Original Article

Lung cancer in Asian Indian females: Identification of disease-specific characteristics and outcome measures over a 12-year period

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ABSTRACT

Aim: Globally, the incidence of lung cancer amongst women appears to be increasing. We aimed to compare the socio-epidemiological and clinical characteristics of lung cancer amongst men and women from a large cohort at a tertiary care hospital in Northern India. **Methods:** Records of patients diagnosed with lung cancer between January 2008 and March 2020 were reviewed. Baseline epidemiological data, clinical characteristics, histologic profiles, treatment administered, and survival were compared between males and females. **Results:** A total of 2054 male and 438 female patients were included in analysis. Compared to males, female patients were younger [median age, 56 vs. 60 years, $P < 0.001$)], less likely to be working, less educated beyond secondary level and less likely to be smokers (29.1% vs. 84.9%, $P < 0.0001$). No difference in baseline performance status was observed. Females were more frequently diagnosed with adenocarcinoma (54.2% vs. 30.2%, $P = <0.0001$), stage IV disease (70.8% vs. 63%, $P = 0.001$), and had higher rate of EGFR mutation (37.2% vs. 21.5%, $P < 0.0001$). There was no difference in the proportion of females receiving cancer-specific therapy. Multivariate Cox proportional hazards model revealed higher progression-free survival [median 9.17 vs. 7.23 months; $P = 0.007$] and overall survival [median 13.80 vs. 9.10 months respectively, $P = 0.001$] amongst females compared to males. **Conclusion:** Amongst a large cohort of lung cancer, females demonstrated several distinct and characteristic demographics as well as disease-related features, especially better survival outcomes.

KEY WORDS: Female, India, lung cancer

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INTRODUCTION

Lung cancer is one of the leading causes of cancer and cancer-related mortality in India and worldwide.[1] In India, lung cancer constitutes 6.9 per cent of all new cancer cases and 9.3 per cent of all cancer-related deaths in both sexes.[2] In recent years, the proportion of adenocarcinoma appears to be increasing with the rising incidence of lung cancer in females being one of the postulated reasons.[3] In general, the profile of lung cancer in females is less well studied; however, it is reported that several differences exist in risk factors, histology, prognosis and survival in women compared to men with lung cancer.[4] The contribution of certain unique factors, such as exposure to indoor biomass, malnutrition and post-tubercular scarring of the lungs is likely but not well elucidated. Hence, the present study aimed to compare various clinical and outcome characteristics of lung cancer between men and women and attempt to identify certain unique phenotypes to define the disease especially in females.

MATERIALS AND METHODS

This was a retrospective, analytical, observational study carried out at a tertiary care hospital in New Delhi, India. Patients with pathologically (histology or cytology) proven lung carcinoma diagnosed between January 2008 and March 2020 in the lung cancer clinic of the tertiary care hospital in India were included. Baseline demographic data (age, sex, employment, education, comorbidities) clinical characteristics, smoking history, histologic profiles, treatment details and survival parameters were compared between male and female patients. Cancer staging was done using the Tumour, Node, Metastasis (TNM) system of the 7th and 8th Ed of the American Joint Committee on Cancer (AJCC) and the Union for International Cancer Control (UICC).[5,6] The pathological differentiation between adenocarcinoma (ADC) and squamous cell carcinoma (SCC) was done primarily using the IHC markers TTF-1 and p40 from 2013 onwards, and for small cell lung cancer (SCLC) using chromogranin and synaptophysin. Epidermal growth factor receptor (EGFR) mutation and anaplastic lymphoma kinase (ALK) rearrangement were detected using immunohistochemistry (IHC). The modified Karnofsky Performance Scale (KPS) and Eastern Cooperative Oncology Group Scale (ECOG) were used for assessment of performance status.[7] Various forms of treatment administered, such as chemotherapy, radiotherapy, both, or only palliative care were recorded. All eligible subjects were administered a first-line chemotherapy regimen comprising a doublet combination based on the morphology. The regimens used were: carboplatin plus paclitaxel/pemetrexed for ADC; carboplatin plus paclitaxel/gemcitabine for SCC; and carboplatin plus paclitaxel for NSCLC-not otherwise specified (NSCLC-NOS), in three-weekly cycles for a total of 4–6 cycles. Maintenance chemotherapy in non-progressive disease comprised of pemetrexed or gemcitabine for ADC and SCC, respectively. Targeted therapy was initiated in 2014 and comprised of oral gefitinib/erlotinib or osimertinib (for EGFR mutations), and crizotinib (for ALK and ROS1 mutations). Immunotherapy with nivolumab was administered to eligible patients wherever feasible based on cost logistics. Response assessment was done using the RECIST 1.1 criteria.[8] Overall survival (OS) was calculated from date of definitive diagnosis to date of death or last known follow-up. In cases where the last follow-up was within a month of data censoring, the patients were considered to be on continuous follow-up. If the patient did not follow up for more than a month, attempts were made to contact the patient telephonically. Patients were followed from the date of registration to the date of death and were censored at the date they were last known to be alive, i.e., date of the last follow-up either in person or telephonically. Progression-free survival (PFS) was calculated from date of treatment to date of progression, documented after response assessment.

Statistical methods

Statistical analysis was performed using Stata statistical analysis software. A descriptive analysis was performed. Categorical variables were expressed as frequency (percentages), and quantitative variables were expressed as mean ± standard deviation or median interquartile range. Statistical significance was calculated using Pearson's Chi-square test, and results were deemed statistically significant if $P < 0.05$. Progression-free survival (PFS) and overall survival (OS) were evaluated using a multivariate Cox proportional hazards model and depicted as Kaplan–Meier curve.

RESULTS

Patient characteristics

Following database review, 2054 male patients and 438 female patients were included in the final analysis. Supplementary Figure 1 shows the proportion of females affected with lung cancer from 2008 to 2020. The differences in baseline characteristics are tabulated in Table 1. It was observed that females had an earlier median age of disease diagnosis (56 vs. 60 years, $P < 0.001$), were less likely to be employed in a job (5.4% vs. 73.3%, $P < 0.0001$), less likely to be educated beyond the secondary level (23.1% vs. 41.4%, $P < 0.0001$), less likely to be smokers (current and/or reformed) (29.1% vs. 84.9%, $P < 0.0001$) and less likely to be heavy smokers (smoking index more than 450) (29.2% vs. 58.2%, $P < 0.0001$), compared to males. No difference in the baseline KPS or ECOG status was observed. Mean duration from symptoms onset to first doctor visit was similar for males and females (70 days vs. 71 days, $P = 0.48$).

Disease-specific variables amongst the two groups

Compared to males, female subjects with lung cancer were significantly more likely to have adenocarcinoma morphology (54.2% vs. 30.2%), metastatic disease at

Table 1: Comparison of baseline demographic characteristics and disease-specific comparison between males and females with lung cancer

Variable	Males (*n*=2054)	Females (*n*=438)	*P*
Age (years)	60 (53-66)	56 (48-63)	<0.0001
Unemployed (%) (*n*=2033)	91 (5.4%)	255 (73.3%)	<0.0001
Completed secondary education or higher (*n*=2446)	837 (41.4%)	98 (23.1%)	<0.0001
Smokers (current and/or reformed) (*n*=2354)	1659 (84.9%)	116 (29.1%)	<0.0001
Smoking index>450 (*n*=1260)	682 (58.2%)	26 (29.2%)	<0.0001
Mean duration of symptoms prior to first presentation to doctor (days)	70 (10-90)	71 (10-90)	0.485
KPS (Karnofsky Performance Scale) ≥70 (*n*=2148)	1339 (76.1%)	276 (70.9%)	0.688
ECOG ≥3 (*n*=2076)	282 (16.5%)	80 (21.4%)	0.186
Morphology (*n*=2394)			
Adenocarcinoma	598 (30.2%)	225 (54.2%)	<0.0001
Squamous cell carcinoma	641 (32.4%)	72 (17.3%)	
Small cell carcinoma	312 (15.8%)	49 (11.8%)	
Stage 4 disease (*n*=2041)	1064 (63.0%)	250 (70.8%)	0.001
EGFR mutation positivity (*n*=409)	62 (21.5%)	45 (37.2%)	<0.0001
ALK rearrangement positivity (*n*=953)	24 (3.0%)	16 (10.5%)	<0.0001
ATT received empirically prediagnosis (*n*=2224)	426 (23.2%)	115 (29.6%)	0.007
Alternate forms of medicine received (*n*=1070)	71 (8.1%)	9 (4.6%)	0.217
Lung cancer-specific treatment received (*n*=2472)	1006 (49.4%)	239 (55.1%)	0.065

All values depicted as median (IQR) or frequency (%)

diagnosis (70.8% vs. 63%), mutations in the EGFR gene (37.2% vs. 21.5%), and ALK rearrangements (10.5% vs. 3%).

[Table 1] Lung cancer-specific treatment was administered to similar proportions of males and females, although females were more likely than males to receive empirical antitubercular treatment prior to the lung cancer diagnosis. (29.6% and 23.2% respectively).

Survival analysis

After administering first-line therapy, as either chemotherapy or targeted therapy, the objective response rate (ORR), defined as complete remission or partial response, was similar in females and males (59.4% vs. 54.7% respectively, $P = 0.37$).

Compared to males, females demonstrated significantly better PFS [median (IQR), 9.17 (4.5–17.6) months vs. 7.23 (3.5–14.8) months; $P = 0.007$] and OS [median (IQR), 13.8 (5.3–29.2) months vs. 9.1 (3.6–20.7) months respectively, $P = 0.001$]. [Figure 1 (a and b)].

A univariate and multivariate analysis was performed to analyze the factors affecting the OS and PFS in females [Tables 2 and 3] and males [Tables 4 and 5]. On univariate analysis in males, factors that significantly affected PFS included age, ECOG, KPS, small cell carcinoma histology and smoking status. Factors affecting OS in males on univariate analysis included age, ECOG, KPS, small cell carcinoma, EGFR mutation, smoking status and smoking index more than 300. However, on multivariate analysis, only performance status (ECOG more than or equal to 3 and KPS more than or equal to 80) significantly affected PFS and OS in males.

On univariate analysis in females, factors that significantly affected PFS included ECOG, KPS more than or equal

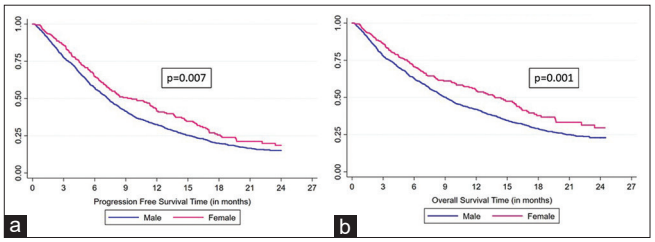

Figure 1: (a) Kaplan–Meier curve depicting progression-free survival amongst males and females with lung cancer. (b) Kaplan–Meier curve depicting overall survival amongst males and females with lung cancer

to 80, small cell carcinoma histology, current smoking status and smoking index more than 600, while for OS it included ECOG, KPS, current smoker and smoking index more than 600. On multivariate analysis in females, only ECOG more than or equal to 3, KPS more than or equal to 80 and small cell carcinoma histology significantly affected PFS, while smoking index more than 600 and KPS significantly affected OS.

DISCUSSION

The main findings of our study are that the females with lung cancer are younger, less likely to receive higher education, more likely to be non-smokers and to receive inappropriate and empirical anti-TB treatment in comparison to males. No differences between genders were observed in the baseline performance status and the rates of receipt of cancer-specific therapy. Females had a better PFS and OS after first-line treatment. The performance status (ECOG more than or equal to 3 and KPS more than or equal to 80) significantly affected PFS and OS in males while performance status and small cell carcinoma histology significantly affected PFS, while smoking index more than 600 and KPS significantly affected OS in females.

Table 2: Univariate and multivariate analysis of factors influencing progression-free survival in females

Variable	Subgroup	*n*	Median PFS days	Univariate Analysis		Multivariate Analysis	
				HR (95% CI)	*P*	HR (95% CI)	*P*
Age (years)	=<45	71	242	1			
	46-70	249	262	1.06 (0.73-1.53)	0.76		
	>70	23	359	0.94 (0.48-1.84)	0.85		
Education Level	Up to Primary Level	262	302	1			
	Above Primary Level	81	229	1.05 (0.75-1.47)	0.79		
Employment	Unemployed	190	239	1			
	Employed	43	302	0.85 (0.55-1.31)	0.46		
Smoking Status	Never Smoker	222	343	1			
	Current Smoker	47	183	1.73 (1.16-2.58)	0.008*	0.68 (0.22-2.17)	0.52
	Reformed Smoker	51	239	1.32 (0.87-2.01)	0.184		
Smoking Index	<100	54	230	1			
	100-300	31	198	1.30 (0.75-2.25)	0.35		
	301-600	28	348	0.91 (0.49-1.67)	0.76		
	>600	14	167	2.44 (1.11-5.38)	0.03*	3.27 (0.96-11.14)	0.058
ECOG	0,1	134	432	1			
	2	101	215	1.93 (1.33-2.80)	<0.001*	0.44 (0.14-1.39)	0.162
	>=3	57	147	2.29 (1.53-3.44)	<0.001*	0.19 (0.04-0.99)	0.049*
KPS	=<60	87	133	1			
	70	72	219	0.75 (0.50-1.11)	0.15		
	80-100	148	432	0.38 (0.26-0.54)	<0.001*	0.07 (0.01-0.31)	0.001*
Cancer type	Adenocarcinoma	60	359	1			
	Squamous Cell Carcinoma	187	324	1.11 (0.72-1.72)	0.63		
	Small Cell Carcinoma	41	177	2.04 (1.18-3.52)	0.01*	2.57 (1.16-5.70)	0.020*
EGFR Mutation	Absent	65	249	1			
	Present	36	331	1.08 (0.63-1.88)	0.76		
ALK Mutation	Absent	63	343	1			
	Present	11	340	1.07 (0.47-2.43)	0.88		

PFS: Progression-free survival, ECOG: Eastern Cooperative Oncology Group, KPS: Karnofsky Performance Status Scale (*$P<0.05$)

Table 3: Univariate and multivariate analysis of factors influencing overall survival in females

Variable	Subgroup	*n*	Median PFS days	Univariate Analysis		Multivariate Analysis	
				HR (95% CI)	*P*	HR (95% CI)	*P*
Age (years)	=<45	71	432	1			
	46-70	247	408	1.03 (0.69-1.55)	0.88		
	>70	23	414	0.84 (0.40-1.77)	0.65		
Education Level	Up to Primary Level	261	439	1			
	Above Primary Level	80	302	1.29 (0.89-1.87)	0.17		
Employment	Unemployed	188	360	1			
	Employed	43	439	0.87 (0.53-1.42)	0.57		
Smoking Status	Never Smoker	221	485	1			
	Current Smoker	46	187	1.89 (1.21-2.94)	0.005*	0.55 (0.15-1.96)	0.357
	Reformed Smoker	51	287	1.46 (0.92-2.29)	0.11		
Smoking Index	<100	54	439	1			
	100-300	30	219	1.64 (0.87-3.10)	0.13		
	301-600	28	348	1.47 (0.76-2.88)	0.26		
	>600	14	177	2.72 (1.14-6.49)	0.02*	4.01 (1.01-15.96)	0.048*
ECOG	0,1	134	665	1			
	2	100	364	2.00 (1.30-3.08)	0.002*	0.33 (0.09-1.25)	0.104
	>=3	56	147	3.44 (2.18-5.42)	<0.001*	0.29 (0.05-1.79)	0.181
KPS	=<60	86	135	1			
	70	72	289	0.55 (0.36-0.85)	0.007*	0.25 (0.07-0.84)	0.024*
	80-100	147	703	0.23 (0.15-0.35)	<0.001*	0.05 (0.01-0.27)	0.001*
Cancer type	Adenocarcinoma	60	408	1			
	Squamous Cell Carcinoma	186	477	1.02 (0.64-1.64)	0.93		
	Small Cell Carcinoma	41	287	1.70 (0.93-3.12)	0.09		
EGFR Mutation	Absent	64	590	1			
	Present	35	788	0.79 (0.37-1.72)	0.56		
ALK Mutation	Absent	63	464	1			
	Present	10	490	0.66 (0.19-2.22)	0.49		

OS: Overall survival, ECOG: Eastern Cooperative Oncology Group, KPS: Karnofsky Performance Status Scale (*$P<0.05$)

Historically, lung cancer has been more prevalent in men than in women; however, this trend seems to be changing in the last few years, with the incidence decreasing in men but continuing to increase in women in several regions of

Table 4: Univariate and multivariate analysis of factors influencing progression-free survival in males

Variable	Subgroup	*n*	Median PFS days	Univariate Analysis		Multivariate Analysis	
				HR (95% CI)	*P*	HR (95% CI)	*P*
Age (years)	=<45	193	252	1			
	46-70	1271	213	1.35 (1.07-1.69)	0.011*	1.24 (0.91-1.68)	0.177
	>70	205	219	1.37 (1.03-1.81)	0.028*	1.31 (0.91-1.88)	0.140
Education Level	Up to Primary Level	981	209	1			
	Above Primary Level	685	232	0.95 (0.83-1.08)	0.402		
Employment	Unemployed	60	199	1			
	Employed	677	214	1.01 (0.72-1.41)	0.945		
Smoking Status	Never Smoker	229	274	1			
	Current Smoker	660	207	1.41 (1.14-1.74)	0.002*	1.14 (0.91-1.88)	0.350
	Reformed Smoker	720	211	1.32 (1.07-1.63)	0.010*	1.18 (0.89-1.55)	0.232
Smoking Index	<100	103	216	1			
	100-300	275	224	0.96 (0.71-1.29)	0.785		
	301-600	384	202	1.12 (0.83-1.49)	0.460		
	>600	437	210	1.12 (0.84-1.49)	0.443		
ECOG	0,1	700	281	1			
	2	451	199	1.39 (1.19-1.62)	<0.001*	1.04 (0.82-1.33)	0.726
	>=3	216	87	3.34 (2.74-4.07)	<0.001*	2.02 (1.39-2.92)	<0.001*
KPS	=<60	328	123	1			
	70	321	214	0.54 (0.45-0.66)	<0.001*	0.81 (0.60-1.09)	0.158
	80-100	777	279	0.39 (0.34-0.47)	<0.001*	0.56 (0.40-0.77)	<0.001*
Cancer type	Adenocarcinoma	537	242	1			
	Squamous Cell Carcinoma	490	222	1.08 (0.91-1.27)	0.367		
	Small Cell Carcinoma	274	182	1.44 (1.19-1.75)	<0.001*	1.21 (0.97-1.51)	0.097
EGFR Mutation	Absent	196	252	1			
	Present	52	250	1.06 (0.73-1.55)	0.747		
ALK Mutation	Absent	128	252	1			
	Present	19	223	0.95 (0.49-1.80)	0.865		

PFS: Progression-free survival, ECOG: Eastern Cooperative Oncology Group, KPS: Karnofsky Performance Status Scale (*$P<0.05$)

Table 5: Univariate and multivariate analysis of factors influencing overall survival in males

Variable	Subgroup	*n*	Median OS days	Univariate Analysis		Multivariate Analysis	
				HR (95% CI)	*P*	HR (95% CI)	*P*
Age (years)	=<45	193	396	1			
	46-70	1267	263	1.49 (1.16-1.93)	0.002*	1.84 (0.67-5.01)	0.235
	>70	204	244	1.58 (1.15-2.15)	0.004*	2.69 (0.82-8.77)	0.102
Education Level	Up to Primary Level	980	250	1			
	Above Primary Level	681	296	0.87 (0.76-1.01)	0.059		
Employment	Unemployed	60	365	1			
	Employed	673	291	0.99 (0.68-1.43)	0.946		
Smoking Status	Never Smoker	229	444	1			
	Current Smoker	658	249	1.73 (1.35-2.20)	<0.001*	1.79 (0.65-4.90)	0.258
	Reformed Smoker	717	255	1.60 (1.26-2.04)	<0.001*	2.11 (0.76-5.87)	0.153
Smoking Index	<100	102	544	1			
	100-300	273	277	1.40 (0.97-2.02)	0.070		
	301-600	383	255	1.65 (1.16-2.35)	0.005*	1.08 (0.46-2.53)	0.860
	>600	436	245	1.69 (1.19-2.40)	0.003*	0.93 (0.38-2.29)	0.875
ECOG	0,1	697	429	1			
	2	449	254	1.53 (1.29-1.82)	<0.001*	0.95 (0.43-2.10)	0.904
	>=3	216	87	3.89 (3.15-4.79)	<0.001*	4.5 (1.24-16.39)	0.022*
KPS	=<60	327	124	1			
	70	320	265	0.50 (0.41-0.62)	<0.001*	0.85 (0.36-2.02)	0.711
	80-100	774	423	0.34 (0.28-0.40)	<0.001*	0.29 (0.10-0.82)	0.019*
Cancer type	Adenocarcinoma	537	294	1			
	Squamous Cell Carcinoma	488	351	0.89 (0.75-1.07)	0.225		
	Small Cell Carcinoma	274	202	1.39 (1.13-1.70)	0.002*	2.72 (0.51-14.51)	0.241
EGFR Mutation	Absent	193	447	1		0.63 (0.25-1.57)	0.318
	Present	51	1040	0.46 (0.25-0.85)	0.013*		
ALK Mutation	Absent	125	544	1			
	Present	19	382	1.06 (0.49-2.29) *n*	0.876		

OS: Overall survival, ECOG: Eastern Cooperative Oncology Group, KPS: Karnofsky Performance Status Scale (*$P<0.05$)

the world.[9,10] The reasons are likely to be multifactorial, with changing smoking habits, environmental toxic substances/biomass exposure especially in women residing in rural regions, along with better accessibility to

healthcare facilities allowing increasing female population to seek medical care.

Women in our cohort had an earlier age of lung cancer diagnosis than men (median age, 56 years versus 60 years), a finding that has been reported previously as well.[11] It must be noted, however, that the mean age of Indian lung cancer patients is lesser than that reported in most European and American studies.[4]

Amongst our cohort, lesser females were educated beyond the secondary level and were less likely to be in a job. Lung cancer incidence itself may vary by education level. The incidence rates of lung cancer have been reported to be higher in patients who were non-graduates, compared to college graduates. Furthermore, a lower educational status influenced smoking habits and the inability to quit.[12] The likelihood of undergoing definite investigations and cancer treatment is lesser in patients who have lower educational status. This has translated into a higher mortality in this group of patients.[13]

Cigarette smoking continues to be the leading cause of lung cancer; the incidence of lung cancer in a society largely reflects the prevalent smoking patterns, and some Western studies have shown that the smoking rates amongst women have even surpassed that of men.[14] However, in the present study, the smoking rates were lower in females. The increasing trend of lung cancer in females in our study therefore may be explained by other non-tobacco exposures, such as air pollution or poor environmental/urban air quality. Another important result from the study is that a higher smoking index (more than 600) led to a poor overall survival in females. This has been well documented in literature, with studies showing a dose–dependent relationship between smoking and poor survival. Possible reasons being greater oxidative stress leading to damage of DNA thereby leading to mutation.[15]

Performance status is an important parameter for assessing suitability for administering definitive therapy and prognosis and is affected by several disease characteristics such as duration of symptoms and disease stage.[16] In the present study, no significant difference was seen between the two groups in terms of performance status in spite of the fact that a higher proportion of females were diagnosed when disease had already metastasized. However, we found performance status to be an important parameter affecting both PFS and OS in both the genders on multivariate analysis.

Globally, as well as in India, the most common histological type of lung cancer currently is adenocarcinoma.[17,18] Studies have also shown that there are histological differences in lung cancer between men and women, with adenocarcinoma being more common in females, as was observed in our study as well.[19] Apart from smoking patterns, several non-smoking related factors may be responsible for gender differences in lung cancer morphology, such as genetic alterations, passive smoking, age at onset of smoking (women begin to smoke at a later age), different nicotine metabolism in women, occupational exposure, diet, etc.[20] It must be noted, however, that our estimates of morphological differences between males and females may not be entirely accurate, as this includes results from the time when IHC was not routinely performed to differentiate ADC from SCC.

As expected, the proportion of EGFR positivity was higher in females as compared with males. This has been reported in another Indian study as well.[21] Previously, it has been shown that a significant proportion of patients with lung cancer have an advanced stage of disease at presentation (Stage 3B and 4).[22] One of the potential reasons could be increased availability and practice of performing baseline PET scan.[23] A large database study involving more than 30000 patients reported a higher proportion of males with advanced stage lung cancer as compared with females, a finding that is contrary to the current study.[24] The possible reasons could be related to several factors such as lack of education/awareness of the disease, inappropriate treatment, social responsibilities socio-cultural discrimination, etc., The fact that late diagnosis of disease portends a poor prognosis is well known and documented.

In our study, the proportion of females who received empirical treatment with antitubercular medicines was higher than in males. It is now well documented that the high prevalence of tuberculosis leads to significant delay in diagnosis of lung cancer due to the tendency of giving 'therapeutic anti-TB trial' in patients presenting with respiratory symptoms mimicking TB. Multiple studies across India, including from our centre, have shown that approximately 18–20% of patients with lung cancer receive an inappropriate course of anti-TB medications for varying periods of time, thereby leading to inordinate delay in cancer diagnosis of up to 3 months. It is imperative that these delays be minimized by improving disease awareness amongst physicians and patients both, and encouraging early referrals to higher centres to achieve early diagnosis.[25–28] Indian patients also have an initial preference for alternate forms of treatment such as homeopathy and Ayurvedic medicines for their disease. In our study, males were more likely to receive such forms of treatment in comparison to females, and statistically significant difference was not demonstrated. However, it is also noteworthy that the proportion of females who received definitive treatment was similar to males, irrespective of prediagnosis differences in the treatment administered.

Following first-line treatment, females demonstrated better PFS and OS than males. Generally, it has been reported that lung cancer outcomes in females are superior, more so in early-stage NSCLC and particularly in adenocarcinoma.[24] Data from the Eastern Cooperative Oncology Group (ECOG) Trial comparing gender

differences in survival found similar response rates of 19% in both the groups; however, the median survival time for women was 9.2 months which was significantly better than that for males (7.3 months).[29] Similar data has been reported in a cohort of more than 40000 patients, wherein relative survival was lower in men than in women.[30] Our study demonstrates improved survival rates in a cohort of women comprising predominantly advanced disease, thus depicting the real-life scenario in this country.

We acknowledge some obvious limitations in our study. This was a retrospective cohort analysis from a single centre, thereby limiting the generalizability of results. Secondly, due to a long retrospective chart review going back more than a decade, some data was missing. Thirdly, not all eligible patients were tested for mutations either due to non-availability of the test before 2013 or lack of adequate tissue in the diagnostic specimen. Fourth, not all patients received definitive chemotherapy or targeted therapy due to various factors such as unwillingness, poor performance status or economical constraints. Fifth, although the treatment protocols were by and large uniform for the cancer type, some variability in regimen and duration is to be expected and hence, no conclusion can be drawn regarding superiority of one regimen over another. Overall, however, this is one of the few studies from the Indian subcontinent, and probably the largest that primarily focuses on the gender differences in lung cancer demographics and treatment outcomes in a real-life setting. We were also able to identify several distinct clinico-social and phenotypic characteristics specific to females with lung cancer and those which influence survival. This information may be useful for prehospital education, spreading awareness about disease, and early referrals for diagnosis and initiation of appropriate treatment.

CONCLUSION

Females with lung cancer have better survival and demonstrate several distinct phenotypic characteristics compared to males. Appropriate measures based on this knowledge may help in early diagnosis and development of therapeutic strategies to obtain improved outcomes.

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Conflicts of interest

There are no conflicts of interest.

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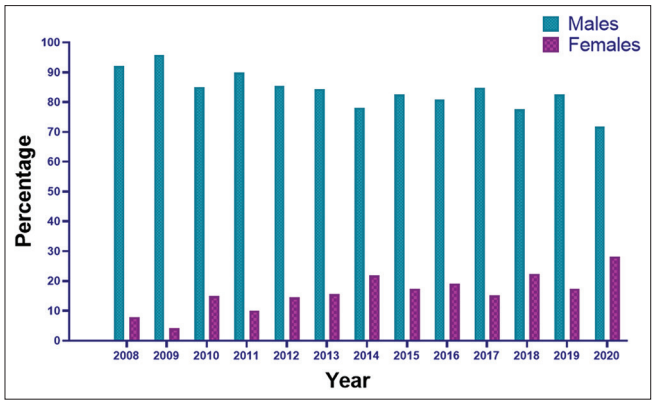

Supplementary Figure 1: Year-wise distribution of male and female lung cancer patients