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Prevalence and Determinants of Chronic Respiratory Diseases in Patients with Lung Cancer in a Tertiary Care Setting in India

Chronic Respiratory Diseases in Lung Cancer

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ABSTRACT: **Background:** Chronic respiratory diseases (CRDs) frequently coexist with lung cancer and may adversely influence clinical outcomes. However, data from India on the prevalence and determinants of CRDs among lung cancer patients remain limited.

Objectives: To estimate the prevalence of CRDs and identify associated factors among patients with lung malignancies in a tertiary care setting.

Methods: A retrospective observational study was conducted among 192 adult patients with histopathologically confirmed lung cancer at a tertiary care hospital in Kerala, India (June 2020–June 2022). Data on sociodemographic factors, behavioural exposures, comorbidities, and CRDs were extracted from medical records. CRDs included chronic obstructive pulmonary disease (COPD), asthma, interstitial lung disease (ILD), and prior tuberculosis (TB). Associations were assessed using χ^2/Fisher's exact test and log-binomial regression. Adjusted prevalence ratios (APR) with 95% confidence intervals (CI) were reported.

Results: The prevalence of CRDs was 19.4%, with COPD being the most common (15.6%), followed by asthma (5.2%). The majority of patients were male (75%) and aged ≥60 years. Multivariable analysis showed that age 70-79 years (APR=8.05; 95% CI: 1.09-59.27), ≥80 years (APR=10.07; 95% CI: 1.29-78.25), hypertension (APR=1.96; 95% CI:

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1.18-3.27), and prior TB (APR=2.85; 95% CI: 1.75-4.64) were independently associated with CRDs. Smoking and diabetes were not statistically significant after adjustment.

Conclusions: Nearly one in five lung cancer patients had coexisting CRDs, predominantly COPD. Increasing age, hypertension, and prior TB were key determinants. Integrated screening and management of CRDs in lung cancer care may improve clinical outcomes in resource-limited settings.

INTRODUCTION

Lung cancer is still one of the primary reasons for cancer deaths across the globe. This condition claimed approximately 1.8 million lives and was responsible for around 18% of all cancer deaths, while about 2.2-2.5 million patients were diagnosed with this disorder annually [1,2]. Although some diagnostic and treatment techniques have improved, the overall prognosis of lung cancer remains quite poor since it usually involves a late diagnosis and the presence of other disorders [3]. Besides tobacco smoking that accounts for almost 85% of cases, other risk factors include environmental pollutants, occupational exposure, and pre-existing pulmonary conditions [1,4].

Chronic respiratory diseases (CRDs) are a group of chronic non-transmissible illnesses, which include various pulmonary conditions like chronic obstructive pulmonary disease (COPD), asthma, interstitial lung disease (ILD), and tuberculosis (TB). As mentioned above, COPD ranks among the most common causes of death worldwide and is prevalent in LMICs [5]. Overall prevalence of CRDs is increasing across the globe due to constant exposure to different risk factors, namely cigarette smoking, biomass fuel exposure, and air pollution [6]. Such diseases are marked by chronic inflammation, remodeling of airways, and lung tissue injury, possibly contributing to the malignant nature of such cases [7].

A link between CRDs and lung cancer appears to be multifactorial in its essence. Inflammation has been considered an essential factor in the link between respiratory diseases and the development of malignancies, driven by genetic alterations and abnormal cell proliferation [7,8]. Studies have found that people suffering from certain lung diseases, including COPD and TB, exhibit a high incidence of lung cancer compared to those without any respiratory disorders [9,10]. Besides, smoking and other risk factors that can contribute to the development of both types of disease also affect their interconnection. Co-morbidity of CRDs also significantly impairs outcomes of treatment and overall prognosis among patients with lung cancer.

In India, the prevalence of lung cancer as well as other chronic respiratory diseases seems to increase, driven by lifestyle factors, urbanization, and exposure to environmental agents. Nonetheless, there is still insufficient information available regarding such associations in the local population. Therefore, this study aims to determine the prevalence of chronic respiratory diseases and identify associated factors among patients diagnosed with lung malignancies in a tertiary care hospital in Kerala, India.

METHODS

This hospital-based retrospective observational study was conducted at a tertiary care teaching hospital in Kerala, India, and included patients diagnosed with lung malignancies between June 2020 and June 2022. The study population comprised adult patients aged 18 years and above with a histopathologically confirmed diagnosis of primary lung malignancy who were managed at the study centre during the study period. Patients with incomplete or missing medical records and those with coexisting malignancies were excluded.

A total of 192 eligible patient records were included using a complete enumeration approach. Data were collected retrospectively from medical records using a structured data extraction form, which captured sociodemographic variables (age and sex), behavioural risk factors (smoking status and biomass fuel exposure), clinical characteristics (type and stage of lung cancer), comorbidities (diabetes mellitus, hypertension, and history of tuberculosis), and the presence of chronic respiratory diseases (CRDs).

Chronic respiratory diseases (CRDs) were defined as diseases of the airways and other structures of the lungs characterised by long duration and slow progression**,** and include conditions such as chronic obstructive pulmonary disease, asthma, occupational lung diseases, pulmonary hypertension, and other chronic lung conditions [11]. Patients were categorised according to the diagnosis documented in the medical records. For this study, CRDs included chronic obstructive pulmonary disease, bronchial asthma, interstitial lung disease, and a history of pulmonary tuberculosis, as documented by treating physicians in the

medical records. The primary outcome variable was the presence of any CRD (yes/no), and independent variables included age group, sex, smoking status, biomass fuel exposure, diabetes mellitus, hypertension, and prior tuberculosis.

Data were entered into Microsoft Excel and analysed using Stata version 14 (StataCorp LLC, College Station, TX, USA). Categorical variables were summarised as frequencies and percentages, and the prevalence of CRDs among lung cancer patients was calculated as proportions. Associations between independent variables and CRD status were assessed using the χ^2 test or Fisher's exact test, as appropriate, and unadjusted prevalence ratios (UPR) with 95% confidence intervals (CI) were estimated. Variables with a p-value < 0.20 in the bivariate analysis were included in the multivariable model. Log-binomial regression analysis was performed to identify independent predictors of CRDs, and adjusted prevalence ratios (APR) with 95% confidence intervals were reported. A p-value <0.05 was considered statistically significant.

As this was a retrospective record-based study, there is a possibility of information bias due to incomplete or inaccurate documentation, and selection bias due to the single-centre design, which may limit generalisability. No formal sample size calculation was performed, and the number of eligible cases available during the study period determined the sample size. There is no involvement of patients or the general population in this study. Ethical approval for this study was obtained from the Institutional Ethics Committee (Reference No: ECASM-AIMS-2024-370, date of approval: 6 August 2024). The requirement for informed consent was waived because of the retrospective nature of this study. The study complied with the principles of the Declaration of Helsinki.

RESULTS

As demonstrated in ***Table 1***, the majority of the subjects studied were old age people, with 38% falling within the age group of 70–79 years, while 31.3% fell within 60–69 years. Out of the total number of study subjects, 75% were males. Smoking background was observed in 27.1% of the patients, while biomass exposure occurred in only 1% of the subjects. Common comorbidities included diabetes mellitus, which affected 34.4% of the patients, and hypertension, which affected 44.3% of them (***Figure 1***). Other medical problems included family history of cancer and TB, which affected 4.2% and 7.8% of patients, respectively. Lung cancers were 90.6% of the cases, of which adenocarcinoma (66.1%) was the most common subtype, followed by squamous cell carcinoma (19.3%). Advanced stage (stage IV) occurred in 70.3% of cases, thus suggesting late diagnosis in many *cases* ***(Table 2).***

The Proportion of Chronic Respiratory Diseases in Lung Cancer is shown in(***Figure 2)***. CRD was found in 19.4% of the subjects under investigation. Of the various types of respiratory diseases, COPD (15.6%) and asthma (5.2%) were the most common, while ILD and TB affected 1% and 0.5% of the subjects, respectively.

Factors associated with chronic respiratory disease (CRDs) are shown in ***Table 3*** through bivariate analysis. Advanced age was significantly associated, where those with age 70-79 years (UPR 12.66, 95% CI 1.77-90.56, p = 0.011) and those with age ≥80 years (UPR 14.82, 95% CI 1.93-114.08, p = 0.010) had an increased risk of developing CRD relative to those aged between 51-59 years. Smokers (UPR 1.87, 95% CI 1.06-3.32, p = 0.032), hypertensive patients (UPR 2.05, 95% CI 1.12-3.73, p=0.019), and history of tuberculosis (UPR 2.27, 95% CI 1.13-4.56, p=0.021) were also significantly associated with CRD. Other factors like sex, diabetes, biomass fuel exposure, and cancer type did not show significant associations.

The results for the multivariable regression analysis are provided in ***Table 4***. People belonging to the age category of 70-79 years had a significantly greater chance of having CRDs (APR=8.05, 95% CI: 1.09-59.27, p=0.041), similar were people who belonged to the age group of ≥80 years (APR=10.07, 95% CI: 1.29-78.25, p=0.027). On the other hand, although there was a greater chance in the case of people between the ages of 60-69 years (APR=4.06, 95% CI: 0.53-31.41), that was not statistically significant (p=0.179). Hypertensive patients had higher odds of CRDs (APR=1.96, 95% CI: 1.18-3.27, p=0.009). The presence of tuberculosis was found to be significantly related.

Table 1. Distribution of sociodemographic and clinical characteristics (N=192)

Variables	Frequency	Percentage (%)
Age (in years)		
<50	9	4.69

51-59	33	17.19
60-69	60	31.25
70-79	73	38.02
≥80	17	8.85
Sex		
Female	48	25.00
Male	144	75.00
Smoking status		
Yes	52	27.08
No	140	72.92
Biomass fuel exposure		
Yes	2	1.04
No	190	98.96
Diabetes Mellitus		
Yes	66	34.38
No	126	65.62
Hypertension		
Yes	85	44.27
No	107	55.73
Family history of malignancy		
Yes	8	4.19
No	183	95.81
History of Tuberculosis		
Yes	15	7.81
No	177	92.19

Table 2: Distribution of types and subtypes of Lung cancer along with staging (N=192)

Variables	**Frequency**	**Percentage (%)**
Types of Lungs Cancer		
NSCLC	174	90.6
SCLC	17	8.9
Both	1	0.5
Subtype		
Adenocarcinoma	127	66.1

Large cell carcinoma	1	0.5
Small cell carcinoma	19	9.9
Squamous cell carcinoma	37	19.3
Others	8	4.2
Staging		
Stage I	8	4.2
Stage II	18	9.4
Stage III	31	16.1
Stage IV	135	70.3

Table 3. Factors associated with Chronic Respiratory Disease (CRD): Bivariate Analysis (N=192)

Variable	**CRD n (%)**	**No CRD n (%)**	**UPR**	**95% CI**	**P-value**
Age group (years)					
> 68	30 (81.08)	84 (54.19)	Ref	-	-
< 67	07 (18.92)	71 (45.81)	**3.62**	**1.50-8.74**	**0.004**
Sex					
Male	30 (20.98)	113 (79.02)	1.44	0.68-3.06	0.345
Female	7 (14.58)	41 (85.42)	Ref	-	-
Type of Cancer					
NSCLC	33 (19.19)	140 (80.81)	Ref	-	-
SCLC	4 (23.53)	13 (76.47)	1.23	0.49-3.05	0.660
Others	0 (0.00)	2 (100.00)	-	-	-
Smoking status					
Non-smoker	22 (15.71)	118 (84.29)	Ref	-	-
Smoker	15 (28.80)	37 (71.20)	**2.17**	**1.02-4.61**	**0.040**
Biomass fuel exposure					
Yes	1 (50.00)	1 (50.00)	4.27	0.26-70.02	0.268
No	36 (18.90)	154 (81.10)	Ref	-	-
Diabetes Mellitus					
Yes	17 (25.76)	49 (74.24)	1.83	0.88-3.81	0.099
No	20 (15.90)	106 (84.10)	Ref	-	-
Hypertension					
Yes	23 (27.06)	62 (72.94)	**2.46**	**1.18-5.16**	**0.015**

No	14 (13.21)	93 (86.79)	Ref	-	-
History of TB					
Yes	6 (40.00)	9 (60.00)	**3.14**	**1.04-9.46**	**0.034**
No	31 (17.61)	146 (82.39)	Ref	-	-

UPR=Unadjusted prevalence ratio

Table 4. Factors associated with Chronic Respiratory Disease (CRD): Multivariable Regression Analysis (N=192)

Variable	**APR**	**95% CI**	**P-value**
Age group (in years)			
> 68	Ref	-	-
< 67	**3.35**	**1.35-8.38**	**< 0.01**
Smoking status			
Non-smoker	Ref	-	-
Smoker	1.49	0.89-2.52	0.132
Biomass fuel exposure			
Yes	**2.25**	**1.01-5.08**	**0.05**
No	Ref	-	-
Diabetes Mellitus			
Yes	0.74	0.34-1.64	0.46
No	Ref	-	-
Hypertension			
Yes	**2.56**	**1.11-5.86**	**0.03**
No	Ref	-	-
History of TB			
Yes	**3.69**	**1.06-12.79**	**0.04**
No	Ref	-	-

APR=Adjusted prevalence ratio

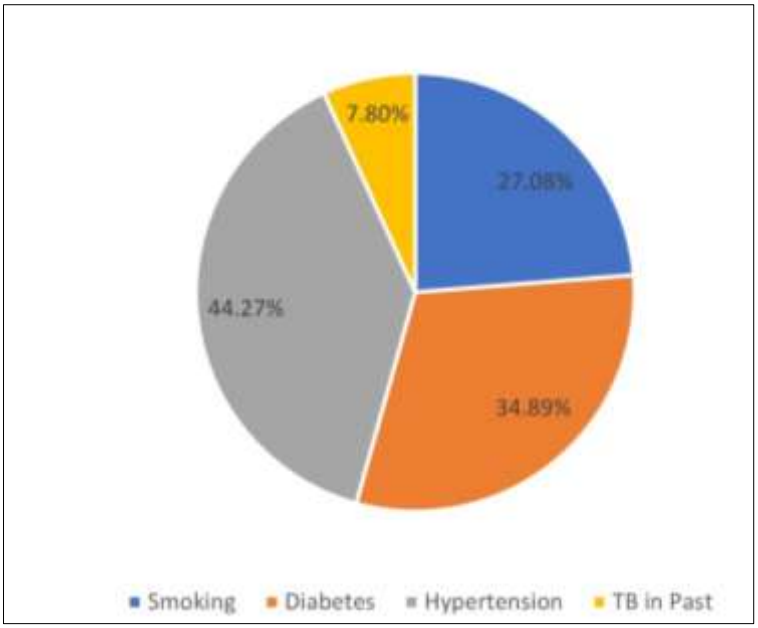


Fig 1. Comorbidities in Lung Cancer

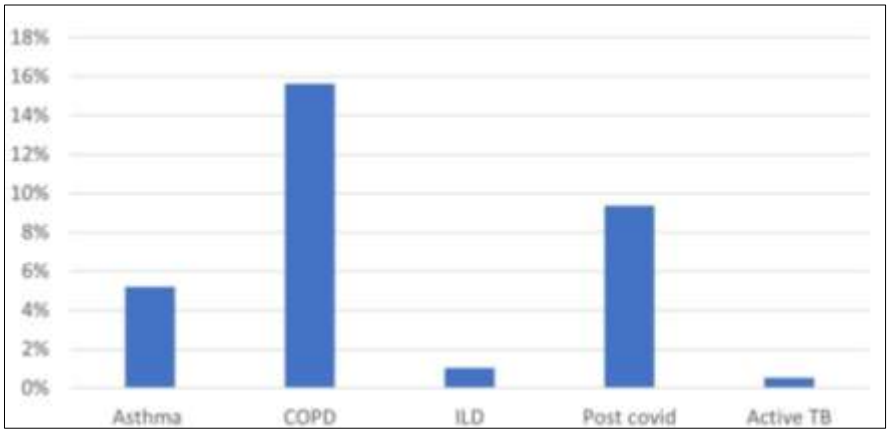


Fig 2. Proportion of Chronic Respiratory Diseases in Lung Cancer.

DISCUSSION

In our study cohort of 192 participants, there was a considerable burden of chronic respiratory diseases. Out of all the diagnoses, Chronic obstructive pulmonary disorder (COPD) came out to be the most common after malignancy. It is consistent with the findings of Sharma *et al.,*in which they found the prevalence of COPD to be 15.6% among the population aged 25 and above in a multicenter Indian study (SWORD Study) performed on 25,177 adults [12]. This indicates that even among the people suffering from lung malignancy, COPD could be an important concomitant illness. It has been included under the scope of NPCDCS (National Programme for Prevention and Control of Cancer, Diabetes, Cardiovascular Diseases & Stroke) in India, but still there is poor awareness regarding the illness among the public population of the country, as reported by the Ghorpade *et al.,*study [13]. The lack of awareness may delay the detection of the disease, making the individual prone to developing malignancy [14, 15].

The incidence of asthma in our study sample was 5.2%, which is similar to the results reported by Salameh *et al.,*where around 2% of asthma patients were found to suffer from cancers, especially lung cancer, during their long-term follow-up period [16]. The chronic inflammation in asthma, according to the antigenic stimulation model, can increase carcinogenesis [17]. In contrast,

the enhanced immune surveillance mechanism proposes a possible protective effect against cancer due to increased elimination of carcinogens in the respiratory system [18]. Thus, the relationship between asthma and lung cancer is unclear and requires further research. The incidence of interstitial lung disease (ILD) in our sample was 1%. Some previous reports have shown a correlation between ILD and the development of lung cancer, where the incidence rate of ILD in lung cancer patients was 6.4%, with a median duration of 16.3 months between ILD and lung cancer diagnosis [19]. This correlation has been attributed to persistent inflammation with proliferation of fibroblasts resulting in damage to epithelial cells and genetic alteration in tumour suppression pathways such as p53 [20,21].

Tuberculosis (TB) also became a relevant aspect for our investigation. Although active cases were not common, previously treated cases of TB were evident in 7.8% of cases, which is similar to the prevalence rate of 10.6%, reported in a multicenter study conducted in Kerala [22]. According to the existing theories, inflammation caused by TB infection results in the formation of a micro-environmental milieu promoting DNA damage due to reactive oxygen species, which in turn promotes carcinogenesis [23, 24]. In addition to this, Liao *et al.,*have found that a previous history of TB disease increases the risk of mortality among lung cancer patients [10]. Bronchiectasis was not seen in any of our patients; however, earlier systematic reviews have suggested that patients suffering from bronchiectasis are at a greater risk of developing lung cancer compared to patients without bronchiectasis [25]. This further supports the role of chronic airway remodeling and inflammation as contributing mechanisms in lung carcinogenesis.

The proportion of individuals with hypertension in this study was found to be 44.3%, similar to the rates observed in a cross-sectional study conducted among cancer patients by Kibret et al [26]. Furthermore, the pooled cohort studies conducted in Australia and New Zealand have shown that hypertensive individuals are characterized by a higher incidence and mortality of cancer compared with normotensive individuals, thus underlining the impact of vascular dysfunction in the development of the disease [27]. Notably, despite the well-known risk factors such as a positive family history of malignancy, which contributes to the development of cancers with odds ratios of 1.5-2.8, the percentage of participants with a family history of malignancies in this study amounted to only 4.2% [25,26].

Bivariate and multivariate analysis revealed that older age (70-79 years old [APR=8.05, p=0.041] and ≥80 years old [APR=10.07, p=0.027]), hypertension (APR=1.96, p=0.009), and a history of TB (APR=2.85, p<0.001) were significant predictors of CRDs in the population of lung cancer patients. The older patients' age was associated with an increased likelihood of being diagnosed with a CRD. Moreover, the odds of being diagnosed with a CRD were doubled in hypertensive subjects and tripled in patients with a history of TB. These findings highlight the complex interplay between infectious, inflammatory, and metabolic comorbidities in the pathogenesis of chronic respiratory impairment among lung cancer patients.

Some of the strengths of this study were that it was conducted with a clear scope of identifying the burden of CRDs among patients with lung cancer, as there is not much Indian literature available on this topic. Nonetheless, the strengths of the study are undermined by its weaknesses in being a univariate analysis carried out at one center retrospectively. The presence of selection bias is inevitable, and the absence of confirmation through spirometry results may have resulted in inaccurate measurement of the prevalence of CRDs.

CONCLUSION

Many cases of lung cancer patients showed an association with the presence of other CRDs, mainly COPD. Risk factors included advanced age, hypertension, and history of TB. Enhancing the screening program for CRDs, together with that for lung cancer, might benefit patients, as it would ensure prompt action by health care providers.

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Author Contributions

All authors contributed to the study conception and design. Material preparation and data collection were performed by **Athul S Pramod Nair, Gokulakrishnan G**, and **Nithya Haridas**. Data Analysis and dissemination were performed by **Akhilesh**

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Human Ethics and Consent to Participate: Ethical approval for this study was obtained from the Institutional Ethics Committee (Reference No: **ECASM-AIMS-2024-370**, date of approval: 6 August 2024). The requirement for informed consent was waived because of the retrospective nature of this study.

Consent to publish: Not Applicable.

Clinical trial number*:* Not applicable

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