

SOCIO-DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF LUNG CANCER PATIENTS IN NORTH MACEDONIA

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Abstract

Lung cancer disease is one of the most common causes of mortality in the world, coming right after cardiovascular diseases. It is a big and is a special problem in the highly developed countries, especially in the USA, but also in developing countries.

The reason for the research is the fact that the number of newly diagnosed and death cases from lung cancer is constantly growing, especially in the last few years.

The aim of the study is to determine the influence of socio-demographic factors in the occurrence of lung cancer (gender, age, national and ethnic origin, place of residence) and smoking as the main risk factor associated with this neoplasm.

The research is a descriptive study in which 82 patients with pathohistologically confirmed lung cancer participated. It was implemented at the Institute for Oncology and Radiotherapy at the clinical center in Skopje for a period of 3 months.

A total of 82 patients were registered from Institute for Oncology and Raditherapy in Skopje, North Macedonia who were diagnosed with primary lung cancer. Of all, 64.7% of them were males and 35.3% were females. Histologically, 51.2% had adenocarcinoma, 25.6 had squamous cell carcinoma, 20.7% had small cell carcinoma and 7.4% had no small cell carcinoma.

It was observed that the proportion of females diagnosed with primary lung cancer is increasing. Patients get diagnosed at a later stage of the disease, which calls for screening and early detection of lung cancer.

Keywords: Lung cancer, death, smoking, gender

Introduction

Lung cancer is one of the leading causes of cancer deaths in the world. GLOBOCAN 2018 database shows that approximately 2.1 million people were affected with lung cancer in 2018, with a reported estimate of 1.8 million deaths [1].

In North Macedonia, lung cancer constitutes 13.12% of all cancer-related deaths [2,3]. Lung cancer is the leading cause of cancer among men and the second leading cause in women [3].

Developed countries show an increase in the women population with cancer explained by the increased population of women smokers coming to par with men. However, a decrease in rates of smoking among men in developed countries, explains plateauing of lung cancer rates in men [2].

Since first described in 1912, the major cause of lung cancer is cigarette smoke inhalation; amounting to up to 90% of all causes of lung cancer [4].

A multicenter study in Europe by Boffetta P and Pershagen G [5] showed that tobacco smoking is associated with increased odds of developing lung cancer. Also a study done in New Mexico by Humble CG *et al.* showed that the cumulative risk of lung cancer in heavy smokers is approximately 30% compared with a less than 1% risk in nonsmokers [6].

Other major risk factors include occupational asbestos exposure, radon, indoor smoke from cooking and heating, chronic obstructive pulmonary disease (COPD) [7], and genetic factors.

In developing countries like North Macedonia, patients reach the primary care physician with symptoms and are then referred to higher centers. First-level investigations and symptom management happen at the primary care level.

Although cases may be detected incidentally, clinical manifestations of lung cancer are very common. Clinical symptoms include cough, dyspnea, hemoptysis, chest pain, hoarseness of voice, fever, and loss of weight/appetite. Lung cancer is also associated with metastatic symptoms and paraneoplastic syndromes.

The diagnostic evaluation involves assessing the stage of the disease, histological grading and genotype, presence of metastasis, and associated paraneoplastic syndromes.

This study focuses to describe the socio-demographic and clinical characteristics of lung cancer patients in North Macedonia.

Materials and Methods

The research is a descriptive study in which 82 patients with pathohistologically confirmed lung cancer participated. It was implemented at the Institute for Oncology and Radiotherapy at the clinical center “Mother Teresa” in Skopje.

The research data were collected using a specially designed survey questionnaire consisting of 40 questions related to the socio-demographic characteristics of the patients (gender, age, place of residence, profession, marital status, education), questions related to the potential risk factors associated with the occurrence of BC (cigarette smoking habit, occupational exposure to carcinogenic substances, air pollution, stress, genetic factor) as well as issues related to the disease itself (pathohistological finding, cancer localization, diagnosis and treatment).

Our research lasted for a period of 3 months.

Statistical analysis

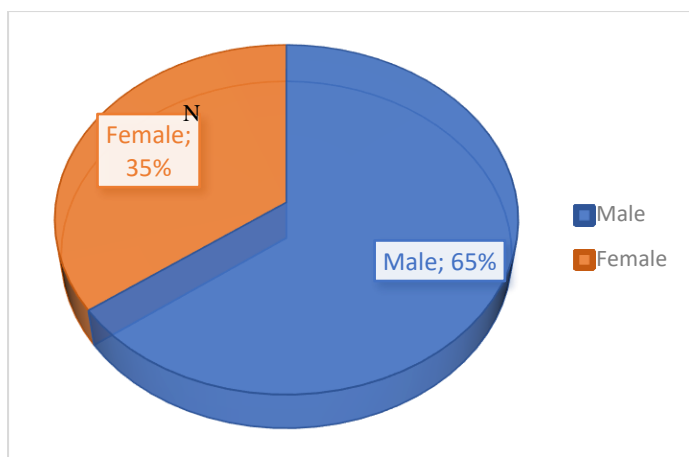
The data were entered into an Excel worksheet and analysis was performed using the Statistical Package for the Social Sciences (SPSS) 23 and Statistica. Data on continuous measurements were presented as mean and standard deviation and results on categorical measurements were presented in number (%).

Results

A total of 82 patients with primary lung cancer in the period of three months from May (2023) to August (2023) were included in the study. Of all, 64.7% of them were males and 35,3% were females.

Table 1. Distribution of patients by sex.

Sex	Patients	
	Number	%
Male	53	65
Female	29	35
Total	82	100%



Graphic 1. Distribution of patients by sex.

The mean age of the study population was 66.54 ± 8.4 years. The youngest patient is 46 years old, and the oldest is 84 years old.

The study included a wide range of age groups, which showed the highest population (75%) in the age groups of 55–64 years and 65–75 years followed by 25% in the age groups of <55–59 years and >75 years. Our study also shows lung cancer is mostly seen in males (64.7%) when compared with females (35.3%), with a male: female ratio (M: F) of 5:3.

Table 2. Average age of patients with lung cancer.

Patiens	N	<u>+SD</u> Mean	min	max
Age	82	66.54 ± 8.4	46	84

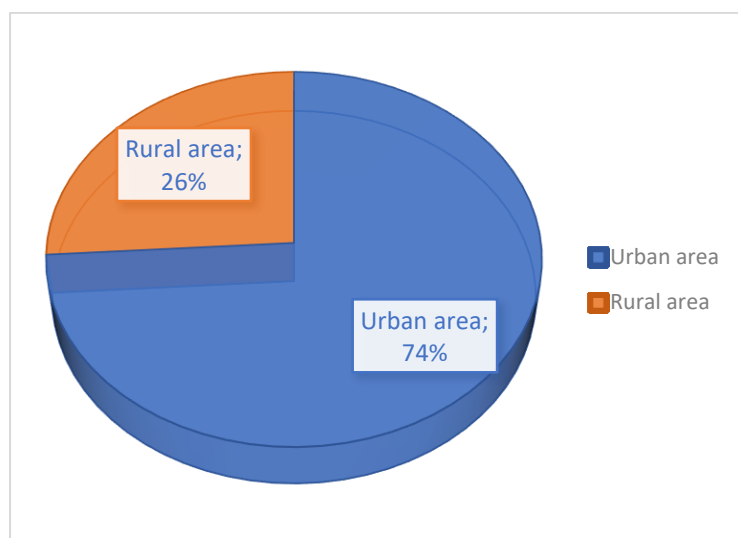
Table 3. Age of patients with lung cancer.

Age	Patiens	
	Number	%
<55 years	12	15
55-64 years	25	30
65-74 years	37	45
>75 years	8	10
Total	82	100

Most of the patients 61 (74%) live in the urban area, and less 21 (26%) live in the rural area.

Table 4. Distribution of patients by place of residence.

Place of residence	Patients	
	Number	%
Urban area	61	74
Rural area	21	26
Total	82	100

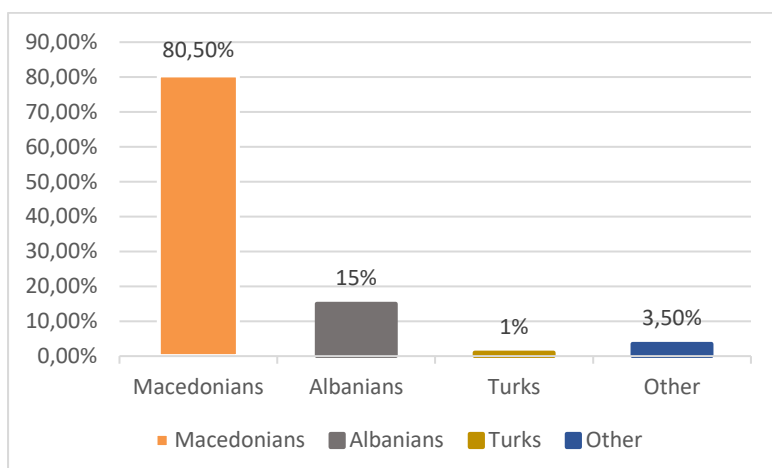


Graphic 2. Distribution of patients by place of residence.

In terms of nationality, the majority are Macedonians 66 (80.5%), then Albanians 12(15%), Turks 1 (1%), and other nationality 3 (3.5%), and according to religious affiliation, the largest percentage belongs to patients with the Orthodox religion (80%), and a smaller percentage (20%) to patients with the Muslim religion.

Table 5. Distribution of patients by nationality.

Nationality	Patients	
	Number	%
Macedonians	66	80.5
Albanians	12	15
Turks	1	1
Other	3	3.5
Total	82	100



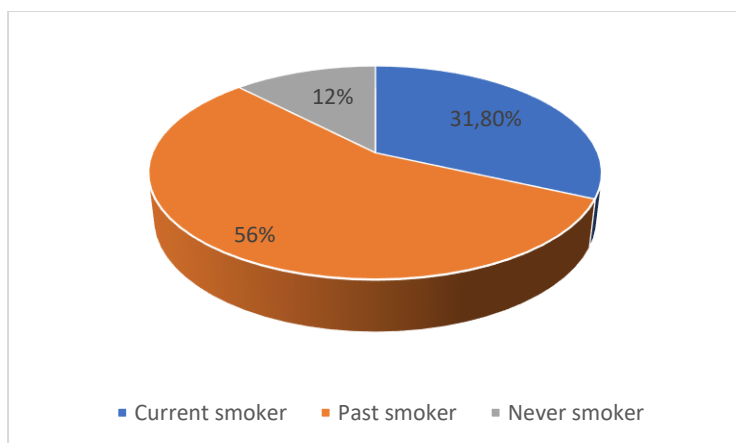
Graphic 3. Distribution of patients by nationality.

On assessing the available smoking history data, males 48 (90.6%) of total 53 and 24 (82.8) female of total 29 have smoked in their lifetime. Table 5 shows that 26 (31.8%) patients continue to smoke after a diagnosis of lung cancer was made and 46 (56%) patients stopped smoking thereafter.

It also shows that 10 (12.2%) patients with lung cancer have never smoked in their lifetime.

Table 6. Distribution of patients by smoking history.

Smoking history	Patients	
	Number	%
Current smoker	26	31.8
Past smoker	46	56
Never smoker	10	12.2
Total	82	100

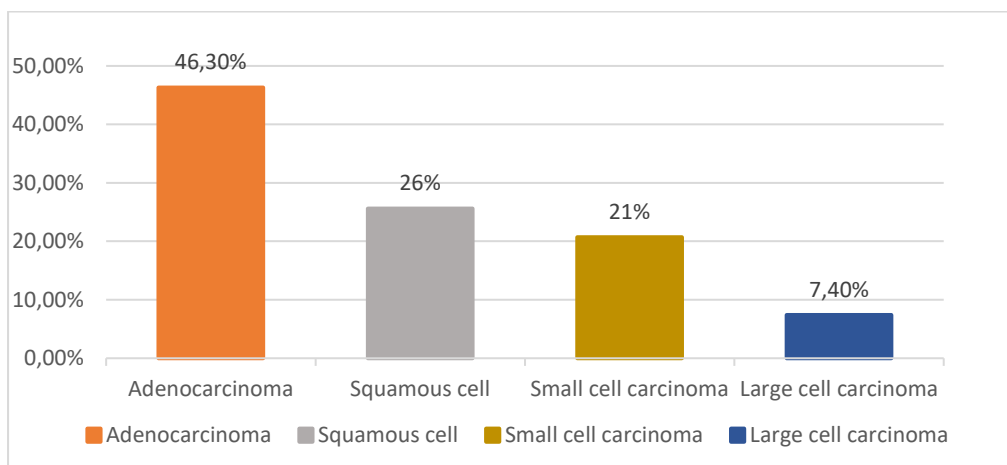


Graphic 4. Distribution of patients by smoking history.

Our study shows that the most common pathological type was adenocarcinoma (46.3%) and it was the most common among both males and females; followed by squamous cell carcinoma (25.6%) and small cell carcinoma (20.7%). Large cell carcinoma was the least common (7.4%) and was present in males and females.

Table 7. Pathological types of lung carcinoma.

Pathological types	Patients	
	Number	%
Adenocarcinoma	38	46.3
Squamous cell	21	25.6
Small cell carcinoma	17	20.7
Large cell carcinoma	6	7.4
Total	82	100



Graphic 5. Pathological types of lung carcinoma.

Table 8 shows a list of presenting symptoms of lung cancer with cough (present in 78%) and breathlessness (present in 72%) being the predominant ones. Other noted symptoms include weakness (60%), chest pain (45%), hemoptysis (30.5%), bone pain (15.9%) and fever (4.9%).

Table 8. Symptoms of lung cancer.

Symptoms of lung cancer	Patients	
	Number	%
Cough	64	78
Breathlessness	59	72
Weakness	49	60
Chest pain	37	45
Hemoptysis	25	30.5
Bone pain	13	15.9
Fever	4	4.9

Discussion

Our study aims to analyze the epidemiology, demographic, clinical, and histological profile of primary lung cancer by collecting data from Institute of Oncology and Radioterhapy in Skopje, North Macedonia.

The mean age of the study population was $66,54 \pm 8.4$ years. Over the decades, there has been an increase in the mean age group of diagnosed lung cancer patients. It was 52.1 years before 1985 and increased to 54.6 years after 1985 [8].

Recent studies on the global level show their mean age group similar to our study indicating that the occurrence is most common in the elderly age groups [9,11].

This is in line with the latest US preventive task force recommendation of screening for lung cancer in smokers from 50 to 80 years [12].

The incidence and mortality have historically always been male-predominated and continue to be so according to the global cancer statistics 2020 [13].

Our study data showed 64.7% males and 35.3% females with M:F ratio of 5:3. This similar decrease in M:F ratio is supported by many studies in the United States indicating that the incidence curve of females is plateauing while that for males is decreasing [14-16].

Since first described in 1912, cigarette smoke inhalation is the major cause of lung cancer amounting to up to 90% of all causes. [3,7,17,18].

In addition, 55.3% of the patients were smokers with a large majority being males (55.1%) and just 0.13% constituting females. A study done by Kshetrimayum *et al.* in Lucknow showed a similar drastic difference between male and female smokers in India. [19] However, Western studies show that an increasing trend of female smokers is resulting in identical risk between men and women [2].

In addition, 26% of the smokers in our study population continue to smoke, which can increase the all-cause mortality, recurrence, and development of new primary cancers [20].

Our study also shows that 12.2% were nonsmokers.

Nonsmoking-related lung cancers can be attributed to other etiologies like second-hand smoke, occupational asbestos exposure, radon, indoor smoke from cooking and heating, previous history of chemoradiation, genetic, and environmental factors. However, more research is required in

this area as no clear etiology and screening guidelines are stated for nonsmokers, despite their increasing incidence rates [21].

Most patients present with symptoms due to the locoregional spread, metastasis, or paraneoplastic syndromes. Our study data showed that the most common symptoms were cough (78%), breathlessness (72%), weakness (60%), chest pain (45%), hemoptysis (30.5%), and fever (4.9%).

International studies [19,22,23,24] showed cough and breathlessness to be the most common presentations followed by chest pain and weight loss. This showed a similar pattern of symptoms in our study compared with other studies.

About the pathological types of lung cancer, adenocarcinoma (46.3%) was the most common pathological type overall among both males and females; followed by squamous cell carcinoma (25.6%) and small cell carcinoma (20.7%). Large cell carcinoma was the least common (7.4%) and was present in males and females.

However, our study is consistent with many recent studies showing that adenocarcinoma has surpassed squamous cell carcinoma [9,25,26].

This change in trend can be attributed to the changing smoking patterns and the increasing incidence of lung cancer in females and nonsmokers [20,26,27].

In our study most of the patients 61 (74%) live in the urban area, and less 21 (26%) live in the rural area. According to this data, but also the data obtained from researches at the global level, the way of life and excessive urbanization increase the risk of the occurrence of this neoplasm. [28, 29].

Religious differences regarding the appearance of this neoplasm arise from lifestyle, culture, socialization, diet, etc.

In terms of nationality, the majority are Macedonians 66 (80.5%), then Albanians 12 (15%), Turks 1 (1%), and other nationality 3 (3.5%), and according to religious affiliation, the largest percentage belongs to patients with the Orthodox religion, and a smaller percentage to patients with the Muslim religion.

With increasing industrialization, urbanization, fast-paced lifestyles, and access to tobacco worldwide, the incidence of lung cancer globally is expected to continue to rise in the coming decades.

Conclusion

It was observed that the proportion of females diagnosed with primary lung cancer is increasing. Patients get diagnosed at a later stage of the disease, which calls for screening and early detection of lung cancer. As it accounts for the highest mortality among all other cancers, there is high scope for prevention and screening strategies.

References

1. Ferlay J, Colombet M, Soerjomataram I, Mathers C, Parkin DM, Piñeros M, et al. Estimating the global cancer incidence and mortality in 2018: GLOBOCAN sources and methods. *Int J Cancer*. 2019;144:1941–53. doi: 10.1002/ijc.31937. [PubMed] [Google Scholar].
2. Thun MJ, Carter BD, Feskanich D, Freedman ND, Prentice R, Lopez AD, et al. 50-year trends in smoking-related mortality in the United States. *N Engl J Med*. 2013;368:351–64. doi: 10.1056/NEJMsa1211127. [PMC free article] [PubMed] [Google Scholar].
3. Barta JA, Powell CA, Wisnivesky JP. Global Epidemiology of Lung Cancer. *Ann Glob Health*. 2019 Jan 22;85(1):8. doi: 10.5334/aogh.2419. PMID: 30741509; PMCID: PMC6724220.
4. Alberg AJ, Samet JM. Epidemiology of lung cancer. *Chest*. 2003;123(1 Suppl):21S–49. doi: 10.1378/chest.123.1_suppl. 21s. [PubMed] [Google Scholar].
5. Boffetta P, Pershagen G, Jöckel K-H, et al. Cigar and pipe smoking and lung cancer risk: A multicenter study from Europe. *Journal of the National Cancer Institute*. 1999; 91(8): 697–701. DOI: 10.1093/jnci/91.8.697 [PubMed] [CrossRef] [Google Scholar].
6. Humble CG, Samet JM. Smoking and lung cancer in New Mexico. *Am J Public Health*. 1986;76:1361. doi: 10.2105/ajph. 76.11.1361. [PMC free article] [PubMed] [Google Scholar].

7. Young RP, Hopkins RJ, Christmas T, Black PN, Metcalf P and Gamble GD. COPD prevalence is increased in lung cancer, independent of age, sex and smoking history. *European Respiratory Journal*. 2009; 34(2): 380–386. DOI: 10.1183/09031936.00144208 [PubMed] [CrossRef] [Google Scholar].
8. Bharate Ramesh Tukaram, Mhaisekar D G, Anil Maske. Clinical profile of lung cancer patients. *MedPulse International Journal of Medicine*. 2017;1:54–8. Available from: <https://www.medpulse.in/Medicine> . [Google Scholar].
9. Kaur H, Sehgal IS, Bal A, Gupta N, Behera D, Das A, et al. Evolving epidemiology of lung cancer in India: Reducing non-small cell lung cancer-not otherwise specified and quantifying tobacco smoke exposure are the key. *Indian J Cancer*. 2017;54:285–90. doi: 10.4103/ijc.IJC_597_16. [PubMed] [Google Scholar].
10. Prasad R, James P, Kesarwani V, Gupta R, Pant MC, Chaturvedi A, et al. Clinicopathological study of bronchogenic carcinoma. *Respirology*. 2004;9:557–60. doi: 10.1111/j. 1440-1843.2004.00600.x. [PubMed] [Google Scholar].
11. Dey A, Biswas D, Saha SK, Kundu S, Kundu S, Sengupta A. Comparison study of clinicoradiological profile of primary lung cancer cases: An Eastern India experience. *Indian J Cancer*. 2012;49:89–95. doi: 10.4103/0019-509X.98930. [PubMed] [Google Scholar].
12. Krist AH, Davidson KW, Mangione CM, Barry MJ, Cabana M, Caughey AB, et al. Screening for lung cancer: US Preventive services task force recommendation statement. *JAMA*. 2021;325:962–70. doi: 10.1001/jama.2021.1117. [PubMed] [Google Scholar].
13. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics. 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2021;71:209–49. doi: 10.3322/caac. 21660. [PubMed] [Google Scholar].
14. Fu JB, Kau TY, Severson RK, Kalemkerian GP. Lung cancer in women: Analysis of the national surveillance, epidemiology, and end results database. *Chest*. 2005;127:768–77. doi: 10.1378/chest. 127.3.768. [PubMed] [Google Scholar].
15. Edwards BK, Brown ML, Wingo PA, Howe HL, Ward E, Ries LA, et al. Annual report to the nation on the status of cancer, 1975-2002, featuring population-based trends in cancer treatment. *J Natl Cancer Inst*. 2005;97:1407–27. doi: 10.1093/jnci/dji289. [PubMed] [Google Scholar].
16. Thomas L, Doyle LA, Edelman MJ. Lung cancer in women: Emerging differences in epidemiology, biology, and therapy. *Chest*. 2005;128:370–81. doi: 10.1378/chest. 128.1.370. [PubMed] [Google Scholar].
17. Pearl R. Tobacco smoking and longevity. *Science*. 1938;87:216–7. doi: 10.1126/science.87.2253.216. [PubMed] [Google Scholar].
18. Hill A, Doll R. Smoking and carcinoma of the lung;Preliminary report. *Br Med J*. 1950;2:739–48. doi: 10.1136/bmj.2.4682.739. [PMC free article] [PubMed] [Google Scholar].
19. Kshetrimayum S, Srivastava A, Kant S, Verma AK, Prakash V, Bajaj DK, et al. A study of the sociodemographic, clinical, pathological and radiological profile of lung cancer in a tertiary care center. *Int J Adv Med*. 2016;3:920–7. doi: 10.18203/2349-3933.ijam20163724. [Google Scholar].
20. Parsons A, Daley A, Begh R, Aveyard P. Influence of smoking cessation after diagnosis of early stage lung cancer on prognosis: systematic review of observational studies with meta-analysis. *BMJ*. 2010 Jan 21;340:b5569. doi: 10.1136/bmj.b5569. PMID: 20093278;PMCID: PMC2809841. [PMC free article] [PubMed] [Google Scholar].
21. Sun S, Schiller JH, Gazdar AF. Lung cancer in never smokers--A different disease. *Nat Rev Cancer*. 2007;7:778–90. doi: 10.1038/nrc2190. [PubMed] [Google Scholar].
22. Pandhi N, Malhotra B, Kajal N, Prabhudesai RR, Nagaraja CL, et al. Clinicopathological profile of patients with lung cancer visiting Chest and TB Hospital Amritsar. *Scholars Journal of Applied Medical Sciences*. 2015;3:802–9. [Google Scholar].
23. Buccheri G, Ferrigno D. Lung cancer: Clinical presentation and specialist referral time. *Eur Respir J*. 2004;24:898–904. doi: 10.1183/09031936.04.00113603. [PubMed] [Google Scholar].

24. Kocher F, Hilbe W, Seeber A, Pircher A, Schmid T, Greil R, et al. Longitudinal analysis of 2293 NSCLC patients: A comprehensive study from the TYROL registry. *Lung Cancer*. 2015;87:193–200. doi: 10.1016/j.lungcan.2014.12.006. [PubMed] [Google Scholar].
25. Ramani V, Bijit C, Vinu S, Belagutti JS, Radheshyam N. Clinicopathological profile of lung cancers at an institute from South India—A record based retrospective cohort study. *Adv Lung Cancer*. 2020;09:41–54. doi: 10.4236/alc.2020.93005. [Google Scholar].
26. Panigrahi MK, Saka VK, Jaganathan V, Sinnassamy M, Narahari NK. Changing trend of clinical and epidemiological profile of lung cancer –Experience from a tertiary care centre in southern India. *J Clin Diagnostic Res*. 2018;12:LC01–3. doi: 10.7860/JCDR/2018/36768.12148. [Google Scholar].
27. Travis WD, Brambilla E, Noguchi M, Nicholson AG, Geisinger KR, Yatabe Y, et al. International association for the study of lung cancer/american thoracic society/european respiratory society international multidisciplinary classification of lung adenocarcinoma. *J Thorac Oncol*. 2011;6:244–85. doi: 10.1097/JTO.0b013e318206a221. [PMC free article] [PubMed] [Google Scholar].
28. U.S. Cancer Statistics: Lung Cancer Stat Bite | CDC.
29. Lung cancer statistics | World Cancer Research Fund International (wcrf.org).