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Histopathological study of lung cancer: Rate of different types of bronchogenic carcinoma of follow up cases in Benghazi Medical Centre

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Original Research Article

Abstract

Introduction: Lung cancer has transformed from a relatively rare disease to a worldwide health problem and a major global health concern. It is the second most common cancer in both men and women, after prostate and breast cancer respectively. It has become the leading cause of cancer-related death.

Aim: This study is conducted to shed the light on the rate of different types of lung cancer among patients who were diagnosed and treated at Benghazi Medical Center.

Material and methods: The current study was a retrospective study, carried on 269 Case of confirmed primary lung cancer diagnosed between the years 2015, to 2018. Data was collected from the Oncology Department of Benghazi Medical Center. The data was analyzed using SPSS version 23, and was plotted into tables and figures by Microsoft Excel 2010.

Results: This study revealed that the common age group of patients was between 61–70 years, with a mean age of 62.3±3.75 (SD) years. The disease was more common in males than females. Most of the patients were active smokers, and about 92.9% of the patients have no past medical history of respiratory diseases. Non-small cell carcinoma was the commonest type of lung cancer (71.4%), out of which adenocarcinoma represented 54% of the cases. Almost all (92.9%) cases were presented with stage IV of the cancer at the time of diagnosis, which meant that the cancer was already metastasized to distant organs. In about 72.5% of the cases, the tumor was in the right side of the lung, in the upper region. There was a statistically significant difference between the mean age of males and females. Also, there was a significant relationship between the adenocarcinoma subtype of NSCLC (None Small Cell Lung Cancer) and patients with no past respiratory diseases.

Conclusion: lung cancer is an aggressive malignant tumor which was very common among smoking Libyan males and usually associated with high mortality rate.

Keywords: bronchogenic carcinoma, squamous cell carcinoma. adenocarcinoma, smoking, small cell carcinoma.

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Introduction

Cancer is one of the major causes of death worldwide. Metastasis is the leading cause of cancer-related mortality (1).80-90% of cancers are caused by external environmental factors (carcinogens). In 2018, an evaluation of 2.2 million infection-attributable cancer cases was diagnosed globally. Lung cancer has been transformed from uncommon disease into a worldwide trouble and public health problem. In 1900, about 140 lung cancer cases had been published in medical literature, subsequently, findings of lung tumors in autopsied cadavers started to rise dramatically (2). Lung cancer is the second most common cancer in men after prostate cancer and in women after breast cancer. Annually, more patients die of lung cancer than of colon, breast, and prostate cancers combined (3).

A previous study in Libya, conducted between 1981 and 1985, found that lung cancer was the most common tumor (22.4%), among males who had been heavy smokers for 20 years or more (4). In the eastern part of Libya, lung cancer was the most common cancer among males, constituting 18.9% (5). In the central region of Libya, a previous study revealed that lung cancer ranked third (7.7%), following breast cancer and colorectal cancer (6).

Although, in 2004, research revealed that lung and breast cancer were the commonest causes of cancer deaths in eastern Libya (7). Still, there is Lack of the updated records about the incidence of cancer in Libya, both for the cancer in general and lung cancer in specific. Therefore, the trends of lung cancer distribution in Libya have to be compared to the regional and world wide data as this data can help improve the services provided by cancer facilities in many Libyan cities.

The aim

This study was conducted to determine the prevalence of different types of lung cancer among follow-up cases at the Oncology Department of Benghazi Medical Center during the period of time from January 1, 2015, to December 31, 2018.Also, it aimed to find out the possible relationship between the risk factors and types of lung cancer.

Patients & methods

This research was are prospective cohort study. A total of 269 cases of bronchogenic carcinoma was collected from the archive of Benghazi Medical Centre in the period from January2015 to December, 2018. Among many lung biopsy samples, only lung biopsy with malignant tumor were included in this study and the hematoxylin and eosin (H&E)-stained sections from all cases were examined under light microscope to determine the type of the tumor.

The histological diagnosis of bronchogenic carcinoma was correlated to many general factors, including age, gender, smoking status, past medical history of respiratory diseases, and family history of lung cancer. In addition, the site of the tumor, the size of the tumor, the stage of the cancer at the

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time of presentation, and the presence of metastas is were also being studied in this research. That is according to the information available in the files of these patients. Data was arranged in tables and was analyzed by IBM SPSS version 23. The results were posted in figures using Microsoft Excel 2010 as well as by SPSS.

Results

Age distribution

In this study, out of the 269-studied lung cancer cases, the mean age of the patients was 63 years(figure.1)

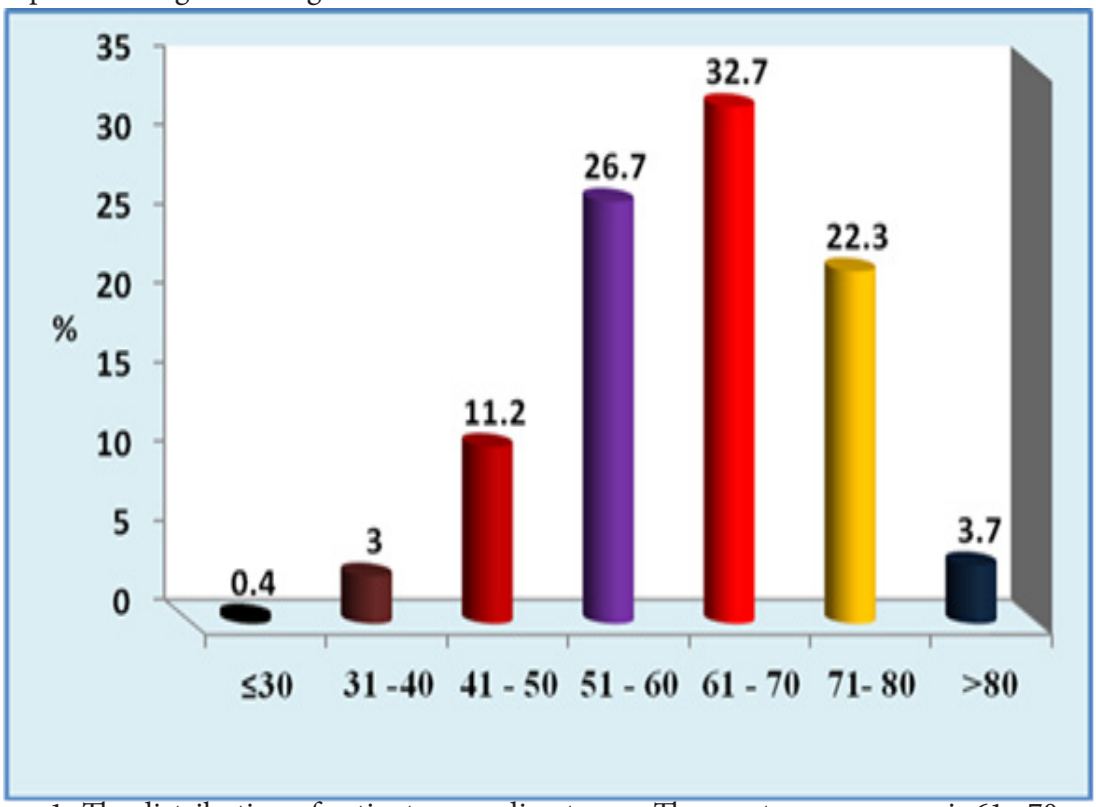

Figure 1- The distribution of patients according to age: The most common age is 61– 70 years, followed by the 51-60 years old.

Sex distribution

Among the 269studied cases, about 90% of the cases were males, while a small percentage of cases were females (less than 10%) (figure.2)

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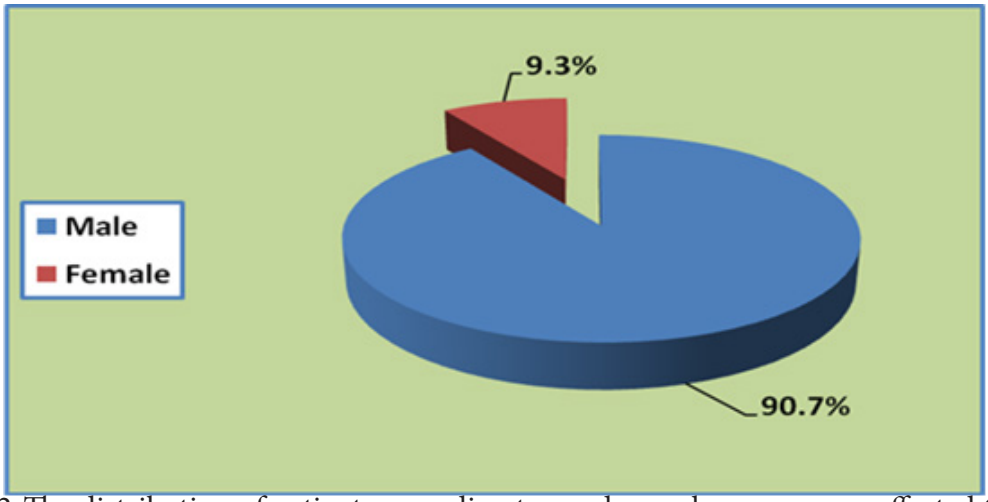

Figure 2-The distribution of patients according to gender, males were more affected than females with ratio of 10:1 respectively.

Smoking status distribution

In this study, more than 98% of patients were smokers, only a small percentage were nonsmokers with mean smoking duration of 40 years.

Family history, tumor subtype, and site

Most of the patients did not have family history of lung cancer.

More than 71% were diagnosed with NSCLC, out of which 54% had adenocarcinoma & 26% squamous cell carcinoma (figure 3). The majority of the recorded cases were infected in the upper part of the right lung (figure 4).

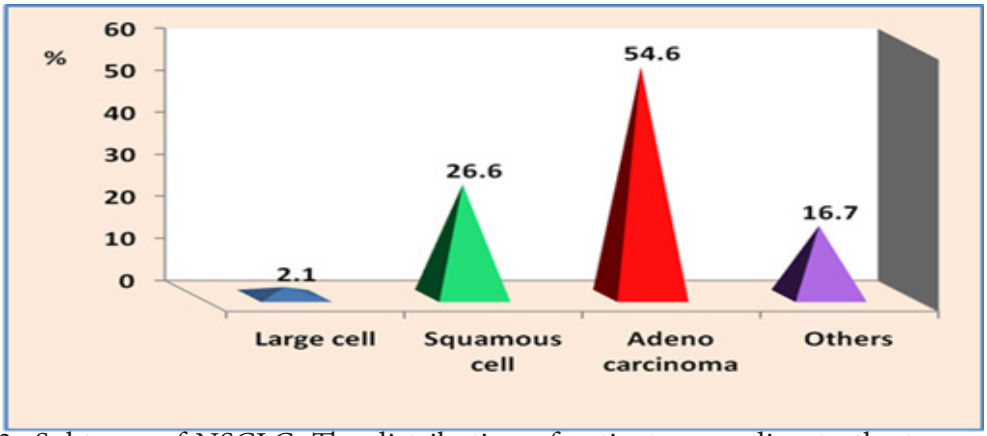

Figure 3- Subtypes of NSCLC: The distribution of patients according to the types of none small cell lung cancer. Adenocarcinoma was the most common type followed by squamous cell carcinoma.

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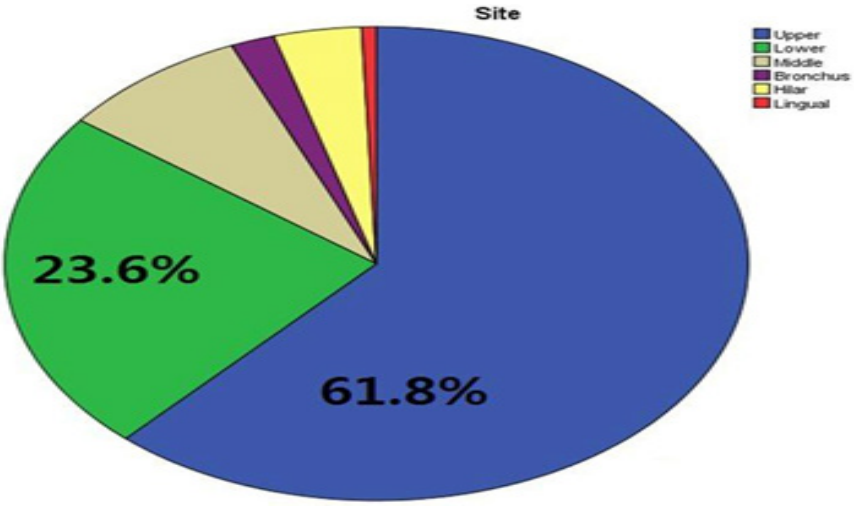

Figure 4- Distribution of patients according to the site of lesion; upper lobe was more affected than the other lung parts.

Previous respiratory diseases

The study of the distribution of patients according to previous respiratory diseases, revealed that 83.8 % of the patients had no previous history of RD(respiratory diseases) while only 6.8 % of had past chronic obstructive pulmonary disease(COPD) (figure 5)

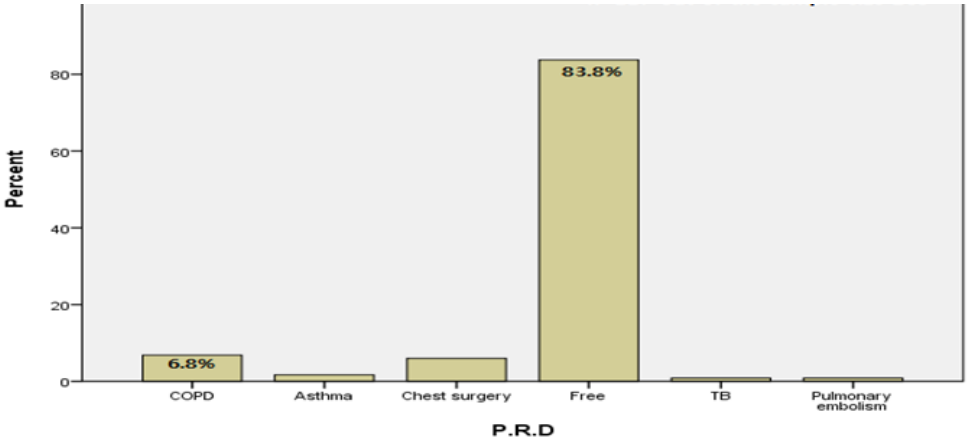

Figure5-Previous respiratory disease (PRD) distribution; PRD had no relation with lung cancer as most of the cases were with free medical history.

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Tumor stage and site of metastasis

In the time of presentation, more than 85% of patients were in the IV stage (figure 6) with metastasis in more than one organ, bone and brain were the most common sites of metastasis (figure7).

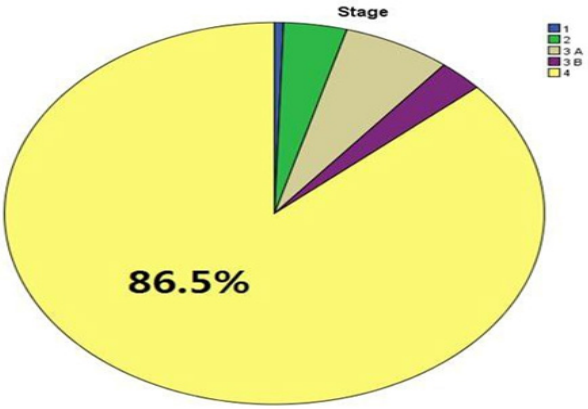

Figure 6- The distribution of patients according to stage of tumor, most of the patient were in stagre IV at the time of presentaion

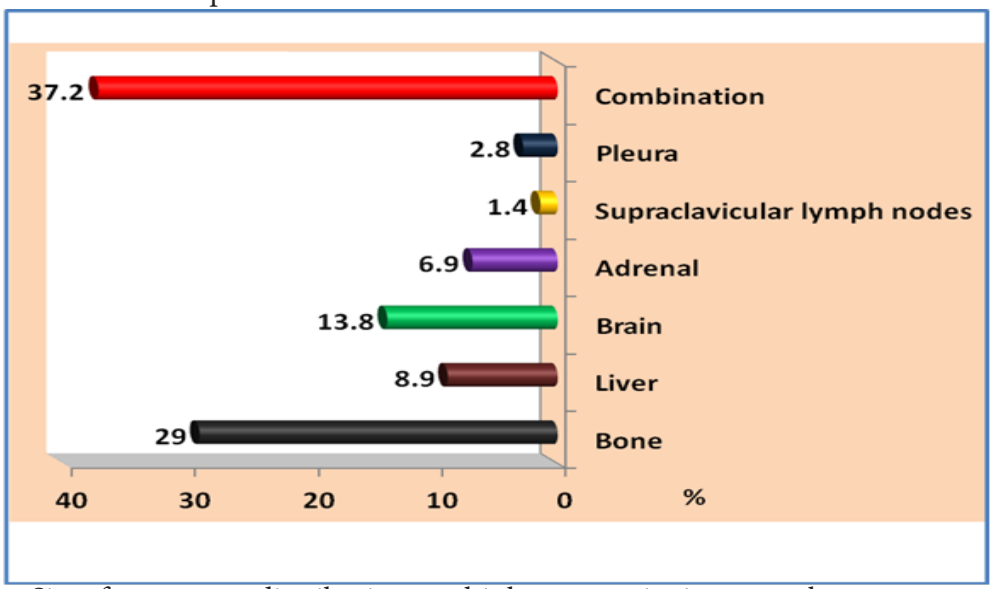

Figure 7- Site of metastases distribution, multiple metastatic sites were the commonest type of presentation followed by bone metastasis and then brain, liver and adrenal gland.

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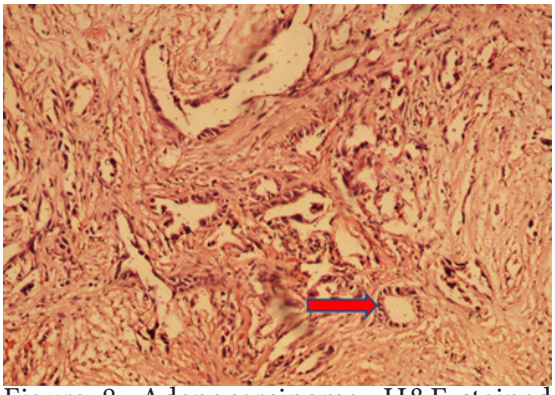

Figure 8: Adenocarcinoma: H&E-stained section from intra parenchymal tumor shows enlarged irregular glandular spaces lined by pleomorphic cells with enlarged nuclei (red arrow), decrease stroma between glandular pattern. (X100)

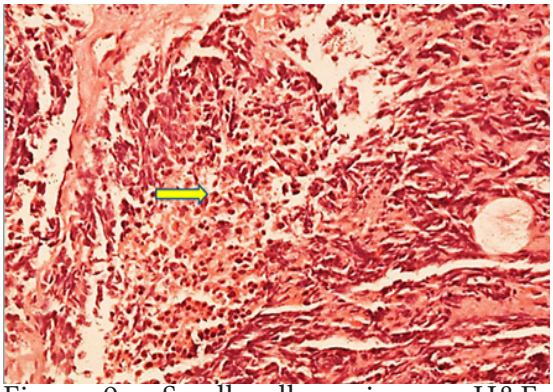

Figure 9: Small cell carcinoma: H&E-stained section from tumor in right bronchus inter Medius shows sheets of small dark round cells with round to oval hyperchromatic nuclei and scanty cytoplasm (yellow arrow). (X 200)

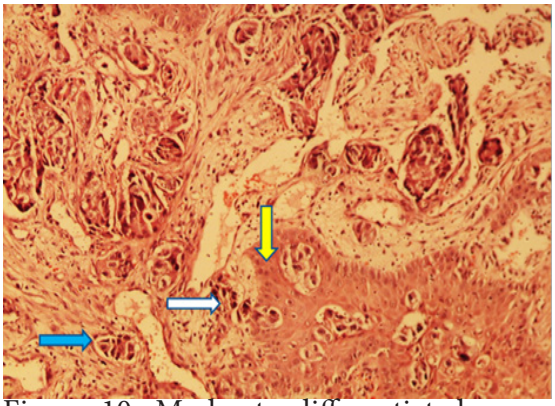

Figure 10: Moderate differentiated squamous cell carcinoma: H&E stained section from tumor in left upper bronchial wall shows fibrous tissue lined by hyperplastic squamous epithelium (yellow arrow) and infiltrated by clusters of malignant squamous cells (blue arrow), prescnce of intercellular bridge (white arrow), no evidence of keratin pearls (X100)

Discussion

Lung cancer is the second most common cancer in both men after prostate cancer and women after breast cancer. Annually, more patients die of lung cancer than of colon, breast, and prostate cancers combined (3).

The mean age of patients results resemble previous results of research done in the eastern part of Libya (8) and in other Arab countries (9). On the contrary the mean age of patients with lung cancer in USA is 71 years (10) probably, due to better quality of life and health service.

In Libya, men are more likely to develop lung cancer than women. This was proven by this study and a previous study in 2004 (8). The increase of the risk of lung cancer in males is

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also comparable with previous study done by Tol win et al. (12) who found that the male cases represent 53% and female cases (47%) of the sample size. This difference in disease distribution according to gender in our community reflecting the habit of smoking is not common between females in Libya

The predominance of the NSCLC between our patients was similar to the findings of a German study in which adenocarcinoma (figure 8) was the leading cell subtype in young male and female patients with lung cancer, whereas, among older male patients, squamous cell carcinoma (figure 9) was predominant (11). In an Egyptian study, adenocarcinoma in the sample size was the predominant, but it was more common in females than males (13).

The histological types of lung cancer in a recent study showed that 71.4% of the sample size diagnosed as NSCLC and only 6.3% were diagnosed as SCLC (figure 10) while 22.3% were diagnosed as lung cancer without classifying. Thai AA et al found that about 85% of all lung cancer cases were NSCLC, and 15% were SCLC (14).

Regarding NSCLC subtypes, the result showed that adenocarcinoma was the most common subtype (54.6%), followed by squamous cell carcinoma (26.6%), and large cell carcinoma was only 2.1%. This is consistent with a previous study done in USA where they found that adenocarcinoma was the most common histologic finding (54.7%), followed by squamous cell (29.4%) (15).

The current study revealed that lung cancer occurs more in the right lung (64.4 %) than the left lung (35.6 %) which is consistent with a previous study done by JiaB. et al (16). Left and right-side lung cancers might have different biological and gene mutation features. Tumors with epidermal growth factor receptor (EGFR L858) mutation are most commonly located on the right side, whereas tumors without EGFR mutation are found on the left side of the lung (17).

EGFR is a protein on cells that helps them grow. A mutation in the gene for EGFR can make it grow too much, which may cause cancer. About 32% of NCSLC cases all over the world involved an EGFR mutation. The most common subtype to have an EGFR mutation was adenocarcinoma (18).

In the present study, 86.5% of the recorded cases were diagnosed at stage IV, this result seems to be higher than the results obtained by Bryan S et al in Canada, where 49.6% of new diagnosed lung cancer cases presented at stage IV (19). This difference is probably due to the delay in seeking medical help in our cases and much better medical services in the western countries. This stage of lung cancer means that the cancer cells are already metastasized to distant organs, and according to recent studies, the target organs in order were the bone (29%) was the common site of spreading, followed by the brain (13.8%), the liver 8.9%, the adrenal gland (6.9%), in addition to pleura (2.8%) and supra clavicular lymph nodes (1.4%) of recorded cases with metastasis (n=145).

In Sweden, a study showed that the target metastasized organs were as follows: the brain (47%) was the common site of spreading, fol-

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lowed by the bone (39%), the liver (35%), the respiratory sys(22%) (20).About (46.7%) of females in this study showed the high percentage of bone metastasis than male who constitute only (27%).

Both preclinical and clinical research have found sex-based differences in bone metastasis development; these findings are most likely connected to the regulation of hormones and underlying biology associated with sexual dimorphism. Future research should focus both in vitro and in vivo on the idea that feminization of bone marrow by sex steroid delivery, or blockage can change results (21).

Regarding to smoking state in this study,(98.3%), were smokers and one of them was a female, a case of non-smoker female was diagnosed as lung cancer without classifying the type, but the male cases were diagnosed with adenocarcinoma lung cancer. This corresponds to a result of study on non-smoker patients in Egypt, where they found that adenocarcinoma was the most common subtype between un smokers (22). In addition to passive smoking as a risk factor for lung cancer in non-smokers, many researches revealed that radon exposure and domestic fuel smoke, infections such as Mycobacterium tuberculosis, and Human Papilloma Virus are also risk factors. Other less factors include inflammatory diseases such as asthma and sarcoidosis (23). The World Health Organization believes that lung cancer deaths globally will continue to increase largely as a result of raise in tobacco use, which is the leading risk factor for lung cancer. Despite efforts to curb tobacco smoking, there are about 1.1 billion smokers in the world, and if the current trends carry on, that number would increase to 1.9 billion by 2025 (24).

Concerning family history of the cancer, we found that there was a positive family history of lung cancer in (16%) of patients as well as positive family history of cancer in other organ away from the lung (44%), other patients have no family history of a cancer anyway (40%), whereas in Japan Yoshida K et al found that family history of lung cancer in first-degree relatives was associated with an elevation of risk of lung cancer among both genders (25). Adenocarcinoma subtype of NSCLC was the predominant subtype, while, in USA squamous cell carcinoma subtype of NSCLC was the most associated with familial history of lung cancer (26).

On the subject of past history of respiratory diseases, the current study revealed that about (83.8%) of patients presented with lung cancer had no history of respiratory diseases while only (6.8%) of patients had past history of COPD, this result is somewhat different from previous study by Brenner DR et al, where they concluded that past history of lung diseases are associated with an increased risk of lung cancer with the evidence among never smokers supporting a direct relationship between previous lung diseases and lung cancer (27). In present study (6.8%) of the patients with past history of COPD, there were four patients diagnosed with NSCLC, two patients with adenocarcinoma and two patients with squamous cell carcinoma. A previous study showed that the positive history of COPD could be a risk group for the

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development of lung cancer, especially adenocarcinoma subtype (28, 29).

The majority of patients in our study were from Benghazi city, and this might be due to presence of an oncology department in this city or it could be related to the increased population of Benghazi, Moreover, the presence of Al Hawari Cement Factory in Benghazi, was considering as one of the major air pollution sources in the area throughout several years of production.

In current study, most of the patients were diagnosed in stage IV, a late stage where the cancer has already spread to distant organs, this is most probably due to delay presentation of patient and late diagnosis by physicians even with early presentation of patient (30).

A study in England by Kotecha J.et al referred the delay of presentation by patients to non-recognition of symptoms, anxiety and denial(30).

In Denmark, a study by Bjerager M et al referred the reasons for the delay in proper diagnosis of lung cancer in primary health care to using chest x-ray without suspicion of a cancer, symptoms not related to lungs, waiting of laboratory investigation and unclear of appointment of follow up (31). In 2022, many studies applying low dose CT have stated the ability to diagnose lung cancer early and a survival hope to those screened (32).

Conclusion

1.The recent study showed that bronchogenic carcinoma was a very common cancer in Benghazi, and the smoker male patients with a mean age of 63 years and 58 years for females.

2.NSCLC type of lung cancer was the most common type of lung cancer(71.4%) among different age group.

3.Adenocarcinoma subtype of NSCLC was the predominant type in this study, specifically in patients with no past medical history of respiratory diseases

4.Most of the patients presented with stage IV of the cancer which means that the cancer has already metastasized away from the lung.

Limitations

The large issue in this study was lack of some data from the patient's file in oncology department of Benghazi medical center.

Recommendations

1.It is important to increase the level of awareness in the society about the two most common causative factors related to lung cancer, smoking and inhalation of radon gas. The authorities have to sets a plan for measuring such radioactive natural gas in different areas of the country.

2.There is need to establish a high technical procedure for proper recording and good history taking for the cancer cases.

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