

## Original Research Article

# Clinicopathological spectrum of peripheral lung tumors in resected lung specimens: a single institutional study in a tertiary care centre

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## ABSTRACT

**Background:** Lung cancer is the most common cancer and by far the leading cause of cancer death among both men and women in the world. In Kashmir, in the recent study, Lung carcinoma was found to be second common in males and sixth in females in Kashmir. This study was carried out to study the demography, clinical presentation, risk factors and histopathological pattern of peripheral lung tumours in resected specimens and to evaluate the added advantage of Immunohistochemistry for enhancing the diagnostic accuracy.

**Methods:** It was a five-year study conducted in the Department of Pathology, SKIMS and the cases from June 2009 to April 2012 were analysed retrospectively while the cases from June 2012 to May 2014 were evaluated prospectively. A total of 97 cases with peripheral lung tumor in whom resection was done were studied.

**Results:** Majority of the cases were seen in males (84.53%) in the fifth decade of life. Cough was the most common symptom, present in 58.76% patients. Right lung was involved in majority of the cases, 57.95% and left lung was involved in 42.04%. Maximum growth size as seen on gross examination was 8 cm and minimum were 1 cms. Most common histopathological subtype was squamous cell carcinoma seen in 64.94% followed by adenocarcinoma seen in 19.58% of the patients. Lymph nodes were involved in 41 cases (52.56%) and were free in 37 patients (47.43%). IHC was done wherever required and was consistent with histopathology.

**Conclusions:** To improve the therapeutic results of lung cancers efforts for early detection and treatment are essential. Timely intervention with the help of surgery, histopathology and immunohistochemistry are hence very helpful.

**Keywords:** Lung, Pathology, Smoking, Tumors

## INTRODUCTION

Lung cancer is the most common cancer and by far the leading cause of cancer death among both men and women in the world.<sup>1</sup> In India lung cancer was thought to be rare, but as per the data given in first All India report (AIR) 2001-2002, in males the lung cancer is the leading cancer in 8 of the 12 Population Based Cancer Registration (PBCR's) (ICMR, 2001-2002).<sup>2</sup>

In Kashmir in the recent study period (2000-2012) conducted by the Departments of Hospital Administration and Radiation Oncology, Lung carcinoma was found to be second common in males and sixth in females in Kashmir.<sup>3</sup>

Authors carried out this study to find out the demographic, clinical, and histological characteristics and risk factors of lung cancer in a referral tertiary center in Kashmir.

A variety of benign and malignant tumors arise in the lung of which 90 to 95% are carcinomas, 5% bronchial carcinoids, 2 to 5% mesenchymal and other miscellaneous tumors.<sup>4</sup> The lungs are common sites of metastatic disease.<sup>5</sup> More than 90% of lung carcinoma patients are over 40 years of age at the time of diagnosis.<sup>6</sup>

The most common presenting symptom is Cough; however, symptoms may vary according to the different tumor subtype.<sup>7</sup>

The most important risk factor for lung carcinoma is cigarette smoking and 87% of lung carcinomas occur in active smokers or those who have stopped smoking recently.<sup>8</sup>

Approximately 10 to 15% of all lung cancers arise in never smokers.<sup>9</sup> The present study attempted to evaluate the cases of lung cancers at a tertiary care hospital in Kashmir.

**METHODS**

The study was conducted at the Sher-i-Kashmir Institute of Medical Sciences (SKIMS), Srinagar, Kashmir (India), in the department of pathology. The cases from June 2009 to April 2012 were analysed from the Department of Medical Records retrospectively while the cases from June 2012 to May 2014 were evaluated prospectively. A total of 97 cases with peripheral lung tumor (primary or metastatic) in whom resection was done in the form of lobectomy, bilobectomy, pneumonectomy or segmentectomy were studied, out of 97 patients 49 were in prospective group and 48 were in retrospective series.

**Study population**

All cases were patients admitted in hospital for surgical resection of peripheral lung tumors.

**Inclusion and exclusion criteria**

- The study included only the peripheral tumours in resected specimens of lungs over the period already mentioned.
- Cases found to be non-neoplastic after histopathological examination were excluded.
- Detailed clinical information as per proforma was gathered. Immunohistochemistry was done only wherever required.

**Statistical analysis**

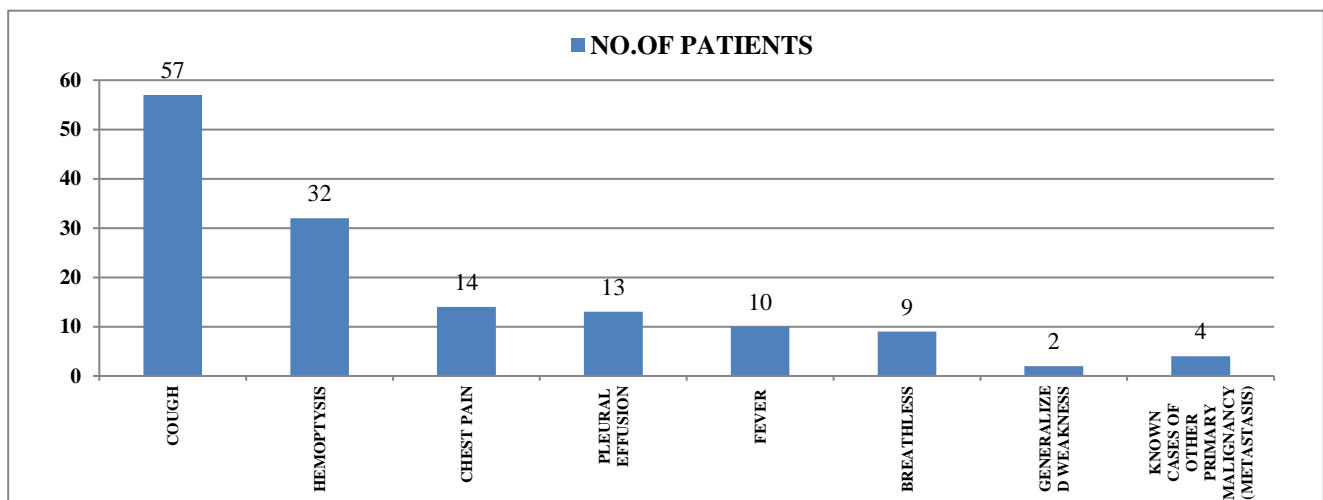
Statistical data was carried out using SPSS 16.

**RESULTS**

A total of 97 cases with peripheral lung tumor (primary or metastatic) in whom resection was done in the form of lobectomy, bilobectomy, pneumonectomy or segmentectomy were studied. In the present study following observations were made.

In this study mean age of presentation was 59.91 years. Maximum number of cases i.e. 39(40.20%) were in the age range of 50-59 years and a younger age of presentation was noted in females as compared to males. Males represented 84.53 percent (82/97) and females represented 15.46 percent (15/97) of the patients. Male: Female ratio was 5.6:1. 57(58.76%) cases were from urban areas while 40(41.23%) cases were from rural areas. Cough was the most common symptom, present in 57(58.76%) patients. The frequency of various symptoms is represented in (Figure 1).

Right lung was involved in majority of the cases, 57.95% (51 patients) and left lung was involved in 42.04% (37 patients).



**Figure 1: Frequency of various symptoms.**

Maximum growth size as seen on gross examination was 8 cm and minimum were 1 cms. The tumor configuration was found to be necrotic in maximum number of cases i.e. 47(48.45%), 42(43.29%) were Grey/white firm, 5(5.15%) were cavitary and no well-defined growth was seen in 3(3.09%) cases. Histopathological subtypes and gender distribution are represented in (Table1). Out

of 20 Adenocarcinomas 4 were reported as papillary type, 3 as BAC and 1 as lepidic predominant. Out of 4 metastases, 2 were that of Ewings sarcoma, 1 was MPNST and 1 was Adenocarcinoma of colon. Among male's Squamous cell carcinoma was the predominant type seen in 59 cases (71.95%) and in females it was adenocarcinoma seen in 7 cases (46.66%).

**Table 1: Various histopathological subtypes and their gender distribution.**

Histopathological subtypes	Male	Female	Total	Percentage
Squamous cell carcinoma	59	4	63	64.94
Adenocarcinoma	12	7	19	19.58
Large cell carcinoma	3	2	5	5.15
Metastasis	3	1	4	4.12
Small cell carcinoma	1	1	2	2.06
Mesothelioma	2		2	2.06
Lymphoma	1		1	1.03
Chondroid Hamartoma	1		1	1.03
Total	82	15	97	100 %

It was seen that Lymph nodes were involved in 41 cases (52.56%) and were free in 37 patients (47.43%). In 19 patient's lymph nodes were either not sent or retrieved in the specimen.

Tumor emboli were seen in 55 cases (58.51%), absent in 39 cases (41.48%) and in 3 cases lymphovascular invasion was not determined (in hamartoma, in Non Hodgkins Lymphoma and in Malignant peripheral nerve sheath tumor).

**DISCUSSION**

Lung cancer is the most common cancer worldwide. Each year more people die of lung cancer than of colon, breast and prostate cancers combined.<sup>1</sup> Lung cancer kills 85% to 90% of its victims.<sup>10</sup> To improve the therapeutic results of these cancers efforts for early detection and treatment are essential. Surgery is still regarded the most effective method in controlling the primary tumor, provided a complete resection is possible and risks of procedure are low.

In this study maximum number of cases i.e. 39(40.20%) in the age group 50-59 years followed. Mean age of presentation in this case was 59.91 years. Results were consistent with the study conducted by Stojic J et al, who found that the most patients operated for lung cancer were in the age group of 51-60 years.<sup>11</sup> In this study females were affected at younger age than males. The above findings were comparable with international studies.<sup>12-14</sup> Males comprised 84.53%(n=82) and females comprised 15.46%(n=15) of all the cases. The male:female ratio was 5.46:1. The previous studies on

lung carcinoma from Kashmir showed different results for sex distribution. In a study by Nafae et al, at Chest Disease Hospital and SMHS Hospital, Srinagar, Kashmir all lung tumors were reported in males.<sup>15</sup> Khan et al, found male:female ratio of 11.3:1. Thus, in this study, authors have found that increasing number of lung carcinoma cases are now being reported in females in Kashmir.<sup>16</sup>

In the current study 75.23% (n=73) were smokers and 24.74% (n=24) were nonsmokers. The smoker: nonsmoker ratio was 3.04:1. Among males, smokers constituted 85.36% (n=70) and among females, smoking history was positive only in 20% (n=3 cases). A previous study by Khan et al, reported smoking history in 88% males and none of the female patients had history of smoking. A rise in the incidence of smoking in females could be a reason for increasing incidence of Lung carcinoma in females.<sup>16</sup>

The presenting symptoms in the decreasing order of frequency were cough (58.76%), hemoptysis (32.98%), chest pain (14.43%), pleural effusion 13.40%, fever (10.30%), breathlessness (9.27%) and generalized weakness 2.06%. Most of the other studies revealed similar findings and most common symptoms were found to be cough, dyspnoea and chest pain.<sup>17</sup>

Bronchoscopy was available in 75 cases. In all cases it was reported as normal study. The peripheral tumors as those where no growth was visible on bronchoscopy or grossly it was seen in the peripheral region beyond the subsegmental bronchi. RJ Shiner et al, defined peripheral lesion as one that was not seen within bronchial tree at fiberoptic bronchoscopy.<sup>18</sup> In a study by Harubumi Kato

et al, it was defined as a lesion located in an airway more peripheral than subsegmental bronchi.<sup>10</sup> In a study by Oscar Auerbach et al it was studied that peripheral tumors are increasing with corresponding increase in centrally originating bronchial carcinoma.<sup>19</sup>

CT Scan revealed contrast enhancing mass in >80% cases. In 5 cases it was reported as cavitary lesion, in 4 cases as collapse, in 2 cases as suggestive of metastasis and in 1 case as infective pathology. Additional information like presence/ absence of lymphadenopathy, effusion and pleural or rib infiltration were also reported on the CT Scans. The size of tumor, presence or absence of LAP/necrosis, type of growth as reported on CT scan were corresponding well with the same as seen grossly in the specimen received. Thus, CT scan serves as an important diagnostic tool in the peripheral lung tumors where fiberoptic bronchoscopy was found to be normal. Other studies in the past have shown the specificity of 82.9%, sensitivity of 66.7% and total accuracy of 80% on CT scans.<sup>17</sup>

This study showed right lung involvement in 57 cases (58.76%) and left lung involvement in 40 cases (41.23%). This was found consistent with the study done by Sharif Abd el Aziz et al, observed right lung involvement in 60.0% and left lung involvement in 40.0%.<sup>17</sup>

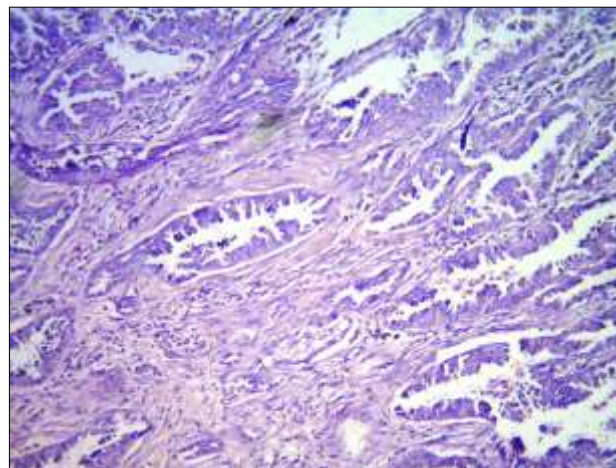
Size of the tumor as seen grossly was divided into five groups (<2 cms; 2.1 to 4 cms; 4.1 to 6 cms; 6.1 to 8 cms and >8.1 cms). 37 cases (38.14%) cases had tumor size in the range of 4.1 to 6cms. 28 cases (28.86%) had tumor size in the range of 2.1 to 4 cms. <2 cms size was seen in 15 cases (15.46%), 6.1 to 8 cms size was seen in 13 cases (13.40%) and 1 case was having tumor size >8.1 cms. Mean tumor diameter recorded was 4.89cms. In three cases no well-defined growth was seen grossly.

These results were comparable to other studies which reported tumor size as 0 to 3 cm in 72 cases; 3.1 to 6 cm in 154 cases and >6 cms in 88 cases out of 314 total cases seen.<sup>17,20</sup>

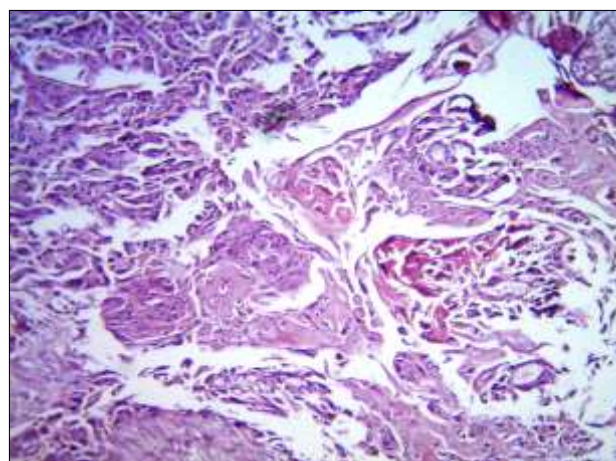
The commonest histological subtype was Squamous cell carcinoma seen in 63 cases (64.94%). Adenocarcinoma was the second most common subtype seen in 19 cases (19.58%). Large cell carcinoma was reported in 5 cases (5.15%), metastasis in 4 cases (4.12%), small cell carcinoma and Mesothelioma 2 cases (2.02% each), Lymphoma and Chondroid Hamartoma 1 case each (1.03% each). Most of the Squamous cell carcinoma were well to moderately differentiated. Two cases of Squamous cell carcinoma were reported as Basaloid variant and one as non-keratinizing type. Four cases of Adenocarcinoma were reported as papillary variant, three as BAC and one as mucinous lepidic predominant. One mesothelioma was reported as epithelial variant and one as lymph histiocytic variant. The case of lymphoma was reported as NHL B-Cell type. Out of four secondary tumors two were that of Ewings sarcoma, one was of

MPNST and one was of colonic adenocarcinoma. All the four cases were already operated before for primary malignancy and had received therapy for the same.

Squamous cell carcinoma has been reported as predominant type in most of the studies.<sup>17,20-22</sup> However, study by Sherif Abd El Aziz et al, and Wahbah M et al, showed Adenocarcinoma as the commonest histological subtype followed by Squamous cell carcinoma.<sup>17,23</sup>



**Figure 2: Tumor cells with abundant cytoplasm, hyperchromatic nuclei and prominent nucleoli in a case of squamous cell carcinoma (10X).**

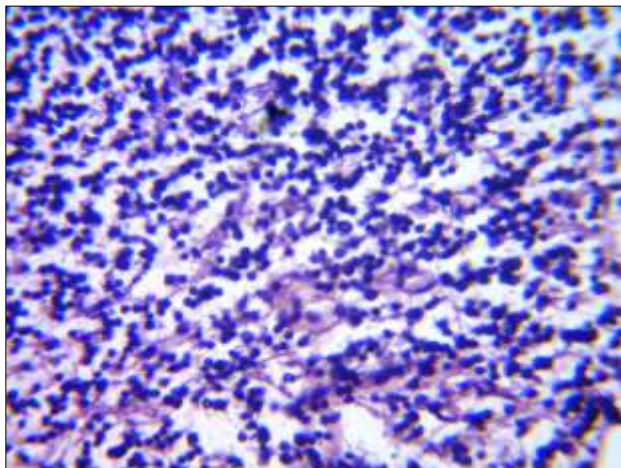


**Figure 3: Tumor cells forming glands in a case of adenocarcinoma (10X).**

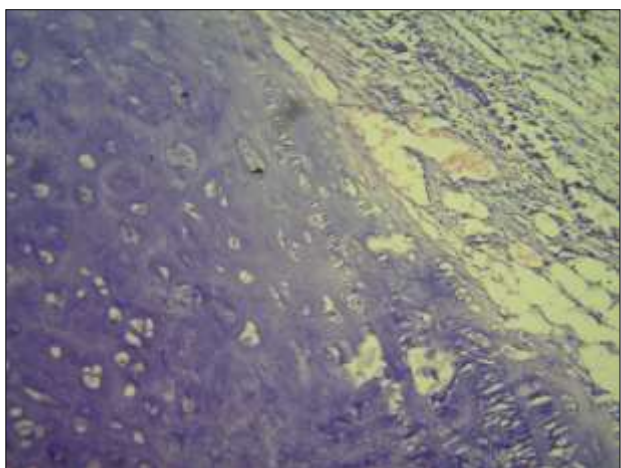
The histological subtypes found among males and females were different in the current study. Similarly, subtypes varied among smoker and nonsmoker group and among various age groups. Among male's squamous cell carcinoma was the commonest histological subtype seen in 59 cases (71.95%) (Figure 3) followed by Adenocarcinoma (Figure 2) in 12 cases. Among females it was Adenocarcinoma in 7 cases (46.60%) followed by Squamous cell carcinoma in 4 cases. Squamous cell carcinoma was the most common subtype in older age



group and among smokers and Adenocarcinoma was the predominant type among younger patients and nonsmokers. Since in this study most of the females were nonsmokers with younger age of presentation, that partly explains the above results



**Figure 4: Monotonous sheets of tumor cells in a case of lymphoma (40X).**



**Figure 5: Mature cartilage in case of hamartoma.**

The past studies have shown varying results. In one study most common histologic types as squamous cell carcinoma (33%) and adenocarcinoma (30%): Squamous cell carcinoma in men (36%) and adenocarcinoma in women (56%).<sup>24</sup> Another study showed adenocarcinomas occurred more frequently at early ages among both men and women.<sup>25</sup> In another study a strong association with smoking was found where out of 58 cases of lung carcinoma 51% were found to be adenocarcinoma (n=29).<sup>26</sup>

IHC was done in 19 cases. (Figure 4 and 5) In all the cases results were consistent with histopathological diagnosis. On IHC the case of NHL was found to be positive for CD20 (diffusely), MPNST showed focal positivity for S-100, both cases of Mesotheliomas were

positive for Calretinin and HMBE-45 and negative for TTF-1, both cases of Ewings sarcoma were positive for CD99 and TTF-1 negative, metastatic colonic adenocarcinoma was positive for CK-20 and negative for CK-7 and TTF-1, four papillary adenocarcinomas were positive for TTF-1 and eight cases of poorly differentiated squamous cell carcinomas were positive for p63.

## CONCLUSION

The most common histological subtype was Squamous cell carcinoma followed by adenocarcinoma affecting mostly males in the fifth decade. However, an increasing incidence in females was observed. Similar to other studies throughout the world this study also found a close association between lung cancer and smoking. IHC wherever required was done and was found to be consistent with histopathology.

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*Ethical approval: The study was approved by the Institutional Ethics Committee*

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