Original Article

Prevalence of chronic obstructive pulmonary disease in India: A systematic review and meta-analysis

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ABSTRACT

Background and Objective: The prevalence of chronic obstructive pulmonary disease (COPD) is increasing worldwide. There is a lack of national-level estimates on the magnitude of COPD in India. Hence, we estimated the prevalence of COPD among adults in India. **Methods:** We searched PubMed, Embase, Cochrane Library, Google Scholar, and Scopus and included community-based cross-sectional studies reporting data on the prevalence of COPD among adults based on spirometry. A random-effects model was used to estimate the pooled prevalence of COPD. **Results:** In the eight identified studies, (pooled sample of 8,569 individuals), the estimated prevalence was 7.4% (95% confidence interval: 5.0%–9.8%), I^2 = 95.4% (P < 0.001). The prevalence was higher among males, in the urban area, and the northern region. **Conclusion:** Adequate training and resources should be provided to diagnose COPD at primary health care level for early management. A nationwide population-based survey is indicated to provide reliable estimates of the burden to inform evidence-based community-based interventions.

KEY WORDS: Adults, chronic obstructive pulmonary disease, community, cross-sectional, India, prevalence

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INTRODUCTION

Globally, chronic obstructive pulmonary disease (COPD) is among the leading causes of morbidity and mortality.[1] COPD was estimated to be the sixth leading cause of death in 2019.[2] According to the 2017 GBD study, of all the chronic respiratory diseases, COPD contributed 50% of all cases and 69% of years lived with disability.[3] More than 90% of COPD-related deaths occur in low- and middle-income countries (LMICs).[4] Apart from causing a huge economic burden, COPD causes disability and impairs the quality of life, loss of productivity, increased hospital admissions, and premature mortality.[5] The global prevalence of COPD, as per the estimates by Adeloye *et al*. is 11.37% (95% confidence interval [CI]: 10.76–11.96).[6] A review by Rehman *et al*. in 2019, to estimate the economic burden of COPD in Europe reported that the annual per-patient cost of work productivity loss was highest in Germany (€5735) and lowest in Greece (€998).[7]

The diagnosis of COPD requires a broader approach which includes assessment based on symptoms, risk factors, and spirometry.[8] The prevalence of COPD is underestimated as most symptoms such as cough and dyspnea are ignored by the patients until they worsen, and are not confirmed by objective lung function tests.[9-11] Spirometry is necessary to

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diagnose COPD, and is increasingly used in epidemiological studies to objectively assess airway obstruction.[12-14] Even with increasing consensus on the use of spirometry, cut-off points for detecting airway limitation vary.[15] There is a lack of national-level estimates on the burden of COPD in India. Previous studies have attempted to review the status of COPD in India qualitatively.[16] Moreover, many of the estimates are based on varying definitions and diagnostic criteria of COPD. Hence, in order to address the above-mentioned methodological issues, we conducted a systematic review and meta-analysis to estimate the prevalence of COPD among adults diagnosed by spirometry in India.

SEARCH STRATEGY

A comprehensive literature search was conducted for studies published since their inception to December 31, 2020, in the following databases: Medline through PubMed, Embase, Cochrane Library, Scopus, and Google Scholar, without any language restriction, using MeSH terms and keywords. We used the Preferred reporting items for systematic review and meta-analysis statement for reporting systematic review and meta-analysis as a guide for this study.[17]

INCLUSION AND EXCLUSION CRITERIA

The eligible studies were identified by performing an initial screening of identified titles and abstracts, followed by a full-text review. We included only those studies which adhered to the following criteria: (1) it was a population/community-based cross-sectional study, (2) reporting prevalence of COPD among the Indian population, (3) diagnosis of COPD based on spirometry, and (4) sufficient data were available in the article to extract both the numerator and denominator for the prevalence of COPD. Exclusion criteria were as follows: (1) studies assessing the burden of COPD among patients with other chronic conditions such as kidney disease and heart failure because they might show higher than expected prevalence and (2) letters, abstracts, conference papers, review articles, modeling studies, and studies not conducted on humans.

STUDY SELECTION, DATA EXTRACTION, AND QUALITY ASSESSMENT

Two independent reviewers (RAD and SKG) screened all the titles and abstracts of retrieved records. All duplicates were removed after verifying the recent version. Reference lists of the retrieved studies were also searched for additional sources. The full-text studies were retrieved for the selected abstracts, and the final inclusion in the review was based on full-text reading. There was a complete agreement between the two reviewers. A data extraction form was developed in Microsoft Excel, which was used to extract information on author name, year of publication, place, location, sample size, the proportion of females, criteria used and the reported prevalence of COPD. Risk of bias assessment was done based on the Critical Appraisal Skills Programme checklist.[18]

DATA SYNTHESIS AND STATISTICAL ANALYSIS

We provided summary estimates of the prevalence of COPD and used 95% CI to gauge the precision of the summary estimate. The standard error was calculated using the prevalence and sample size from each included studies. The meta-analysis was performed by package *metan*[19] in STATA[20] version 14.0 (Stata Corporation, College Station, TX, USA), using random-effects model, weighted by the inverse of the variance. I^2 statistic was calculated to estimate the amount of heterogeneity. Publication bias was assessed by the visual inspection of funnel plot and the small-study effect was assessed by Egger's test. Subgroup analysis was done based on study setting, geographical region, and gender. Sensitivity analysis was done by excluding studies that used other than GOLD criteria and by excluding the study undertaken exclusively on women participants.

RESULTS

Overall, 770 studies were initially retrieved from the databases and through cross-references. After removing the duplicates (101 studies), 669 studies (titles and abstracts) were screened for inclusion criteria, of which, a total of 32 eligible abstracts were selected, and their full-texts were screened. Finally, eight studies satisfied the inclusion criteria and were included in this meta-analysis [Figure 1].

CHARACTERISTICS OF STUDIES INCLUDED IN THE META-ANALYSIS

This review includes 8,569 individuals, of which 50.8% are females. The majority of the studies used GOLD criteria to diagnose COPD except the study done by Gupta *et al*.[21] where forced expiratory volume during the 1st s (FEV_1)/forced vital capacity (FVC)<lower limit of normal (LLN) criteria was used to classify COPD [Table 1]. The studies conducted by Koul *et al*.[22] and Christopher *et al*.[23] reported estimates of the prevalence of COPD by both cut-offs; for the calculation of the summary estimate, we considered the FEV_1/FVC<LLN criteria. Out of eight studies, three studies[21,22,24] were conducted in the urban region, and three were from south. The study by Mukherjee *et al*.[25] was conducted exclusively on women participants in Burdwan, Birbhum, Hooghly, Nadia, and South 24-Pargans districts of West Bengal. All the studies included in this meta-analysis diagnosed COPD based on either or both of the two above-mentioned cut-offs. As per GOLD criteria, patients with FEV1/FVC (forced expiratory volume in the first second/forced vital capacity) ratio of <0.7 are considered to have airway obstruction, and based on the obtained values, the patient is classified into any one of the 4 categories, i.e. GOLD stage 1 (mild): ≥80%; stage 2 (moderate): 50%–79%; stage 3 (severe): 30-49; and stage 4 (very severe) <30%.[26] Postbronchodilator FEV1/FVC < LLN, defined as a z-score for FEV1/FVC below the 5th percentile derived from population-based normative data adjusted for age, sex, and ethnicity.[27]

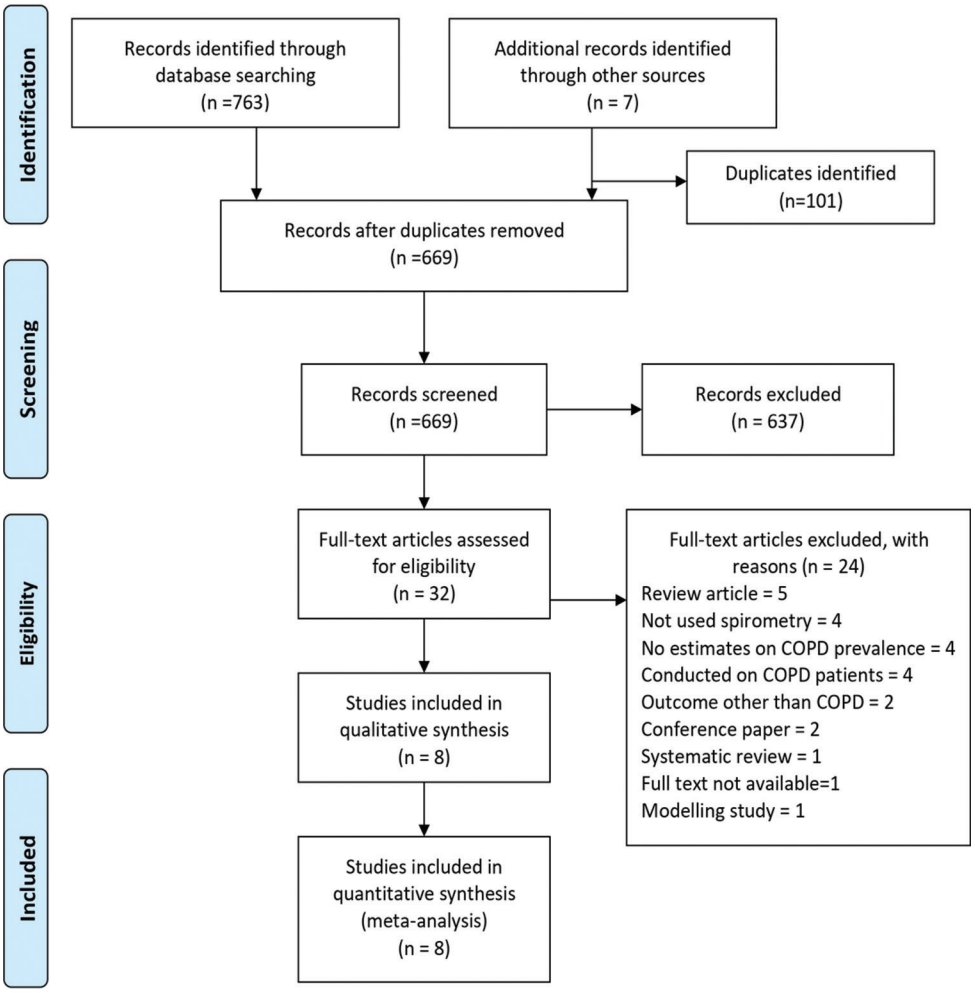

Figure 1: Flow of selection of studies for meta-analysis

PREVALENCE OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN INDIA

The prevalence of COPD from the eight studies ranged from 2.4% in a cross-sectional study done by Johnson *et al*.[28] in Southern India, to 16.1% by Koul *et al*.[22] conducted in Northern India [Table 2]. The random-effects pooled estimate for the prevalence of COPD among the Indian population was 7.4% (95% CI: 5.0%–9.8%) [Figure 2]. There was significant heterogeneity between the studies. Heterogeneity test showed I^2 value of 95.5% and $P < 0.001$.

SUBGROUP ANALYSIS

Prevalence of chronic obstructive pulmonary disease-based on gender

Out of the eight studies, gender-wise prevalence was reported in five studies. The prevalence of COPD among males and females were 11.4% (95% CI: 6.0%–16.9%) and 7.4% (95% CI: 5.2%–9.6%), respectively. We did not observe any decrease in heterogeneity among this sub-group. There was a significant difference in the heterogeneity between the studies as shown in Figure 3 ($P < 0.001$).

Prevalence of chronic obstructive pulmonary disease-based on study setting

Out of the eight studies, three studies were conducted in an urban area. The prevalence of COPD in the rural and urban areas was 5.6% (95% CI: 3.3%–6.8%) and 11.4% (95%CI: 7.6%–15.2%), respectively. We did not observe any decrease in heterogeneity. There was significant difference in the heterogeneity between the studies of rural and urban setting as shown in Figure 4 ($P < 0.001$).

Prevalence of chronic obstructive pulmonary disease-based on geographical distribution

Out of the eight studies, four studies are conducted in the northern part of India, three studies in the southern part of India, and one study in the east. The prevalence of COPD in these regions was 10.4%, 3.7%, and 6.8%, respectively. We observed a mild decrease in heterogeneity in the southern part of India. There was a significant difference in the heterogeneity between the studies based on geographical region as shown in Figure 5 ($P < 0.001$).

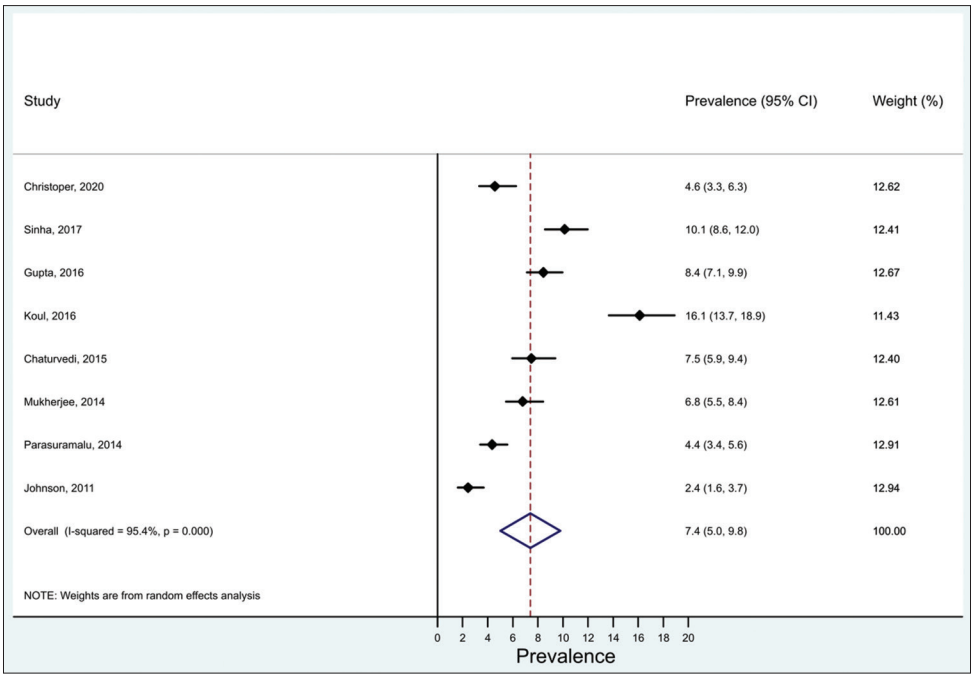

Figure 2: Forest plot of the meta-analysis for the prevalence of chronic obstructive pulmonary disease

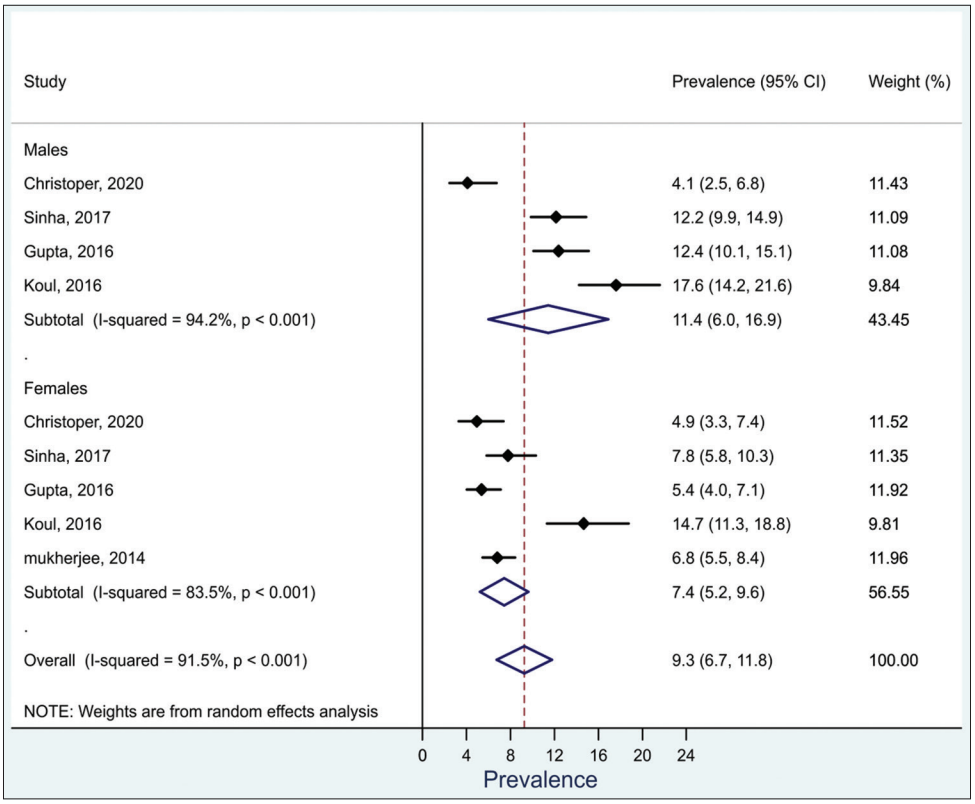

Figure 3: Forest plot of the meta-analysis for the prevalence of chronic obstructive pulmonary disease based on gender

QUALITY ASSESSMENT

Across the nine quality domains evaluated, majority of the studies met five or more of the quality criteria [Table 3]. Three studies met all the quality criteria assessed.[23,24,28] Five studies did not mention CIs in their main results. The sample size of three studies was not based on pre-study considerations of statistical power. Three studies did not clearly explain the methods of selection of the participants. All the eight studies had measurements that were likely to be valid and reliable and achieved a satisfactory response rate.

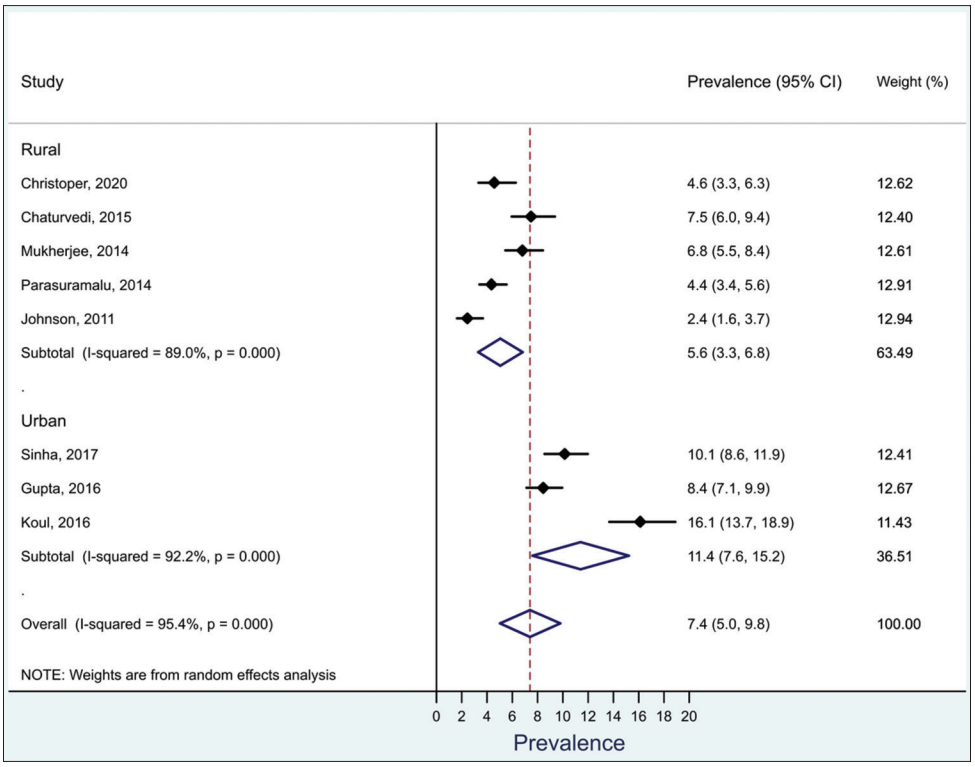

Figure 4: Forest plot of the meta-analysis for the prevalence of chronic obstructive pulmonary disease based on study setting

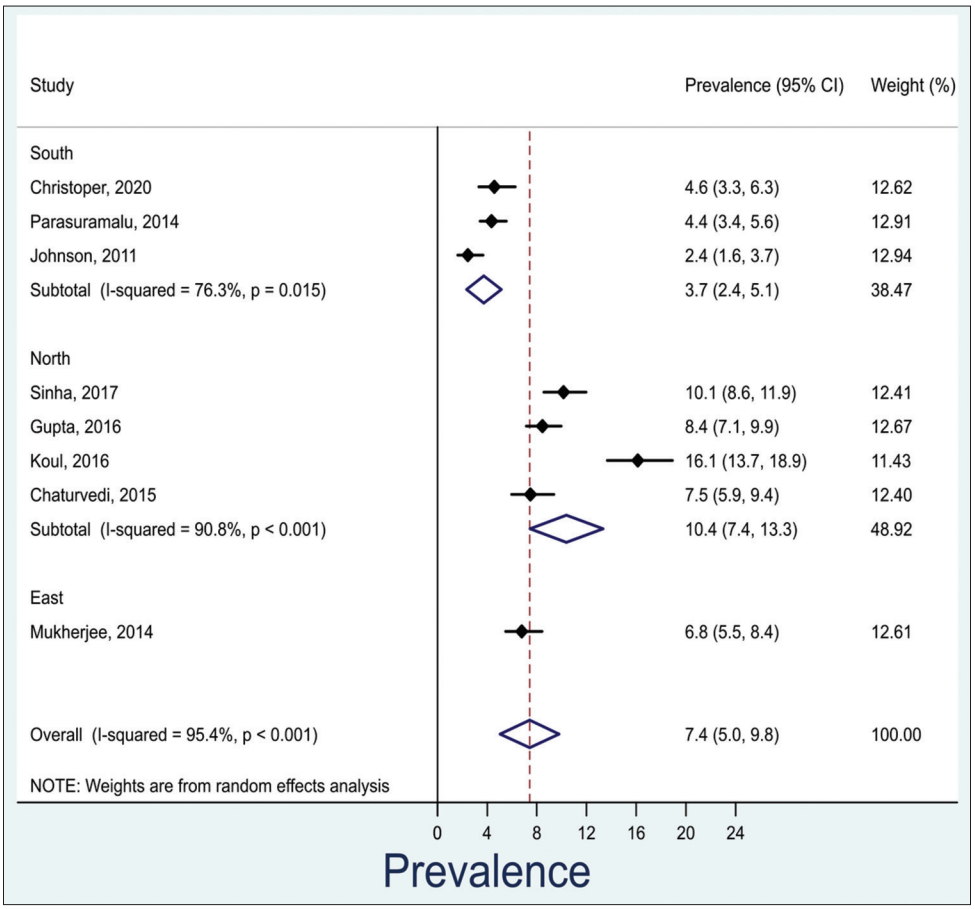

Figure 5: Forest plot of the meta-analysis for the prevalence of chronic obstructive pulmonary disease based on geographical location

Table 1: Characteristics of studies included in the meta-analysis

Author	Year of publication	Place	Study setting	Study period	Response rate (%)	Age (mean±SD/ age group)	Criteria used	Proportion of females
Christopher *et al*.[23]	2020	Tamil Nadu, Vellore	Rural	2018	96.4	51.3±12.9	FEV_1/FVC < LLN	56.6
Sinha *et al*.[24]	2017	New Delhi, Mehrauli	Urban	2012-2013	99	46±13	GOLD	46
Gupta *et al*.[21]	2016	Uttar Pradesh, Ghaziabad	Urban	NA	98.1	64.5	FEV_1/FVC < LLN	56.2
Koul *et al*.[22]	2016	Kashmir, Bandipora	Urban	2010	86.9	≥40	FEV_1/FVC < LLN	46
Chaturvedi *et al*.[43]	2015	Uttar Pradesh, Muzaffarnagar	Rural	2014-2015	89.8	44.88±11.7	GOLD	48.2
Mukherjee *et al*[25]	2014	West Bengal	Rural	NA	97.9	23-43	GOLD	Only women participants
Parasuramalu *et al*.[44]	2014	Karnataka, Bangalore	Rural	2008	100	47.39±10.3	GOLD	51.5
Johnson *et al*.[28]	2011	Tamil Nadu, Tiruvallur	Rural	2007	99.1	30-70	GOLD	NA

GOLD: Global initiative for chronic obstructive lung disease, FEV_1: Forced expiratory volume during the 1st s, FVC: Forced vital capacity, LLN: Lower limit of normal, NA: Not available, SD: Standard deviationa

Table 2: Prevalence of chronic obstructive pulmonary disease among adults

Author	Year of publication	Sample size	Prevalence of COPD (%)				
			Overall	Male	Female	Urban	Rural
Christopher *et al*.[23]	2020	1015	4.6	4.1	4.9	NA	4.6
Sinha *et al*.[24]	2017	1203	10.1	12.2	7.8	10.1	NA
Gupta *et al*.[21]	2016	1493	8.4	12.4	5.4	8.4	NA
Koul *et al*.[22]	2016	757	16.1	17.6	14.7	16.1	NA
Chaturvedi *et al*.[43]	2015	908	7.5	NA	NA	NA	7.5
Mukherjee *et al*.[25]	2014	1119	6.8	NA	6.8	NA	6.8
Parasuramalu *et al*.[44]	2014	1400	4.4	NA	NA	NA	4.4
Johnson *et al*.[28]	2011	900	2.4	NA	NA	NA	2.4

COPD: Chronic obstructive pulmonary disease, NA: Not available

PUBLICATION BIAS

The funnel plot demonstrated a mild asymmetry [Figure 6]. Moreover, the *P* value for Egger's test was observed to be 0.01, implying publication bias.

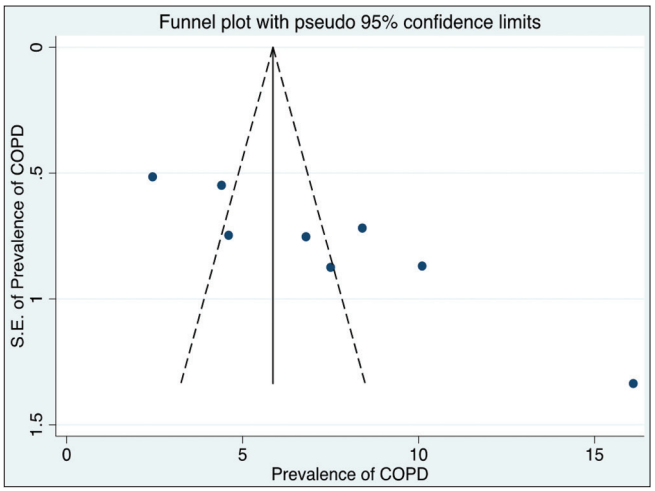

Figure 6: Funnel plot for assessing publication bias

SENSITIVITY ANALYSIS

Sensitivity analysis was performed by removing three studies[21-23] that had classified COPD based on LLN criteria; it showed a decrease in the prevalence of COPD from 7.4% (95% CI: 5.0-9.8%) to 6.2% (95% CI: 3.6–8.8). The pooled estimate after removing one study conducted exclusively on women participants by Mukherjee *et al*.[25] showed no substantial change.(7.5% [95%CI: 4.8–10.2]).

DISCUSSION

We conducted a systematic review and meta-analysis of data from eight studies involving 8,569 participants and found a pooled prevalence of COPD of 7.4% (95% CI: 5.0–9.8) among adults in India. The studies included in this review had high heterogeneity among them. We conducted subgroup analysis based on gender, geographical region, and study setting, but we could not find the reason for heterogeneity.

A systematic review conducted to determine the prevalence of COPD in India by McKay *et al*. in 2012 reported that the prevalence ranges from 6.5%–7.7% from 16 eligible studies.[16] This estimate is similar to our pooled estimate. The projections based on the COPD prevalence estimation model among 12 Asia-Pacific regions by regional COPD working group in 2003,[29] reported that the prevalence of COPD is 6.3% which is closer to our study's estimate. Another global systematic review and meta-analysis conducted by Halbert *et al*. in 2006 on COPD prevalence reported a pooled estimate of 8.9% (95% CI: 2.1–26.4) based on 26 studies, which is similar to our study's estimate.[30] In the 2005, Burden of Obstructive Lung Disease study conducted in 12 sites across the world by Buist *et al*. reported that the prevalence of COPD was 10.1%, which is a little higher than our estimate.[31]

Another systematic review and meta-analysis done by Adeloye *et al*. reported the prevalence of COPD of 11.4% (95% CI: 10.8–12.0) from 123 eligible studies among

Table 3: Risk of bias assessment of the studies included in the meta-analysis

Question	Christopher *et al.*	Sinha *et al.*	Gupta *et al.*	Koul *et al.*	Chaturvedi *et al.*	Mukherjee *et al.*	Parasuramalu *et al.*	Johnson *et al.*
Did the study address a clearly focused question/issue?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Was the research method (study design) appropriate for answering the research question?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Was the method of selection of the participants (employees, teams, divisions, organizations) clearly described?	Yes	Yes	No	Yes	No	No	Yes	Yes
Could the way the sample was obtained introduce (selection) bias?	No	No	Yes	No	No	Yes	No	No
Was the sample of participants representative with regard to the population to which the findings will be referred?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Was the sample size based on prestudy considerations of statistical power?	Yes	Yes	No	No	Yes	No	Yes	Yes
Was a satisfactory response rate achieved?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were the measurements (questionnaires) likely to be valid and reliable?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were confidence intervals given for the main results?	Yes	Yes	No	No	No	No	No	Yes

adults globally.[43] This prevalence is higher than the estimate from our study. The possible reason for the disparity in the prevalence is that the former had included estimates of COPD prevalence from all the six WHO regions. Studies included in their review diagnosed COPD using varied cut-offs like FEV_1/FVC <75%, FEV_1/FVC <65%, FEV_1/FVC <70%, and FEV_1/FVC<LLN, which might be the reason for the high prevalence of COPD whereas, the studies included in this systematic review and meta-analysis had included only the latter two cut-offs. The difference in estimates could also be due to the race of the population included in this study which consists of the population which belongs to Mongoloid and Indo-Aryan race. This is supported by the evidence from various studies, which says that the prevalence of COPD may vary by race and ethnicity.[32-35]

A systematic review and meta-analysis on COPD prevalence on adults by Ntritsos *et al*. reported a pooled prevalence of 9.23% (95% CI: 8.16–10.36) from 194 eligible studies, and this estimate is a little higher than our estimate.[36] The reason might be that the former study has included studies that have diagnosed COPD based on patient-reported, spirometry diagnosed, and physician-diagnosed cases. Furthermore, the study population included belongs to LMIC, upper-middle, and high-income countries.

Epidemiological studies undertaken to estimate the prevalence of COPD varies with the criteria used to diagnose COPD. The majority of the studies conducted are based on FEV_1/FVC<70%. Some subject experts claim that the fixed cut-off has no statistical basis and is arbitrary.[37] It may overestimate COPD in the elderly because the elasticity of the lung decrease as the age increases, thereby reducing the FEV_1 more than the FVC value.[38] Hence, using this criterion will lead to underestimation in young adults and overestimation in elderly people. To resolve such issues in the classification of COPD, the American Thoracic Society/European Respiratory Society advocates using LLN criteria, which is defined as the value below the lower 5th percentile of a reference population is considered abnormal.[39,40] However, the usage of this definition in the studies selected in this review is very less (3/8). However, some studies suggest that LLN may miss some people with COPD.[41] This variation in COPD diagnosis is more prominent in LMICs, where cases such as bronchiectasis, tuberculosis, or some other obstructive airway disease are more prevalent and may be misdiagnosed as COPD.[42] Apart from this, the population structure, age-range, and increased rates of smoking might be the reason for the high heterogeneity observed in this meta-analysis. We explored the reason for heterogeneity by performing subgroup analysis based on gender, geographical region, and study setting, and there was no decrease in the heterogeneity.

Even though spirometry is recognized as a standard tool to diagnose COPD, still it is being under-utilized among the primary care level leading to misdiagnosis. Strong political will and funding are crucial for any successful program. Hence, adequate training and resources should be provided to the primary care physicians to correctly diagnose COPD and start on appropriate treatment to prevent their complications and the quality of life.

In total, we identified eight studies, which allowed us to pool results from 8,569 participants. The findings of this systematic review and meta-analysis should be interpreted with the follow limitations. Even though we followed a comprehensive search strategy, we did not include the grey literature which might affect the pooled estimate. The pooled prevalence estimate from this study has to be interpreted cautiously as there is high heterogeneity among the studies.

CONCLUSIONS

Our findings suggest a high prevalence of COPD in India among adults. This suggests the need to have a nationwide community-based survey to estimate the true burden of COPD using robust and uniform methodology. This would be useful for planning and implementation of community-based control measures and also for their monitoring and evaluation.

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Conflicts of interest
There are no conflicts of interest.

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