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#### **Research Article**

# COPD in India: A Review of the Impact of Biomass Smoke Exposure on COPD Risk

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#### Abstract

COPD is the third leading cause of death worldwide and has a particular impact on the population of India. About 53 million people are affected by COPD in India, and this disease disproportionately affects those in the low-middle income class. This review explores the global impact of COPD and its impact on the population of India. Within the country, there is also regional and gender variation in the impact of COPD. Moreover, the contribution of biomass smoke exposure on the development of COPD is particularly pronounced in India. We conducted a literature search on common databases of publications that discuss the risk of biomass exposure on development of COPD, particularly in India. Identifying differences and recognizing the importance of biomass smoke exposure will allow for future efforts to reduce their impact on the population of India.

# **INTRODUCTION**

The prevalence of chronic respiratory diseases has been increasing [1], with a 39.8% increase in the prevalence of chronic respiratory diseases between 1990 and 2017. An estimated 544.9 million people globally live with chronic respiratory diseases [1]. Estimates of the prevalence of chronic obstructive pulmonary disease (COPD) range. One study suggested that 384 million cases of COPD, comprising 11.7% of global prevalence, occurred in 2010 [2]. Globally, estimates suggest 328 million people had COPD in 2015 [3]. The incidence of COPD was estimated at 11.7 per 1,000 people per year based on spirometry but only 5.8 per 1,000 per year based on medical record documentation - almost a twofold difference - reinforcing the potential for underestimation of COPD impacts on global health [4]. COPD is currently the third leading cause of death worldwide (WHO) and is estimated to have a global disease mortality of 3.2 million in the year 2015 [5].

Significant heterogeneity exists globally in incidence and impact of COPD. COPD incidence is estimated around 0.2% in Japan, around 37% in the United States of America (USA), and between 2.1%-26.1% in Europe [4]. A large cohort study in the Netherlands estimated a baseline prevalence of 4.7% with a incidence rate of 8.9/1000 person years resulting in a cumulative prevalence of 13.6% over the course of the study [4]. Similarly, a study of a population in Oregon, USA based on the Burden of Obstructive Lung Disease (BOLD) Initiative estimated that the prevalence of COPD Global Initiative for COPD (GOLD) stage 2 or greater is 11.8% in men and 8.5% in women [6]. Other studies from the USA suggest prevalence from 10-20% based on spirometry and 18% when self-reported [6].

Ninety percent of patients with COPD live in the low and lower-middle income countries (LMIC) [7]. These countries are defined by the World Bank as countries with a gross national income per capita of \$1,035 or less (low income) or a gross national income per capita between \$1,036 to \$4,045 (lowermiddle income) in 2019 [8]. Moreover, more than 90% of COPDrelated deaths occur in LMIC [9]. LMIC have a higher proportion of under-diagnosis of COPD and have worse morbidity and mortality compared to higher income countries [10]. Potential etiologies of this disparity include limited healthcare access, higher prevalence of asymptomatic younger individuals, poor health literacy, and underreporting of symptoms [10]. Whereas studies from high income countries suggest prevalence of up to 37%, a 2016 study of a population in India suggested a prevalence of 5.7% to 17% based on spirometry and only 1% to 10% based on patient self-reporting [11]. A study in southern Ethiopia estimated a prevalence of 17.8% for COPD [12]. These combined data suggest the potential for underreporting in these countries resulting in lower prevalences compared to higher income countries. In addition, the economic impact of COPD is significant, and estimates suggest that COPD will cost LMIC 1.7 million euros by 2030 [13].

COPD prevalence is directly correlated with increased age and tobacco smoke exposure. The incidence is higher in older age, men, and smokers [4]. With each 10year increase in age, the pooled odds ratio estimate is 1.94 [6]. The disease is male predominant, with estimates of 50 to 55% male predominance in the USA and India, respectively [10]. The main risk factors for the development of COPD are tobacco smoking and ambient particulate matter, household air pollution, occupational particulates, ozone, and second-hand smoke [5]. These risk

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factors account for 73.3% of DALYs due to COPD [5]. It is important to note that air pollution is the third leading cause of COPD [5]. Population-based air pollution and ozone-levels in many of the world's most populated countries has increased in the past 10 years, including in India, and continues to be high in China [14].

In 2015, 3.2 million people died from COPD, which was an increase of 11.6% compared with the year 1990 [5]. In a global burden of disease study between 1990 and 2015, COPD accounts for 1,273 disability-adjusted life years (DALY) per 100,000 people for men and 717 DALYs for women [5]. India and China account for 33% of the global population however mortality is disproportionately high with India and China accounting for 66% of global COPD deaths [11].

#### **METHODS**

Review of existing literature regarding COPD and biomass exposure was performed by searching Pubmed and Web of Science databases between the years 2000 and 2020. Search terms used included "COPD" or "chronic obstructive pulmonary disease" AND "biomass" or "biomass exposure" or "biomass smoke" AND "India." Initial results yielded 52 entries in Web of Science and 20 entries in PubMed. Further review allowed exclusion papers that were redundant or did not address biomass smoke exposure risk. Review of references cited in these articles was also performed. In total, 34 studies were eventually included in the review which included observational cohort studies, including population studies, systematic reviews, meta-analyses, and opinion pieces.

#### RESULTS

Estimates suggest that 53 million people in India have COPD [15], with a male-to-female ratio of 1.5-to-1 [16]. Early studies between 1964 and 1995 in India estimate the prevalence of COPD to be between 3 to 8% in men and 2.5 to 4.5% in women [17]. A questionnaire-based study of over 160,000 people across 12 districts estimated an overall prevalence of 3.49% of chronic bronchitis [18]. A subsequent 2012 meta-analysis estimated disease prevalence of chronic bronchitis in rural areas to be between 6.5 to 7.7% [19]. Age-adjusted prevalence in 1990 across all states in India (population 1,316 million) was 5.8% compared with 5.5% in 2016 [19]. A study of patients in Delhi found a disease prevalence of 4% [17]. There is significant heterogeneity in point estimates of COPD prevalence depending on study location and methodology.

The population of India is disproportionately distributed with over 70% of the living in rural areas [22]. In those with lower socioeconomic status, which account for 626 million people, the prevalence of COPD was estimated to 5.8% [20]. In those in the lower-middle socioeconomic status, which account for 92 million people, the prevalence was 5.7% [20]. Disease prevalence is higher in the northern Indian states of Jammu and Kashmir, Himachal Pradeshh, Haryana, Uttarakhand [20]. The BOLD study estimated COPD prevalence in various regions of India using spirometry and found a prevalence of 5.7% in men and 6.8% in women in Pune, 6% in men and 7.6% in women in Mumbai, and 17.3% in men and 14.8% in women in Srinagar [23].The prevalence of COPD increased by 44.2% between 1990 and 2015 [5], and the total number of cases of COPD increased from 28.1 million in 1990 to 55.3 million in 2016 [20]. Chronic respiratory diseases account for 6.4% of DALYs in 2016, increased from 4.5% in 1990<sup>20</sup>. COPD is the eighth leading cause of disability in India [21] and accounts for 4.8% of DALY (5.2% in men and 4.4% in women) [11]. The disease accounts for 75.6% of chronic respiratory disease DALYs in India [20]. The 53.7% of DALYs were attributable to air pollution, 25.4% attributable to tobacco use, and 16.5% attributable to occupational exposures [20]. In the low epidemiological transition level, including Jharkhand, Uttar Pradesh, and Rajasthan, COPD contributes to 1,700 DALYs per 100,000 population, compared with a 1,292 per 100,000 DALY in the high epidemiological transition level areas, such as Punjab and Himachal Pradesh [20]. In 2015, the age-adjusted DALY was over 2,000 [5]. The highest DALY in 2016 were in the states of Rajasthan and Uttar Pradesh [20].

Sex differences have been reported in risk factors for the development of COPD in India. The prevalence of COPD in men compared to woman occurs at a 1.5 to 1 ratio in India [16]. However, tobacco smoking is a predominantly male activity, and tobacco smoking occurs in a ratio of 10 to 1 in men compared to women. This suggests a great role for non-smoking associated risk factors for COPD, particularly in women [16]. Women in villages in India are exposed to an average of 4 to 6 hours of biomass smoke (BMS) per day while cooking [16]. Indoor levels of carbon monoxide, sulfate, and nitric oxide in rural India are dangerously high and remain at unsafe levels up to three hours after cooking [22]. Thus, BMS-induced COPD is pervasive in rural Indian women [16].

Together, COPD, asthma, and other respiratory illnesses are the second leading cause of death in patients ages 25 to 69 years in India, equaling about 10.2% of deaths [11]. COPD alone accounts for 8.7% of total deaths (8.7% in men and 8.6% in women) [20]. COPD is the fourth leading cause of lost life years in many Indian states [21]. Approximately 500,000 people in India annually from COPD, four times the amount of people who die from COPD in the US and Europe [11]. Finally, the economic burden of COPD was estimated to be 35,000 Crores of Rupees (350 billion rupees) [17].

#### **DISCUSSION**

In recent years, BMS exposure has been an emerging area of interest as a risk factor for COPD and as a significant contributor to morbidity and mortality [3]. Compared with 1.1 billion tobacco smokers worldwide, 3 billion people are exposed to BMS in toxic amounts [16]. Similar to tobacco smoke, BMS leads to oxidative stress [24]. Over 2 billion kilograms of biomass fuel are burned daily in open fires and stoves, and household air pollution accounts for up to 4 million deaths annually [7]. This exposure can be equated to smoking two packs of cigarettes daily [25]. Just as smoking is a modifiable risk factor for COPD, so too is BMS exposure, and many green initiatives aimed at reducing the level of BMS in household scross India, including changes such as improved household ventilation and use of solar energy and cooking gas for cooking, among other changes.

Moreover, the effect of biomass smoke begins during peripartum and childhood. BMS-exposure is associated with low

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birth weight, increased infant mortality, reduced lung function, and increased risk of lower respiratory tract infections in children [26]. Several longitudinal studies in children suggest outdoor air pollution leads to delay in lung function development in children and adolescents [3]. In one study, children who grew up in the most polluted communities were five times more likely to have low lung functions (defined as forced expiratory volume in 1 second <80% of expected) compared with children who grew up in the least polluted communities [27].

The pathophysiology of BMS-associated COPD is not fully understood. BMS-associated COPD is a heterogeneous disease that predominantly involves bronchi and is more often associated with respiratory failure and airway hyperinflation compared to tobacco smoking-associated COPD [16]. It is also associated with worse hypoxemia [28]. In a study comparing smokers and nonsmokers with COPD, non-smokers had increased dyspnea, lower PaO2, and lower SaO2 compared with smokers with similar spirometry results [28]. On spirometry, there is usually milder airway obstruction with higher DLCO compared to tobacco smokers [29]. Non-smoking COPD patients have lower forced expiratory volumes in 1 second over forced vital capacity ratios and lower forced expiratory volumes in 1 second compared to predicted values [30]. BMS exposure may also be an important risk factor in the development of TB and lung infections [24]. it is difficult to compare with any accuracy BMS exposure related COPD with other forms, including smoking-associated COPD due to inability to calculate the exact amount of BMS exposure with reasonable accuracy. Patients with BMS-associated COPD have increased eosinophilia, IgE levels [29], anthracotic pigment deposition, and thickening of airway walls and vascular endothelium [29]. Other studies have noted increased elastolytic activity of macrophages and increased levels of C-reactive protein levels in the serum [24]. The disease is associated with lower concentrations of IL-6, IL-8, and mononuclear cells in sputum [28], markers which are known to be associated with tobaccorelated COPD [28]. Patients with BMS exposure COPD have more CD4 inflammatory mediators such as TH2, IL-4 and IL-10 [24]. Serum concentrations of CCL15, CCL27, and CXL13 were higher in patients with BMS exposure but without COPD compared with COPD patients, suggestive a protective role of these cytokine markers [16].

Several studies have demonstrated an independent risk association with BMS exposure. BMS exposure may affect the development of peak lung function and lead to a sharper decline in function [3]. A meta-analysis of 15 studies found an odds ratio of 1.95 with exposure to BMS and COPD development [3]. Similarly, a study of a population in southern Ethiopia found that exposure to BMS had an adjusted odds ratio of 2.05 for development of COPD [12]. Another systematic review of 24 studies focusing on women found that BMS exposed women were 1.38 times more likely to be diagnosed with COPD compared with those who were not exposed to BMS [31], and the association was noted in both urban and rural areas. The pooled odds ratio in rural areas was 1.95 compared with a pooled odds ratio of 1.61 in urban areas [31]. In a study of primary care clinics in several Latin American countries, BMS exposure had an adjusted odds ratio of 2.28 for development of COPD, and tobacco smoking had an adjusted odds ratio of 3.30 [32]. Of these COPD patients included, 40% reported exposure to BMS [32]. In a meta-analysis of 15 studies from various nations including India, BMS exposure was associated with a 2.3 odds ratio of COPD [33]. These phenomena may explain why in never smokers, a female predominance is present [4]. More than 1 in every 4 females with COPD are never smokers [4], and this is probably an underestimation. A study of a selected population of women over 35 years of age near Mexico City also found that the exposure to BMS was 47% in women [34]. The estimated prevalence was 3.1% in people with BMS exposure compared with 2.5% in the overall population suggesting that BMS-exposure related COPD occurs in rural and urban populations alike [34].

#### **CONCLUSION**

COPD is the third leading cause of death worldwide and contributes significantly to morbidity and DALYs. These effects are disproportionate in LMIC such as India. Women in rural India are particularly at risk for BMS-associated COPD given their lifelong exposure to household air pollutants due to social norms. Many studies have demonstrated the increased risk of developing COPD with BMS-exposure. Multiple reviews exist focusing on the epidemiology and prevalence of COPD globally and in various countries, including India. This review focuses particularly on the impact of biomass exposure on the development and progression of COPD in India, a country with high biomass exposure in daily life. This is the first review in recent years to delve into the risk associated with BMS exposure. Recognition of the role of BMS in COPD, particularly in India, is necessary to begin working toward reducing the morbidity and mortality of this very common disease.

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