

CARCINOMA LUNG AMONG SOUTH INDIAN FEMALE PATIENTS: A SINGLE INSTITUTE EPIDEMIOLOGICAL STUDYC. Sanjeeva Kumari¹, M. Adi Lakshmi², John Winkle³, Aparna Suryadevra⁴**HOW TO CITE THIS ARTICLE:**

C. Sanjeeva Kumari, M. Adi Lakshmi, John Winkle, Aparna Suryadevra. "Carcinoma Lung among South Indian Female Patients: A Single Institute Epidemiological Study". Journal of Evolution of Medical and Dental Sciences 2015; Vol. 4, Issue 54, July 06; Page: 9327-9335, DOI: 10.14260/jemds/2015/1356

ABSTRACT: INTRODUCTION: Lung cancer is the major cause of morbidity and mortality worldwide, accounting for more deaths than any other cancer cause. The data on Indian female lung cancer patients is very sparse. So the aim of our study was to analyze the epidemiology and clinical behavior of lung cancer in female patients. **METHODS:** A total of 244 female lung cancer patients treated at MNJIO/RCC from 2010 to 2014 were evaluated retrospectively for the epidemiology and clinical behavior. **RESULTS:** The median age at presentation is 56 years and majority were post-menopausal. Majority of the patients were non-smokers (75%). ECOG PS 0,1,2,3 and 4 was seen in 0.55%, 12.15%, 33.14%, 44.19% and 9.94% of the patients respectively. NSCLC was seen in about 80% of the patients. Among the NSCLC, adenocarcinoma was seen on 61%). The TNM stage at presentation was stage II, III and IV in 1%, 6% and 92% of the patients respectively. Most common site of metastasis was pleura and malignant pleural effusion (57%) followed by bone metastasis (24%). Majority of the patients were stage IV and treated with palliative intent (77%). Among patients treated with chemotherapy only 14% completed planned treatment. But among patients planned with radical CT and RT, 75% completed treatment. At the time of conclusion of the study only 13 (7.18%) were alive and on follow-up. **DISCUSSION & CONCLUSION:** Carcinoma lung in the female South Indian patients is similar in the mean age at presentation to other studies from North India. Majority of the patients in our study were non-smokers, much higher than other studies. NSCLC was common, with adenocarcinoma as the most common subtype. The trend of a shift from squamous cell carcinoma to adenocarcinoma mentioned in western population is confirmed in our study. Pattern of metastases is slightly different among Indian female lung cancer patients, with majority having metastasis to pleura or malignant pleural effusion. In our study majority had a poor ECOG PS and advanced disease and more patients would benefit with best supportive care rather than CT. But patients with early disease can tolerate the aggressive treatment well.

KEYWORDS: Carcinoma lung; Female; India, Epidemiology; Histology; Metastasis.

INTRODUCTION: Lung cancer is the major cause of morbidity and mortality worldwide, accounting for more deaths than any other cancer cause. Lung cancer has been the most common cancer in the world for several decades. While there has been a substantial decline in lung cancer rates in developed countries, incidence rates are rising in the developing countries like China and India.^{1,2,3}

According to the recent GLOBOCAN 2008 report, India showed 47,010 new lung cancer cases among males and 11,557 new lung cancer cases among females. The age standardized incidence/100,000 is reported to be 10.9 for males and 2.5 for females in 2008 in India. Lung cancer has also been the leading cause of disability-adjusted life year (DALY) with 549,000 in males and 127,000 in females in 2004. However robust data on the epidemiological trends in lung cancers from the Indian subcontinent is lacking.^{1,4,5}

ORIGINAL ARTICLE

The variations and trends in histology have been a matter of interest in many studies. Lung cancer (80-90%) is most commonly attributed to smoking.¹ The strength of the association between smoking and lung cancer varies by histology. The majority of the Indian studies showed that squamous cell carcinoma was the most common histological subtype⁶. But recent studies show a possible shift in histology from squamous cell carcinoma to adenocarcinoma in India. The never-smoking cohort is also increasing in females with higher adenocarcinoma rate in comparison to the smokers' group.^{1,7,8,9}

The aim of our study is to assess the female lung cancer patients treated at our institute regarding the epidemiological features, smoking, histological type and the behavior of the disease in these patients.

METHODS: All the female lung cancer patients treated at Mehdi Nawaz Jung Institute of Oncology and Regional Cancer Centre (MNJIO/RCC) from January 2010 to December 2014 were reviewed retrospectively. All female lung cancer patients treated at MNJIO/RCC during this 5 year period were analyzed by retrieving the files from the medical record department of the hospital.

A total of 244 patients were reviewed in detail for this 5 year period. Out of these 181 patients were finally evaluable for our study. Remaining patients (63) were excluded from the study as they had incomplete data for evaluation.

In this single institute retrospective epidemiological study we evaluated each patient for demographics like age at presentation of the disease, menopausal status and history of tobacco use. Performance status (PS) of the patient at presentation assessed by Eastern Co-operative Oncology Group (ECOG) scale was recorded.

All patients had confirmation of lung cancer by histopathology on the biopsy specimen or pleural fluid cytology. Histological type and subtype of malignancy were noted. All cases were staged by using the latest TNM staging and stage of disease at presentation was noted.

All the patients with stage IV disease were assessed for the site of metastasis and all sites of metastasis at presentation were noted.

When patients received treatment, the intent of treatment was noted. Also the type of chemotherapy and radiotherapy was also recorded.

All the patient follow-ups were recorded and the reason for death of patient was recorded.

RESULTS: A total of 244 females with lung cancer were assessed but out of these 181 were included for analysis. Remaining 63 patients were excluded as the data was incomplete on these patients.

Age of patients at presentation ranged from 23 to 89 years with mean age of 56.03 years and median of 56 years. Majority of the females were among 41 to 70 years age group. The peak incidence was in the 5th decade (51 to 60 years). Figure 1 summarizes the age at presentation.

ORIGINAL ARTICLE

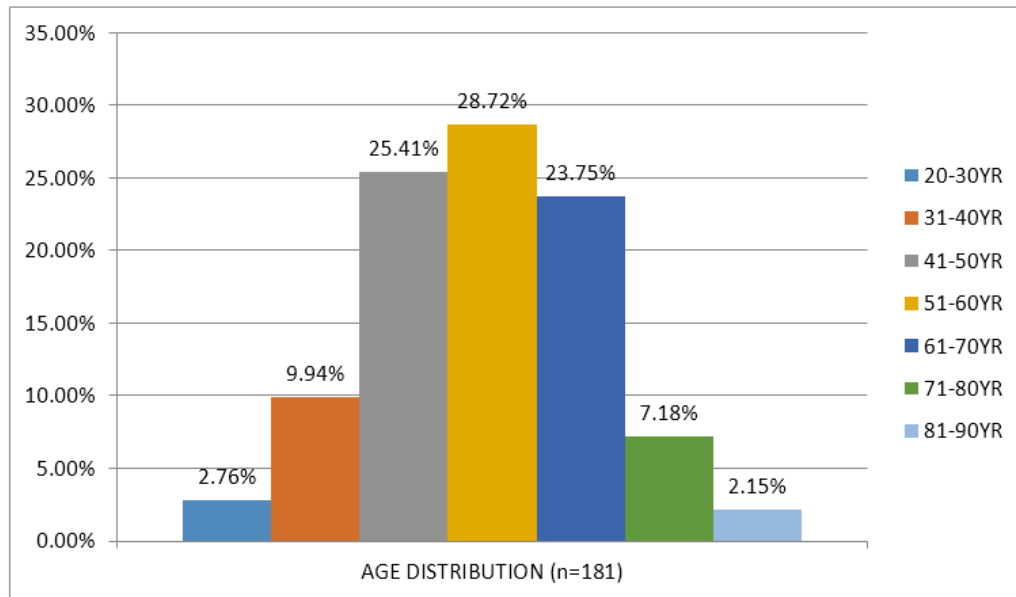


Fig. 1: Graph depicting the age-wise distribution of the female lung cancer patients

Menopausal status of the patients was also noted and majority of the patients were post-menopausal (n=135; 74.58%). The number of pre-menopausal patients was 46 (25.41%).

All patients were assessed for tobacco usage. Majority of the patients were non-smokers (75%). Fifteen percent of the patients had the habit of smoking tobacco while 9.16% patients had the habit of chewing tobacco.

Histopathology of the patients was reviewed in detail. Patients had different histologies but majority were non-small cell lung carcinoma (NSCLC) (n=145; 80.11%). Only 6 patients (3.31%) had small cell lung carcinoma (SCLC). So majority of the patients (80.11%) had NSCLC. SCLC was seen in small number of patients (3.31%). Figure 2 summarizes the histological type in study patients.

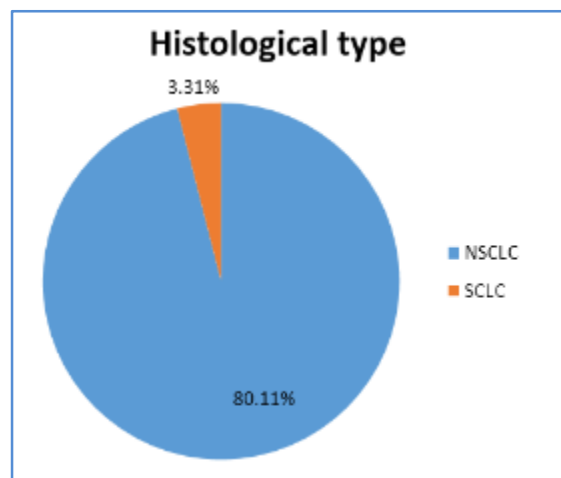


Fig. 2: Graph below showing the 2 most common histological types seen among the female lung carcinoma patients

ORIGINAL ARTICLE

Among the NSCLC, adenocarcinoma (n=111; 61.32%), squamous cell carcinoma (n=21; 11.6%) and large cell carcinoma (n=2; 1.1%) were noted. About 6.07% had NSCLC not otherwise specified.

Other histologies included mesothelioma (n=1; 0.55%), neuroendocrine tumor (n=1; 0.55%) and poorly differentiated carcinoma (n=9; 4.97%). Some patients (n=19; 10.49%) had only cytological evaluation of the pleural fluid which was positive for malignant cells. Graph below summarizes the different histologies seen in these females with lung carcinoma. Graph in figure 3 summarizes subtype of different histologies seen in the study.

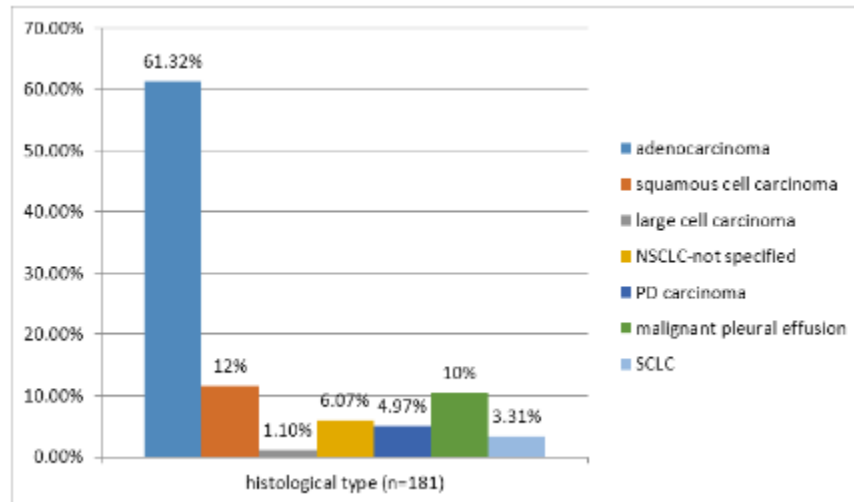


Fig. 3: Graph below summarizes the different histologies seen in the female lung carcinoma patients

Stage at presentation varied from TNM stage II to IV. All 181 patients were staged by the latest AJCC TNM staging for carcinoma lung. Majority of the patients were at TNM stage IV at presentation (n=167; 92.26%). There were no patients with TNM stage 0 or I disease while there were 3 (1.65%) with TNM stage II and 11 (6.07%) with TNM stage III disease. Graph below summarizes the stage wise disease distribution. Figure 4 summarizes the TNM stage at presentation.

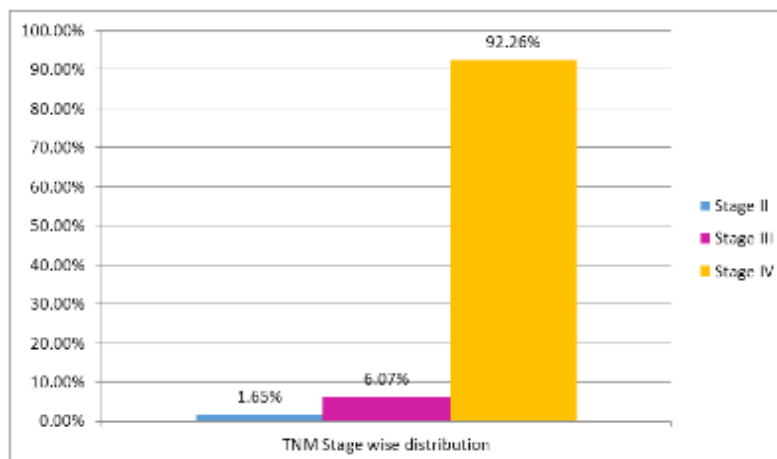


Fig. 4: Graph summarizing the TNM stage of disease at presentation among female lung cancer patients

ORIGINAL ARTICLE

All patients with stage IV disease were assessed for the pattern of metastasis. Most common site of metastasis was pleura and malignant pleural effusion (n=104; 57.45%) followed by bone metastasis (n=44; 24.30%). Thirty seven patients (20.44%) had metastasis at more than 1 site.

Brain metastasis was seen in 12 patients (6.62%), opposite lung metastasis in 19 (10.49%), liver metastasis in 22 (12.15%), adrenal metastasis in 11 (6.07%), pericardial metastasis with effusion in 4 (2.20%) patients was noted. Disease metastasis to scalp and choroid was noted in 1 patient (0.55%) and para-aortic lymphnode metastasis was noted in 1 (0.55%) patient. Graph in figure 5 summarizes the pattern of metastasis seen in the stage IV patients.

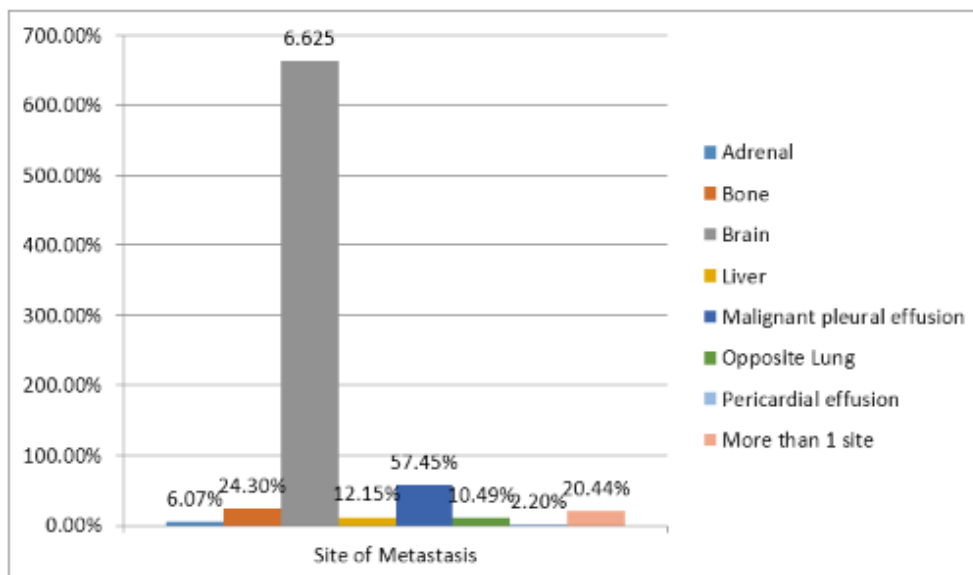


Fig. 5: Graph showing the site of metastasis among the female lung cancer patients shown as percentages

Performance status varied from ECOG scale 0 to 4. ECOG scale PS was 0 for 1 patient (0.55%) while 12.15% had a PS of 1, 33.14% patients had an ECOG PS of 2 and 44.19% had a PS of ECOG 3. A small percentage (9.94%) had a PS of ECOG 4.

Majority of the patients were stage IV and treated with palliative intent (n=140; 77.34%). Only 12 (6.62%) patients were treated with radical intent with chemotherapy (CT) and radiotherapy (RT) and 29 (16.02%) patients received only best supportive care due to poor general condition.

One hundred and eighteen (n=118; 65.19%) patients received CT while RT was given for 33 (18.23%) patients. Among patients treated with chemotherapy 17 patients completed planned treatment (n=17 of 118 cases; 14.4%). Among patients planned with radical CT and RT, 75% (n=9 out of 12) completed treatment. During treatment, 31 (17.12%) patients expired due to disease and/or treatment related complications. At the time of conclusion of the study only 13 (7.18%) were alive and on follow-up.

DISCUSSION: The total cancer incidence rate is lower in India than among Indians in other countries (Singapore, the UK and the US). Rates for certain cancers were higher in India than among Indians living elsewhere. These observations suggest the role of environmental and lifestyle factors as well as possible diagnostic and screening practice differences. Research on these patterns is needed to

advance the understanding of cancer etiology and to develop the means of prevention¹⁰. So the aim of our study was to analyze the epidemiology, pattern of spread and clinical behavior of lung cancer in female patients. The data on Indian female lung cancer patients particularly from Southern India is very sparse.

There appears to be a marginal increase in the mean age of diagnosis of lung cancers in India over the years, it was 52.16 years in 1958-1985 and 54.6 years during 1985-2001.⁶

The mean age at presentation was 56.03 years in our study which was similar to the other studies from North India.¹ Majority of the females were among 41 to 70 years age group with peak incidence in the 5th decade.

The mean and peak ages of lung cancers in India are lower when compared to the studies from the West.¹¹ An Indian study showed significant correlation between advanced age at presentation (>60 years) with a smoking history to squamous histology.¹ However in our study we didn't find such correlation.

The major histologic subtype in women over the last 20 years has been adenocarcinoma, while this subtype has only risen to prominence in men over the past 10 years. The greatest gender difference is seen for squamous cell carcinoma, due to the relatively low risk of this subtype in women. The reasons could be differences in smoking habits or the type of cigarettes smoked.^{12,13,14,15,16}

Hormonal influences may play an important role in the pathogenesis of lung cancer and the survival of lung cancer patients. However, some reports have offered conflicting data regarding the expression and potential influence of hormonal factors in the development of NSCLC.^{12,13,14,15,16}

In our study most of the patients were in their 5th decade or older and so majority were post-menopausal at presentation.

In a large study from Poland, women were more frequently non-smokers than men (18.8% versus 2.4%). Adenocarcinoma patients smoked less intensively than patients with squamous and SCLC both in women (31.4 versus 35.8 and 33.7 packs/year) and in men (38.2 versus 42 and 41.9 packs/year).¹⁷

In our study majority of the patients were non-smokers (75%), which was much higher than that noted in the literature (18.8%).

The majority of the Indian studies showed that squamous cell carcinoma was the most common histological subtype followed by adenocarcinoma and small cell carcinoma⁶. Majority of the patients in our study had NSCLC. Among the NSCLC, adenocarcinoma was the most common histology followed by squamous cell carcinoma.

The trend of a shift from squamous cell carcinoma to adenocarcinoma was subsequently confirmed in some studies. Two possible hypotheses to explain the trend were: the first is the changing patterns in smoking-with the switch from unfiltered to filtered cigarettes. Smoke from filtered milder cigarettes may be more deeply inhaled, resulting in carcinogen deposition more peripherally and giving rise to adenocarcinomas. The second explanation pertains to the nature of carcinogens-polycyclic aromatic hydrocarbons (PAHs) which are inducers of squamous cell carcinomas, while an increase in the yields of carcinogenic tobacco-specific N-nitrosamines (TSNAs) which are inducers of adenocarcinomas.^{7,8,9}

Data regarding clinical stage of cancer were available for 91% with histological diagnosis in the same study.¹⁷ In our study 92% of patients had histological confirmation of the disease and most

ORIGINAL ARTICLE

common histology was adenocarcinoma, consistent with the literature and pathology of the disease. Majority of the patients in our study were non-smokers (75%), consistent with other studies.

A significantly higher percentage of women than men with disseminated diseases was observed (20.3% versus 13.9%; $P < 0.001$) in the literature¹⁷. But in our study majority of the patients presented with advanced disease, stage IV (92.26%) in contrast to the 20% noted in the literature.

Adenocarcinoma is known to spread widely outside thorax by hematogenous dissemination, commonly involving the bones, liver and brain¹⁸. In contrast to the literature, in our study majority of the patients had metastasis to pleura or malignant pleural effusion (57.45%), followed by bone metastasis (24.3%). About 20.44% had metastasis at more than 1 site.

In a study from Poland, majority of patients had a good performance status (0/1 on the ECOG scale) and 11.8% of patients had poor performance status (3/4 on the ECOG scale). There were no difference in performance status between men and women¹⁷. In our study majority of the patients had ECOG PS of 2/3 which was in contrary to the literature.

About 65% of the patients in our study received CT and among these only 14% could complete the planned treatment. This could be because majority of our patients were with advanced and disseminated disease along with poor performance status at presentation.

About 6% of our patients could be treated with radical intent with chemotherapy (CT) and radiotherapy (RT). Among patients planned with radical CT and RT, 75% completed treatment. So patients with early disease could tolerate the aggressive treatment.

Majority of the patients in our study were stage IV and treated with palliative intent (77%) or received only best supportive care (16%) due to poor general condition. May be more number of patients could have benefitted with best supportive care rather than CT as very small number (14%) could complete all the cycles of chemotherapy. At the time of conclusion of the study only 13 (7.18%) were alive and on follow-up.

CONCLUSION: The mean age at presentation among the South Indian female lung cancer patients is similar to other studies from North India with peak incidence in the 5th decade. There is no difference in the age at presentation. Also there was no association between smoking and squamous histology.

Majority of the patients in our study were non-smokers, much higher than other studies. Also most common type on lung cancer among female patients is NSCLC, predominantly adenocarcinoma subtype followed by squamous cell carcinoma which is in contrary to the older Indian studies on carcinoma lung. So the trend of a shift from squamous cell carcinoma to adenocarcinoma mentioned in western population is confirmed in our study.

In our study majority of the patients had a poor ECOG PS and advanced disease at presentation, in contrary to the literature. More number of patients could benefit with best supportive care rather than CT as very small number of female lung cancer patients can complete all the cycles of chemotherapy. We need newer CT schedules designed for South Indian female lung cancer patients presenting with an advanced disease.

Female patients with early disease tolerate the aggressive treatment well. So the Indian females with early stage lung cancer can be treated aggressively.

Pattern of metastases is slightly different among Indian female lung cancer patients, as majority of the female lung cancer patients have metastasis to pleura or malignant pleural effusion followed by bone metastasis rather than hematogenous dissemination.

ACKNOWLEDGEMENT: Staff, Medical Records Department, MNJIO and Regional Cancer Centre, Hyderabad, Telangana, India.

REFERENCES:

1. A Krishnamurthy, R Vijayalakshmi, V Gadigi, R Ranganathan, TG Sagar. The relevance of "Nonsmoking-associated lung cancer" in India: A single-centre experience. *Indian Journal of cancer*. 2012, Volume: 49, Issue: 1, Page: 82-88.
2. Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. *Int J Cancer* 2010; 127: 2893-917.
3. Kanavos P. The rising burden of cancer in the developing world. *Ann Oncol* 2006; 8: 15-23.
4. GLOBOCAN 2002, 2008 database, International Agency for Research on Cancer, World Health Organization. Available at <http://www-dep.iarc.fr/>.
5. World Health Organisation. The Global Burden of Disease: 2004 Update. Geneva, WHO, 2009b. Death and DALY estimates for 2004 by cause for WHO Member States. http://www.who.int/healthinfo/global_burden_disease/estimates_country/en/index.html.
6. Behera D, Balamugesh T. Lung cancer in India. *Indian J Chest Dis Allied Sci* 2004; 46: 269-81.
7. Devesa SS, Bray F, Vizcaino AP, Parkin DM. International lung cancer trends by histologic type: male: female differences diminishing and adenocarcinoma rates rising. *Int J Cancer* 2005; 117: 294-9.
8. Thun MJ, Lally CA, Flannery JT, Calle EE, Flanders WD, Heath CW Jr. Cigarette smoking and changes in the histopathology of lung cancer. *J Natl Cancer Inst* 1997; 89: 1580-6.
9. Stellman SD, Muscat JE, Thompson S, Hoffmann D, Wynder EL. Risk of squamous cell carcinoma and adenocarcinoma of the lung in relation to lifetime filter cigarette smoking. *Cancer* 1997; 80: 382-8.
10. TanujaRastogi, Susan Devesa, PunamMangtani, AleyammaMathew, Nicola Cooper, RoyKaoet al. Cancer incidence rates among South Asians in four geographic regions: India, Singapore, UK and US. *International Journal Epidemiology* (2008) 37 (1): 147-160.
11. Jindal SK, Behera D. Clinical spectrum of primary lung cancer: Review of Chandigarh experience of 10 years. *Lung India* 1990; 8: 94-8.
12. Jennifer B. Fu, MD, T. Ying Kau, PhD, Richard K. Severson, PhD, Gregory P. Kalemkerian, MD. Lung Cancer in Women. Analysis of the National Surveillance, Epidemiology, and End Results Database. *CHEST*. 2005; 127(3): 768-777.
13. Fasco M, Hurteau G, Spivack S. Gender-dependent expression of alpha and beta estrogen receptors in human nontumor and tumor lung tissue. *Mol Cell Endocrinol* 2002; 188: 125-140
14. Omoto Y, Kobayashi Y, Nishida K, et al. Expression, function, and clinical implications of estrogen receptor β in human lung cancers. *Biochem Biophys Res Commun* 2001; 285: 340-347
15. Stabile LP, Davis A, Gubish CT, et al. Human non-small cell lung tumors and cells derived from normal lung express both estrogen receptor α and β and show biological responses to estrogen. *Cancer Res* 2002; 62: 2141-2150
16. Di Nunno L, Larsson L, Rinehart JJ, et al. Estrogen and progesterone receptors in non-small cell lung cancer in 248 consecutive patients who underwent surgical resection. *Arch Pathol Lab Med* 2000; 124: 1467-147.

17. E. Radzikowska, P. Głaz and K. Roszkowski. Lung cancer in women: age, smoking, histology, performance status, stage, initial treatment and survival. Population-based study of 20 561 cases. *Annals of Oncology* (2002) 13 (7): 1087-1093.
18. Martin J. Edelman, David R. Gandara. Pathology and natural history of lung cancer. *Manual of Clinical Oncology*, 7th edition, Section II, chapter 8, page 207.

AUTHORS:

1. C. Sanjeeva Kumari
2. M. Adi Lakshmi
3. John Winkle
4. Aparna Suryadevra

PARTICULARS OF CONTRIBUTORS:

1. Professor, Department of Radiation Oncology, M. N. J. Institute of Oncology & RCC, Hyderabad.
2. Assistant Professor, Department of Radiation Oncology, M. N. J. Institute of Oncology & RCC, Hyderabad.
3. Resident, Department of Radiation Oncology, M. N. J. Institute of Oncology & RCC, Hyderabad.

FINANCIAL OR OTHER**COMPETING INTERESTS:** None

4. Senior Resident, Department of Radiation Oncology, M. N. J. Institute of Oncology & RCC, Hyderabad.

NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:

Dr. C. Sanjeeva Kumari,
Department of Radiation Oncology,
M. N. J. Institute of Oncology & Regional
Cancer Centre, Hyderabad-500004,
Telangana, India.

E-mail: cskumari62@gmail.com
mnjadi1962@yahoo.com
johnwinklemeddia@yahoo.com
surya_aparna@yahoo.com

Date of Submission: 01/05/2015.
Date of Peer Review: 02/05/2015.
Date of Acceptance: 04/06/2015.
Date of Publishing: 03/07/2015.