

# Editorial

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## Lung Cancer In India – Changing Trend

Lung cancer is the most common malignancy across the globe and accounts for very high morbidity and mortality<sup>1</sup>. It is the leading cause of cancer related death in developed countries and is rising at an alarming rate in developing countries including India<sup>2</sup>. There is direct association of tobacco smoking to lung cancer making it the leading preventable cause of death. Lung cancer was a rare disease before the advent of cigarette smoking and was not even identified as a distinct disease until 1761. Since the early 1900's, lung cancer rates have gone up to the extent that now it is a global epidemic. Poor awareness about harmful effects of smoking of various types has led to increased number of patients with lung cancer. Although smoking is considered as one of the major causes of lung cancer, not all smokers develop lung cancer, indicating the role of additional cofactors for lung carcinogenesis. Several studies have been carried out to identify the etiological factors of lung cancer. Various lifestyle factors also play an important role in lung cancer etiology.

The clinical features of lung cancer are quite non specific. Symptoms such as fever, cough, expectoration, hemoptysis, weight loss and anorexia are common to tuberculosis and lung cancer. In India where tuberculosis is rampant, it is not uncommon to find a lung cancer being treated as tuberculosis or chronic obstructive airway disease<sup>3</sup>. Traditional literature mentions that only 20-30% of patients have an operable disease at time of presentation, and the situation has not changed much over decades<sup>4</sup>.

The relative frequency and clinicopathological profile of different histological sub types of primary lung cancer have changed in recent years, probably due to changes in smoking habit, growing popularity of low-tar/ filter cigarettes and exposure to other occupational agents. An increasing occurrence of lung cancer in never smokers is being documented<sup>5</sup>. Globally, lung cancer in never smokers exhibits a remarkable gender bias with ladies accounting for vast majority of the cases. Cancers in never smokers tend to arise in distal airways and the histological pattern favours adenocarcinoma. Molecular studies, especially the TP 53, KRAS and EGFR genes demonstrate distinctly different mutations between lung cancers in smokers versus non smokers<sup>6</sup>. Never-smokers with lung cancer present with more advanced disease,

usually at an earlier age, again suggesting a biologically different disease from tobacco-related lung cancer.

Management of lung cancer has undergone dramatic transformations over the last couple of decades. Targeted or personalized therapy provides an attractive option in subjects with carcinoma lung with the potential of maximizing therapeutic effects to tumour cells without major influence on surrounding normal tissue<sup>8</sup>. The identification of molecular pathways have allowed for better understanding on tumour pathogenesis and prediction of response to agents targeting specific pathways. Some of the specific pathways that have been the targets of detection as well as therapy in carcinoma lung include the mutations in the epidermal growth factor receptor (EGFR), anaplastic lymphoma kinase (ALK) and K-RAS, of which maximum attention has been dedicated to EGFR mutations. The occurrence of EGFR mutations in subjects with non small cell lung carcinoma is between 25-40% and the figure reaches higher proportions if adenocarcinoma cases are examined<sup>9</sup>. Therapy with tyrosine kinase inhibitors like gefitinib and erlotinib doubles the survival rates even in subjects with EGFR mutation positive stage 4 lung carcinoma and the potential to administer these agents orally has revolutionized the treatment of advanced lung cancer<sup>10</sup>. Agents like crizotinib may be beneficial in the minority of subjects with ALK mutation.

Early detection of lung cancer is challenging owing to the relative asymptomatic status of peripheral lesions as well as non specific nature of symptoms. This has lead to the attractive concept of lung cancer screening in an attempt to early diagnosis and therapy, with the hope that this might translate to better survival and outcomes. Early attempts by chest roentgenograph have yielded disappointing results<sup>11</sup>. Renewed interest in the field has ignited from the studies employing low dose CT to detect early tumours. The results published by the National Lung Screening Trial Research Team in 2011 indicated a better detection rate and 20% reduction in mortality due to lung cancer if a screening programme was implemented by an experienced centre<sup>12</sup>. The subject has been the area of limelight and controversy since then, with issues centering around the ideal subject who needs screening, unnecessary procedures performed on subjects with benign lesions with attendant complications, lead time bias, varying growth pattern of tumours etc. A recent article concluded that individuals at high risk of lung cancer who meet the criteria for CT screening in published guidelines should participate in an informed and shared decision making process by discussing the potential benefits, harms, and uncertainties of screening<sup>13</sup>. Given the high incidence of tuberculosis and other granulomatous diseases in the country with consequent presence of benign nodules on radiography, most stake holders in the country including the authors feel that Indian population may not merit a screening programme employing low dose CT.

Disclosures / Conflicts of interest - None

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