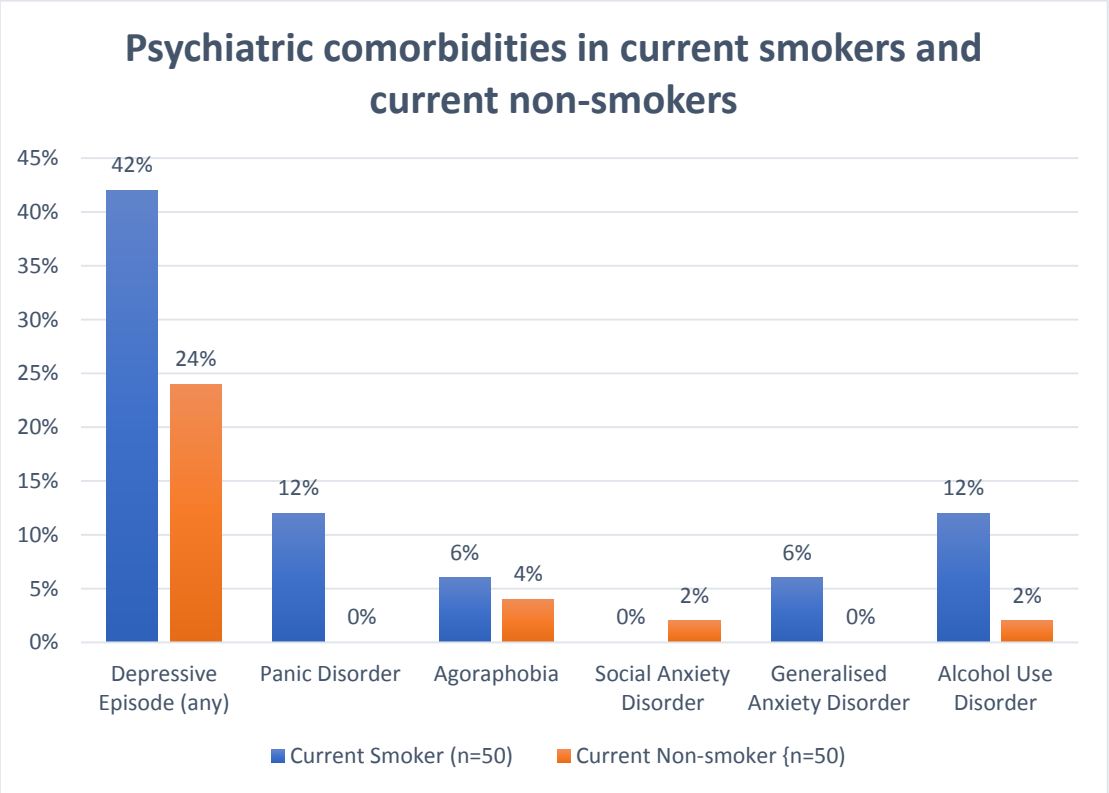
Table 13: Psychiatric comorbidities in current smokers and current non-smokers

Variable		**Current Smokers**		**Current Non-Smokers**		**Total**	**Statistic**	
		n=50	**%**	**n= 50**	**%**	**N=100**	**χ^2**	**P**
Depressive Disorder (Any)[@]	Yes	21	42	12	24	33	3.664	0.056
	No	29	58	38	76	67		
Panic Disorder	Yes	6	12	0	0	6	6.383	0.012*
	No	44	88	0	0	94		
Agoraphobia	Yes	3	6	2	4	5	0.211	0.646
	No	47	94	48	96	95		
Social Anxiety Disorder	Yes	0	0	1	2	1	1.01	0.315
	No	50	100	49	98	99		
Generalised Anxiety Disorder	Yes	3	6	0	0	3	3.093	0.079
	No	47	94	50	100	97		
Alcohol Use Disorder	Yes	6	12	1	2	7	3.84	0.05
	No	44	88	49	98	93		

*significant at p<0.05

[@]Any Depressive Disorder includes current, recurrent or any depressive episode in past

Fig. 3: Psychiatric comorbidities in current smokers and current non-smokers



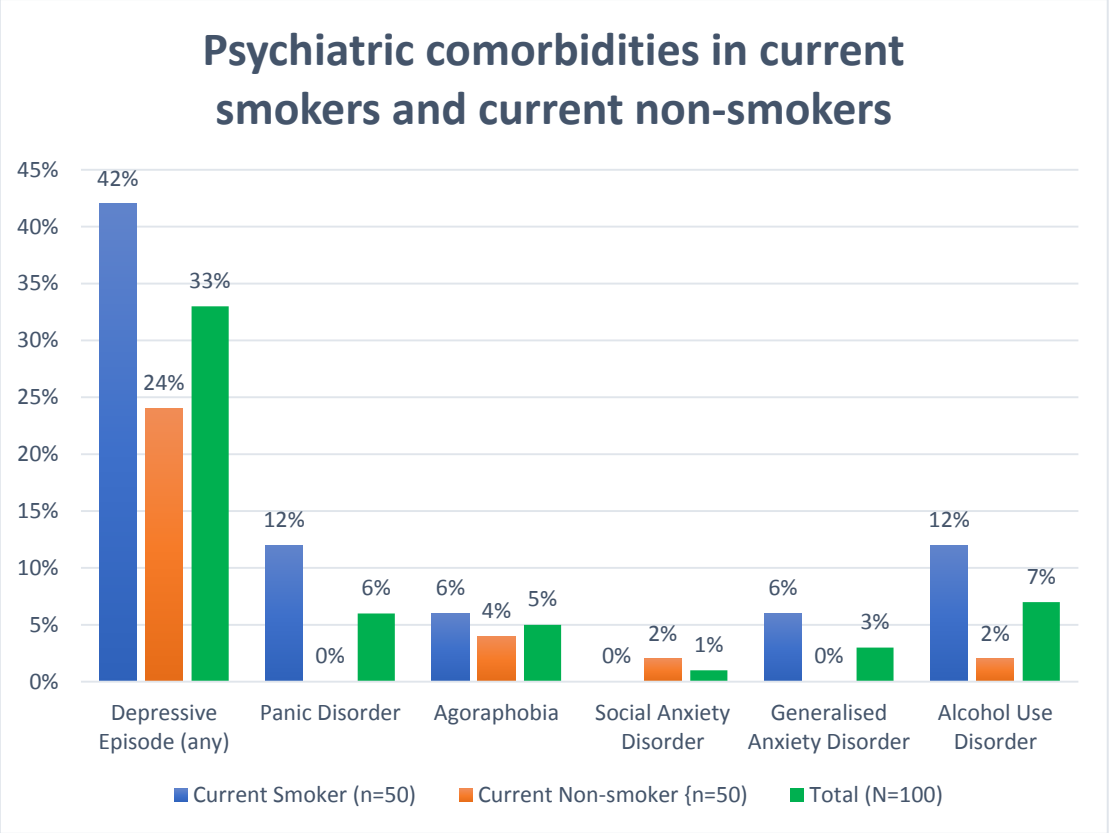


Table 14 represents Psychiatric Illnesses both Lifetime and current, including alcohol use disorder (excluding TUD) in current smokers and current non-smokers. Among the total sample (n=100), 45% of the population suffered from a psychiatric illness during their lifetime. 56% of the current smoker group (n=28) and 34% of the current non-smoker group (n=17) have suffered from a psychiatric illness in their lifetime. There was statistically significant difference in the proportion of lifetime psychiatric illness between the two groups (χ^2= 4.89, p=0.027). In the total sample (n=100), 35% of them were suffering from a current psychiatric illness. 50% of the current smoker group (n=25) and 20% of the current non-smoker group (n=10) were suffering from current psychiatric illnesses. This difference was statistically significant between the two groups (χ^2= 9.89, p= 0.002).

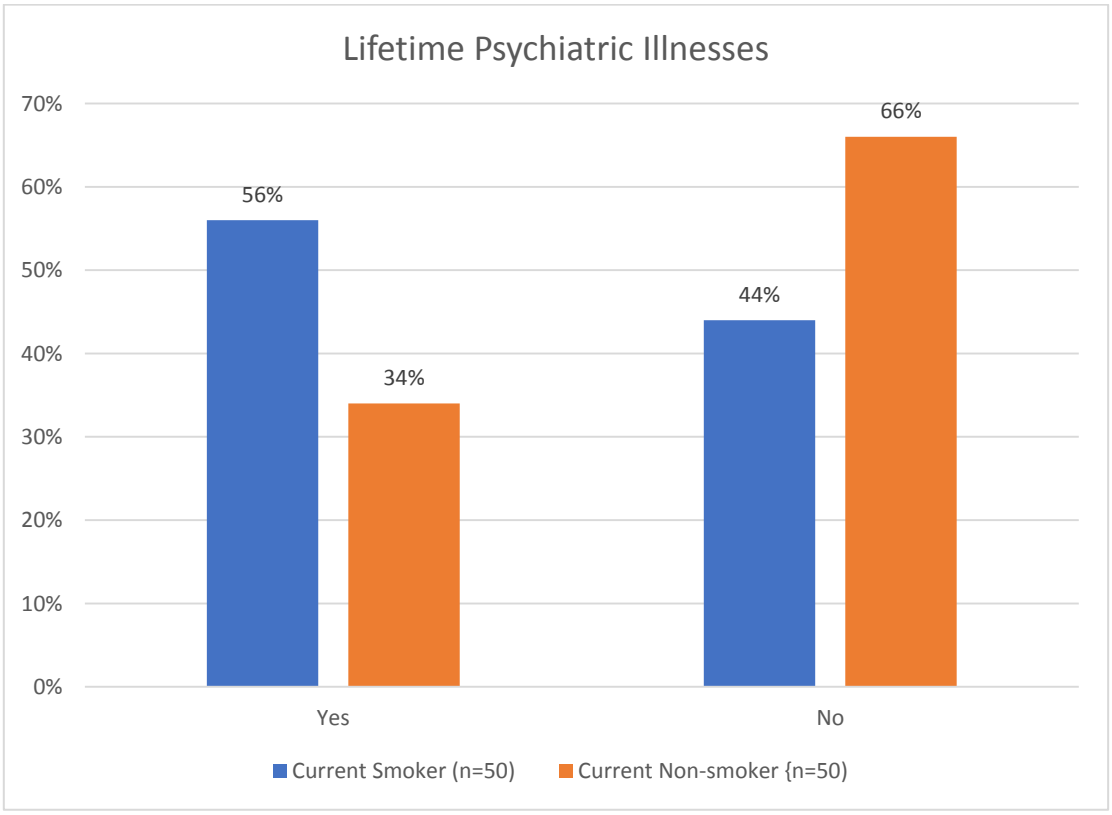
Table 14: Psychiatric Illnesses- lifetime and current (excluding TUD) in current smokers and current non-smokers

Variable		**Current Smoker**		**Current Non-Smoker**		**Total**	**Statistic**
		n= 50	%	n=50	%	N=100	
Lifetime Psychiatric Illnesses (Excluding TUD)	Yes	28	56	17	34	45	χ^2= 4.89, p= 0.027*
	No	22	44	33	66	55	
Current Psychiatric Illnesses (Excluding TUD)	Yes	25	50	10	20	35	χ^2=9.89, p=0.002**
	No	25	50	40	80	65	

*significant at p<0.05

**significant at p<0.005

Fig. 4: Lifetime Psychiatric illnesses in current smokers and current non-smokers



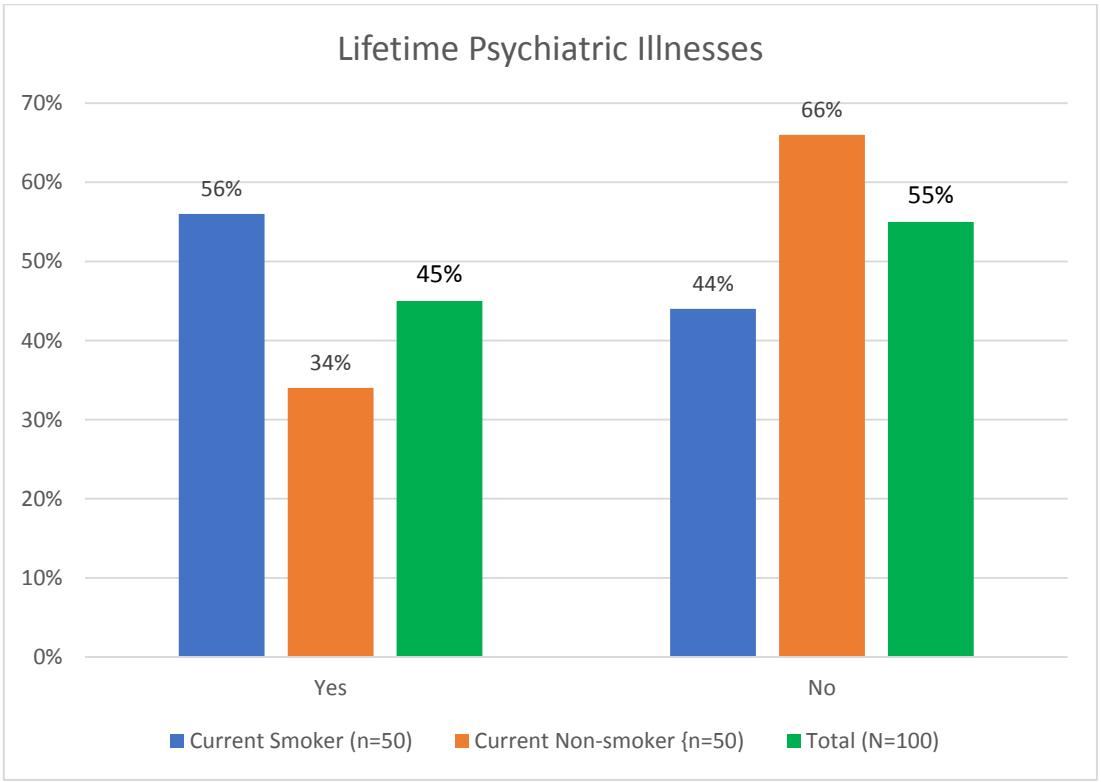
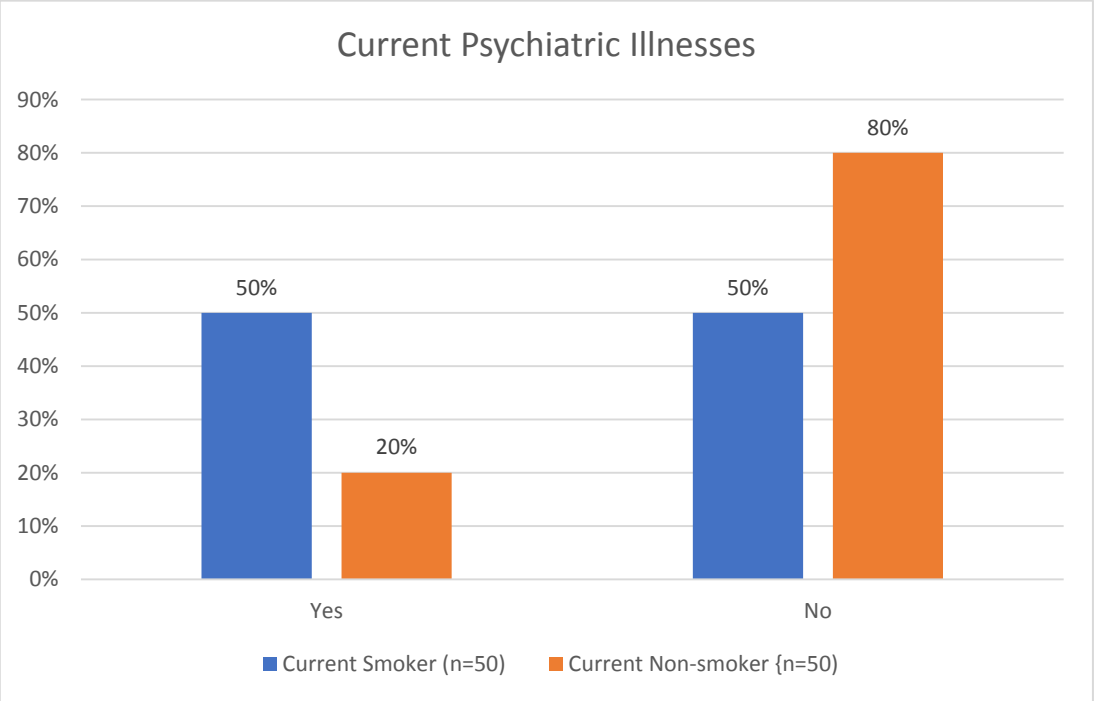


Fig. 5: Current psychiatric illness in current smokers and current non-smokers



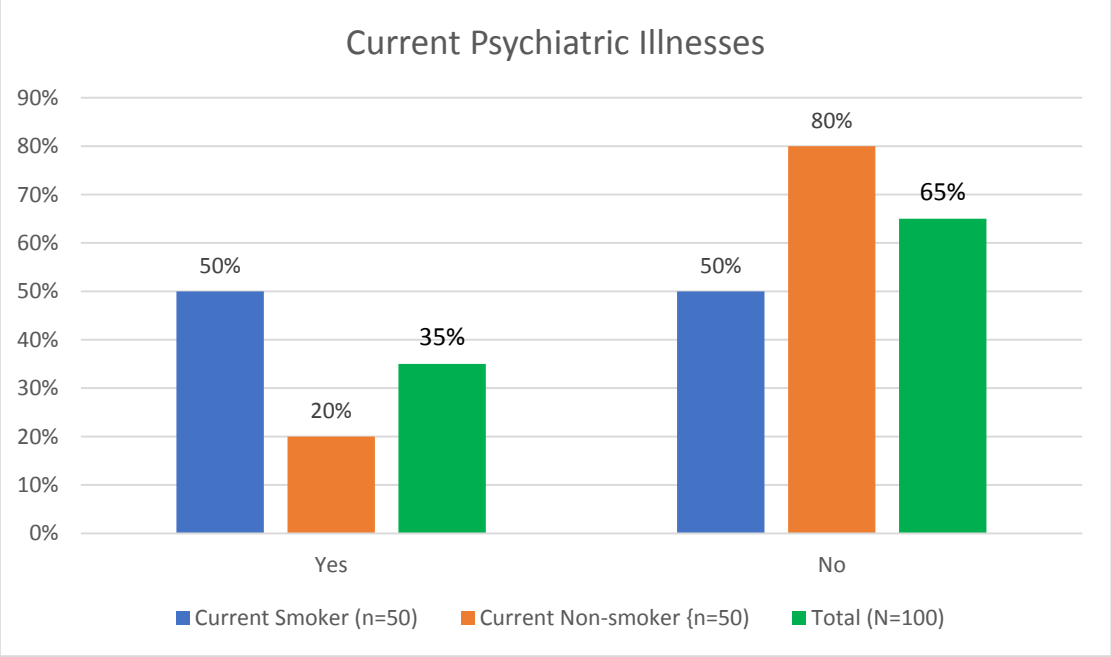


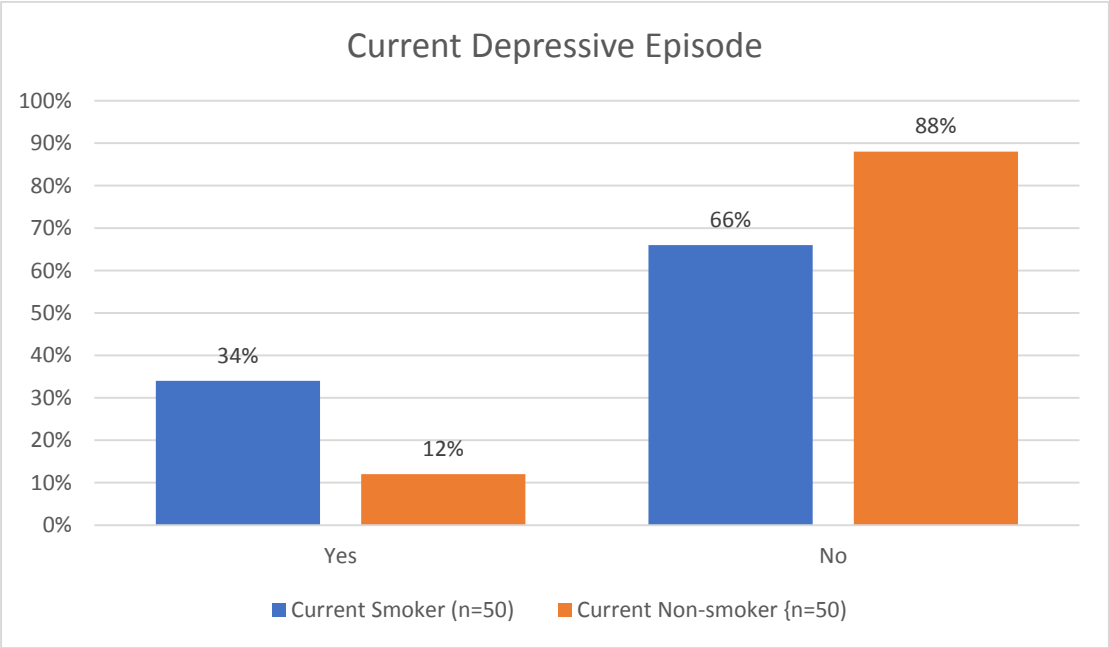
Table 15 shows current depressive episode (for recurrent depressive disorder or for single episode) in current smokers and current non-smokers. Out of the total sample (n=100), 23% of the patients (n=23) were suffering from current depressive episode. 34% of current smokers (n=17) had current depressive episode in comparison to 12% of current non-smokers (n=6) which was a significantly higher proportion (χ^2= 6.83, p=0.009)

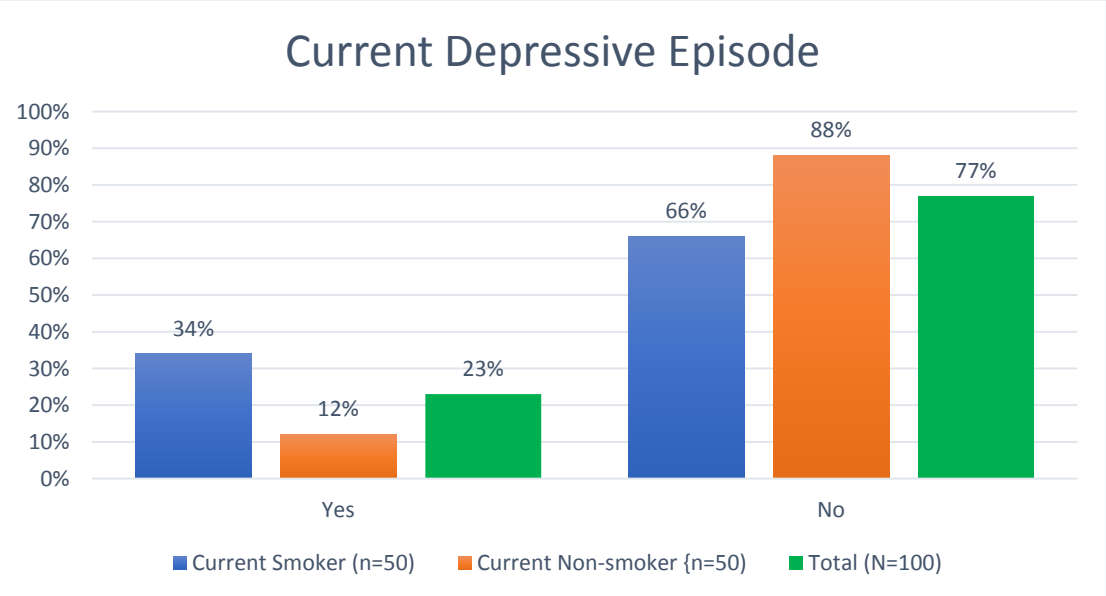
Table 15: Current depressive episode in current smokers and current non-smokers

Variable		Current Smokers		Current Non-Smokers		Total	Statistic
		n= 50	%	n=50	%	N=100	
Current Depressive Episode	Yes	17	34	6	12	23	χ^2= 6.83 (p=0.009)*
	No	33	66	44	88	77	

*significant at p<0.05

Fig. 6: Current depressive episode in current smokers and current non-smokers





Among the total sample (n=100), 19% of the patients had current single depressive episode, 10% had a past history of depressive disorder and 4% had recurrent depressive disorder. The current smokers' group had 42% of the population (n=21) suffering from any type of depressive disorder. 26% of the current smokers' group (n=130 had current single depressive episode, 8% of them (n=4) had past history of depressive disorder and 8% of them (n=4) were suffering from a recurrent depressive disorder. The current non-smokers' group had 24% of the patients (n=12) suffering from any type of depressive disorder. Among the current non-smokers' group, 12% of the patients (n=6) were suffering from current single depressive episode and 12% of the patients (n=6) had suffered from a past history of depressive disorder.

Table 17 shows Patient Health Questionnaire-9 (PHQ-9) scores and Airway Inventory for Respiratory Diseases (AIR) scores in current smokers and current non-smokers. The mean PHQ-9 score of the total sample (n=100) was 3.44 (SD=4, Median= 2, IQR=0,5) and mean AIR score was 3.27 (SD=3.96, Median=2, IQR=0,6). In the current smokers' group, the mean PHQ-9 score was 4.7 (SD=4.8, Median=3.5, IQR=0,8) and whereas mean PHQ-9 score of the current non-smokers' group was 2.18 (SD=2.66, Median=1, IQR=0,4). There was statistically significant difference in the mean PHQ-9 scores of the two groups (U=-2.58, p=0.01). In the current smokers' group, the mean AIR score was 4.9 (SD=4.55, Median=4.5, IQR=0,8) and whereas mean AIR score of the current non-smokers' group was 1.6 (SD=2.34, Median=0, IQR=0,3). There was statistically significant difference in the mean AIR scores of the two groups (U=-3.86, p=0.001).

Table 17: Mean PHQ-9 and AIR scores in current smokers and current non-smokers

Variable	**Current Smoker (n=50)**	**Current Non-Smoker (n=50)**	**Total (N=100)**	**Statistic**	
	Mean(SD) Median(IQR)	Mean(SD) Median(IQR)	Mean(SD) Median(IQR)	Mann-Whitney U Test	
PHQ-9 Score	4.7 (4.76) 3.5(0, 8)	2.18 (2.66) 1 (0, 4)	3.44 (4.04) 2 (0, 5)	-2.58	0.01*
AIR Score	4.9 (4.55) 4.5 (0, 8)	1.6 (2.34) 0 (0, 3)	3.27 (3.96) 2 (0, 6)	-3.86	<0.001***

*significant at p<0.05
***significant at p<0.001

Table 19 shows AIR scores with cut-off score of 8 in current smokers and current non-smokers. Out of the total sample (n=100), 19% (n=19) had AIR score of >8. 34% of the current smokers' group (n=17) and 4% of the current non-smokers' group (n=2) had AIR score of more than 8. This difference between the two groups was statistically significant (p<0.001).

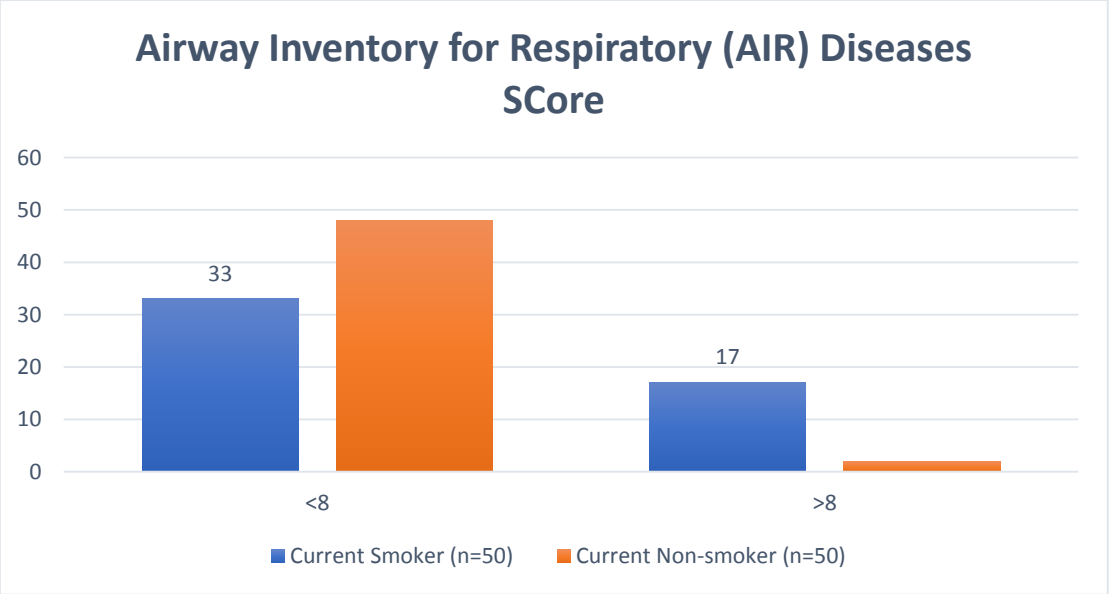
Table 19: AIR scores with cut-off ≥8 in current smokers and current non-smokers

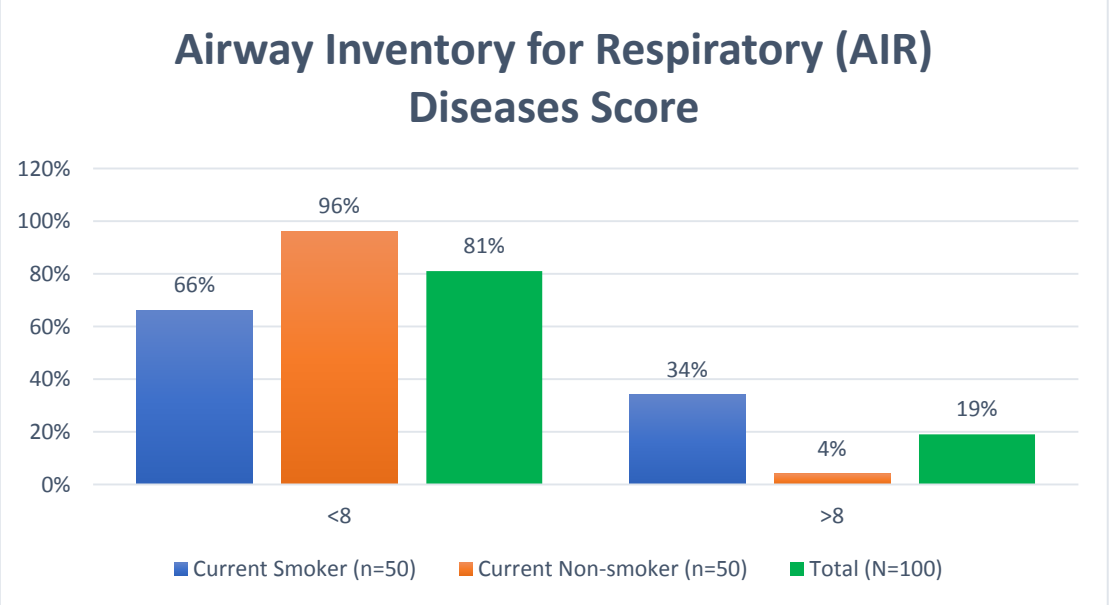
Variable		Current Smoker		Current Non-Smoker		Total	Statistic
		n= 50	%	n=50	%	N=100	
AIR Score	<8	33	66	48	96	81	Fisher's Exact Test (p<0.001)***
	>8	17	34	2	4	19	

***significant at p<0.001

>8 means clinically significant anxiety symptoms

Fig. 8: AIR scores with cut-off ≥8 in current smokers and current non-smokers





Correlation between FTND Scores and PHQ-9 & AIR Scores of Current smokers

The relationships between FTND scores and PHQ-9 scores and FTND scores and AIR scores were analysed with Spearman's rank correlation (Table 20). There was no significant correlation between FTND scores and PHQ scores of current smokers (ρ= 0.222, p=0.122) or between FTND scores and AIR scores of current smokers (ρ= 0.063, p=0.664). So, there was no correlation between the severity of nicotine dependence and severity of depression and anxiety in current smoker COPD patients.

Table 20: Relation of FTND score with severity of depression (PHQ-9) and anxiety (AIR score) among current smokers with COPD

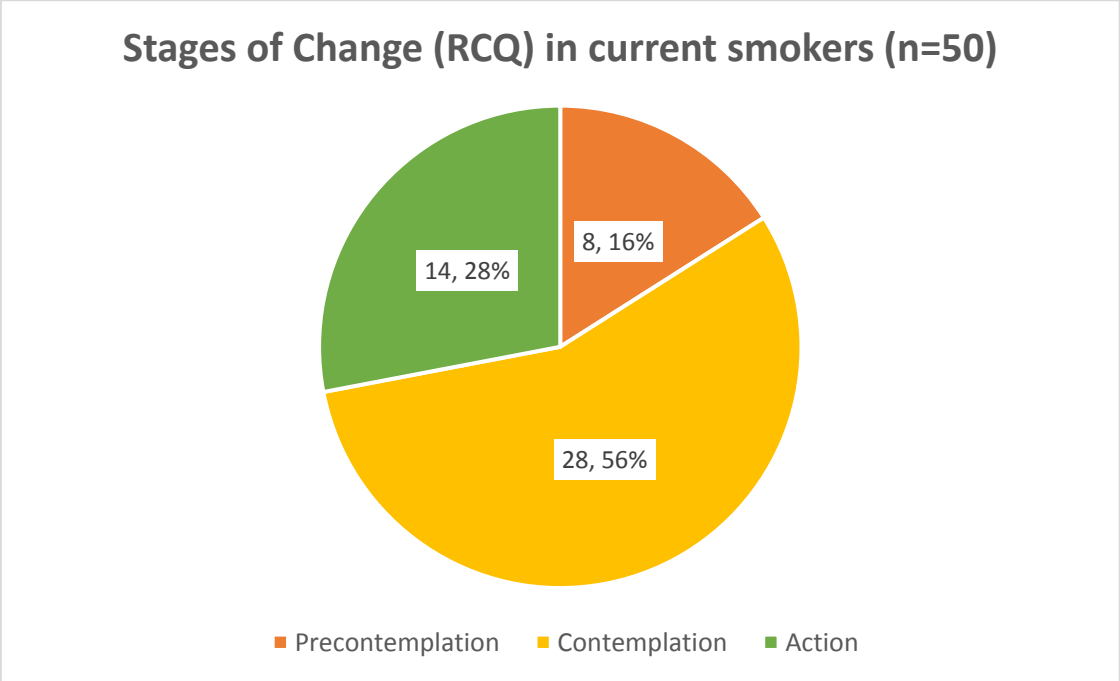
	PHQ-9 score (N=50)	**AIR score (N=50)**
FTND Score	Spearman correlation coefficient, ρ= 0.222	Spearman correlation coefficient, ρ= 0.063
p value	p=0.122	p=0.664

There was significant correlation between AIR scores and PHQ-9 scores of current smokers (ρ=0.597, p<0.001).

Stages of Change in Current Smokers

The current smokers were assessed for the stage of change of change in context of the tobacco use using Readiness to Change questionnaire (Figure 2). More than half (56%) of the current smokers were in contemplation stage as per the RCQ questionnaire scores. 16% of the current smoker group (n=8) were in precontemplation stage and 28% (n=14) were in action stage.

Fig. 9: Stages of Changes as per the RCQ scores in Current smokers



Regression analysis:

The table 21 summarizes the result of binary logistic regression by considering the dependent variables as current smokers with COPD and independent predictors as education status, duration of COPD symptoms, presence of medical co morbidities, presence of lifetime psychiatric diagnoses, current depressive episode, PHQ-9 scores and AIR scores. After multivariable regression analysis (MV[a]), only two variables remained significant.

The multivariable regression analysis revealed that increase in one unit of AIR score in patient with COPD has 24% greater likelihood for being continued smokers. The increase of duration of COPD symptoms by one year (one unit) in patients with COPD has 16 % lesser likelihood for being continued smoker.

Unadjusted odds were calculated first for each of the independent variable. A single adjusted regression model was performed was run with smoking status as dependent variable and sociodemographic variables and medical comorbidity and psychiatric illness related variables as independent variables. The smoking status related variable could not be included for the regression analysis as it would miss the never smoker population of our study.

For educational status, illiterate variable was kept as reference. For primary and middle education, the unadjusted regression coefficient B was -1.82, OR=0.16 (95% CI: 0.04-0.66, p=0.01) and adjusted regression coefficient B was -0.705, aOR=0.5 (95% CI: 0.09-

2.697, p=0.416). For high School, the unadjusted regression coefficient was B=-0.75, OR=0.47 (95% CI: 0.13-1.74, p=0.26) and adjusted regression coefficient B=0.37, aOR=1.45 (95% CI=0.29-7.2, p=0.65). For graduate and above, the unadjusted regression coefficient B=-1.2, OR=0.1 (95% CI: 0.07-1.26, p=0.1) and adjusted regression coefficient B=0.06, aOR=1.06 (95% CI: 0.19-6.099, p=0.945).The unadjusted odds for primary and middle education was statistically significant but when adjusted with the regression model the adjusted odds were not statistically significant.

The unadjusted odds of the duration of COPD symptoms was statistically significant with B=-0.156, OR=0.86 (95% CI: 0.76-0.96, p=0.006). The odds remained statistically significant in the adjusted regression model with B=-0.18, aOR=0.834 (95% CI: 0.736-0.95, p=0.007).

For the presence of medical comorbidity, the unadjusted regression coefficient was B= 0.85, OR=2.3 (95% CI: 0.19-0.97, p=0.04). This finding was statistically significant. When adjusted regression model was performed, the findings were not statistically significant with B=0.638, aOR=0.23 (95% CI: 0.68-5.3, p=0.23).

On calculating unadjusted odds for lifetime psychiatric illness, the regression coefficient was B=0.9, OR=2.5 (95% CI: 1.1-5.5, p=0.03). This finding was statistically significant. The adjusted odds were not significant with B=-0.58, aOR=0.56 (95% CI: 0.09-3.45, p=0.53).

For current psychiatric illnesses, the unadjusted regression coefficient was B= 1.39, OR=4 (95% CI: 1.65-9.7, p=0.002). This finding was statistically significant. In the adjusted regression model, the odds for current psychiatric illness were not statistically significant with B=0.22, aOR=1.25 (95% CI: 0.14-11.49, p=0.85).

The unadjusted regression coefficient for current depressive episode was B=1.33, OR=3.78 (95% CI: 1.34-10.63, p=0.012) which was statistically significant. The adjusted regression coefficient was B=0.81, aOR=2.25 (95% CI: 0.22-22.62, p=0.49) which was not statistically significant.

On calculating unadjusted odds for PHQ-9 scores, the regression coefficient B=0.178, OR=1.2 (95% CI: 1.1-1.34, p=0.003) was statistically significant. The adjusted odds were B=0.08, aOR=1.09 (95% CI: 0.84-1.4, p=0.52). This finding was at the margin of statistical significance.

On calculating the unadjusted odds for AIR score, the regression coefficient B=0.26, OR=1.3 (95% CI: 1.14-1.5, p<0.001) which was statistically significant. When adjusted

regression model was performed, regression coefficient was B=0.22, aOR=1.24 (95% CI: 1.03-1.5, p=0.023). The adjusted OR for AIR score was statistically significant.

Table 21: Regression analysis- Univariate and Multivariate analyses

Variable		Current smoker (n=50)	Current non-smoker (n=50)	Logistic Regression				
				-	B	OR/ aOR	95% CI	p value
Educational Status	**Illiterate**	11 (22%)	4 (8%)	UV	-	-	-	-
				MV[a]	-	-	-	-
	Primary and Middle	8 (16%)	18 (36%)	UV	-1.82	**0.16**	0.04-0.66	**0.01***
				MV[a]	-0.705	0.5	0.091-2.697	0.416
	High School	22 (44%)	17 (34%)	UV	-0.75	0.47	0.13-1.74	0.26
				MV[a]	0.371	1.45	0.29-7.2	0.65
	Graduate and above	9 (18%)	11 (22%)	UV	-1.2	0.1	0.07-1.26	0.1
				MV[a]	0.061	1.06	0.19-6.099	0.945
Duration of COPD symptoms	**Mean**	3.11(3.64)	6.38(6.31)	UV	-0.156	**0.86**	0.76-0.96	**0.006***
				MV[a]	-0.18	**0.834**	0.736-0.945	**0.005***
Presence of Medical Comorbidity		25 (50%)	15 (30%)	UV	0.85	**2.3**	0.19-0.97	**0.04***
				MV[a]	0.66	1.93	0.695-5.391	0.206
Presence of Lifetime psychiatric illness		28 (56%)	17 (34%)	UV	0.9	**2.5**	1.1-5.5	**0.03***
				MV[a]	-0.266	0.766	0.203-2.897	0.695
Presence of Current psychiatric illness				UV	1.386	**4**	1.65-9.7	**0.002****
Current Depressive Episode		17 (34%)	6 (12%)	UV	1.33	**3.78**	1.34-10.63	**0.012***
				MV[a]	0.739	2.09	0.341-12.846	0.424
PHQ-9 Score		4.7 (4.76)	2.18 (2.66)	UV	0.178	**1.20**	1.1-1.34	**0.003****
				MV[a]	0.069	1.071	0.84-1.4	0.588
AIR Score		4.9 (4.55)	1.6 (2.34)	UV	0.26	**1.30**	1.14-1.5	**<0.001*****
				MV[a]	0.22	**1.24**	1.03-1.5	**0.023***
AIR Score of >8		17 (34%)	2 (4%)	UV	2.52	**12.36**	2.68-57.14	**0.001****

*significant at p<0.05
**significant at p<0.005
***significant at p<0.001

Regression Analysis for smoking related variable:

The table 22 summarizes the result of binary logistic regression by considering the dependent variables as current smokers with COPD and independent predictors as type of smoking, duration of smoking and maximum dose of cigarette/bidi per day. Multivariable analysis (MV^b) was done with these smoking- related variables with total sample as current smokers (n=50) and former smoker (n=37).

The unadjusted regression coefficient for the type of smoking was B=1.36, OR=3.89 (95% CI: 1.17-12.8, p=0.03) which was statistically significant. When adjusted regression model was performed, regression coefficient was B=2.205, aOR=9.075 (95% CI: 2.01-10.94, p=0.004). This result was statistically significant (p=0.004).

The duration of smoking had B=0.089, OR=1.09 (95% CI: 1.05-1.1, p<0.001) which was statistically significant. In multivariable analysis, regression coefficient was B=0.103, aOR=1.108 (95% CI: 1.05-1.167, p<0.001), which was statistically significant.

For maximum dose of cigarette/bidi per day, the regression coefficient B=0.022, OR=1.022 (95% CI:0.99-1.06, p=0.186). In multivariable analysis, the regression coefficient was B=0.013, aOR=1.108 (95% CI: 1.05-1.167, p=0.076).

Table 22: Unadjusted Regression Analysis of smoking-related variables

Variable		**Current smoker (n=50)**	**Current non-smoker (n=37)**	**Logistic Regression**				
				-	**B**	**OR/aOR**	**95% CI**	**P value**
Type of Smoking	**Bidi and others**	34 (68%)	33 (89.2%)	UV	1.36	**3.89**	1.17-12.8	**0.03***
	Cigarette	16 (32%)	4 (10.8%)	MV^b	2.205	**9.075**	2.01-10.94	**0.004****
Duration of Tobacco Smoking		38.88 (11.3)	27.03 (11.47)	UV	0.089	**1.09**	1.05-1.1	**<0.001*****
				MV^b	0.103	**1.108**	1.05-1.167	**<0.001*****
Maximum dose of cigarette/ bidi per day		17.88 (13.27)	13.51 (16.82)	UV	**0.022**	1.022	0.99-1.06	0.186
				MV^b	0.013	1.013	0.978-1.05	0.476

*significant at p<0.05

***significant at p<0.001

With the univariate analysis of each of the independent variables, there was increased likelihood of continuing smoking in COPD patients with medical comorbidity (OR=2.3), lifetime psychiatric illness (OR=2.5), current psychiatric illness (OR=4), current depressive episode (OR=3.78), with AIR score>8 (OR=12.36) and cigarette smoking (OR=3.89). There is increased risk in continuing smoking in the COPD patients with increase in PHQ-9 score (OR=1.2), AIR score (OR=1.3) and duration of tobacco smoking (OR=1.09). There is decreased risk of continuing smoking in COPD patients with education status of primary and middle school (OR=0.16). The risk of continuing smoking in COPD patients decreases with increase in duration of COPD symptoms (OR=0.86).

With multivariate regression analysis (MV^{a}), only two of the independent variables had statistically significant association. With increase in one unit of AIR score, there is 24% increased likelihood of continued smoking in COPD patients (aOR=1.24). With increase of duration of COPD symptoms by one year, the COPD patients are 17% less likely to continue smoking (aOR=0.83).

In multivariate analysis ($MV^{b)}$ including only smoking related variables, two out of three independent variable had significant association. With cigarette smoking, there is 9 times more likelihood of continued smoking. With increase in tobacco smoking by one year, the COPD patients are 10% more likely to continue smoking.

Discussion

DISCUSSION

Our study aims to evaluate the association between tobacco smoking status and psychiatric comorbidities among treatment seeking patients with COPD with secondary objectives of assessing the relation of tobacco smoking status with various socio-demographic & clinical variables among treatment seeking patients with COPD and study the relation of severity of nicotine dependence with severity of depression and anxiety among current smokers with COPD.

During the study, 172 patients were screened in order to collect data from 100 patients as per the inclusion and exclusion criteria. 50 current smokers and 50 current non-smokers were taken in the study using purposive sampling method.

Study methodology:

We have included the subjects with age greater than 30 years. The physiological decline in the respiratory functions begins at the age of 30-40 years. Majority of the studies (62%) have included patients with age of more than 40 years. The risk of COPD increases up to 5 times in age >65years as compared to age <40 years(96,97). We have included only male patients as the majority of the patients with COPD coming to the OPD of Department of Pulmonary, Critical Care and Sleep Medicine are males. The prevalence of COPD in males is as high as twice the prevalence of females (96). As per GATS-2 2016-17 survey, the prevalence of tobacco smoking in males was 19% and in females, it was 2% (98).

Most of the studies which assessed for the prevalence of psychiatric morbidities in COPD were cross-sectional studies of COPD patients or case-control studies (49,63,84,99,100). This study has grouped COPD patients on the basis of smoking status.

We took patients who have been visiting in the OPD of Department of Pulmonary, Critical Care and Sleep Medicine for at least 3 months. Three months of duration was kept so that there is sufficient time for assessment and diagnosis of COPD and for any change in the smoking behaviour. Severe comorbid illnesses & clinically unstable patients and those patients with oral steroid intake were excluded as they could act as confounding factors while estimating the prevalence of psychiatric comorbidities.

Patients who were already on any medications for their psychiatric illness were also excluded as it would have improved the scores of PHQ-9 and AIR scales.

There is no universal definition to define current smoker and former smoker. Therefore, operational definitions for our study was framed based on definitions by National Health Interview Survey, National Survey for Drug Use and Health and New Zealand's Ministry of Health (86,88,101).

Socio-demographic factors:

The mean age of the total sample was 59.97 ± 10.12 years. There was no statistically significant difference between current smokers and current non-smokers (60.1 ± 10.74 years vs 59.84 ± 9.66 years).Mean age was comparable with most of the studies on COPD which ranged from 54-67 years(70,72,83–85,102,103).

There was no significant difference between the current smokers and current non-smokers in marital status, occupation, area of residence and the state-wise residence of the patients. Most of the patients among the total sample belonged to Delhi, Uttar Pradesh, and Haryana which are geographically the closest states from AIIMS Delhi.

There was statistically significant difference in the education of the two groups (χ^2=7.954, p=0.046). Post hoc analysis of chi-square test showed that there was higher proportion of illiterate population in the current smokers when compared to current non-smokers. This difference was statistically significant. With univariate analysis, there was decreased likelihood of continuing smoking in COPD patients with education status of primary and middle school (OR=0.16) as compared to illiterate status. This finding was not significant in multivariate regression analysis.

A higher proportion of illiterate population is seen in COPD population with current smokers up to 68.8% (104).Another study evaluating COPD in current smokers and current non-smokers did not find any significant difference(105). The lower educational status may lead to lack of awareness about the disease, treatment modalities, difficulty in lifestyle modification and therefore, such individuals can be non-compliant. Insufficient management of COPD may result in undue stress increasing the risk for psychiatric illnesses as well as continued smoking.

Characteristics of COPD:

The mean duration of COPD symptoms was 4.75 ±5.38 years in the total population. The mean duration of COPD symptoms in the current smokers was less than current non-smokers (3.11 ±3.64 vs 6.38±6.31). The current non-smokers were having the complaints of respiratory illness, eg., breathlessness, cough, etc., from a significantly longer duration when compared to the current smokers' group ($p<0.001$). This finding was similar to findings of *Tashkin et al., 2018,* in which ex-smokers had longer duration of COPD than current smokers, 6 years vs 4.8 years (106). This finding might suggest that there is a slower progress of symptoms of COPD in current non-smokers when compared to current smokers due which the treatment seeking in the current non-smokers occurs much later after the onset of symptoms. In other words, the result suggests that smoking causes rapid progression of COPD which has been widely reported in several studies (4,5,77,107).

There was no significant difference in the severity of COPD between the current smokers and current non-smokers. The current smokers' group had lower proportion of patients with mild COPD as per GOLD criteria when compared to current non-smokers' group (24% vs 38%) and higher proportion of patients with moderate COPD (48% vs 46%) and severe COPD (26% vs 12%). This finding was similar to findings in *Tashkin et al., 2019*, with 66.7% of current smokers with moderate COPD in comparison to 57.4% in the ex-smokers(106). In our study, a higher proportion of the current smokers were having severe or very severe COPD when compared to current non-smokers (28% vs 16%). This finding was similar to findings of *Li et al., 2020*, in which 50% of the active smoker had severe or very severe COPD as compared to only 20% of the non-smokers or passive smokers and *Bajpai et al., 2019,* with 78.7% smokers vs 33.34% non-smokers having severe or very severe COPD(82,108).Smoking cessation may prevent or slow the progression of severity of COPD.

With the univariate analysis with the duration of COPD symptoms, it was found that there is less likelihood of continued smoking in COPD patients with increase in duration in COPD symptoms (OR=0.86). As per the multivariate regression analysis, with the increase of duration of COPD symptoms by one year (one unit) in patients with COPD there is 17% lesser likelihood for being continued smoker. Our results suggest that patient with longer duration of COPD symptoms are more likely to be non-smoker. It is

possible that the non-smokers with COPD might be seeking treatment from a longer duration and therefore they might have received more chances of interaction with the health care workers and would have received frequent cessation advices from them. This statement is supported by the observation of our study for total duration of treatment from OPD of Pulmonary, Critical Care and Sleep Medicine. The current non-smoker's group had longer mean duration of treatment from the OPD of Pulmonary Medicine as compared to the current smokers' group (19.34± 20.19 vs 11.66±11.03, $p<0.05$).

This result is similar to that of *Martínez-González et al., 2018* which found that smoking cessation is associated with chronic COPD symptoms (expectoration) and problems in daily activities due to COPD(109).It is also possible that early appearance of the COPD symptoms might motivate the patients to quit smoking earlier.

It reflects that smokers with COPD have long duration of tobacco use and are severely dependent. Therefore, they need comprehensive and frequent sessions for smoking cessation.

Characteristics of Tobacco Smoking:

The current smokers (n=50) and former smokers (n=37) were assessed for characteristics of smoking. Among the total sample (n=87), 23% of the population smoked cigarettes and 77% of the population smoked bidi or any other smoking form of tobacco. 32% of current smokers were cigarette smokers whereas only 10.8% of former smokers were cigarette consumers. Rest 68% of the current smokers smoked bidi and other smoking forms of tobacco as compared to 89.2% of the current non-smokers. This difference in type of tobacco smoking was statistically significant ($p<0.05$). In univariate analysis, the cigarette smokers with COPD were 3.9 time more likely to be continue smoking as compared to the COPD patients who smoked bidi or any other forms of tobacco ($p<0.05$). With multivariate regression analysis of smoking-related variables, considering continued smoking as dependent variable and independent variables as, namely, type of smoking, duration of smoking and maximum dose of cigarette/bidi per day, the cigarette smokers with COPD were 9 times more likely to continue smoking as compared to those COPD patients who smoked bidi or other forms of tobacco($p<0.005$).

Age of onset of tobacco smoking was 21.83 ±6.92 years among current and former smokers (n=87). Mean age of onset of smoking was almost similar in the current

smokers and former smokers (21.4±7.26 years vs 22.41±6.49 years). This finding was not statistically significant (p=0.2). Majority of regular smokers initiate their smoking tobacco use at an age less than 20 years. In GATS-2 survey of 2016-17, the average age of initiation was 18.9 years. 90% of the daily smoker initiated their tobacco use by age 18 as per UDHHS 2012 data and 83.2% daily smokers by age of 20 years as per *Ali et al., 2020*(110,111).. *Jindal et al.,2006,* also reported age of initiation of smoking as 20.5 years (112). It has been well established that early age of initiation is associated with higher severity of dependence and subsequently difficult cessation (113–115).

The mean duration of use of smoking form of tobacco of the current smokers and former smokers (n=87) was 33.84±12.75. The mean duration of use of tobacco in smoking form was significantly higher in the current smokers' group when compared with the current non-smokers' group (38.88±11.3 years vs 27±11.47 years, p<0.001).

In univariate analysis, there is greater likelihood of continuing smoking in COPD patients with increase in duration of smoking (OR=1.09). In multivariate regression analysis, our study reports even greater likelihood of continuing smoking in COPD patients with increase in duration of smoking (aOR=1.11).

In our sample the current smoker smoked tobacco for a significantly longer duration. The duration of smoking have been associated with severity of nicotine dependence (116). Moreover, the current smokers have higher nicotine dependence than former smokers (117). It could be possible that in our study, because of the severity of nicotine dependence, the current smokers were finding it difficult to quit. Only advice to stop smoking by the treating physician may not be effective for them, and they may require comprehensive smoking cessation intervention (counselling and pharmacotherapy).

The mean maximum dose of cigarette/ bidi per day in the current smokers and former smokers(n=87) was 16±14.95. The mean maximum dose of cigarette/bidi per day of the current smokers' group was significantly higher than the former smokers' group (17.88±13.27 vs 13.51±16.82, U=618.5, p<0.05). This number is much higher than the mean number of cigarettes in the daily cigarette smoker in India which is 6.8 and mean number of bidi smoked by daily bidi smoker per day is 15.1 (98). Patients with COPD have much higher mean maximum dose of cigarette/bidi as compared to the general population. There were no significant findings of maximum dose of cigarette/bidi per day and smoking status in multivariate regression analysis.

The mean total abstinence attempts of the current and former smokers (n=87) was 1.83±1.56. The mean total abstinence attempt in the current smokers' group was greater than former smokers' group (1.92±1.72 vs 1.7±1.3). This difference was not statistically significant (U=895.5, p>0.05). Obviously, there were failed attempts by the current smoker population. Out of the ever smokers, only 4 patients took smoking cessation treatment in the form of counselling or pharmacological management. 3 of them were from the current smokers' group. This difference was statistically not significant (Fisher's exact test value= 0.617). The patients coming for treatment might not have awareness about either the smoking cessation treatments or the source of such treatments. The smokers visiting the OPD of Pulmonary Medicine, Critical Care and Sleep Medicine may be referred to the smoking cessation clinic of Department of Psychiatry to initiate smoking cessation interventions. Previous studies have reported the importance of any smoking cessation intervention alone or in combination significantly improves the outcome of abstinence attempts(75,77).

The current smokers' group was also assessed for the severity of nicotine dependence using FTND scale. The mean score of FTND was 3.94±2.38, with minimum score 0 and maximum score of 9. 68% of the current smokers had FTND score 3 or >3. The mean score of the current smokers' group lies in low-to-moderate dependence as per the scoring of FTND. This was lower than the findings of *Saha et al., 2018* and *Jayakrishnan et al.,2012*, which was 7.8±1.97 in COPD patients 5.04±5.05 in tobacco smokers, respectively(118,119). The findings were similar to the mean FTND score of 4.2±2.4 in tobacco users in the study by *Islam et al., 2019* (120). In our study, the lower mean FTND scores may be due to the concurrent use of smokeless tobacco. The use of smokeless tobacco might lower the requirement of tobacco in smoking form and thus affecting the FTND scores.

20% of the total population (n=100) actively used smokeless form of tobacco at the time of assessment. 24% of the current smoker and 16% of the current non-smoker used smokeless tobacco. This difference was not statistically significant. The finding for total sample was similar to the finding of GATS-2 survey, 21.4% of the Indian population currently use smokeless forms of tobacco as per GATS-2 survey (1)

Characteristics of Alcohol use:

Our study assessed for alcohol use disorder among the two groups. There were 7% of the total sample (n=100) suffering alcohol use disorder. This difference was marginally significant ($p>0.05$). It is almost similar to the prevalence of general population, 5.2% reported by *Ambekar et al.,* (121). However the prevalence of alcohol use or problematic alcohol use has been reported to be 14.5% in COPD patients and 9.3% in population with chronic diseases (122,123). This suggests that the current smokers' group have higher proportion of patients with alcohol use disorder. Concurrent alcohol use with tobacco smoking in COPD patients has been associated with unsuccessful quit attempts and low motivation to quit(71,73,74).

Medical Comorbidities:

In our study, 40% of the total sample (n=100) had medical comorbidities. The current non-smoker had significantly lower proportion of patients with medical comorbidities as compared to current smokers' group (30% vs 50%, $p<0.05$). With the univariate analysis of each of the independent variables, there was increased risk of continuing smoking in COPD patients with medical comorbidity (OR=2.3) but the finding was not significant on multivariate regression analysis.

Tobacco smoking increases the risk of other comorbidities in COPD (124). With the findings of our study, there may be higher comorbidities in smokers with COPD. It is a well-established fact that smoking leads to disease and disabilities (125).

Psychiatric Comorbidities:

Out of the total sample (n=100), 45% of the patients suffered from a diagnosable psychiatric co-morbidity including alcohol use disorder (excluding tobacco use disorder) in their lifetime. 56% of the current smokers' group and 34% of the current non-smokers' group had suffered from any diagnosable psychiatric illness including alcohol use disorder in their lifetime. This difference was statistically significant ($p<0.05$). Also, 35% of the total participants were diagnosed with a current psychiatric illness including alcohol use disorder during the assessment. The proportion of current smoker with a current psychiatric illness including alcohol use disorder was also significantly higher as compared to current non-smokers with COPD ($p<0.005$).

With univariate analysis, there is greater likelihood of continuing smoking in COPD patients with lifetime psychiatric illness (OR=2.5) and current psychiatric illness (OR=4). These results did not remain significant in multivariate regression analysis.

The proportion of lifetime and current psychiatric illness was much higher in this study than the prevalence in the general population. As per the National Mental Health Survey 2015-16 data, lifetime prevalence of any psychiatric illness was 13.7% and current psychiatric illness was 10.6% (121). The proportion of psychiatric illness was much higher than the prevalence in general population. This might be due to concurrent chronic illness, i.e. COPD and substance use, both of which are known to be associated with psychiatric illness. Psychiatric disorders are more common in COPD than in chronic illnesses like coronary heart, stroke , diabetes, asthma, high blood pressure and cancer (37). Another reason for higher proportion of psychiatric illness in our study might be use of purposive sampling method. Our findings are almost similar to the findings in a meta-analysis by *Dare et al., 2019* where pooled prevalence of psychiatric illness with chronic physical diseases was 36.5% (95% CI: 31.4-42.1) (100). The prevalence of psychiatric comorbidities may range from 8% to 80% in the patients with COPD (53). The findings of the prevalence for any psychiatric comorbidity was similar to the findings of *Yin et al., 2017* (40%), *Smith MC, Wrobel JP, 2014*(40%), and several other studies (37,41,44,46,52,54). Smoking has been significantly associated with a concurrent psychiatric illness in patients with COPD (67).

Depressive Disorder:

Out of the total sample (n=100), 33% had suffered from lifetime depressive disorder. 23% of the population were having current depressive episode. As per WHO estimates of 2015, the prevalence of depression in males of age group 55-74 years is 5.5%. In WHO estimates of 2019, the total point prevalence for depression was 10.8% (121,126).The current smokers' group had significantly higher proportion of a current depressive episode as compared to current non-smoker population (34% vs 12%, $p<0.05$). These findings are similar to 2006 BRFSS data where a higher proportion of non-quitters and unsuccessful quitters had current depression when compared to quitters (16.75% vs 8%) (65). COPD causes functional limitations in the activities that would require physical activity such as ambulation, home management, and recreational activities and psychosocial functioning. The amount of perceived need for assistance in daily living in

COPD patients is found to be correlated with depression (127,128). The presence of depressive symptoms have been associated with persistent smoking behaviour (OR=2.3) in the study by *Ng et al.,2007*(129).These findings show that there is an independent link between depression and COPD.

There is evidence of continuation of smoking behavior in the presence of depression(68). With univariate analysis, there was greater likelihood of continuing smoking in COPD patients with current depressive illness (OR=3.78). However, the results did not remain significant in multivariate regression analysis.

The mean PHQ-9 score of the total sample was 3.44±4.04. There was a statistically significant difference in the mean PHQ-9 scores of the two groups (p=0.01). The mean PHQ-9 score of current smokers' group was 4.7±4.76 and of current non-smokers' group was 2.18±2.66. This shows that depressive symptoms are significantly higher in the current smokers' group as compared to current non-smokers' group. With univariate analysis, there was greater likelihood of continuing smoking in COPD patients with increase in PHQ-9 score (OR=1.2). The results did not remain significant in multivariate regression analysis.

There is evidence which bi-directional relation between smoking and depression. Self-medication hypothesis suggests that the depresses patients smoke to alleviate the dysphoric mood, as shown in a 40-year follow up study by *Murphy et al., 2003* (130,131). Other possible reason that has been suggested is common genetic vulnerability factor for smoking and depression (131). Though the underlying mechanism are unclear, there may be multiple mechanism for such bi-directional relation.

Anxiety Disorders:

6% of the total sample had panic disorder and all of them belonged to current smokers' group. This finding was statistically significant ($p<0.05$). The prevalence of panic disorder in our study is similar to findings of *Kunik et al., 2005* and *Pollack et al., 1996.* As per these studies the estimated prevalence of panic disorder in COPD ranges from 6-67%(47,132). The prevalence of panic disorder can be up to ten times higher than the general population (1.5-3.5%)(133).

6% of the current smokers and 4% of the current non-smokers had agoraphobia. 6% of the current smokers' group had generalized anxiety disorder and 2% of the current non-smoker had social anxiety disorder. These findings were not significant.

The mean Anxiety Inventory for Respiratory (AIR) Diseases score of the total sample was 3.27±3.96. The mean AIR score of the current smokers' group was 4.9±4.55 and mean AIR score of the current non-smokers' group was 1.6±2.34. This difference was strongly significant ($p<0.001$). The anxiety symptoms were significantly higher in the current smoker patients with COPD. The AIR score of >8 has 80% sensitivity for diagnosis of anxiety disorder. The AIR score was >8 in 19% of the total sample (n=100). AIR score was >8 in 34% of current smokers' group and 4% of the current non-smokers' group and this difference was statistically significant ($p<0.001$).

With univariate analysis there was increased likelihood of smoking in COPD with AIR score>8 (OR=12.36) and) and increase in AIR score (OR=1.3). The multivariable regression analysis revealed that increase in one unit of AIR score in patient with COPD has 24% greater likelihood for being continued smokers. The findings of our suggest that the likelihood of smoking increases in COPD with anxiety symptoms.

There is evidence of bidirectional relation between smoking and anxiety.

In COPD, the development of anxiety may be due to smoking, aging, hypoxemia as suggested in studies by *Smith & Wrobel, 2014* and *Pumar et al., 2014.* Many studies have shown that cigarette smoking can increase the risk of anxiety, although it has yet to be confirmed. Evidence of anxiety disorder pathogenesis and increasing signs of anxiety may be due to different neurotransmitter pathway, immune system, mitochondrial activity, and epigenetic modulation, however the literature is heterogeneous and sparse in some fields. *Moylan et al., 2013* has reported that cigarette smoke products, including nicotine and other toxic substances, have an effect on all these pathways, thus affecting anxiety disorders(66).

Goodwin et al., 2012 has reported a strong relation between anxiety disorder and smoking as well as between COPD and smoking. The study has also suggested that the relationship between anxiety disorder and COPD was significant due to confounding by smoking and nicotine dependence and the finding was no longer significant after

adjusting for both. This suggest that smoking might be acting as a common risk factor for anxiety disorder and COPD.

Fluharty et al., 2017 reported that there is evidence of association of baseline anxiety symptoms and early or late onset smoking pattern, which supports the self-medication theory (67). *Cuijpers et al.,2007* reported an increased risk of anxiety disorder with smoking. This study also found a significant association between smoking and first incidence of anxiety disorder (134). With support of available data, our study suggests that there is significant association between smoking and anxiety symptoms in COPD patients. It may be possible that continued smoking may be to alleviate the anxiety symptoms. On the other hand, the nicotine withdrawal might worsen the anxiety symptoms resulting in failure in quitting.

The presence of comorbid anxiety and smoking may decrease the adherence to treatment in COPD patients(135). The finding is in congruence with *Piper et al., 2011* where the presence of a anxiety symptoms were associated with impaired ability to quit smoking (136).

As per *Lou et al.,* 2014 the combined effect of anxiety and current smoking increases the death risk by 4.3- fold (59). In the study by *Kupiainen et al., 2012*the presence of psychiatric disorder was associated with low success are of quitting (OR=1.8) (70).This shows that concurrent treatment of anxiety is necessary to help the patient in quitting smoking and to improve management of COPD. It is important to evaluate for the anxiety and depressive symptoms, especially in the COPD patients with active smoking so that adequate treatment for smoking cessation and psychiatric illness can be done simultaneously.

The depression and anxiety have largest impact on the management and outcome of COPD when compared to other comorbidities (40). The presence of psychiatric comorbidity significantly affects the quality of life in COPD(38,58). There is detrimental effect in quality of life in COPD because of comorbid depression and anxiety disorder and has been found to have strongest association with self-reported health status of COPD patients in a systematic review and meta-analysis by *Ioanna et al., 2011* (137).

Correlation between severity of nicotine dependence and PHQ-9 and AIR scores

There was no significant correlation between the FTND score and PHQ-9score (ρ=0.222, p=0.12) or between FTND score and AIR score(ρ= 0.063, p=0.66).As per our knowledge, there were no other studies which examined the correlation between severity of nicotine dependence and depressive or anxiety symptoms using instruments. There is well established association between smoking and anxiety and depression (138–141). However, our study could not replicate this result. The possible reason may be concurrent use of smokeless tobacco which might have resulted in lower FTND scores for smoking form of tobacco. A larger sample for study might be helpful in replicating similar findings in COPD patients.

Stages of change:

In our study, out of 50 current smokers, 8 patients were in pre-contemplation stage, 28 patients were in the contemplation stage, and rest 14 were in action stage. More number of patients were in contemplation or pre-contemplation stage. This finding was similar to *Ivey et al., 2019* and *Hilberink et al., 2006* where a higher proportion of the patients were in the precontemplation or contemplation stage (142,143). This suggests that more than half of the patients in the current smokers' group are thinking or planning to quit smoking. It is well established that smoking cessation is the cornerstone of management of COPD. The review by *Warnier et al.,2013* indicates that pharmacological therapy along with behavioural intervention is the most effective smoking cessation strategy in smokers with COPD (144). Negative experiences associated with smoking cessation attempts or therapies results in lack of motivation in the smoker COPD patients (145). An interview-based study in our study setting might help in recognizing the problems faced by the patients in smoking cessation and making adequate improvement in the smoking cessation treatment. Additionally, frequent and repeated counselling during OPD visits or telephonically might be helpful for improving motivation and improving the stage of change from pre-contemplation, contemplation and action phase to maintenance phase.

LIMITATIONS:

There were certain limitations of the study. Our study had a small sample size. The sample size was kept 100 with 50 patients in each current smoker and current non-smokers' group. Initially, we proposed to keep 99 patients in each group with assumption that the ratio of prevalence in current non-smokers and current smokers is 1:2, with a confidence interval of 95% and power of 75%. Since with the allotted time for completion of thesis could only allow the assessment of 100 patients, the sample size was kept as 100 after the discussion within the department of Psychiatry & NDDTC.

The sampling method used was purposive sampling method and included only treatment seeking COPD patients. Hence, the findings of our study is not generalisable in all COPD population. Small sample size and purposive sample may have led to high level of bias. A more robust methodology and better sampling method would be required to overcome these limitations. The study was done at a single tertiary care centre that is likely to cater population from a geographical area and with higher severity of disease. A multicentric study might eliminate this limitation. The study population consisted of only OPD visiting patients, so the hospitalized or severely ill patients could not be assessed in the study.

Future studies should include a larger sample with three groups if possible. The future studies should be a follow up study to observe the change in smoking behaviour over a duration and impact of the psychiatric comorbidity in the change in smoking behaviour. Future studies should also inculcate intervention for tobacco cessation and should assess barriers in attaining smoking cessation in COPD patients. Regression analysis is one of the strengths of the study. The methodology is explained in detail with study flow and procedure. The results are easy to analyse.

Summary & Conclusion

SUMMARY & CONCLUSION

The present study was done at All India Institute of Medical Sciences, New Delhi in the outpatient Department of Pulmonary, Critical Care and Sleep Medicine. We hypothesized that the current tobacco smokers with COPD have higher rates of psychiatric co-morbidities as compared to current non-smokers with COPD. The aim was to examine the association between tobacco smoking status and psychiatric co-morbidities among treatment seeking patients with COPD.

We recruited 50 current smokers with COPD and 50 non-current smokers with COPD as per the inclusion and exclusion criteria, and assessed them for socio-demographic variables, characteristics of COPD, characteristics of smoking tobacco and other substance use, psychiatric illnesses and stage of change.

All recruited patients were males and with mean age of 59.97±10.16 [60.1 years (SD= 10.74) for current smokers and 59.84 (SD= 9.66) for current non-smokers. 91% of the participants were married. 85% of the participants were literate. 22% of current smokers were illiterate as compared to current non-smokers (8%) which was at the margin of statistical significance ($p<0.05$). Significantly higher proportion of current non-smokers had primary and middle education ($p=0.02$).

Total duration of COPD symptoms was 4.75(5.38) years for total sample [3.11(3.64) years for current smokers and 6.38(6.31) years for current non-smokers]. This finding was statistically significant with $p<0.001$. 32% of the current smokers smoked cigarettes as compared to only 10.8% of the current non-smokers ($p<0.05$).

The mean duration of smoking was significantly higher in the current smokers' group ($p<0.001$). The mean duration of smoking was approximately 12 years greater in current smokers with COPD.

There was higher medical comorbidity in current smokers' group (50% vs 30%, $p<0.05$). In univariate analysis, there was increased likelihood of continued smoking in COPD patients with the presence of a medical comorbidity (OR=2.3) but no such significant association in multivariate regression analysis.

45% of the total sample had lifetime psychiatric illness including alcohol use disorder (excluding Tobacco Use Disorder) and 35% of the total sample had a current psychiatric illness including alcohol use disorder. The proportion of lifetime and current psychiatric illness was significantly higher in the current smokers [lifetime psychiatric illness, $p<0.05$; current psychiatric illness; $p<0.005$).

33% of the total sample had depressive disorder (lifetime). 42% of the current smokers and 24% of the current non-smokers had depressive disorder (lifetime) ($p=0.056$) which was not statistically significant. But the difference in the current depressive episode between the two groups was significant ($p<0.05$). The mean PHQ-9 score, and mean AIR score was significantly higher in current smokers' group [PHQ-9; 4.7(4.76) vs 2.18(2.66), $p<0.05$ & AIR; 4.9(4.55) vs 1.6(2.34), $p<0.001$]. as compared to non-smokers' group. The anxiety and depressive symptoms are significantly higher in the current smokers with COPD.

With correlational analysis (only current smokers) our study found no correlation between severity of nicotine dependence measured with FTND scale and severity of depressive symptoms measured by PHQ-9 scale. There was no correlation between severity of nicotine dependence and severity of anxiety symptoms measured by AIR scale.

The multivariable regression analysis with current smoking as dependent variable and educational status, duration of COPD symptoms, presence of medical comorbidity, lifetime psychiatric disorder, current depressive episode, PHQ-9 score, AIR score as independent variable. Two independent variables had significant findings. First, with increase in one unit of AIR score, there is 24% increased likelihood of continued smoking in COPD patients (aOR=1.24). Second, with increase of duration of COPD symptoms by one year, the COPD patients are 17% less likely to continue smoking (aOR=0.83).

With multiple regression analysis with current smoking as dependent variable and smoking-related variables as independent variables that are, type of smoking, maximum dose and duration of smoking, the odds of type of smoking and duration of smoking were significant. With cigarette smoking, there is 9 times more likelihood of continued smoking. With increase in tobacco smoking by one year, the COPD patients are 10% more likely to continue smoking.

It is necessary to diagnose anxiety symptoms in the COPD patients, which could be part of both anxiety disorders and depressive disorders. The presence of anxiety symptoms may negatively affect the smoking cessation in the COPD patients. The persistence of smoking behaviour has been established to be detrimental for both COPD as well as psychiatric illness.

Smokers in COPD have more severe dependence and longer duration of tobacco smoking and require greater efforts to quit tobacco. Therefore, a comprehensive smoking cessation and more frequent and consistent sessions for smoking cessation are required for smokers with COPD. Moreover, it is known to decrease the quality of life, and would be responsible for further progression of the COPD patients and impact the management of COPD. Therefore, simultaneous diagnosis and management of psychiatric illness is important to expect positive outcome from the treatment.

Future Directions

FUTURE DIRECTIONS

- Future studies should plan a larger sample size with robust methodology and preferably a follow-up study to better study the impact of smoking behaviour of psychiatric comorbidity and COPD management and impact of psychiatric illness on smoking and COPD management.
- Future studies should primarily work on anxiety and depressive symptoms in COPD patients and its impact on illness, treatment, and quality of life.
- Future studies should focus on actively managing smoking in COPD patients as a large proportion our current smokers' group intend to quit smoking or are actively changing their smoking behaviour
- Future studies should find out the effectiveness of different intervention that can be provided at a non-Psychiatry set-up for smoking intervention as well as primary management of anxiety and depressive symptoms. The intervention should include both pharmacological and non-pharmacological intervention (counselling/lifestyle modification/exercises)
- Future studies should work on identifying the risk factor of having psychiatric illness in the smoking patients with COPD so that an early intervention can be planned to improve overall outcome

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Appendices

APPENDIX 1: SEMI-STRUCTURED PROFORMA

I. NAME				
AGE (in completed years)		GENDER	☐ MALE	☐ FEMALE
RELIGION	☐ HINDU ☐ MUSLIM ☐ SIKH ☐ CHRISTIANITY ☐ NOT KNOWN SPECIFY IF OTHER: ……			
OCCUPATION	Specify ……... ☐ Professional ☐ Semi- professional ☐ Highly skilled ☐ Skilled ☐ Semi-skilled ☐ Unskilled ☐ Unemployed			
EDUCATION	☐ Illiterate ☐ Primary ☐ Middle ☐ High School ☐ Intermediate ☐ Graduate ☐ Post Graduate ☐ Professional			
FAMILY INCOME PER MONTH	…….			
MARITAL STATUS	☐ Married ☐ Separated/Divorced ☐ Unmarried			
ADDRESS	…….. City…… State…… Urban/Rural Phone No……..			
Duration since registration for COPD at OPD of Pulmonary Medicine and Sleep, AIIMS Delhi	……..			
Current smoking status	……..			
Smoking status at the time of diagnosis of COPD	…….			
Smoking status at the time of registration in COPD clinic	…….			

Stage of COPD	☐ Mild ☐ Moderate ☐ Severe ☐ Very Severe
Treatment details for COPD	
Treatment details for Tobacco Cessation	Advised- ☐ Yes ☐ No Treatment given-
Details of Tobacco use	Type of smoking…….. Age of onset of smoking…… Duration of use…….. Maximum dose used……. Other forms of tobacco……. Abstinence attempts……. No of attempts in past 1 year……..
Other substance use history	
Medical/Surgical History	

APPENDIX- II: FAGERSTROM TEST FOR NICOTINE DEPENDENCE

Fagerstrom Test for Nicotine Dependence

	PLEASE TICK (✓) ONE BOX FOR EACH QUESTION	
How soon after waking do you smoke your first cigarette?	Within 5 minutes 5-30 minutes 31-60 minutes	☐ 3 ☐ 2 ☐ 1
Do you find it difficult to refrain from smoking in places where it is forbidden? e.g. Church, Library, etc.	Yes No	☐ 1 ☐ 0
Which cigarette would you hate to give up?	The first in the morning Any other	☐ 1 ☐ 0
How many cigarettes a day do you smoke?	10 or less 11 – 20 21 – 30 31 or more	☐ 0 ☐ 1 ☐ 2 ☐ 3
Do you smoke more frequently in the morning?	Yes No	☐ 1 ☐ 0
Do you smoke even if you are sick in bed most of the day?	Yes No	☐ 1 ☐ 0
	Total Score	

SCORE		
	1- 2 = low dependence 3-4 = low to mod dependence	5 - 7= moderate dependence 8 + = high dependence

APPENDIX- III: MINI INTERNATIONAL NEUROPSYCHIATRIC INTERVIEW (MINI) WITH TOBACCO USE DISORDER MODULE 7.0.2

II. MINI INTERNATIONAL NEUROPSYCHIATRIC INTERVIEW (MINI) WITH TOBACCO USE DISORDER MODULE 7.0.2

Patient Name:		***Patient Number:***	
Date of Birth:		***Time Interview Began:***	
Interviewer's Name:		***Time Interview Ended:***	
Date of Interview:		***Total Time:***	

	MODULES	TIME FRAME	MEETS CRITERIA	ICD-10-CM	PRIMARY DIAGNOSIS
A	MAJOR DEPRESSIVE EPISODE	Current (2 weeks)	☐		
		Past	☐		
		Recurrent	☐		
	MAJOR DEPRESSIVE DISORDER	Current (2 weeks)	☐	F32.x	☐
		Past	☐	F32.x	☐
		Recurrent	☐	F33.x	☐
B	SUICIDALITY	Current (Past Month)	☐		☐
		Lifetime attempt	☐	☐ Low ☐ Moderate ☐ High	☐
	SUICIDE BEHAVIOR DISORDER	Current	☐	(In Past Year)	☐
		In early remission	☐	(1 - 2 Years Ago)	☐
C	MANIC EPISODE	Current	☐		
		Past	☐		
	HYPOMANIC EPISODE	Current	☐		
		Past	☐	☐ Not Explored	
	BIPOLAR I DISORDER	Current	☐	F31.0 - F31.76	☐
		Past	☐	F31.0 - F31.76	☐
	BIPOLAR I DISORDER WITH PSYCHOTIC FEATURES	Current	☐	F31.2/31.5/F31.64	☐
		Past	☐	F31.2/31.5/F31.64	☐
	BIPOLAR II DISORDER	Current	☐	F31.81	☐
		Past	☐	F31.81	☐
	OTHER SPECIFIED BIPOLAR AND RELATED DISORDER	Current	☐	F31.89	☐
		Past	☐	F31.89	☐
D	PANIC DISORDER	Current (Past Month)	☐	F41.0	☐
		Lifetime	☐	F40.0	☐
E	AGORAPHOBIA	Current	☐	F40.00	☐
F	SOCIAL ANXIETY DISORDER (Social Phobia)	Current (Past Month)	☐	F40.10	☐
G	OBSESSIVE-COMPULSIVE DISORDER	Current (Past Month)	☐	F42.2	☐
H	POSTTRAUMATIC STRESS DISORDER	Current (Past Month)	☐	F43.10	☐
I	ALCOHOL USE DISORDER	Past 12 Months	☐	F10.10 - F10.21	☐
J	SUBSTANCE USE DISORDER (Non-alcohol)	Past 12 Months	☐	F11.10 - F19.21	☐
	TOBACCO USE DISORDER	Past 12 Months	☐	Z72.0/F17.200	☐

K	ANY PSYCHOTIC DISORDER	Current	☐	F20.81-F29	☐
		Lifetime	☐	F20.81-F29	☐
	MAJOR DEPRESSIVE DISORDER WITH PSYCHOTIC FEATURES	Current	☐	F32.3/F33.3	☐
		Past	☐	F32.3/F33.3	☐
	BIPOLAR I DISORDER WITH PSYCHOTIC FEATURES	Current	☐	F31.2/F31.5/F31.64	☐
		Past	☐	F31.2/F31.5/F31.64	☐
L	ANOREXIA NERVOSA	Current (Past 3 Months)	☐	F50.01/F50.02	☐
M	BULIMIA NERVOSA	Current (Past 3 Months)	☐	F50.2	☐
MB	BINGE-EATING DISORDER	Current (Past 3 Months)	☐	F50.81	☐
N	GENERALIZED ANXIETY DISORDER	Current (Past 6 Months)	☐	F41.1	☐
O	MEDICAL, ORGANIC, DRUG CAUSE RULED OUT			☐ No ☐ Yes ☐ Uncertain	
P	ANTISOCIAL PERSONALITY DISORDER	Lifetime	☐	F60.2	☐

IDENTIFY THE PRIMARY DIAGNOSIS BY CHECKING THE APPROPRIATE CHECK BOX.
(Which problem troubles you the most or dominates the others or came first in the natural history?) ——→

APPENDIX-IV: PATIENT HEALTH QUESTIONNAIRE-9 (PHQ-9)

PATIENT HEALTH QUESTIONNAIRE-9 (PHQ-9)

Over the last 2 weeks, how often have you been bothered by any of the following problems? *(Use "✔" to indicate your answer)*	**Not at all**	**Several days**	**More than half the days**	**Nearly every day**
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself — or that you are a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed? Or the opposite — being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9. Thoughts that you would be better off dead or of hurting yourself in some way	0	1	2	3

FOR OFFICE CODING 0 + _____ + _____ + _____

=Total Score: _____

If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

Not difficult at all	**Somewhat difficult**	**Very difficult**	**Extremely difficult**
☐	☐	☐	☐

Developed by Drs. Robert L. Spitzer, Janet B.W. Williams, Kurt Kroenke and colleagues, with an educational grant from Pfizer Inc. No permission required to reproduce, translate, display or distribute.

नाम → | Date

पिछले दो सप्ताह में, आपको नीचे लिखी समस्याओं से कितने दिन परेशानी का सामना करना पड़ा?

PHQ-9	अपना उत्तर देने के लिए (✓) के चिन्ह का प्रयोग करें	एक भी दिन नहीं	कई दिन	आधे से ज्यादा दिन	हर दिन
1	कोई भी काम करने में कोई खुशी नहीं होती और नाही कोई चाहत होती है।	0	1	2	3
2	उदास रहना हर वक्त निराशा में रहना	0	1	2	3
3	नींद का ना आना या फिर सोए रहने में असहित होना या बहुत ज्यादा सोए रहना	0	1	2	3
4	थकावट सी रहना या कमजोरी महसूस करना	0	1	2	3
5	खाने को दिल नहीं चाहता जरूरत से ज्यादा खाना	0	1	2	3
6	अपने आप में बुरा महिसूस करना जिंदगी में असफल समझना क्युकि आप अपनी और परिवार की देख-भाल नहीं करते	0	1	2	3
7	किसी भी काम में मन नही लगता जैसे की कुछ पढ़ना या लिखना या दूरदर्शन (T.V) देखना	0	1	2	3
8	इतनी आहिसता चलने और बातें करने हो कि लोग आप को रोगी समझने लगें इस का उलट - की आप हर समय बहुत जल्दी में और बेचैनी में रहते हो	0	1	2	3
9	आप यह सोचें की ऐसी जिंदगी से बे मौत अच्छी है। या फिर अपने को नुकसान करना चाहें।	0	1	2	3

APPENDIX-V: AIRWAY INVENTORY FOR RESPIRATORY DISEASES

ANXIETY INVENTORY FOR RESPIRATORY DISEASES

I have had worrying thoughts going through my mind.				
Not at all	Occasionally	Frequently	Almost all the time	
I have felt very frightened or panicky.				
Not at all	Occasionally	Frequently	Almost all the time	
I have felt worked-up and/or upset.				
Not at all	Occasionally	Frequently	Almost all the time	
I have had fear of losing control and/ or falling apart.				
Not at all	Occasionally	Frequently	Almost all the time	
I have worried about experiencing panic.				
Not at all	Occasionally	Frequently	Almost all the time	
I have found it hard to relax.				
Not at all	Occasionally	Frequently	Almost all the time	
I have had sudden and intense feelings of fear and/ or panic.				
Not at all	Occasionally	Frequently	Almost all the time	
I have felt generally anxious.				
Not at all	Occasionally	Frequently	Almost all the time	
I have felt nervous or on-edge.				
Not at all	Occasionally	Frequently	Almost all the time	
I have had thoughts that something bad might happen.				
Not at all	Occasionally	Frequently	Almost all the time	
TOTAL SCORE				

ANXIETY INVENTORY FOR RESPIRATORY DISEASES

रेस्पिरेटरी रोगों के लिए घबराहट/चिंता सूची

अपने पिछले दो हफ्तों को ध्यान में रखकर सबसे उचित विकल्प चुने |

1.मेरे दिमाग में चिंता करने वाले विचार चलते रहते हैं ।				
बिल्कुल नहीं	**कभी कभी**	**बार-बार**	**लगभग हमेशा**	
2.मैंने बहुत डरा या घबराया हुआ महसूस किया है।				
बिल्कुल नहीं	कभी कभी	बार-बार	लगभग हमेशा	
3.मैंने व्याकुल और / या परेशान महसूस किया है।				
बिल्कुल नहीं	कभी कभी	बार-बार	लगभग हमेशा	
4.मुझे अपना नियंत्रण खोने का और/या टूटने का डर हुआ है।				
बिल्कुल नहीं	कभी कभी	अक्सर	लगभग हर समय	
5.मैं घबराहट का सामना करने के बारे में चिंतित हूँ ।				
बिल्कुल नहीं	कभी कभी	बार-बार	लगभग हमेशा	
6.मैंने यह पाया है की मुझे आराम मिलना मुश्किल है।				
बिल्कुल नहीं	कभी कभी	बार-बार	लगभग हमेशा	
7.मैंने डर और / या घबराहट को अचानक और बहुत तेज़ महसूस किया है।				
बिल्कुल नहीं	कभी कभी	बार-बार	लगभग हमेशा	
8.मैंने आम तौर पर चिंतित महसूस किया है।				
बिल्कुल नहीं	कभी कभी	बार-बार	लगभग हमेशा	
9.मैं नर्वस या बौखलाया हुआ महसूस किया है।				
बिल्कुल नहीं	कभी कभी	बार-बार	लगभग हमेशा	
10.मुझे ये विचार आते है की कुछ बुरा हो सकता है।				
बिल्कुल नहीं	कभी कभी	बार-बार	लगभग हमेशा	
कुल स्कोर				

APPENDIX-VI: ALCOHOL USE DISORDERS IDENTIFICATIONS TEST (AUDIT)

AUDIT questionnaire

Please circle the answer that is correct for you

1. How often do you have a drink containing alcohol?

· Never
· Monthly or less
· 2-4 times a month
· 2-3 times a week
· 4 or more times a week

2. How many standard drinks containing alcohol do you have on a typical day when drinking?

· 1 or 2
· 3 or 4
· 5 or 6
· 7 to 9
· 10 or more

3. How often do you have six or more drinks on one occasion?

· Never
· Less than monthly
· Monthly
· Weekly
· Daily or almost daily

4. During the past year, how often have you found that you were not able to stop drinking once you had started?

· Never
· Less than monthly
· Monthly
· Weekly
· Daily or almost daily

5. During the past year, how often have you failed to do what was normally expected of you because of drinking?

· Never
· Less than monthly
· Monthly
· Weekly
· Daily or almost daily

6. During the past year, how often have you needed a drink in the morning to get yourself going after a heavy drinking session?

· Never
· Less than monthly
· Monthly
· Weekly
· Daily or almost daily

7. During the past year, how often have you had a feeling of guilt or remorse after drinking?

· Never
· Less than monthly
· Monthly
· Weekly
· Daily or almost daily

8. During the past year, have you been unable to remember what happened the night before because you had been drinking?

· Never
· Less than monthly
· Monthly
· Weekly
· Daily or almost daily

9. Have you or someone else been injured as a result of your drinking?

· No
· Yes, but not in the past year
· Yes, during the past year

10. Has a relative or friend, doctor or other health worker been concerned about your drinking or suggested you cut down?

· No
· Yes, but not in the past year
· Yes, during the past year

Scoring the AUDIT

Scores for each question range from 0 to 4, with the first response for each question (eg never) scoring 0, the second (eg less than monthly) scoring 1, the third (eg monthly) scoring 2, the fourth (eg weekly) scoring 3, and the last response (eg. daily or almost daily) scoring 4. For questions 9 and 10, which only have three responses, the scoring is 0, 2 and 4 (from left to right).

A score of 8 or more is associated with harmful or hazardous drinking, a score of 13 or more in women, and 15 or more in men, is likely to indicate alcohol dependence.

Saunders JB, Aasland OG, Babor TF et al. Development of the alcohol use disorders identification test (AUDIT): WHO collaborative project on early detection of persons with harmful alcohol consumption — II. Addiction 1993, 88: 791–803.

नाम: .....

दिनांक: ..... **जन्मतिथि:** .....

शराब आपके स्वास्थ्य को प्रभावित कर सकती है। विशेष कर तब जब आप किसी तरह की चिकित्सा ले रहें हों। हम चाहते हैं कि आप स्वस्थ रहें और शराब से होने वाले कुप्रभावों को हम कम कर सकें।

निम्नलिखित प्रश्न आपके शराब पीने की आदतों से संबंधित है। निचे एक बार में शराब पीने की मात्रा दर्शायी गयी है।

अपने उत्तर को गोल घेर दें	0	1	2	3	4
आप शराब की कम से कम एक पेग कितना सेवन करते हैं?	कभी नही	महीने में एक बार या कम	महीने में 2-4 बार	सप्ताह में 2-3 बार	सप्ताह में 4 से ज्यादा
जिस दिन आप शराब का सेवन करते हैं, उस दिन आप कितना पेग पीते हैं?	1 या 2	3 या 4	5 या 6	7 या 9	10 या ज्यादा
किसी एक अवसर पर आप शराब की चार या उससे ज्यादा पेग कितनी बार सेवन करते हैं?	कभी नही	माह से कम	मासिक	साप्ताहिक	लगभग प्रतिदिन
गत वर्षो में कितनी बार.....					
.....आपने ये जाना की जब आप पीना शुरू करते हैं तब खुद को रोक नहीं पाते?	कभी नही	माह से कम	मासिक	साप्ताहिक	लगभग प्रतिदिन
.....पीने के कारण आप वो करने में अक्षम रहें जो आप कर सकते थे?	कभी नही	माह से कम	मासिक	साप्ताहिक	लगभग प्रतिदिन
.....आपको सुबह में तरोताजा महसूस करने के लिए शराब पीना पड़ा, क्युंकि पिछली रात को आपने ज्यादा पी ली थी?	कभी नही	माह से कम	मासिक	साप्ताहिक	लगभग प्रतिदिन
.....पीने के बाद आपको अपराधबोध या पश्चाताप हुआ है?	कभी नही	माह से कम	मासिक	साप्ताहिक	लगभग प्रतिदिन
.....पीने वाली रात की घटनाओं को आप याद करने में अक्षम रहे हैं?	कभी नही	माह से कम	मासिक	साप्ताहिक	लगभग प्रतिदिन
	0	2			4
क्या आपके पीने की वजह से आपको खुद या किसी अन्य को अघात पहुचा है?	नहीं	हाँ पर गत वर्ष में नहीं			हाँ, गत वर्ष में
क्या आपके कोई सम्बन्धी , दोस्त, चिकित्सक या अन्य कोई स्वास्थ्यकर्मी आपकी शराबपीने की आदत को ले कर चिंतित हैं और वो चाहते हैं कि आप शराब पीना कम करें?	नहीं	हाँ पर गत वर्ष में नहीं			हाँ, गत वर्ष में
				कुल योग	

शराब की एक पेग की मानक मात्रा

फलों के रस के साथ मिश्रित वाइन	: 12 औंस
बियर	: 12 औंस
80 . ूफ़ वाली अल्कोहल	: 1.5 औंस
वाइन	: 5 औंस
ब्रांडी, शराब या मद्यपेय	: 4 औंस

Translated by : Dr. Kaushal Kumar Savera, RA(H), CRU(H), Siliguri
Back Translated by : Dr. Gurudev Choubey, RO(H), Scientist II, CRU(H), Siliguri

AUDIT 1/24/11

APPENDIX -VII: READINESS TO CHANGE QUESTIONNAIRE

READINESS TO CHANGE QUESTIONNAIRE

The following questionnaire is designed to identify how you personally feel about your smoking/tobacco right now. Please read each of the questions below carefully, and then decide whether you agree or disagree with the statements. Please tick the answer of your choice to each question. Your answers are completely private and confidential.

	Strongly Disagree	Disagree	unsure	Agree	Strongly Agree	
1. I don't think I use tobacco too much.	☐	☐	☐	☐	☐	☐ P
2. I am trying to use/tobacco less than I used to.	☐	☐	☐	☐	☐	☐ A
3. I enjoy my tobacco use , but sometimes I use too much.	☐	☐	☐	☐	☐	☐ C
4. Sometimes I think I should cut down on my tobacco use	☐	☐	☐	☐	☐	☐ C
5. It's a waste of time thinking about my tobacco use	☐	☐	☐	☐	☐	☐ P
6. I have just recently changed my tobacco habits.	☐	☐	☐	☐	☐	☐ A
7. Anyone can talk about wanting to do something about tobacco use, but I am actually doing something about it.	☐	☐	☐	☐	☐	☐ A
8. I am at the stage where I should think about using less tobacco	☐	☐	☐	☐	☐	☐ C
9. My tobacco use is a problem some times.	☐	☐	☐	☐	☐	☐ C
10. There is no need for me to think about changing my tobacco habit	☐	☐	☐	☐	☐	☐ P
11. I am actually changing my tobacco habits right now.	☐	☐	☐	☐	☐	☐ A
12. using less tobacco would be pointless for me.	☐	☐	☐	☐	☐	☐ P

Readiness to Change Questionnaire

		पूरी तरह से असहमत	असहमत	अनिश्चित	सहमत	पूरी तरह से सहमत	
1	मुझे नही लगता कि मैं बहुत अधिक तंबाकू इस्तेमाल करता हूँ						P
2	मैं कम से कम तंबाकू इस्तेमाल करने की कोशिश कर रहा हूँ						A
3	मुझे तंबाकू लेने में आनंद आता है लेकिन कभी कभी मैं बहुत ज्यादा तंबाकू ले लेता हूँ						C
4	मुझे अपने तंबाकू के सेवन में कटौती करना चाहिए						C
5	मेरे तम्बाकु लेने के बारे में सोचना समय की बर्बादी है						P
6	मैंने अभी हाल ही में अपनी तंबाकू लेने की आदतों को बदल दिया है						A
7	कोई भी तंबाकू सेवन के बारे में कुछ करने की इच्छा के बारे में बात कर सकते हैं लेकिन मैं वास्तव में इसके बारे में कुछ कर रहा हूँ						A
8	मैं एक ऐसी स्थिति में हूँ जहा से मुझे अब अपना तंबाकू सेवन कम करने के बारे में सोचना चाहिए						C
9	मेरा तंबाकू लेना कभी कभी समस्या बन जाता है						C
10	मुझे मेरे तंबाकू लेने की आदत को बदलने के बारे में सोचने का कोई मतलब नहीं						P
11	मैं वास्तव में अभी मेरी तंबाकू लेने की आदतों को बदलने वाला हूँ						A
12	कम तंबाकू लेना मेरे लिए व्यर्थ होगा						P

APPENDIX-VIII: PARTICIPANT INFORMATION SHEET

Participant Information Sheet

DATE……

Title: Association of Tobacco Smoking with Psychiatric Co-morbidities among Patients with Chronic Obstructive Pulmonary Disease

Principal investigator: Dr. Mahendra Singh Uikey **Contact no:** 8770409157
Chief guide: Dr. Prabhoo Dayal
Contact address: Junior Resident, Department of Psychiatry, AIIMS, New Delhi - 29

Introduction:
You are being invited to voluntarily take part in a research study "**Association of Tobacco Smoking with Psychiatric Co-morbidities among Patients with Chronic Obstructive Pulmonary Disease".** Before you make a decision, it is important for you to understand why this study is being done and what it will involve. Please take time to understand the following information carefully. Please do not hesitate to ask if there is anything that is not clear or if you would like more information. Take time to decide whether you wish to take part in this study. If you do take part, you will be asked to sign a consent form.

1. **Aims and methods of the research:** The study will be conducted at OPD of Department of Pulmonary Medicine and Sleep, AIIMS Delhi. Those individuals who are participating in the study according to inclusion and exclusion criteria would be interviewed using Semi-Structured Questionnaire, MINI, PHQ-9, AIR, FTND (in current smokers), AUDIT (if there is positive history of alcohol), RCQ (in current smokers). It will study the socio-demographic profile, severity and duration of COPD, psychiatric comorbidities, mainly anxiety and depression and their severity. In participants with history of alcohol use the study will identify alcohol use disorders using AUDIT. In current smokers, the study will assess for dependence on tobacco using FTND and motivation to quit smoking using RCQ. The study will assess for any association between psychiatric comorbidities and tobacco smoking in COPD patients. It will also compare the prevalence of psychiatric comorbidities in non-smokers COPD patients and smoker COPD patients.

2. **Expected duration of the subject participation:** You will be required to undergo a face-to-face interview which will last for approximately 70 minutes. Before beginning the interview, it is important that you read this document and understand the purpose of this study and nature of your involvement.

3. **Benefit out of study**: Psychiatric comorbidities are common in COPD patients. Information obtained will help in finding its association with tobacco smoking, alcohol use and sociodemographic factors. If you are found to be having any psychiatric comorbidity, you will be provided treatment for it. Also, you will be counselled and motivated to seek treatment for your problem with addiction.

4. **Risk to the subject associated with the study:** As the study only involves face-to-face interviews to generate information, the participants are not expected to be exposed to any additional risks due to the study.

5. **Confidentiality of participants and records:** No identifying information about you will be collected as part of this study. The information obtained from this study will be kept with utmost confidentiality. Nothing you say will be read by anyone other than the research team. You will be anonymous in any written and verbal reports of the study and your name will not be quoted or referred to anywhere.

6. **Compensation:** There is no provision of any compensation for participation in this study.

7. **Nature of participation:** Your participation in this study is completely voluntary. You are free to withdraw from the study at any time without citing any reason and without your legal rights being affected. You are also free to just participate in the interview and not refer anyone else for the same. Non-participation in this study will not affect any service / treatment which you may wish to receive.

8. **Sample collection and costs:** The study does not involve any collection of blood or any other samples from you. There are no cost implications on you for participation in this study.

9. **Next steps:** If you are willing to participate in this study after being given an opportunity to ask any questions, you will be asked to sign a consent form. Subsequently, you will be asked to respond to a questionnaire which will take about 70 minutes to complete.

10. **Human Rights:** To know more about the study or to submit any complaints regarding the study, please contact:

Member Secretary, Ethics Committee
All India Institute of Medical Sciences,
New Delhi
Phone: 011-26594579

प्रतिभागी सूचना पत्रक

दिनांक .....

शीर्षक: स्थायी अवरोधक फुफ्फुसीय रोग (सीओपीडी) के मरीजों में तम्बाकू धूम्रपान और मनोवैज्ञानिक सह-रोगों के बीच सम्बन्ध

प्रमुख अन्वेक्षक: डॉ महेंद्र सिंह उइके **संपर्क संख्या:** 877040157

मुख्य मार्गदर्शक: डॉ प्रभु दयाल

संपर्क पता: जूनियर रेजिडेंट, मनोचिकित्सा विभाग, एम्स, नई दिल्ली - 29

प्रस्तावना:

आपको स्वेच्छा से एक शोध अध्ययन में भाग लेने के लिए आमंत्रित किया जा रहा है **"स्थायी अवरोधक फुफ्फुसीय रोग (सीओपीडी) के मरीजों में तम्बाकू धूम्रपान और मनोवैज्ञानिक सह-रोगों के बीच सम्बन्ध"**| निर्णय लेने से पहले, यह समझना आपके लिए महत्वपूर्ण है कि यह अध्ययन क्यों किया जा रहा है और इसमें क्या शामिल होगा। कृपया निम्नलिखित जानकारी को ध्यान से समझने के लिए समय निकालें। कृपया यह पूछने में संकोच न करें कि यदि कुछ भी स्पष्ट नहीं है या यदि आप अधिक जानकारी चाहते हैं। यह तय करने के लिए समय लें कि क्या आप इस अध्ययन में भाग लेना चाहते हैं। यदि आप भाग लेते हैं, तो आपको एक सहमति फॉर्म पर हस्ताक्षर करने के लिए कहा जाएगा।

1. **अनुसंधान के लक्ष्य और तरीके:** अध्ययन पल्मोनरी मेडिसिन एंड स्लीप, एम्स दिल्ली विभाग के ओपीडी में आयोजित किया जाएगा। वे लोग जो शामिल करने और बहिष्करण मानदंडों के अनुसार अध्ययन में भाग ले रहे हैं, उनका अर्ध-संरचित प्रश्नावली का उपयोग करके साक्षात्कार किया जाएगा, मिनी, पीएचक्यू-9, एआईआर, एफटीएनडी (वर्तमान धूम्रपान करने वालों में), ऑडिट (यदि शराब का सकारात्मक इतिहास है), आरसीक्यू (वर्तमान धूम्रपान करने वालों में) का प्रयोग किया जायेगा। यह सामाजिक-जनसांख्यिकीय प्रोफ़ाइल, सीओपीडी की गंभीरता और अवधि, मनोवैज्ञानिक सह-रोग, मुख्य रूप से चिंता और अवसाद और उनकी गंभीरता का अध्ययन करेगा। अल्कोहल के इतिहास के साथ प्रतिभागियों में ऑडिट का उपयोग कर अल्कोहल उपयोग-विकारों की पहचान की जाएगी। मौजूदा धूम्रपान करने वालों में, एफटीएनडी का उपयोग करके तम्बाकू पर निर्भरता का आंकलन और आरसीक्यू का उपयोग करके धूम्रपान छोड़ने के लिए प्रेरणा का आकलन किया जायेगा। यह अध्ययन सीओपीडी रोगियों में मनोवैज्ञानिक सह-रोग और तंबाकू धूम्रपान के बीच किसी भी संगठन के लिए मूल्यांकन करेगा। यह गैर-धूम्रपान करने वाले सीओपीडी रोगियों और धूम्रपान करने वाले सीओपीडी रोगियों में मनोवैज्ञानिक सह-रोग के प्रसार की तुलना भी करेगा।

2. **विषय भागीदारी की अपेक्षित अवधि:** आपको आमने-सामने साक्षात्कार करना होगा जो लगभग 70 मिनट तक चलेगा। साक्षात्कार शुरू करने से पहले, यह महत्वपूर्ण है कि आप इस दस्तावेज़ को पढ़ लें और इस अध्ययन के उद्देश्य और अपनी भागीदारी की प्रकृति को समझें।

3. **अध्ययन से लाभ**: सीओपीडी रोगियों में मनोवैज्ञानिक सह-रोग आम हैं। प्राप्त जानकारी तम्बाकू धूम्रपान, शराब के उपयोग और समाजशास्त्र संबंधी कारकों के साथ अपने सहयोग को खोजने में मदद करेगी। यदि आपको कोई मनोवैज्ञानिक सह-रोग मिलता है, तो आपको इसके लिए उपचार प्रदान किया जाएगा। इसके अलावा, आपको व्यसन के साथ अपनी समस्या के इलाज के लिए सलाह दी जाएगी और प्रेरित किया जाएगा।

4. **अध्ययन से जुड़े विषय पर जोखिम:** अध्ययन के रूप में केवल जानकारी उत्पन्न करने के लिए आमने-सामने साक्षात्कार शामिल हैं, प्रतिभागियों को अध्ययन के कारण किसी भी अतिरिक्त जोखिम के संपर्क में आने की उम्मीद नहीं है।

5. **प्रतिभागियों और अभिलेखों की गोपनीयता:** इस अध्ययन के हिस्से के रूप में आपके बारे में कोई पहचान जानकारी एकत्र नहीं की जाएगी। इस अध्ययन से प्राप्त जानकारी को अत्यंत गोपनीयता के साथ रखा जाएगा। आप जो कुछ भी कहेंगे, वह शोध दल के अलावा किसी अन्य व्यक्ति द्वारा नहीं पढ़ा जाएगा। आप अध्ययन की किसी भी लिखित और मौखिक रिपोर्ट में अज्ञात होंगे और आपका नाम प्रस्तुत नहीं किया जाएगा या कहीं भी संदर्भित नहीं किया जाएगा।

6. **मुआवजा:** इस अध्ययन में भागीदारी के लिए किसी मुआवजे का कोई प्रावधान नहीं है।

7. **भागीदारी की प्रकृति:** इस अध्ययन में आपकी भागीदारी पूरी तरह से स्वैच्छिक है। आप बिना किसी कारण बताए और आपके कानूनी अधिकारों के प्रभावित किए बिना किसी भी समय अध्ययन से हटने के लिए स्वतंत्र हैं। आप साक्षात्कार में भाग लेने के लिए भी स्वतंत्र हैं और इसके लिए किसी और को संदर्भित नहीं करते हैं। इस अध्ययन में गैर-भागीदारी किसी भी सेवा / उपचार को प्रभावित नहीं करेगी जिसे आप प्राप्त करना चाहते हैं।

8. **नमूना संग्रह और लागत:** अध्ययन में आपके रक्त या किसी अन्य नमूने का संग्रह शामिल नहीं है। इस अध्ययन में भाग लेने के लिए आपके लिए कोई लागत प्रभाव नहीं है।

9. **अगला कदम:** यदि आप किसी भी प्रश्न पूछने का मौका देने के बाद इस अध्ययन में भाग लेने के इच्छुक हैं, तो आपको एक सहमति फॉर्म पर हस्ताक्षर करने के लिए कहा जाएगा। इसके बाद, आपको एक प्रश्नावली का जवाब देने के लिए कहा जाएगा जिसमें पूरा होने में लगभग 70 मिनट लगेंगे।

10. **मानवाधिकार:** अध्ययन के बारे में और अध्ययन के बारे में कोई शिकायत जमा करने के लिए, कृपया संपर्क करें:

सदस्य सचिव, नीतिशास्त्र समिति
अखिल भारतीय आयुर्विज्ञान संस्थान,
नई दिल्ली
फोन: 011-26594579

APPENDIX- IX: PARTICIPANT INFORMED CONSENT FORM

Participant Informed Consent Form (PICF)

Participant identification number: ……...

Title: Association of Tobacco Smoking with Psychiatric Co-morbidities among Patients with Chronic Obstructive Pulmonary Disease

Principal Investigator: Dr Mahendra Singh Uikey **Contact No.-** 8770409157

Contact address: Junior Resident, Department of Psychiatry, AIIMS, New Delhi - 29

The contents of the information sheet dated ……. that was provided have been read carefully by me / explained in detail to me, in a language that I comprehend, and I have fully understood the contents. I confirm that I have had the opportunity to ask questions.

The nature and purpose of the study and its potential risks / benefits and expected duration of the study, and other relevant details of the study have been explained to me in detail. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal right being affected.

I understand that the information collected about me from my participation in this research and sections of any of my medical notes may be looked at by responsible individuals from AIIMS. I give permission for these individuals to have access to my records.

I give my full, free and willing consent to take part in the above study.

---------- Date:

(Signature / Left Thumb Impression) Place:

Name of the Participant: _____

Son / Daughter / Spouse of: _____

Complete postal address: _____

This is to certify that the above consent has been obtained in my presence.

---------- Date:

Signatures of the Principal Investigator Place:

1) Witness – 1	2) Witness – 2
----------	----------
Signature	Signature
Name: ……	Name: …….....

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<u>प्रतिभागी सूचित सहमति फॉर्म (पीआईसीएफ)</u>

प्रतिभागी पहचान संख्या: .....

शीर्षक: स्थायी अवरोधक फुफ्फुसीय रोग (सीओपीडी) के मरीजों में तम्बाकू धूम्रपान और मनोवैज्ञानिक सह-रोगों के बीच सम्बन्ध

प्रधान अन्वेक्षक : डॉ महेंद्र सिंह उइके **संपर्क** संख्या- 8770409157

संपर्क पता: जूनियर रेजिडेंट, मनोचिकित्सा विभाग, एम्स, नई दिल्ली - 29

सूचना पत्र की सामग्री ..... जो प्रदान किया गया था, उसे मेरे द्वारा सावधानी से पढ़ा गया है / विस्तार से समझाया गया है, एक भाषा में जिसे मैं समझता हूं, और मैंने सामग्री को पूरी तरह से समझ लिया है। मैं पुष्टि करता हूं कि मुझे प्रश्न पूछने का अवसर मिला है।

अध्ययन की प्रकृति और उद्देश्य और इसके संभावित जोखिम / लाभ और अध्ययन की अपेक्षित अवधि, और अध्ययन के अन्य प्रासंगिक विवरणों को विस्तार से समझाया गया है। मैं समझता हूं कि मेरी भागीदारी स्वैच्छिक है और मैं किसी भी समय बिना किसी कारण के, मेरी चिकित्सा देखभाल या कानूनी अधिकार प्रभावित होने के बिना वापस लेने के लिए स्वतंत्र हूं।

मैं समझता हूं कि इस शोध में मेरी भागीदारी से मेरे बारे में एकत्र की गई जानकारी और मेरे किसी भी मेडिकल नोट के अनुभाग एम्स से जिम्मेदार व्यक्तियों द्वारा देखे जा सकते हैं। मैं इन व्यक्तियों के लिए अपने रिकॉर्ड तक पहुंचने की अनुमति देता हूं।

मैं उपर्युक्त अध्ययन में भाग लेने के लिए अपनी पूर्ण, स्वतंत्र और इच्छुक सहमति देता हूं।

---------- तिथि:

(हस्ताक्षर / बाएं अंगूठे का निशान) स्थान:

प्रतिभागी का नाम: _____

पुत्र / बेटी / पति / पत्नी: _____

पूरा डाक पता: _____

यह प्रमाणित करना है कि उपर्युक्त सहमति मेरी उपस्थिति में प्राप्त की गई है।

---------- दिनांक:

प्रधान अन्वेषक हस्ताक्षर स्थान:

1) साक्षी - 1

हस्ताक्षर

नाम: .....

2) साक्षी - 2

हस्ताक्षर

नाम: .....

APPENDIX- X: ETHICAL CLEARANCE

INSTITUTE ETHICS COMMITTEE FOR POST GRADUATE RESERACH
ALL INDIA INSTITUTE OF MEDICAL SCIENCES
ANSARI NAGAR, NEW DELHI 110029
Room No 102, 1st Floor Old O.T. Block,
Tel No 4579 (Internal), 26594579 (Direct)

Dated: 20.07.2018

Dr. Mahendra Singh Uikey
Junior Resident
Deptt. of Psychiatry
AIIMS, New Delhi

Ref. No. IECPG-310/18.07.2018

Through Guide: Dr. PrabhooDayal,

Sub: Association of tobacco smoking with psychiatric co-morbidities among patients with chronic obstructive pulmonary disease

Dear Dr. Uikey

This has reference to your above mentioned protocol. The protocol was discussed in the Ethics Committee for Post Graduate research (Clinical Science) meeting held on 18.07.2018 at 3:00 P.M. in the Ethics Committee room, AIIMS, and the following members of the ethics committee for post graduate research attended the meeting.

1. Dr. S.K. Maulik, Professor Deptt. of Pharmacology, AIIMS - Acting Chairman
2. Dr.PushpendraVerma, Consultant, Deptt. of TB & Chest Diseases LHMC, New Delhi - Member
3. Dr. Jagriti Bhatia, Professor, Deptt. of Phramacology, AIIMS - Member
4. Dr.Surabhi Vyas, Associate Professor, Deptt. of Radiodiagnosis, AIIMS - Member
5. Dr. Rohit Bhatia, Prof. Deptt. of Neurology - Member
6. Dr.VimiRewari, Prof. Deptt. of Anesthesiology, AIIMS - Member
7. Dr. BanusriVelpandian, Advocate, Legal Person- Member
8. Dr. B.K. Das, Professor, Deptt. of Microbiology - Member
9. Dr. Sanjeev Sinha, Professor, Deptt. of Medicine, AIIMS- Member-Secretary

The protocol has been approved from ethical angle w.e.f. 18.07.2018 subject to the following conditions:

- The approval is valid for the period of the conduct of study according to this protocol under the responsibility **Dr. Mahendra Singh Uikey,**
- No significant changes to the research protocol should be made and implemented without prior consent of the IEC and any changes/deviations from the protocol which increase the risk for the subjects should be submitted to the IEC and approved by it prior to implementation.
- It is hereby confirmed that neither you nor any of the study team members have participated in the voting/decision making procedures of the committee.
- IEC should be informed about all SAE's occurring in the study as per DCGI guidelines. The Study progress report should be made available to the IEC for review every 6 months and completion report must be submitted along with PDF format of the thesis protocol at iecpgcompletionreport@gmail.com.

With best regards,
Yours truly,

Sanjeev Sinha

Dr. Sanjeev Sinha
Member-Secretary
Ethics Committee for Post Graduate Research