# Histopathological Types in Iraqi Patients with Lung Cancer: Which is the Most Common?

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**ABSTRACT**:
**Background**: The frequency of lung cancer histopathological types has significantly changed over the last decades; adenocarcinoma has replaced squamous cell carcinoma (SCC) as the most common histopathological type of lung cancer. The aim of this study is to assess the frequency of histopathological types among patients with lung cancer. **Method**: In total, 210 lung cancer patients (158 male and 52 female) were included in this study. Age, sex, histopathological type, smoking habits, and stage of disease were all recorded. **Results**: The mean age of patients was $61.71 \pm 10.69$ years; adenocarcinoma was the most common histopathological type of lung cancer (41.9%), followed by SCC (37.6%). Squamous cell carcinoma was the most common type in men (40.5%). 92.3% of patients with small cell lung cancer and 91.1% of patients with SCC were cigarette smokers. At the time of diagnosis, most of the patients had advanced stages. **Conclusion**: Adenocarcinoma is the most common histopathological type of lung cancer in all patients, with SCC still the most common type in men. SCC and SCLC had the oldest mean age. Most patients presented with stages III and IV at diagnosis.

**INTRODUCTION**:
Historically, in 1912, the first monograph on lung cancer was published by Adler, when lung cancer was a rare disease, and in the middle of the last century, the association between lung cancer and smoking cigarettes was established (1, 2). Nowadays, lung cancer is the second most common type of cancer in the world and the most common cause of cancer-related death (3). Non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC) are the two main types of primary lung cancer. NSCLC accounts for 85% of lung cancer, which is classified as adenocarcinoma, squamous cell carcinoma (SCC), large cell carcinoma, and other subtypes (4). Squamous cell carcinoma was previously reported as the most common type of NSCLC as a result of cigarette smoking, but in the last decades, adenocarcinoma incidence has increased and replaced squamous cell carcinoma as the most common type of NSCLC. Adenocarcinoma has a high prevalence among non-smokers and females, and the increase in incidence among smokers is thought to be related to the use of filter cigarettes (5). Small cell lung cancer is more aggressive than NSCLC, and the incidence has declined in the last few decades. SCLC is highly linked to cigarette smoking (6). In Iraq, lung cancer is the second most common cancer (7). The objective of this study is to assess the frequency of histopathological types of lung cancer among a group of Iraqi patients with lung cancer and compare it with global data.

**METHOD**:
Two hundred and ten patients were involved in this study. It's a descriptive study carried out between March 2021 and December 2022. All patients in this study were approved to have primary lung cancer by tissue biopsy (true cut, bronchial, or excisional). Patients diagnosed with fine needle aspirate, cytology (sputum, bronchial wash, pleural effusion), patients with lung secondary disease, and any other pathology (mesothelioma, sarcoma, lymphoma, etc.) rather than lung cancer were excluded from this study. Data from patients with lung cancer was collected after taking their permission during

their visit to the oncology unit using a structural form that included: sex, age, smoking habits, type of diagnostic sample, histopathology type, and clinical and radiological staging of disease at diagnosis. The World Health Organization (WHO) histopathological classification was used to classify primary lung cancer, including NSCLC and small cell lung cancer. NSCLC is subdivided into adenocarcinoma, squamous cell carcinoma, large cell carcinoma, and other sub type (8). The American Joint Committee on Cancer (AJCC) Cancer staging manual , eighth edition was used for staging of the disease in to four stages (I, II, III, IV) according to the investigations (9). We classified patients according to their smoking pattern as follows: smoker: a patient who smoked 100 cigarettes or more during their lifetime; non-smoker: a patient who has never smoked or who smoked less than 100 cigarettes

during their lifetime; and heavy smoker: a patient who smoked 20 cigarettes or more per day. Statistical package for social sciences (SPSS version 22 software) was used for descriptive analysis of the data.
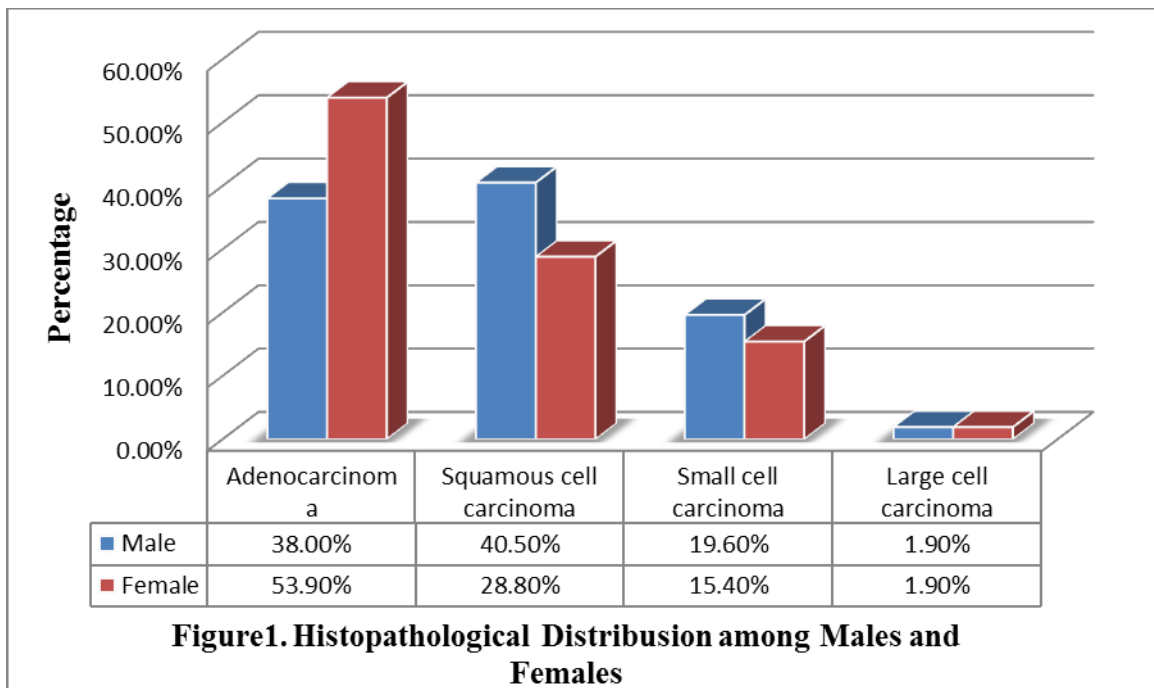
## RESULTS:
In this study, 210 patients with primary lung cancer, 158 (75.2%) male and 52 (24.8%) female, were included. The mean age of patients was 61.71±10.69 years. Among the study group, adenocarcinoma was the most common histopathological type of lung cancer 88 (41.9%), followed by SCC 79 (37.6%) and SCLC 39 (18.6%). The mean age of patients with adenocarcinoma was 59.35±12.01 years younger than the mean age of patients with SCC and SCLC but older than the mean age of patients with large cell carcinoma [Table 1].

| Table 1. Descriptive Data for Cases | | | | | | |
|---|---|---|---|---|---|---|
| Sex: | Number n. | Percentage % | Younger age/year | older age/year | Mean age | Std. Deviation |
| Male | 158 | 75.2% | 37 | 87 | 62.59 | ±10.31 |
| Female | 52 | 24.8% | 36 | 85 | 59.05 | ±11.47 |
| Both | 210 | 100% | 36 | 87 | 61.71 | ±10.69 |
| Histopathology type: | | | | | | |
| Adenocarcinoma | 88 | 41.9% | 36 | 85 | 59.35 | ±12.01 |
| Squamous cell carcinoma | 79 | 37.6% | 41 | 87 | 63.89 | ±9.19 |
| Small cell carcinoma | 39 | 18.6% | 38 | 80 | 63.30 | ±9.42 |
| Large cell carcinoma | 4 | 1.9% | 44 | 63 | 55.25 | ±8.99 |

In this study, lung cancer was most frequently diagnosed in 75 (35.7%) patients aged 55-64 years; all histopathological types were most frequent at this age, except SCLC, which was highest diagnosed at age 65-74 years [Table 2]. Among male patients, SCC was the most common histopathological type with 64 (40.5%), while adenocarcinoma was the most common histopathological type among female patients with 28 (53.9%), as shown in [Figure 1].

| Table 2. Age Distribution Among Histopathological Types | | | | | | |
|---|---|---|---|---|---|---|
| Histopathology | Age /year n. (%) | | | | | |
| | 35- 44 y | 45- 54 y | 55- 64 y | 65- 74 y | 75-84 y | 85-90 y |
| Adenocarcinoma | 9 (10.2%) | 21 (23.9%) | 27 (30.7%) | 19 (21.6%) | 11 (12.5%) | 1 (1.1%) |
| Squamous cell carcinoma | 3 (3.8%) | 8 (10.1%) | 33 (41.7%) | 24 (30.4%) | 10 (12.7%) | 1 (1.3%) |
| Small cell carcinoma | 1 (2.6%) | 6 (15.4%) | 13 (33.3%) | 16 (41%) | 3 (7.7%) | 0 (0%) |
| Large cell carcinoma | 1 (25%) | 1 (25%) | 2 (50%) | 0 (0%) | 0 (0%) | 0 (0%) |
| Total | 14 (6.7%) | 36 (17.1%) | 75 (35.7%) | 59 (28.1%) | 24 (11.4%) | 2 (1%) |

**Figure1. Histopathological Distribusion among Males and Females**

| | Adenocarcinoma | Squamous cell carcinoma | Small cell carcinoma | Large cell carcinoma |
|---|---|---|---|---|
| ■ Male | 38.00% | 40.50% | 19.60% | 1.90% |
| ■ Female | 53.90% | 28.80% | 15.40% | 1.90% |

We found that 168 patients (80%) were cigarette smokers and 42 (20%) were non-smokers. Among smokers, 142 (84.5%) patients were heavy smokers. Out of 168 smokers, 139 (82.7%) were males and 29 (17.3%) were females. 92.3% of patients with SCLC and 91.1% of patients with SCC were cigarette smokers. Adenocarcinoma was the most common histopathological type among non-smokers, with 31 (35.2%) patients [Table 3].

**Table 3. Histopathological Distribution Between Smokers and Non-smokers**

| | Adenocarcinoma | Squamous | Small Cell | Large Cell |
|---|---|---|---|---|
| **Smokers** | 57 (64.8%) | 72 (91.1%) | 36 (92.3%) | 3 (75%) |
| **Non-Smokers** | 31 (35.2%) | 7 (8.9%) | 3 (7.7%) | 1 (25%) |
| **Total** | 88 | 79 | 39 | 4 |

| Histopathological Distribution According to Smoking Status and Sex | | | | |
|---|---|---|---|---|
| | **Smokers** | | **Non-Smokers** | |
| **Histopathology** | Male | Female | Male | Female |
| **Adenocarcinoma** | 47 (27.9%) | 10 (6%) | 13 (31%) | 18 (42.9%) |
| **Squamous cell carcinoma** | 60 (35.7%) | 12 (7.1%) | 4 (9.5%) | 3 (7.1%) |
| **Small cell carcinoma** | 29 (17.3%) | 7 (4.2%) | 2 (4.7%) | 1 (2.4%) |
| **Large Cell carcinoma** | 3 (1.8%) | 0 (0%) | 0 (0%) | 1 (2.4%) |
| | 139 (82.7%) | 29 (17.3%) | 19 (45.2%) | 23 (54.8%) |
| **Total** | 168 (80%) | | 42 (20%) | |

At the time of diagnosis, most of the patients had advanced stages: 113 (53.8%) were stage IV and 79 (37.6%) were stage III. Only 18 (8.6%) patients had early stage disease (I, II). Most patients with adenocarcinoma and SCLC presented with distant metastases of 62 (70.5%) and 20 (51.2%), respectively, while most SCC patients 42 (53.2%) were diagnosed at stage III [Table 4].

**Table 4.  Distribution of Lung Cancer Histopathological Types According to the Stage of Disease at Diagnosis**

| Histopathology | Stages of Disease No. (%) | | | | |
| --- | --- | --- | --- | --- | --- |
| | Stage I | Stage II | Stage III | Stage VI | Total n. |
| Adenocarcinoma | 1 (1.1%) | 6 (6.8%) | 19 (21.6%) | 62 (70.5%) | 88 |
| Squamous cell carcinoma | 0 (0%) | 8 (10.1%) | 42 (53.2%) | 29 (36.7%) | 79 |
| Small cell carcinoma | 0 (0%) | 1 (2.6) | 18 (46.2) | 20 (51.2%) | 39 |
| Large cell carcinoma | 1 (25%) | 1 (25%) | 0 (0%) | 2 (50%) | 4 |
| Total | 2 (1%) | 16 (7.6%) | 79 (37.6%) | 113 (53.8%) | 210 |

## DISCUSSION:

In recent decades, there has been a significant increase in adenocarcinoma among the histopathological types of lung cancer in both sexes, accompanied by a significant decrease in squamous cell carcinoma and small cell carcinoma, as reported in the United States, Japan, France, and other countries. These changes could be explained by the use of filtered cigarettes and the tobacco control program that began earlier in developed countries than in developing countries (5, 10, 11, 12). In our study, adenocarcinoma was the most prevalent histopathological category, accounting for 41.9% of cases, followed by SCC with 37.6%. According to studies conducted in Jordan and France, adenocarcinoma accounts for 55.3% and 51.9%, respectively, while SCC accounts for 30.2% and 22.1%, respectively (13, 11). SCLC accounts for 18.6% of patients in our study, which is higher than the 16%, 14%, and 12.6% rates reported in Turkey, the United States, and France, respectively (14, 5, 11). Although all histopathological types of primary lung cancer are related to smoking, the incidence of squamous cell carcinoma and small cell carcinoma is significantly associated with tobacco smoking, so the incidence has declined as a result of the decrease in tobacco smoking in the last few decades (15). In 2023, lung cancer will be the third most common cancer in newly diagnosed cases in the United States, accounting for 12.2%. Among American people, lung cancer is most frequently diagnosed at ages 65-74, with a median age at diagnosis of 71 years (16). Whereas in our study, 35.7% of patients were diagnosed at ages 55-64, similar to an Indian study that reported nearly one third of patients diagnosed at 55-64 years of age (17). In this study, the mean age of patients was 61.71±10.69 years, nearly similar to the mean age in the Jordanian study of 63.8±11.8 years and younger than that reported in a cohort study in France of 67.8±10.3 years (13, 11). The mean age of patients with adenocarcinoma in our study

was 59.35±12.01 years younger than SCC 63.89±9.19 years, whereas the mean age of Jordanian patients with adenocarcinoma was 62.74±11.9 years, which is also younger than SCC 65.42±11.6 years (13).

In general, the incidence of all histopathological types of lung cancer in males was higher than in females, but by the time the incidence of adenocarcinoma in females increased, the gender gap in lung cancer incidence narrowed (18).

A cohort study in France found that adenocarcinoma was significantly increasing in both males and females (47.3% of males and 60.6% of females). While SCC accounts for 26.9% of males and 13.1% of females (11).

Whereas in our study, SCC is still the most common histopathological type in males, accounting for 40.5%, and among female patients, adenocarcinoma was the most common type (53.9%).

Our results are comparable to those of an Iranian study, which found that SCC is the most commonly diagnosed histopathology type among Iranian males and adenocarcinoma among Iranian females (19). Similar to that observed in the North Greece study, squamous cell carcinoma is highly prevalent in males at 46.9% and adenocarcinoma in females at 43.2% (20).

Geographical differences in smoking habits reflect the difference in distribution of lung cancer histopathological types between societies, as the smoking gap between males and females decreases in developed societies compared to developing societies, where smoking is more prevalent in males than females (21).

SCC and SCLC are more strongly correlated with tobacco smoking than adenocarcinoma, which is mainly diagnosed in non-smokers and women (14, 21). This is strongly correlated with our findings; nearly 90% of patients with SCLC and SCC were smokers, and among non-smokers, adenocarcinoma was the most common type (73%). Most lung cancer patients present with

locally advanced or metastatic disease, which reduces the chance of cure. Even in developed countries, about half of patients present with distant metastasis, as reported in the United States at 53%, and in France at 57.6%, and nearly 21% of patients are diagnosed with localized disease (16, 11).

A study in Turkey found that about 50% of patients had metastatic disease at diagnosis. Also, a study in India showed 44.8% of patients had metastatic disease and 14.6% had localized disease only (14, 17). Our study found that only 8% of patients were diagnosed with stages I and II and nearly 57.6% with metastatic disease. A late diagnosis reduces the chance of lung cancer being cured. Nguyen et al. suggested that lung cancer screening programs and advances in diagnosis might increase the detection of localized disease that can be cured (10).

In conclusion, adenocarcinoma is the most common histopathological type of lung cancer in all patients, with SCC still the most common type in men. Lung cancer was most frequently diagnosed at ages 55-64, and among histopathological types, SCC and SCLC had the oldest mean age. About 90% of patients with SCLC and SCC were smokers. Most patients presented with stages III and IV at diagnosis. Therefore, these alarming results need an effective tobacco control program, improved facilities for early diagnosis of disease, and a lung cancer screening program in order to improve lung cancer prognosis and survival.

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