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Epidemiology and Histopathology of Lung Cancer in Pakistan Compared with Other South Asian Countries

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Abstract

Lung cancer is one of the major causes of cancer deaths throughout the world and its impact is increasing in south Asian countries. While all of these countries lie within the same geographic area, there are differences in lung cancer frequency, pathological patterns, genetic changes, and environmental exposures associated with lung cancer. The purpose of this review was to investigate and compare the epidemiological and histopathological features of lung cancer in Pakistan with other south Asian countries like India, Bangladesh, Sri Lanka and Nepal. Studies on incidence, mortality, pathological changes and risk factors with regard to lung cancer were included. Lung cancer is one of the frequently mentioned cancers in Pakistan and also causes a significant mortality rate in the country annually. Incidence and mortality are lower than in some Asian countries but the overall burden of disease is increasing. Many studies report the most common histopathological type as adenocarcinoma. Indoor smoke exposure to biomass fuel and occupational exposures are still considerable contributory factors to the development of disease, with smoking still being the top risk factor. Pakistan had a higher proportion of male patients, late diagnosis, and less access to modern techniques of molecular diagnosis and targeted therapy compared to neighboring countries. The overall epidemiological and histopathological parameters of lung cancer in Pakistan are similar to other countries of south Asia. Enhanced cancer surveillance, early screening facilities and molecular testing are crucial to improved cancer management and cancer-related deaths reduction.

Keywords: Lung cancer, Epidemiology, Histopathology, Adenocarcinoma, Smoking, Cancer registry

Introduction:

Lung cancer is still one of the most fatal cancers in the world and the primary cause of cancer related mortality worldwide (International Agency for Research on Cancer, 2020). Millions of new cases are diagnosed worldwide each year and many of the deaths are due to the fact that the disease is often not diagnosed until an advanced stage (Sheikh et al., 2022). This burden is more severe in low-middle income countries where health care resources and/or early screening facilities are less available (The Lancet Regional Health–Southeast Asia, 2024). The South Asian region is made up of densely

populated countries like Pakistan, India, Bangladesh, Sri Lanka, Nepal and Bhutan. Over the past few decades the incidence of lung cancer in this region has steadily increased (Moore et al., 2015). This increase can be attributed to several factors such as cigarette smoking, exposure to biomass fuel smoke, environmental pollution, and exposure to harmful substances at the workplace and rapid industrialization (Raaschou-Nielsen et al., 2013). Although these countries share similar risk factors there are differences in regards to disease patterns, histological subtypes and prognosis (The Lancet Regional Health–Southeast Asia, 2024). Pakistan has many challenges in the field of lung cancer prevention and treatment due to these variations and its associated risk factors such as lifestyle habits, health care system, genetic susceptibility, and access to diagnostic facilities (Sheikh et al., 2022). Smoking rates are still high among men and awareness of early signs and routine screening is still low in the general population (Ahmad et al., 2005). Furthermore, there is no complete national cancer registry system and the bulk of available data comes from regional cancer registries (Ikram et al., 2023). A large percentage of patients are diagnosed in advanced stages when treatment options become limited and survival chances decreased significantly (Bhurgri, 2004). The current review emphasizes the epidemiology and histopathology of lung cancer in Pakistan, and highlights the comparison of available results with lung cancer in neighboring south Asian countries. Incidence trends, pattern of mortality, pathological subtypes, molecular features and key environmental and lifestyle risk factors are discussed. It also pinpoints existing problems and opportunities for further enhancement of health care policies and cancer control programs. Global and Regional Burden of Lung Cancer Global overview Lung cancer is one of the more prevalent cancers in the world today, and the leading cause of cancer death for both men and women. International cancer statistics released in 2020 shows that it is the second most common cancer after breast cancer (International Agency for Research on Cancer, 2020). Due to its severity and mortality, the disease remains a significant health care problem. There are many more cases of non-small cell lung cancer (NSCLC), which makes up almost 85% of lung cancer cases worldwide (Travis et al., 2017). Adenocarcinoma is the most common, then squamous cell and large cell carcinomas. A smaller number of cases are small cell lung cancer (SCLC), which is regarded as more aggressive due to its fast growth and early spread to the distant parts of the body. The countries with the highest age-standardized incidence rates include mostly east Asian countries, especially China and North Korea (Li et al., 2023). South Asian countries, in comparison, have lower rates of incidence. But with the escalating population growth, consumption of tobacco and environmental pollution, along with ageing pollution, the total incidence of lung cancer in South Asia is still steadily increasing (Saleh Iniya et al., 2015). Burden of Lung Cancer in South Asia in South Asian countries, lung cancer is a major contributor of cancer cases per year. In most cancer centers in the region, lung cancer is the primary or second leading cancer in males. The burden of disease varies from country to country, although there are some similarities in the geographical and lifestyle factors, differences in smoking patterns, health care systems, environmental exposures, and cancer registration facilities. The incidence and mortality rates of cancers in Pakistan are relatively low compared to some of its neighboring countries but the limited cancer registration systems may underestimate the burden of the disease (Ikram et al., 2023). The high prevalence of tobacco consumption and the huge population of India results in the highest number of lung cancer cases in the region (Moore et al., 2015). There is also a rising trend of patient numbers reported in Bangladesh and Nepal, and National cancer reporting systems are relatively robust in Sri Lanka. Male predominance is seen consistently across south Asia – this is primarily because smoking is more prevalent among males than females. Some countries have poor access to screening programs and diagnostic facilities, which leads to delayed diagnosis and thus poor survival (Sheikh et al., 2022).

Epidemiology Lung Cancer Pakistan: Incidence and Mortality

Lung cancer is one of the leading cancers reported in Pakistan and contributes significantly to cancer related deaths every year (Sheikh et al., 2022). Based on the available international and regional statistics, the disease makes up a significant number of the cases of new cancer diagnosis in the country. While the incidence and mortality rates in Pakistan are low as compared to many Asian countries, experts suggest that the true figures could be higher than what has been reported (Ikram et al., 2023). These relatively low rates may be due to under diagnosis, lack of complete reporting systems and lack of a fully functioning nationwide cancer registry. What is not recorded are many cases in both rural and underdeveloped areas, where the people lack access to health care (Bhurgri, 2004). These obstacles have not prevented lung cancer from still being a very big health problem, particularly for men.

Cancer Registry Systems and Data Limitations

The main challenge in realizing the burden of lung cancer in Pakistan is the absence of a comprehensive national cancer registry (Ikram et al., 2023). The majority of the information available is from original cancer registries, like the Karachi cancer registry and the Punjab cancer registry, that primarily gather data from large urban centers (Bhurgri, 2004). Consequently the statistics available may not be representative of the situation in rural populations and of smaller provinces. There has been an effort to improve national cancer data collection in recent years, however important areas of gap remain (Ikram et al., 2023). Available statistics are sometimes based on statistical modelling instead of actual national reporting, impacting on the quality of available statistics. Despite these restraints, the published literature overwhelmingly demonstrates that such factors as smoking, late presentation and male preponderance are significant characteristics of lung cancer and Pakistan (Sheikh et al., 2022; Bano et al., 2023). The distribution of population by age, gender and demography Male gender is more prone to lung cancer in Pakistan. The majority of published studies report a ratio of 3:4 of males to females (Bhurgri et al., 2006). This difference is significantly related with the greater smoking prevalence among male Pakistani population as compared to the female population (Ahmad et al., 2005). Smoking cigarettes remains the primary risk factor and use of smokeless tobacco products and bidis play a factor in disease developments in some communities. The disease is commonly diagnosed in middle age and the elderly. Unfortunately, many of the patients only turn to the doctors when the cancer is in an advanced stage. All the studies carried out in Pakistan have shown that the majority of patients at the stage IV of the disease have limited treatment options and significantly lower chances of survival (Emerging trends in lung cancer presentation, 2024). The low level of public awareness, financial constraints, social obstacles and lack of organized lung cancer screening programs in health care systems are all associated with delayed diagnoses.

Urban and Rural Differences

In Pakistan, most of the cancer diagnosis and therapeutic centers are located in the major cities like Karachi, Lahore, Rawalpindi, Peshawar, etc. (Badar et al., 2016). Patients in rural areas and in smaller provinces sometimes have a hard time evaluating specialized oncology services. Due to long distances and time lag in referral systems, many patients were brought to tertiary hospitals in the late stage of the disease (Emerging trends in lung cancer presentation, 2024). Major hospital-based studies have revealed that a high percentage of lung cancer cases are registered in urban areas, especially in Karachi and Lahore (Bhurgri et al., 2006; Badar et al., 2016). This pattern, however, may be a reflection of referral patterns and not true geographic distribution of the disease. Under reporting and delayed diagnosis may be due to limited health care infrastructure in the rural areas.

Comparative Epidemiology Pakistan v/s other south Asian Countries: India

India has a large population of approximately 1.4 billion and a relatively well-developed cancer surveillance system with various population-based cancer registries as part of the national cancer registry program (NCRP). Lung cancer is also the most common form of cancer in India, accounting for about 10.6% of the total cancer burden, of which over 100,000 new cases are expected by the year 2022 (Moore et al., 2015). A higher percentage is seen in the northern and north eastern parts of the country, and this is mainly attributed to smoking and biomass fuel smoke in the home. One of the remarkable facts in India is that even non-smokers have a relatively high lung cancer incidence when compared to the western countries, which might be an indication of rules governing indoor air pollution and genetic susceptibility. Roughly 22-33 % of Indian NSCLC cases of adenocarcinoma have EGFR mutations (Mok et al., 2015). This rate is below that of some countries in east Asia, but molecular diagnostic facilities in Pakistan are much more advanced than in other countries, with advanced sequencing only available in a few labs.

Bangladesh

Bangladesh has a relatively high burden of lung cancer in south Asia with the estimated incidence rate to be approximately double that of India and higher than Pakistan (Moore et al., 2015). Major contributing factors are very high tobacco consumption, very high occupations in tanning and textiles and very high exposure to air pollution. Case-control studies suggest a very strong association between smoking and lung cancer of around odds ratio = 9.7. But the lack of registry infrastructure hinders the ability to make accurate national estimates and conduct wide-spread epidemiological surveillance.

Sri Lanka

Sri Lanka has a working national cancer registry and lung cancer incidence rate of approximately 6.2 per 100,000 population, which is slightly higher than Pakistan (The Lancet Regional Health–Southeast Asia, 2024). Most cases are caused by tobacco smoking, and almost 84 % of all lung cancer cases among males are related to exposure to tobacco. There have been several case-control studies indicating a strong association between smoking and lung cancer. Sri Lanka has better diagnostic and treatment facilities compared to some neighboring countries, which makes better cancer staging, management outcomes.

Nepal:

Lung cancer burden is high in Nepal as compared to health care system strength (Subedi et al., 2021). Studies with several hundred smokers have demonstrated almost a 5x greater risk of lung cancer. Environmental exposure is important as firewood and dung are used as fuel largely for cooking and heating, particularly in rural and high-altitude regions (World Health Organization, 2018). These are the practices that are major sources of indoor air pollution. The cancer registry systems are under development and a large part of the national data is derived by modelling (Subedi et al., 2021).

Regional Overview

Across south Asia, lung cancer patterns show both similarities and differences. India and Bangladesh generally report higher absolute case numbers, while age-standardized rates are broadly comparable across the region (Moore et al., 2015). Male dominance is consistent in all countries, while lung cancer in women is more often linked to indoor pollution and non-smoking-related adenocarcinoma, frequently associated with EGFR mutations (Mok et al., 2015). Late diagnosis is common throughout south Asia, especially in countries with weaker health care infrastructure such as Pakistan and Bangladesh (Sheikh et al., 2022). Molecular diagnostic availability remains highest in India.

The Major Types and Who Classification Lung Cancer Falls into Two Broad Categories:

Non-small cell lung cancer (NSCLC) (approximately 85% of cases) and small cell lung cancer (10-15%) (Travis et al., 2017). NSCLC can also be subdivided into 3 categories: adenocarcinoma, squamous cell carcinoma and large cell carcinoma. The modern classification systems stress the importance of histology along with molecular and immunohistochemical markers for the proper diagnosis (Osmani et al., 2018). An adenocarcinoma originates from glandular epithelial cells and is usually found in the peripheral lung. It is more prevalent among non-smokers, women and Asian races. Squamous cell carcinoma develops in the bronchial epithelium, and smoking is a major risk factor. When other types are excluded, the diagnosis of large cell carcinoma is made when the tumor is poorly differentiated. SCLC is a very aggressive neuroendocrine tumor that is rapidly spreading with early metastasis (Travis et al., 2017).

Histopathology in Pakistan

Adenocarcinoma is emerging as the most prevalent form of lung cancer in Pakistan, and it was found in approximately 38% of lung cancers in various hospital-based studies (Sheikh et al., 2022; Bano et al., 2023). Squamous cell carcinoma is the second most common type of lung cancer, with small cell and large cell carcinoma coming after (Emerging trends in lung cancer presentation, 2024). The increasing trend of adenocarcinoma is consistent with what has been observed worldwide and could be associated with changes in cigarette design, the rising incidence of non-smokers, and the advances in the diagnosis of cancer. Yet there are still patients for whom there is limited immunohistochemistry and molecular testing facilities, and fall into the category of NSCLC-NOS (Osmani et al., 2018).

Regional Histological Pattern

In south Asia, adenocarcinoma is usually the most common type, and is similar to squamous cell carcinoma based on a tobacco exposure pattern (The Lancet Regional Health–Southeast Asia, 2024). Increase of population who use bidi or unfiltered tobacco regularly, consistently and heavily is associated with squamous cell carcinoma which constitutes approximately 10-15% of cancer cases in the region.

Squamous Cell Carcinoma

SCC generally occurs in the central airways and is strongly associated with smoking particularly among older men. It exhibits keratinization and intercellular bridges histologically and is stained positive for markers like p40, ck5/6 (Osmani et al., 2018). It is still more prevalent in areas with high consumption of unfiltered tobacco products. In countries where bidi smoking is prevalent such as Bangladesh, the rate of SCC could be relatively high.

Adenocarcinoma

Adenocarcinoma, the most common form of tumor, has become the most common type of tumor in the South Asian region and especially in Pakistan (Sheikh et al., 2022). It is secreted from glandular tissue found at the periphery of the lungs and is seen in non-smokers, especially women who could be exposed to indoor pollution. In the modern classification, there are different subtypes, such as adenocarcinoma in situ and lipidic-predominant patterns, which have prognostic significance (Travis et al., 2017). It is therefore important to make a histological diagnosis for targeted therapy as EGFR mutations are more common in adenocarcinoma (Mok et al., 2015).

SCLC is a highly aggressive neuroendocrine tumor which is closely associated with smoking. It is a fast-growing, early-spreading tumor that is chemo sensitive but tends to recur. It is composed of small cells with little cytoplasm and ends with granular chromatin, which is the final stage when the cells are viewed under the microscope (Travis et al., 2017). Neuroendocrine markers: synaptophysin and CD56 are typically positive. Treatment is quite different from NSCLC and typically depends on platinum-based chemotherapy alone and not radiation therapy.

Risk Factors in South Asia. Tobacco smoking

Tobacco use is the single largest risk factor for lung cancer, accounting for most deaths worldwide, particularly in south Asia, and comes in a variety of forms such as cigarettes, bidis, hookah and smokeless tobacco such as gutka and naswar (Ahmad et al., 2005; Alam, 1998). Bidis used in India, Bangladesh and Nepal have more harmful chemicals than cigarettes. The association of smoking and lung cancer in Pakistan is very high and in some populations the odds ratio of lung cancer among smokers has been reported as high as 9-22 (Sheikh et al., 2022). Hookah smoking is also prevalent in the culture, and it is also a source of exposure to carcinogens. Smokeless tobacco products also raise the risk of cancer systemically because of the absorption of these carcinogens.

Indoor Air Pollution

Biomass fuels (wood, dung and crop residues) are a significant risk factor in rural South Asia due to indoor pollution (Raaschou-Nielsen et al., 2013). Poor ventilation results in poor exposure to particulate matter and carcinogenic chemicals. Women are the more affected ones because they are more exposed while cooking. This exposure is definitely linked to lung cancer among non-smokers, especially adenocarcinoma.

Outdoor Air Pollution

Today, air pollution, particularly fine particulate matter (PM2.5), is known to be a significant carcinogen. Long-term exposure is an important factor in lung cancer risk (Raaschou-Nielsen et al., 2013). Pollution levels in Lahore, Karachi, Delhi and Dhaka are often much higher than WHO standards. This adds up to an overall environmental risk if combined with indoor air pollution and smoking.

Occupational Exposure

High levels of lung cancer are associated with exposure to asbestos, silica, heavy metals and diesel exhaust from industries (Raaschou-Nielsen et al., 2013). Monitoring of occupational health is weak in South Asia particularly informal labor sectors. Construction, mining and industrial workers are subjects at high risk, and cases are under-reported because there are no surveillance systems in place.

Tuberculosis screening and lung screening

Pulmonary tuberculosis is a common condition in south Asia and has been associated with an increased risk for lung cancer. Scars in the lungs may be a risk factor for future malignancy, especially adenocarcinoma. In several studies, smoking was not the only factor that increased the risk of TB, TB history was also an important independent risk factor.

Molecular and Genomic Landscape Egfr Mutations

The most clinically relevant EGFR gene activating mutations in non-small cell lung cancer (NSCLC), particularly in adenocarcinoma, include mutations in the 19th exon (exon 19 deletions) and the 21st exon (exon 21 substitutions) (Mok et al., 2015). In the large PIONEER study that included 1482 patients from Asian countries, the rate of EGFR mutations was found to be higher (51.4%) than in western populations (around 10-15%). There is however, variation within Asia with lower frequency reported in India (approx. 22%) than in several east and south east Asian countries (Mok et al., 2015). Systematic data are limited in Pakistan because there is a lack of access to molecular diagnostics. EGFR testing is currently available in only a few laboratories across the country, and is even more limited in advanced genomic sequencing facilities. The data available indicate that the mutation rate of Pakistani adenocarcinoma patients is generally comparable to that in India (approximately 22-30%). These mutations are more prevalent in females, never-smokers and adenocarcinoma histology – an emerging subset throughout south Asia.

Alk/Ros1 Rearrangement:

ALK gene rearrangements are found in about 5-7% of NSCLC patients, and ROS1 rearrangements in about 1-2% of patients. These genetic changes are clinically relevant as they are well known for targeted therapeutics. Lung cancer with an abnormal ALK gene now has more effective drugs called

ALK inhibitors, such as crizotinib, alectinib, and ceritinib, that have helped to improve survival. Availability of molecular testing for south Asians varies to a wide extent. In India, access is relatively good with a significant volume of biomarker testing being done in the major centers; though, in Pakistan such biomarker testing is limited to a few tertiary care hospitals in big cities.

Kras and Other Genetic Alteration

KRAS mutations are one of the most prevalent driver mutations in NSCLC worldwide, with prevalence in western populations potentially being as high as approximately 30%. In Asian populations, mutations in the KRAS gene are less common, which may be due to differences in smoking habits and tumor biology (Mok et al., 2015). In emerging therapeutic targets, KRAS G12C has emerged as a key target in recent years, as new targeted therapies have been developed. The other interesting and actionable mutations such as BRAF V600E, HER2 (ERBB2), MET exon 14 skipping and RET rearrangements are also clinically relevant, but less frequently tested in Pakistan and Bangladesh because of financial constraints and laboratory infrastructure.

Pd-L1 Expression and Immunotherapy

PD-L1 is a significant biomarker for prognosis of response to immune checkpoint inhibitors (ICIs). In some of the big cancer institutes in India, a significant number of cases get tested for PD-L1. PD-L1 testing is not widely available in Pakistan and only occurs in certain private or tertiary care hospitals. Likewise, expensive drugs that target PD-L1/PD-1 (pembrolizumab and atezolizumab) are not widely available. There is no national data of percentage of PD-L1 expression levels in lung cancer patients of Pakistan. This makes a big difference in cancer care around the region.

The Clinical Presentation and stage at Time of Diagnosis. Pakistan

Persistent cough (approximately 49%), hemoptysis (around 33%) and chest pain (about 35%) were the most frequently reported symptoms for lung cancer patients in Pakistan (Emerging trends in lung cancer presentation, 2024). They are not specific and may be confused with TB and are common to chronic respiratory illnesses like COPD, which causes a delay in the diagnosis. The age range in which patients are diagnosed is relatively wide, from 45-75 years. One of the concerns is the high number of cases – up to 80% – with advanced metastatic disease (stage IV) (Sheikh et al., 2022; Bano et al., 2023). Cases are presented at a late stage, which reduces the number of treatment options available and is an important reason for poor survival. Most cases are only detected when symptoms are severe, as routine screening programs are not in place, including the low dose CT scanning of high-risk individuals.

The Distribution of Stages in South Asia

The diagnosis of many diseases is delayed in the South Asian region, though the percentage of late diagnosis differs from country to country. Studies have shown that about 65-75% of the patients present at stage III & IV, which is slightly lower than the figures reported from Pakistan (Moore et al., 2015). However, Sri Lanka, which has a relatively robust health care system and referral system, may be able to achieve a bit earlier detection in stain cases. But in the region as a whole, early-stage lung cancer (I or II) is rare, unless there are organized screening programs. Health care challenges and opportunities.

Challenges in Pakistan

There are several systemic issues confronting Pakistan in the treatment of lung cancer. An important constraint is the absence of an adequate and complete national cancer registry which makes it difficult to obtain reliable estimates of cancer burden and outcomes (Ikram et al., 2023). The diagnostic facility like bronchoscopy, biopsy, immunohistochemistry and molecular testing is limited to certain main cities like Karachi, Lahore and Islamabad (Badar et al., 2016). Consequently, there is a significant portion of the population who are either not able to access a diagnosis or not able to access a diagnosis in a timely fashion. Chemotherapy and radiotherapy are available in public hospitals, but there are

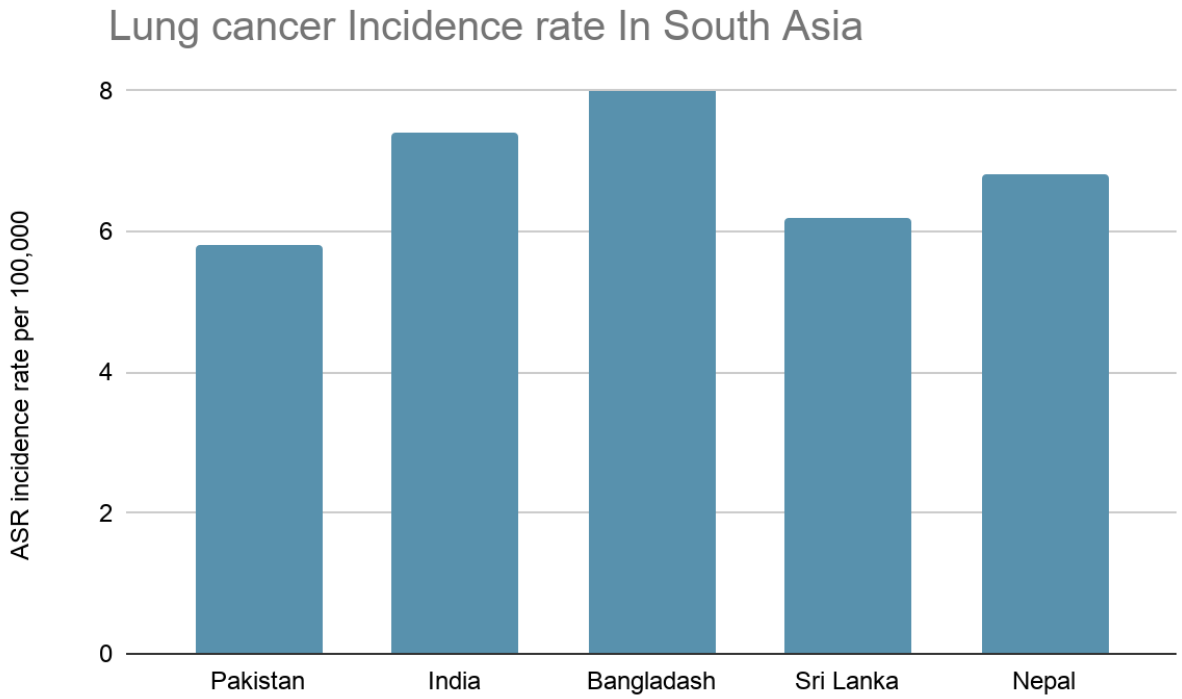
times when treatment continuity may be impacted by drug shortages and resource limitations. Medications that are more sophisticated, like tyrosine kinase inhibitors or immunotherapy, are widely unavailable in public health care facilities or in external programs for using these drugs. Progress has been made in recent years, such as national cancer reporting systems (Ikram et al., 2023). But, for substantial impact, long term investment in infrastructure, trained personnel and tobacco control is crucial.

Opportunities for Improvement

The mortality due to lung cancer can be substantially decreased in Pakistan and the south Asian region by implementing several strategies. The strongest tobacco control policies – such as higher taxes, public education and the banning of heavy advertising – continue to be the most effective prevention strategies (Ahmad et al., 2005). Selective screening with low-dose computed tomography in high-risk patients may help to enhance the early detection of cancer, and international research has shown a reduction of lung cancer deaths of approximately 20-25% by using the technique (National Lung Screening Trial Research Team et al., 2011; de Koning et al., 2020). The enhancement of the cancer registry system at provincial and district level will help to enhance the accuracy of the data and improve health planning (Ikram et al., 2023). Increased lab capacity for IHC and low-cost molecular testing (EGFR testing via PCR) would provide greater access to targeted therapy, which has significant efficacy in certain patient populations. Regional cooperation among the south Asian countries could be achieved in research, clinical trials, and data sharing, evidence could be generated that's more reliable and better cancer care for a population of more than 1.5 billion people.

Comparison of Epidemiology of Lung Cancer in Pakistan V/S Other South Asia Countries

Histological subtype	Pakistan	India	Bangladesh	Sri Lanka	Nepal
Adenocarcinoma	~38%	~35-40%	~30-35%	~33%	~30%
Squamous cell	~30%	~25-30%	~35-40%	~30%	~35%
SCLC	~12-15%	~10-12%	~10-15%	~12%	~10%
Large cell	~8-10%	~8-10%	~8-10%	~8%	~8%
NSCLC-NOS/other	~10-15%	~10-15%	~10-15%	~10%	~12%



COUNTRIES

Histological subtype	Pakistan	India	Bangladesh	Sri Lanka	Nepal
Adenocarcinoma	~38%	~35-40%	~30-35%	~33%	~30%
Squamous cell	~30%	~25-30%	~35-40%	~30%	~35%
SCLC	~12-15%	~10-12%	~10-15%	~12%	~10%
Large cell	~8-10%	~8-10%	~8-10%	~8%	~8%
NSCLC-NOS/other	~10-15%	~10-15%	~10-15%	~10%	~12%

Conclusion:

Lung cancer is still a major and fluctuating public health problem in Pakistan and in the rest of South Asia. Many factors are related to each other and contribute to disburden, which include a high level of indoor and outdoor air pollution, delayed diagnosis, lack of health care infrastructure, and widespread tobacco smoking. Lung cancer is the third most prevalent type of cancer in Pakistan, mainly seen in older males. Histologically, adenocarcinoma is now the most common subtype, as is also the case in neighboring South Asian nations (Sheikh et al., 2022). But Pakistan has other problems because of its weak cancer registry system, scarcity of diagnostic facilities and availability of only few cancer treatment facilities (Ikram et al., 2023). From the histopathological point of view, adenocarcinoma is now the predominant type of tumor in the area, surpassing squamous cell carcinoma. This change is associated with changes in smoking status and the rising prevalence amongst non-smokers, especially women who are exposed to biomass fuel and indoor air pollution. In Pakistan, clinically important genetic alterations like EGFR mutations are present in nearly 22-30% of NSCLC adenocarcinoma patients (Mok et al., 2015). Even so, molecular diagnostic testing is mainly restricted to big cities, making its role and value at a national level in combating the burgeoning lung cancer burden in Pakistan fairly limited. Strengthening of the national cancer registration system, implementation of strong tobacco control policies, feasibility of lung cancer screening programs, and the expansion of both histopathology and molecular diagnostic services are some of the key priorities. Furthermore, targeted therapies and immunotherapy are key to ensuring equity of access to insurances. Regional cooperation among South Asia could help facilitate knowledge sharing, and help speed up the advancement of outcomes for this under-served patient population.

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