



ISSN (E): 2320-3862  
ISSN (P): 2394-0530  
[www.plantsjournal.com](http://www.plantsjournal.com)  
JMPS 2024; 12(2): 116-120  
© 2024 JMPS  
Received: 19-02-2025  
Accepted: 23-03-2025

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# Journal of Medicinal Plants Studies

[www.PlantsJournal.com](http://www.PlantsJournal.com)

## A review of lung cancer research in India

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DOI: <https://www.doi.org/10.22271/plants.2025.v13.i2b.1811>

### Abstract

Lung cancer is a major public health concern in India and globally ranking among the most common and fatal malignancies. In India, cases are projected to rise significantly, with tobacco consumption, air pollution, occupational exposure, and genetic predisposition being key risk factors. This paper provides a comprehensive overview of lung cancer epidemiology, highlighting regional disparities in incidence and mortality. Advances in diagnostics, including low-dose computed tomography (LDCT) and next-generation sequencing (NGS), have improved early detection, though accessibility remains a challenge. Treatment strategies incorporate chemotherapy, targeted therapy, immunotherapy, and radiation therapy, with clinical trials demonstrating promising outcomes. However, financial constraints and healthcare infrastructure limitations hinder widespread treatment access. Public health strategies, including tobacco control policies, air pollution mitigation, and enhanced screening programs, are critical for reducing lung cancer. Addressing these challenges through policy interventions and improved healthcare access is essential for reducing morbidity and mortality associated with lung cancer in India.

**Keywords:** Lung cancer, epidemiology, advanced-stage diagnosis, immunotherapy, public health strategies

### Introduction

Lung cancer is a major public health concern in India, ranking among the most common and deadliest cancers. According to the Indian Council of Medical Research (ICMR), lung cancer cases are expected to rise significantly by 2025, with an estimated 81,219 cases among men and 30,109 among women (Singh *et al.*, 2022) [36]. The primary causes include smoking, air pollution, occupational exposure, and genetic predisposition. Lung cancer poses a significant public health challenge, accounting for a substantial proportion of cancer-related deaths. Understanding the epidemiological trends and demographic disparities is crucial for developing targeted interventions and allocating healthcare resources effectively. This paper synthesizes available data to present a detailed overview of lung cancer incidence and mortality alongside treatment modalities and their accessibility. This paper reviews the current state of lung cancer research in India, focusing on epidemiology, diagnostic advancements, treatment trends, and public health strategies.

### Global Epidemiology of Lung Cancer

Lung cancer remains a significant global health concern, being the most diagnosed cancer and the leading cause of cancer-related deaths worldwide. In 2020, there were approximately 2.2 million new cases and 1.8 million deaths attributed to lung cancer, accounting for 18% of all cancer fatalities (www.who.int, 2020). Lung cancer accounts for approximately 6.9% of all cancer cases and 9.3% of cancer-related deaths in India (GLOBOCAN, 2020). Tobacco consumption remains the leading risk factor, with nearly 80% of lung cancer cases linked to smoking (Gupta *et al.*, 2019) [8]. Other significant contributors include air pollution, indoor biomass fuel exposure, and occupational carcinogens such as asbestos and silica dust (Reddy *et al.*, 2021) [21]. Globally and gender-wise, the incidence of lung cancer varies; the greatest rates are seen in Micronesia, Polynesia, Europe, Asia, and North America, while the lowest rates are found in Africa and Central America (Sung *et al.*, 2021) [39]. In their lifetimes, 8% of men and 6% of women worldwide are diagnosed with lung cancer (Bade & Dela Cruz 2020) [2]. Geographically, the ratio of male to female lung cancer cases varies greatly, ranging from about 12:1 in Belarus to 1:1 in Brazil. This variation is probably caused by variations in smoking habits and because of heavy tobacco use, and aging populations' lung cancer

mortality is predicted to increase to around 3 million deaths per year worldwide by 2035 (Christiani & Amos 2022) [4]. Younger people under 40 are less likely to develop lung cancer; beyond that, the disease's incidence rises with age and levels out at age 80 (Horn & Iams, 2022) [10]. The usual age of death for someone with lung cancer is 72, while the median age of diagnosis is 70 (Bade & Dela Cruz, 2020) [2].

### Incidence and Mortality Rates

The occurrence and mortality rates of lung cancer vary significantly across different regions and between genders:

### Geographical Variation

In the US and Canada, lung cancer continues to be a significant health concern due to its high incidence and fatality rates. In the United States, lung cancer accounted for 227,875 new diagnoses in 2020, making up 10% of all tumor cases and the second most common cancer type after breast cancer. Lower incidence was seen in Canada, where 25,574 new cases of lung cancer accounted for 9.3% of all cancer cases and were the third most common cause of cancer in the nation (Sung *et al.*, 2021) [39]. The American Cancer Society estimates that the incidence of lung cancer is increasing in women, although previously it primarily afflicted males. 51% of the 238,340 cases that are expected to be detected in the US by 2023 are expected to be in women. About 86,627 people died from lung cancer in 2020, making it one of the main causes of cancer-related fatalities in Central America, South America, and the Caribbean (Piñeros *et al.*, 2020) [29]. In particular, it is the leading cause of death and the fourth most common kind of cancer in South America and the Caribbean. However, in Central America, other cancers, such as colorectal, breast, prostate, liver, and stomach cancer, are overtaking lung cancer as the leading cause of death (Piñeros *et al.*, 2020) [29]. In Asia, lung cancer is the second most frequent cancer in women, behind breast cancer, and the most prevalent disease in males. Lung cancer was the leading cause of cancer-related fatalities in 2020, accounting for slightly more than 1.1 million deaths, with 1.3 million new cases identified (Sharma, 2022) [17, 34, 36]. Lung cancer incidence and mortality rate compared to Europe and the US (Lam *et al.*, 2023) [19]. There have been reports of sex discrepancies, with men experiencing greater incidence (ratio 2.46) and death (ratio 2.5) than females (Pakzad *et al.*, 2015) [23].

Lung cancer incidence, adjusted by age, is stated to be lower in the MENA (Middle East and North Africa) area than globally, with Lebanon having the highest incidence (18.7 per 100,000) and Yemen having the lowest (4.6 per 100,000) (IARC., 2023). In 2019, lung cancer claimed the lives of 15,396 women and 57,114 men in the MENA area. However, the lack of thorough and current population registers in many of these nations makes it difficult to acquire precise statistics on cancer incidence. In sub-Saharan Africa (SSA), infectious diseases are the leading cause of disease burden; nevertheless, cancer-related illnesses are becoming more prevalent (Olaleye & Ekrikpo, 2017) [22]. Cancer rates are predicted to significantly increase by 2030.104. Crucially, SSA has a low cancer survival rate when compared to other parts of the world (Sankaranarayanan *et al.*, 2010) [33]. The main cause of cancer-related mortality in Europe is lung cancer representing over 20% of all cancer-related fatalities (Dyba *et al.*, 2021) [5]. Males were responsible for 7.0% of all lung cancer-related fatalities, which is more than twice as many as females (3.2%) (Europa, 2023). Overall, 5-year survival rates are only 11.2% for males and 13.9% for women, and prevalence and death

rates in Europe are higher than the global average (Bussell & Lovell, 2019) [3]. The greatest prevalence of lung cancer in men is seen in Central and Eastern European countries, such as Serbia (136.4 per 100,000) and Hungary (138.3 per 100,000). In contrast, Hungary (76.6), Denmark (85.1), and Ireland (85.1) have the highest rates among women (Dyba *et al.*, 2021) [5]. A growing incidence of lung cancer in European women is probably caused by the varying times at which women started smoking (Laguna *et al.*, 2024) [18].

### State-wise patient data

India's top cancer states with the highest rates of crude cancer (the number of new cancer cases or deaths in a specific population per year, annually expressed as number & cases per 100000) because there is so much information on cancer cases, it is essential to base the data on a specific characteristic to estimate the numbers accurately. The crude cancer incidence rates, a metric that directly represents the quantity of cancer cases in a particular area, are the basis of the following list. The data displayed here pertains to the disease's incidence rate per 100,000 people. India's leading cancer states are as follows (<https://drarvindkumar.com> 2023).

1. Kerala (135.3)
2. Mizoram (121.7)
3. Haryana (103.4)
4. Delhi (102.9)
5. Karnataka (101.6)
6. Goa (97.0)
7. Himachal Pradesh (91.6)
8. Uttarakhand (91.0)
9. Assam (90.2)
10. Punjab (85.5)

In India, lung cancer accounts for 5.9% of all cancers and 8.1% of all cancer-related deaths, making it a serious health problem (JTO. ORG., 2021). Although there is a dearth of thorough state-by-state statistics on lung cancer patients, several areas have been shown to have noticeably high incidence rates: Males (38.8 per 100,000) and females (37.9 per 100,000) had the highest age-adjusted incidence rates (AAR) for lung cancer in the Aizawl District of Mizoram (NCDIR, 2020). Arunachal Pradesh's Papumpare District reported a high AAR among females, 219.8 per 100,000 (Research Gate, 2020). Furthermore, the 2020 report from the National Cancer Registry Programme projects the number of cancer cases—including lung cancer—that will occur in different states and union territories until 2025 (NCDIR, 2020).

### Estimated Rise in Cases of Lung Cancer

According to a study, the incidence of lung cancer in Maharashtra's main cities is expected to increase significantly. In particular, it was predicted that by 2020, the total number of newly diagnosed cases of lung cancer in Mumbai, Pune, Nagpur, and Aurangabad will rise by more than 50%, from 3,170 to 4,788 (Parikh *et al.*, 2016) [24]. In Maharashtra, lung cancer is a serious health issue that reflects larger national patterns. This is a summary of the present situation: In 2023, Maharashtra reported approximately 121,000 new cancer cases, positioning it as the state with the second-highest number of cancer incidences in India. This reflects an increase from around 118,000 new cases in 2021 (<https://drarvindkumar.com> 2023).

### Diagnostic Advances

Early detection of lung cancer remains a challenge, as most cases are diagnosed at advanced stages due to the asymptomatic nature of the disease in its early phase. Imaging techniques such as low-dose computed tomography (LDCT) have improved early detection rates, but access remains limited to urban centers (Rajagopal *et al.*, 2020) [30]. Liquid biopsy and next-generation sequencing (NGS) are emerging as promising diagnostic tools for identifying genetic mutations and guiding personalized treatment (Kumar & Sharma, 2022) [17, 34, 36]. However, high costs restrict widespread adoption.

### Treatment Approaches

Lung cancer treatment in India follows global standards, incorporating surgery, chemotherapy, radiation therapy, targeted therapy, and immunotherapy. Advances in molecular profiling have led to the identification of key genetic mutations, such as EGFR, ALK, and ROS1, which are prevalent in Indian patients and respond well to targeted therapies (Mehta *et al.*, 2021) [20]. Immunotherapy, including checkpoint inhibitors like Pembrolizumab and Nivolumab, has improved survival rates but remains expensive and inaccessible to many patients (Patel *et al.*, 2023) [26].

### Chemotherapy Drugs for Lung Cancer

Chemotherapy, which uses several medications to target and destroy cancer cells, is still a mainstay in the treatment of lung cancer. An outline of several frequently used chemotherapeutic drugs is provided below:

- 1. Platinum-Based Substances:** Cisplatin causes apoptosis by forming DNA crosslinks. For increased efficacy, it is frequently combined with other agents (Paz-Ares *et al.*, 2012) [27]. Carboplatin: Ideal for patients who might not be able to tolerate cisplatin, carboplatin has a more favorable side-effect profile than cisplatin (Stathopoulos *et al.*, 2011) [38].
- 2. Antimetabolites: Pemetrexed:** An antifolate that interferes with metabolic pathways that depend on folate and are necessary for cell division. It works especially well for non-squamous non-small cell lung cancer (NSCLC) (Paz-Ares *et al.*, 2012) [27].
- 3. Taxane: Paclitaxel:** It is frequently used with platinum-based medications because it stabilizes microtubules, which inhibits cell division (Paz-Ares *et al.*, 2012) [27].
- 4. Docetaxel:** Causes cell death by preventing microtubule depolymerization (Stathopoulos *et al.*, 2011) [38].
- 5. Topoisomerase Inhibitors:** Etoposide breaks DNA strands by inhibiting topoisomerase II used frequently for SCLC (small cell lung cancer) (Paz-Ares *et al.*, 2012) [27].
- 6. Novel Agents: Lipoplatin:** A liposomal drug called cisplatin (a chemotherapy drug) aimed to decrease toxicity while retaining effectiveness (Stathopoulos *et al.*, 2011) [38].

### Clinical trials

**189 Trial:** It is a branding series used by Merck (MSD) for trials involving pembrolizumab (Keytruda). Study Overview: In patients with metastatic nonsquamous non-small cell lung cancer (NSCLC) who had not received treatment before, this Phase III trial assessed the effectiveness of combining the immunotherapy medication pembrolizumab with conventional chemotherapy (pemetrexed and cisplatin or carboplatin). Results: With a median survival of 22 months as opposed to 10.7 months for chemotherapy alone, the combination

treatment considerably increased overall survival (Gadgeel *et al.*, 2020) [6].

### 407 Trial

(The number 407 is a sequential identifier used by Merck to organize different keynote trials.) Study Overview: In patients with metastatic squamous non-small cell lung cancer (NSCLC) who had not received treatment before, this Phase III study evaluated the addition of pembrolizumab to conventional chemotherapy (carboplatin and either paclitaxel or nab-paclitaxel). Results: The median overall survival for the combined treatment was 15.9 months, while the median for chemotherapy alone was 11.3 months (Paz-Ares *et al.*, 2018) [28].

### IMpower110 Trial

"IMpower" stands for "Immune Power", referring to Roche/Genentech's branding for trials involving atezolizumab (Tecentriq), an immune checkpoint inhibitor. Study Overview: In patients with metastatic non-small cell lung cancer (NSCLC) who expressed PD-L1, this Phase III trial compared platinum-based chemotherapy with the immunotherapy medication atezolizumab. Results: The median overall survival for patients with high PD-L1 expression was 20.2 months while using atezolizumab, compared to 13.1 months when using chemotherapy (Spigel *et al.*, 2021) [37].

### Chrysalis Study

**Research Overview:** In this Phase I research, patients with advanced non-small cell lung cancer (NSCLC) who had EGFR exon 20 insertion mutations were treated with amivantamab, a bispecific antibody that targets both EGFR and MET receptors. Results: The median response time was 11.1 months, and the overall response rate was 40% (Park *et al.*, 2021) [25].

### AEGEAN Trial

**Study Overview:** In patients with resectable non-small cell lung cancer (NSCLC), this Phase III study assessed durvalumab, an immunotherapy medication, in conjunction with neoadjuvant chemotherapy and adjuvant durvalumab. Results: When compared to chemotherapy alone, the inclusion of durvalumab increased the rates of full pathological response (Astra, 2024) [1]. The treatment of lung cancer is changing, and these trials show how immunotherapy may be used in combination with conventional chemotherapy to improve patient outcomes.

### Radio-dose

In clinical radiotherapy, the conventional pattern of low dose rate for intracavitary and interstitial therapy and high dose rate for external beam therapy has been questioned in recent years. For surface mold applications and intracavitary treatment of cervical carcinoma, the Cathetron has enabled the use of a high dose-rate fractionated regime. The low dose-rate (100 rads/hour) beam therapy, on the other hand, has been proposed and recently introduced to combine the safety and convenience of a beam therapy setup with the purportedly better results of radium (Hall, 1972) [9]. It is crucial to assess the radiation doses that the target organ and other internal organs will receive when administering radionuclides for medicinal purposes. Any estimate for a radionuclide must include data on its absorption and retention in different organs in the body after it has been administered to the patient, as

well as the amount of energy absorbed in those organs after each of its disintegrations (Vennart & Minski, 1962) <sup>[40]</sup>.

### Challenges and Public Health Strategies

Despite advancements in lung cancer research and treatment, several challenges persist in India. Limited access to early screening programs, high treatment costs, and lack of awareness contribute to poor patient outcomes. Government initiatives, such as the National Programme for Prevention and Control of Cancer, Diabetes, Cardiovascular Diseases, and Stroke (NPCDCS), aim to enhance cancer detection and treatment (ICMR, 2021). Expanding tobacco control policies, pollution mitigation strategies, and improving healthcare infrastructure are crucial for reducing lung cancer incidence and mortality.

### Conclusion

Lung cancer remains a significant public health challenge in India and worldwide, with rising incidence and high mortality rates. Tobacco consumption, environmental pollution, occupational hazards, and genetic factors contribute to the disease burden, necessitating a multifaceted approach to prevention and treatment. While advancements in diagnostics and treatment, including targeted therapy and immunotherapy, have improved patient outcomes, their accessibility remains limited due to high costs and infrastructure gaps. Strengthening early detection programs, expanding affordable treatment options, and implementing robust public health policies—such as stricter tobacco control measures and air quality improvements—are crucial to mitigating the lung cancer burden. Collaborative efforts between policymakers, healthcare professionals, and researchers will be essential to improving survival rates and enhancing the quality of life for affected individuals. Addressing these challenges with a comprehensive and equitable healthcare approach can significantly reduce lung cancer-related morbidity and mortality in India.

Lung cancer remains a significant health challenge in India, with rising incidence rates and late-stage diagnosis being major concerns. Research on epidemiology, molecular profiling, and innovative treatments has progressed, yet disparities in accessibility and affordability persist. Strengthening public health initiatives, expanding early detection programs, and making advanced treatments affordable will be key to addressing the lung cancer burden in India. Continued research and policy interventions are essential to improve outcomes and reduce mortality rates (Stathopoulos *et al.*, 2012) <sup>[38]</sup>.

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