An-Najah National University
Faculty of Graduate Studies

Lung Cancer and Associated Risk Factors in the West Bank

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Committee Decision

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This thesis was defended successfully on the 18th of June 2003 and approved by:

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Dedication

TO MY BELOVED MOTHER WHOM I OWE MUCH

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Abstract

Since no previous studies were carried out on large scale regarding lung cancer status and associated risk factors in Palestine, the current study aimed at evaluating the status of the disease and the possibly associated risk factors among the Palestinian inhabitance of the West Bank area. This was achieved through reviewing and analyzing the available patient's files form the period 1997-2000. Files for previous years were excluded due to several problems associated with the used filing systems prior the transfer of authority to the Palestinians. A total of 286 files were reviewed and the collected data was then analyzed using SPSS.

The over all prevalence rate of lung cancer in the West Bank area excluding Jerusalem was 18/100,000. The highest rates were found in the districts of Jenin (24.4) and Tulakrem (22.9). This low prevalence, compared to the internationally reported, is due to multi factorial reasons among which is under-registration, details are shown in text.

The most prevalent histological type in the study population was adenocarcenoma and was represented by 31.5%; squamous cell carcinoma was the second common histological type (24.8%).

Highest prevalent areas were Jenin and Tulkarem, where charcoal production in the former and industrial fumes in the later are significant, also farming is predominant in both areas.

In conclusion, we believe that there is an urgent need to have better national method for cancer registration as well as an urgent need to evaluate risk factors associated with the observed increased incidence of lung cancer in the districts of Tulkarem and Jenin.

Chapter I

Introduction

1.1 What is Lung Cancer?

The lungs are two sponge-like organs found in the chest cavity. The right lung is divided into 3 sections, called lobes. The left lung has 2 lobes. During breathing, air goes into the lung through the trachea (windpipe). The trachea divides into tubes called the bronchi, which divide into smaller branches called the bronchioles. At the end of the bronchioles are tiny air sacs known as alveoli (Figure 1). Many tiny blood vessels run through the alveoli, absorbing oxygen from the inhaled air into your bloodstream and releasing carbon dioxide. Taking in oxygen and getting rid of carbon dioxide are the lungs' main function. A lining, called the pleura surrounds the lungs. This lining protects your lungs and facilitates their sliding motion as they expand and contract during breathing.

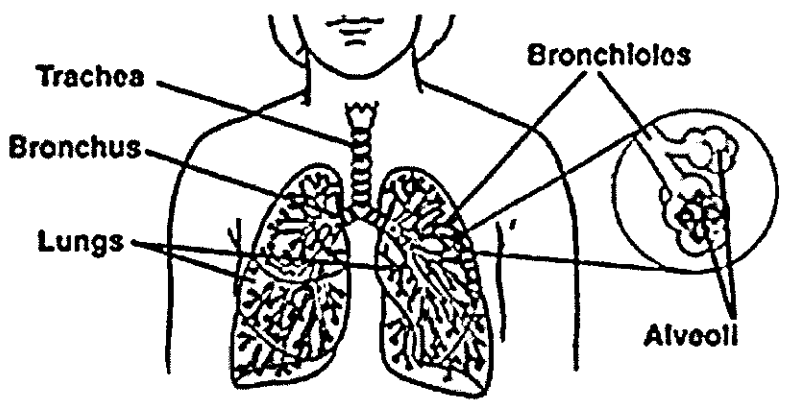

Figure 1. Anatomy of the Lungs

Lung cancers are thought to develop over a period of many years. First, there may be areas of precancerous changes in the lung. These changes do not form a mass or tumor. They cannot be seen on an X-ray and they do

not cause symptoms, however, precancerous changes can be found by analyzing cells in the lining of the airways of smoke-damaged lungs. These precancerous changes often progress to true cancer. These cancer cells may produce chemicals that cause new blood vessels to form nearby. These new blood vessels nourish the cancer cells, which can continue to grow and form a tumor large enough to see on X-rays.

1.2 Types of Lung Cancer

The histological classification of primary lung neoplasm recommended by the world health organization in 1981 is be used. The term lung cancer is usually reserved for tumors arising from the respiratory epithelium (bronchi, bronchioles, and alveoli). Mesotheliomas, lymphomas, and stromal tumors usually are given a pathologic diagnosis distinct from epithelial lung cancer. Four major cell types make up 88 percent of all primary lung neoplasms. These are squmous or epidermoid carcinoma, small cell carcinoma, adenocarcinoma, and large cell carcinoma. The remains include undifferentiated carcinomas, carcinoids, and bronchial gland tumors. The various cell types have different natural histories and responses to therapy, and thus a correct histologic diagnosis by an experienced pathologist is the first step to correct treatment (Fauci, 1998).

1.2.1 Small Cell Lung Cancer

Small Cell Lung Cancer is named for the size and appearance of the cancer cells. Although each of the cells is small, they can multiply quickly and form large tumors, and can spread to lymph nodes and other organs such as the bones, brain, adrenal glands, and liver. This type of cancer often starts in the bronchi and toward the center of the lungs. Small cell lung cancer is almost always caused by smoking. The occurrence of this type among non-smokers seems to be rare. Other names for SCLC are oat cell carcinoma and small cell undifferentiated carcinoma.

Subtypes of small cell lung cancer include: (Hirsch *et al.*, 1988)

*Small cell carcinoma

*Mixed small cell/large cell carcinoma

*Combined small cell carcinoma (small cell lung cancer combined with neoplastic squamous and/or glandular components).

1.2.2 Non-small Cell Lung Cancer

The cells in these sub-types differ in size, shape, and chemical make-up and these include :

1. Squamous Cell Carcinoma: It is associated with a history of smoking and tends to be found centrally, near a bronchus .

2. Adenocarcinoma: It is usually found in the outer region of lung. People with one type of adenocarcinoma, known as bronchioloalveolar carcinoma tend to have a better prognosis than those with other lung cancer types.

3. Large-Cell Undifferentiated Carcinoma: It may appear in any part of the lung and it tends to grow and spread quickly resulting in a poor prognosis (Kreyberg *et al.*, 1981).

1.3 Clinical Manifestations and Mode of Presentation

Although 5 to 15 percent of patients are detected while a symptomatic, usually on a routine chest radiograph, the vast majority of patient's present with some sign or symptom. Signs and symptoms secondary to central or endobronchial growth of the primary tumor include cough, hemoptysis, wheeze and stridor, dyspnea, and postobstructive pneumonitis. Sings and symptoms secondary to the prepheral growth of the primary tumor include pain from pleural or chest wall involvement, cough, dyspnea on a restrictive basis, and symptoms of lung abscess resulting from tumor cavitation. Signs and symtoms related to the regional spread of tumor in the thorax include tracheal obstruction, esophageal compression with dysphagia, recurrent laryngeal nerve paralysis with hoarseness (Fauci, 1998).

1.4 Diagnosis and Staging

1.4.1 Early Diagnosis

The screening of asymptomatic persons at high risk for lung cancer by means of sputum cytology and chest radiographs has not been proved effective. Studies using these screening procedures found a prevalence of lung cancer of 4 to 8 cases per 1000 persons. With follow-up screening every 4 months, four new cases of lung cancer are found per 1000 persons followed per year. These lung cancer are detected 72 percent of the time by radiograph alone and 20 percent by cytology alone, while 6 percent are detected by both methods. In contrast to non-screened patients, 90 percent of these screened patients who developed lung cancer are asymptomatic, 62 percent have respectable lung cancer, and 53 percent of all the new cases are postoperative stage I with a 5-year survival probability of 45 percent. However there was no difference in the survival rate between the screened and non-screened group of smoking males 45 years of age or older. Newer screening methods involving fluorescent bronchoscopy and molecular analysis will be analyzed in clinical trials in the hope of improving the detection of lung cancer before metastases develop (Fauci, 1998).

1.4.2 Screening and Establishing a Tissue Diagnosis of Lung Cancer

Once signs, symptoms, or screening studies suggest lung cancer, it is necessary to establish a tissue diagnosis of malignancy, to determine the

histologic cell type, and to stage the patient for appropriate treatment. In the initial evaluation of each patient, tumor tissue should be obtained so that a histologic diagnosis of cancer and tumor cell type can be made. Tumor tissue can be obtained by a firberoptic bronchoscopy; by node biopsy during mediastinoscopy; from the operative specimen at the time of definitive surgical resection; by percutaneous biopsy of an enlarged lymph node, soft tissue mass, lytic bone lesion, bone marrow, or pleural lesion; by fine-needle aspiration of thoracic or extrathoracic tumor masses using computed tomography (CT) guidance; or from an adequate cell block obtained from a malignant pleural effusion. In the vast majority of cases, the pathologist should be able to definitely make a diagnosis of epithelial malignancy and make the crucial distinction of small cell from non-small cell lung cancer (Fauci, 1998).

At present it is believed that screening with chest X-ray plus sputum cytology detect lung cancer at an earlier stage, but this would be expected in a screening test whether or not it was effective at reducing mortality. In general, uncertainty in interpretation of results from completed studies has led to conflicting positions in the medical community and confusion in populations at risk regarding the value of chest X-ray screening (Ahrendt *et al.*, 1999).

1.4.3 Spiral CT

There are intensive efforts to improve lung cancer screening with newer technologies, including low-dose helical computed tomography (LDCT) and molecular techniques (Henschke *et al.,* 1999; Swensen *et al.*, 2002). LDCT is far more sensitive than chest radiography. In a recent screening study (Swensen *et al.,* 2002). CT detected almost 6 times as many stage I lung cancers as chest radiography and most of these tumors were 1 cm or less in diameter (Gohagan *et al.*, 1995)

1.5 Causes and Risk Factors

The most important risk factor for lung cancer is tobacco use. Cigarette smoking has been definitively established by epidemiologic and preclinical animal experimental data as the primary cause of lung cancer (Schottenfeld and Fraumeni, 1996; Smoking and Health, 1995; Gazdar and Minna, 1997). This causative link has been widely recognized since the 1960s, when national reports in Great Britain and the United States brought the cancer risk of smoking prominently to the public's attention (American Cancer Society, 1999). The percentages of lung cancers estimated to be caused by tobacco smoking in males and females are 90% and 78%, respectively. Cigar and pipe smoking also have been associated independently in case-control and cohort studies with increased lung cancer risk (Smoking and Health 1995) and (Gazdar and Minna, 1997). The cigar risks are of particular

concern because of the recent increase in cigar use in the United States (Roth *et al.*, 1995).

Passive smoking is also implicated in causing lung cancer (Hackshaw *et al.*, 1997). Environmental tobacco smoke has the same components as inhaled mainstream smoke, although in lower absolute concentrations, between 1% and 10% depending on the constituent. Carcinogenic compounds in tobacco smoke include the polynuclear aromatic hydrocarbons, including the classical carcinogen benzo-a-pyrene and the nicotine-derived tobacco-specific nitrosamine, 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone. Experiments on rodents showed that total doses of such compounds that are similar to doses received by humans in a lifetime of smoking induce pulmonary tumors (Cinciripini *et al.*, 1997). Elevated biomarkers of tobacco exposure, including urinary cotinine, tobacco-related carcinogen metabolites, and carcinogen-protein adducts, are seen in passive smokers (McCann *et al.*, 1992; Hecht *et al.*, 1993; Finette *et al.*, 1998 and Parsons *et al.*, 1998).

Several other carcinogens are associated with lung cancer in a smaller proportion of cases, including asbestos and radon (Mollo *et al.*, 2002). There is a dose-response relationship between asbestos exposure and lung cancer risk, and it is evident that asbestos exposure is synergistic with smoking in increasing this risk. In miners, radon, independently and increasingly with smoking, is an established lung cancer risk factor.

Epidemiologic data on radon in the home as a risk factor for lung cancer have been preliminary and limited (American Cancer society, 2002).

Lung cancer is considered to be the end-stage of multi-step carcinogenesis. Suggestive evidence of genetic damage is the association of cigarette smoking with the formation of the DNA adducts in human lung tissue. An unequivocal link between tobacco smoke and lung carcinogenesis has been established by molecular data (Mao *et al.*, 1997).

In general, exposure to carcinogens seems to result in damage or modifications to DNA (Sekido *et al.*, 1998). Oncogenes are genes present in the cells DNA and carry out normal functions (regulate growth and development) but have the potential to make a normal cell turn cancerous. Abnormal change within such genes may induce excessive production of chemical signals that interrupt normal cell growth and leads to cancer. On the other hand some genes are thought to be protective against cancer and viruses causing badly damaged cells to self-destruct (apoptosis). If such genes are damaged or absent then the risk of cancer seems to increase. Evidence for such role came from studies on the *p*53 gene where deletions in that gene region are found to be associated with a range of cancers (Suzuki *et al.*, 1992; Husgafvel-Pursiainen and Kannio, 1996 and Hernandez-Boussard and Hainaut, 1998). Association between chromosomal abnormalities and cancer were also well documented (Thompson *et al.*, 1991).

Lack of normal replication for certain genes was also reported to be prevalent (Curry *et al.,* 1999), among young smokers. It is believed that young smokers are more susceptible to genetic damage in their lungs from tobacco smoke than adults.

Some genes are known as tumor suppressers and mainly involved in inhibiting abnormal cells from forming tumors. Evidence for that came from studies on the gene *p*53 (a tumor suppresser) as it was found that this gene is almost always defective in cases of small cell lung cancer, and in approximately half of non small cell lung cancer cases. Because of the defect in the gene, it does not stop the reproduction of tumor cells as it should (Sekido *et al.,* 1998 and Hernandez-Boussard and Hainaut, 1998).

Previous studies have found that people with lung tumors have breaks in a particular region on their chromosomes, and that certain abnormalities in chromosome structures are known to be early steps in the development of lung cancer. It was also found that smokers had much more fragility in a site on the chromosome, called FRA3B, located in a region where structural abnormalities are commonly found in patients with lung cancer (Jorge and William, 1989).

Women exposed to cooking fumes from rapeseed oil appeared to be at increased risk of lung cancer, and there was some evidence that fumes from linseed oil may have also contributed to the risk. Lung cancer risks also increased with total number of years cooking (Metayer *et al.*, 2002).

1.6 Treatment of Lung Cancer

In general the treatment of lung cancer is dependent on:

- The type of lung cancer (non-small cell or small cell)
- stage
- The general health of the patient (performance status and co-morbidities)

A wide variety of treatments and combinations of treatments may be used to control lung cancer, and/or to improve quality of life by reducing symptoms (Weick *et al.,* 1991)

1.6.1 Non small cell lung cancer

The only curative treatment of lung cancer is surgery if patient can tolerate that include stage I, II (Fauci, 1998). Treatment for stages III and VI mainly involved chemotherapy, which has very poor response (Le Chevalier *et al.*, 1994). Radiation therapy is mainly preoperative in par coast tumor, and to relieve pain and plural effusion.

1.6.2 Small cell lung cancer

As it is always spread, small cell lung cancer practically have no special treatment, however, chemotherapy and radiation therapy result in good response but to very limited periods (Fauci, 1998).

1.7 Prevention

1.7.1 Smoking Prevention and Cessation

Substantial harm to the public health occurs from the smoking habit. Compared with nonsmokers, smokers exhibit a dose-dependent increase in

the risk of dying from lung, head and neck, bladder, and other cancers (Schottenfeld and Fraumeni 1996; The Health Benefits of Smoking Cessation, 1990). Conversely, substantial benefits accrue to the public health from smoking cessation. Avoidance of tobacco use is the most effective measure for preventing lung cancer. Evidence suggests that the preventive effect of smoking cessation depends upon the duration and intensity of prior smoking and upon time since cessation. A 30% to 50% reduction in lung cancer mortality risk has been noted after 10 years of cessation (Schottenfeld and Fraumeni 1996; The Health Benefits of Smoking Cessation, 1990; Cinciripini *et al.*, 1997; Fiore *et al.,* 1996).

1.8 Prevalence and mortality of Lung Cancer

It is estimated that (American Cancer Society, 2002) during 2002, there will be about 169,400 new cases of lung cancer (90,200 among men and 79,200 among women). Lung cancer will account for about 13% of all new cancers. The average age of people diagnosed with lung cancer is 60; it does not usually occur in people under the age of 40.

Lung cancer is the leading cause of cancer deaths among both men and women. There will be an estimated 154,900 deaths from lung cancer (89,200 among men and 65,700 among women) in 2002, accounting for 28% of all cancer deaths (American Cancer Society, 2002). More people die of lung cancer than of colon, breast, and prostate cancers combined.

The 1-year survival rate (the number of people who live at least 1 year after their cancer is diagnosed) for lung cancer was 41% in 1997, the last year for which we have national data. This had not changed in 10 years.

The 5-year survival rate for all stages of lung cancer combined is only 15%. This has not changed over many years. For people whose cancer is found and treated early with surgery, before it has spread to lymph nodes or other organs, the average 5-year survival rate is about 48%. However, only 15% of people with lung cancer are diagnosed at this early, localized stage.

The 5-year survival rate refers to the percent of patients who live at least 5 years after their cancer is diagnosed. Many of these patients live much longer than 5 years after diagnosis, and 5-year rates are used to produce a standard way of discussing prognosis. Five-year relative survival rates exclude from the calculations patients dying of other diseases, and are considered to be a more accurate way to describe the prognosis for patients with a particular type and stage of cancer. Of course, 5-year rates are based on patients diagnosed and initially treated more than 5 years ago. Improvements in treatment often result in a more favorable outlook for recently diagnosed patients.

1.9 Aims of the study

Until now, no large scale study neither on the prevalence of cancer cases in general nor lung cancer in particular were reported and the only available data represent small reports on the incidence released by the Palestinian Ministry of Health. The current study aims at:

1. Study the prevalence of lung cancer and histological types in the various districts of the West Bank area of Palestine for the years 1997-2001.
2. Search for possible risk factors associated with lung cancer in the region.
3. Search for possible association between possible risk factors and lung cancer histological types.

Chapter II

Methodology

2.1 Study population and design

In 1999, the Palestinian Cancer registry published its first description of cancer incidence in the West Bank and Gaza. A second issue in this respect was published in 2001. Data presented in these reports were based on data collected from three referral oncology centers covering the northern (Al-Watani Hospital at the City of Nablus) and southern (Bet-Jala Hospital at the city of Bet-Jala) parts of the West Bank and from Al-Shefa Hospital at the City of Gaza. None of these centers seems to have a system that insures high degree of completeness of the registry.

No registry files were available before the year 1997. All registry files for the years 1997- 2000 (286), in the AL-Watani and Bet-Jala centers, were reviewed. For each case information about the gender, age, place of residence, diagnosis of tumor, date of diagnosis, smoking status, carrier, family history of tumor were collected. Missing data regarding the previously mentioned information were observed. Such data was clarified in the results section. Due to the limited referral number of living diagnosed cases in both centers, it was difficult to collect accurate data concerning lung cancer status, especially with respect to lung cancer types. For lung cancer types we relied on patients files in addition to reports of diagnosis reported by professional laboratories for diagnosis.

2.2 Statistical Analysis

Statistical analysis was performed using Statistical Package for Social Sciences (SPSS). Frequencies and percentages were calculated and Chi-Square test was performed to investigate the significance in the association of the different variable to the incidence frequency of lung cancer. Correlation were considered significant if the observed significance level (*P* value) was <0.05.

3.1 Incidence of Lung Cancer in Various Districts

Data presented in table 1 shows the frequency of cancer cases in the various districts of the West Bank area of Palestine. With the exception of Jerusalem district, a slight variation in the total number of lung cancer cases per 100,000 populations was observed and the highest numbers of cases were found in Jenine and Tulkarem districts.

Table 1. Frequencies of lung cancer and the incidence rate per 100,000 populations among the various districts of the West Bank of Palestine.

District	Population	Lung Cancer Cases	Lung Cancer 100000
Jenin	253637	62	24.4
Tulkarem	134949	31	22.9
Salfeet	49045	7	14.2
Jericho	33180	6	18.08
Ramallah	216921	37	17.06
Nablus	262909	42	15.98
Betlahem	138568	27	19.48
Qalqelia	73095	13	17.79
Hebron	410312	30	7.31
Jerusalem	337384	5	1.48

3.2 Frequency of the Various Lung Cancer Types

Data presented in table 2 represent the frequency of the various types of lung cancer among the study population. The percentages of 31.5%, 24.8% and 11.2% were found for adenocarcinoma, squamous and small cell carcinoma, respectively. Other histolological types were represented with small percentages. Undiagnosed cases were represented by 25.2% of total cases.

Table 2. Frequency of the various lung cancer types among the study population

Lung Cancer Type	Frequency (%)
Large cell carcinoma	13 (4.5)
Squamous cell carcinoma	71(24.8)
Adenocarcinoma	90(31.5)
Small cell carcinoma	32(11.2)
Other	08(2.8)
Un-identified	72(25.2)
Total	286(100)

3.3 Lung Cancer and Age

Data presented in table 3 shows that both adenocarcinoma (42.1%) and squamous cell carcinoma (33.2%) were the most prevalent types among the study population followed by small cell carcinoma (14.9%). It is also clear that the prevalence of almost all types shows an increased frequency with increasing age. Variations in the prevalence rates among the various age groups were of no statistically significant values ($P = 0.520$)

Table 3. Association between age and lung cancer types

Age Group		Large cel carcinom	Squamous ce carcinoma	Adenocarcinom	Small cell carcinoma	Othe	Total
<30	Count	-	2	7	1	1	11
	% within gro	-	18.2%	63.6%	9.1%	9.1%	100%
	% of Total	-	0.9%	3.3%	0.5%	0.5%	5.1%
31-40	Count	1	3	12	4	-	20
	% within gro	5%	15%	60%	20%	-	100%
	% of Total	0.5%	1.4%	5.6%	1.9%	-	9.3%
41-50	Count	2	13	18	5	2	40
	% within gro	5%	32.5%	45%	12.5%	5%	100%
	% of Total	0.9%	6.1%	8.4%	2.3%	0.9%	18.7%
51-60	Count	4	24	26	14	2	70
	% within gro	5.7%	34.3%	37.1%	20%	2.9%	100%
	% of Total	1.9%	11.2%	12.1%	6.6%	0.9%	32.7%
>60	Count	6	29	27	8	3	73
	% within gro	8.2%	39.7%	37%	10.9%	4.1%	100%
	% of Total	7.8%	13.6%	12.6%	3.7%	1.4%	34.1%
Total	Count	13	71	90	32	8	214
	%	6.1%	33.2%	42.1%	14.9%	3.7%	100%

3.4 Lung Cancer and Gender

Data presented in table 4 shows the association between lung cancers types and gender. Data presented in the same table clearly shows that adenocarcinoma (42.1%) and squamous cell carcinoma (33.2%) were the most prevalent histological types among both males and females, however, the rates within groups clearly shows that adenocarcinoma was with a much higher frequency among females (63.9%) compared to that observed among males (37.6%). With respect to the frequency of almost all of the other types except small cell carcinoma, males showed a higher frequency than females.

Variations in the prevalence rates of the various types were statistically significant ($P = 0.028$) and in favor of males.

Table 4. Association between lung cancer types and gender

Gender		Large cell carcinoma	Squamous cell carcinoma	Adenocarcinoma	Small cell carcinoma	Other	Total
M	count	12	67	67	26	6	178
	% within group	6.7%	37.6%	37.6%	14.6%	3.4%	100%
	% of tota	5.6%	31.3%	31.3%	12.1%	2.8%	83.2%
F	count	1	4	23	6	2	36
	% within group	2.8%	11.1%	63.9%	16.7%	5.6%	100%
	% of tota	0.5%	1.9%	10.7%	2.8%	0.9%	16.8%
Total	count	13	71	90	32	8	214
	%	6.1%	33.2%	42.1%	14.9%	3.7%	100%

3.5 Lung Cancer and Occupation

Data presented in table 5 shows the frequency of the various lung cancer types in association with occupation. Around 54% (154 out of 285)

of the study populations were reported to have jobs of which around 50% were farmers. The most common lung cancer types among all job classes were adenocarcenoma, squamous and small cell carcinoma, respectively. No any clear association between job type and lung cancer type was observed, however, it seems that the most lung cancer cases were among farmers (49.4%), followed by workers (14.9%), house wife (11%), clerical (10.4%) and industry (9.1%). Statistical analysis showed no significant variations in the occurrence of any cancer type and job type ($P = 0.639$).

Table 5. Association between lung cancer types and occupation type

Occupation		Large cell carcinoma	Squamous cell carcinoma	Adenocarcinoma	Small cell carcinoma	Other	Total
Farmer	count	5	24	29	16	2	76
	% within grou	6.6%	31.6%	38.1%	21%	2.6%	100%
	% of Total	3.2%	15.6%	18.8%	10.3%	1.3%	49.4%
House Wife	ount	-	2	11	4	-	17
	% within grou	-	11.8%	64.7%	23.5%	-	100%
	% of Total	-	1.3%	7.1%	2.5%	-	11%
Clerical	ount	-	5	9	1	1	16
	% within grou	-	13.3%	56.3%	6.3%	6.3%	100%
	% of Total	-	3.2%	5.8%	0.6%	0.6%	10.4%
Worker	ount	-	14	5	2	2	23
	% within grou	-	60.9%	21.7%	8.7%	8.7%	100%
	% of Total	-	9.1%	3.2%	1.3%	1.3%	14.9%
Industry	ount	1	6	5	1	1	14
	% within grou	7.1%	42.9%	35.7%	7.1%	7.1%	100%
	% of Total	0.6%	3.9%	3.2%	0.6%	0.6%	9.1%
Petroleum	ount	-	1	1	-	-	2
	% within grou	-	50%	50%	-	-	100%
	% of Total	-	0.6%	0.6%	-	-	1.3%
Driver	ount	-	2	1	-	-	3
	% within grou	-	66.7%	33.3%	-	-	100%
	% of Total	-	1.3%	0.6%	-	-	1.9%
Without	count	-	-	2	1	-	3
	% within group	-	-	66.7%	33.3%	-	100%
	% of Total	-	-	1.3%	0.6%	-	1.9%
Total	cou						
	%	3.9%	35.1%	40.9%	16.2%	3.9%	100%

3.6 Distribution of Lung Cancer Types within the Various Districts

Data presented in table 6 represent the distribution of lung cancer histological types among the various districts (according to the filing systems for the period 1997 till the year 2001. Although, adenocarcinoma, squamous cell carcinoma and small cell carcinoma were the most common types in the various districts, it was found that squamous cell carcinoma is more predominant in Jenin, Qalqelia and Hebron in comparison with other districts. On the other hand a noticeable high incidence for adenocarcinoma was observed in both Tulkarem (68.4%) and Ramalla (58.1%) districts. Variations in the rates of the various lung cancer types within the districts were statistically significant ($P = 0.008$).

Table 6. Distribution of lung cancer histological types within the various districts

District		Large cell carcinoma	Squamous cell carcinoma	Adenocarcinoma	Small cell carcinoma	Other	Total
Jenin	count	6	13	10	10	2	41
	% within district	14.6%	31.7%	24.4%	24.4%	4.9%	100%
	% of total	3.1%	6.7%	5.1%	5.2%	1%	21%
Qalqelia	count	1	6	5	1	1	14
	% within district	7.1%	42.9%	35.7%	7.1%	7.1	100%
	% of total	0.5%	3.1%	2.6%	0.5%	0.5%	7.2%
Nablus	Count	2	11	13	2	1	29
	% within district	6.9%	37.9%	44.8%	6.9%	3.4%	100%
	% of total	1%	5.6%	6.7%	1%	0.5%	14.9%
Selfeet	Count	-	3	3	2	-	8
	% within district	-	37.5%	37.5%	25%	-	100%
	% of total	-	1.5%	1.5%	1%	-	4.1%
Tulkarem	Count	2	2	13	2	-	19
	% within district	10.5%	10.5%	68.4%	10.5%	-	100%
	% of total	1%	1%	6.7%	1%	-	9.7%
Betlahem	count	-	7	8	3	3	21
	% within district	-	33.3%	38.1%	14.3%	14.3%	100%
	% of total	-	3.6%	4.1%	1.5%	1.5%	10.8%
Ramallah	count	-	8	18	5	-	31
	% within district	-	25.8%	58.1%	16.1%	-	100%
	% of total	-	4.1%	9.2%	2.6%	-	15.9%
Hebron	count	-	9	8	3	1	21
	% within district	-	42.9%	38.1%	14.3%	4.8%	100%
	% of total	-	4.6%	4.1%	1.5%	.05%	10.8%
Jerusaler	count	-	3	3	-	-	6
	% within district	-	50%	50%	-	-	100%
	% of total	-	1.5%	1.5%	-	-	3.1%
Jericho	count	-	2	-	3	-	5
	% within district	-	40%	-	60%	-	100%
	% of total	-	1%	-	1.5%	-	2.6%
Total	count	11	64	81	31	8	195
	%	5.6%	32.8%	41.5%	15.9%	4.1%	100%

3.7 Lung Cancer and Smoking

Data presented in table 7 represent the association of lung cancer types and the smoking status of the study population. According to the available data in the filing system, only 183 cases out of 286 cases were specified as smokers or nonsmokers and the data regarding the rest of lung cancer cases in this respect were missing. Out of 183 cases, 159 (86.9%) were smokers. The percentages of 32.8, 30.1 and 14.2 were found for squamous, adenocarcenoma, small cell carcinoma, respectively. Other histological types were represented by small percentages. The percentages of 1.6, 9.3 and 2.2 were found for squamous, adenocarcenoma, small cell carcinoma among the nonsmokers population, respectively. Other histological lung cancer types were missing among this group. Statistical analysis revealed a significant variation between the occurrence of the various lung cancer types and the smoking status of the study population in favor of the smokers ($P = 0.013$).

Table 7 Association between lung cancer types and smoking status

Smoking Status		Large cell carcinoma	Squamous cell carcinoma	Adenocarcinoma	Small cell carcinoma	Other	Total
Smoker	Count	11	60	55	26	7	159
	% within grou	6.9%	37.7%	34.6%	16.3%	4.4%	100%
	% of total	6%	32.8%	30.1%	14.2%	3.8%	86.9%
Non Smoker	Count	-	3	17	4	-	24
	% within grou	-	12.5%	70.8%	16.7%	-	100%
	% of total	-	1.6%	9.3%	2.2%	-	13.1%
Total	Count	11	63	72	30	7	183
	%	6%	34.4%	39.3%	16.4%	3.8%	100%

CHAPTER IV

Discussion and Concluding Remarks

In Palestine, available data regarding the incidence of cancer types in general and lung cancer in particular is limited. The only available data in this respect was released by the Ministry of health, the National Cancer Registry in 1999 and covering only 1998.

In the West Bank area of Palestine, hospital or clinic based registry is not available, however, 2 oncology centers (Al-Watani and Bet Jala Hospitals) are assigned as treatment and registry centers. Such arrangements are most likely not enough to cover the area as patients may not come to these centers or seek treatment outside the country. In most developed countries at least a number of regional population-based registries are found and many have a single registry for the entire country, thus on expect that our system for counting and describing cancer will miss some cases and so cannot be reliable.

In addition to the poor registry system, there are other factors which leads to under estimation of the prevalence of lung cancer, these factors are:

- Related to the occupation of the West Bank by Israel, and the presence of the Intifada (Palestinian resistance) which will make transportation extremely difficult.
- Related to the limited financial resource, as most of our patients are not insured.

- Related to the lung cancer itself, as its symptoms can mimic the underlying COPD.

The most interesting observation in the study is the finding that the highest lung cancer cases 24.4 and 22.97/ 100,000 for Jenin and Tulkarem districts, respectively.

Employment in farming occupation is a characteristic feature in both districts, thus one should think of exposure to fumes of herbicides and pesticides as a major risk factor for developing lung cancer in these districts. It is also worth noting that farmers in these districts were evaluated for there knowledge of handling such chemicals in a study conducted by the Applied Research Institute at Jerusalem (ARIJ, 1998) and the results of this study indicate the miss handling of such chemicals and impose a great concern on the health of farmers. Association between pesticides and small lung cancer was reported by Brownson *et al.*, 1993, where exposure to insecticides, pesticides and herbicides seems to play a major role in lung cancer among men. This finding is in support of our findings as small cell lunge cancers constitute around 25% of cancer cell types in Jenin district (see table 6). A recent study in Gaza Strip also showed highly significant correlation between cancer risk and the use of most types of pesticides (Safi, 2002). This study provides more evidence in support of our suggestion on the involvement of these chemicals in development of lung cancer.

One should also point out that these districts are known for their air pollutions due to the presence of large number of quarries. In addition air pollution generated by the Israeli industrial zone in the district of Tulkarem and that generated due to the traditional use of wood to produce charcoal in the district of Jenin. Such environmental conditions and long time exposure to fine dust particles from polluted air are expected to play a role in carcinogenesis and development of lung cancer (Pope *et al.*, 2002).

It is worth noting that the majority of lung cancer cases were from the town of Yabad in Jenin district, which is known as the major production area for charcoal in the West Bank. Since no previous studies seems to link lung cancer with charcoal production, it is important to search for the possible links between the used charcoal production method and lung cancer in this town.

The finding of 25.2% of un-identified lung cancer cases in this study (see table 2) strongly indicates the lack of accurate reporting and the need of good registry system in our region. With respect to the frequency of the various types of lung cancer, our data is in agreement with that reported by Kenji *et al.*, 2001 were adenocarcenoma is found to be the major lung cancer type and represent 31.5% of the studied cases with median age of 61.7 years, however, the finding of 25.2% undiagnosed cases in our study may significantly alter the frequency.

In our patient population, squamous cell carcinoma represented by 24.8% with median age of 66.7 years and was the second predominant lung cancer type. Such finding is also in agreement with that reported by Kenji *et al.,* 2001. Again the findings of 25.2% undiagnosed cases in our study propose a real threat towards the accuracy of our judgment with respect to the frequency of the various lung types in our population.

The finding of the various lung types among the various age groups also confirms that both adenocarcinoma and squamous cell carcinoma types were the most prominent types of lung cancer in our population (see table 3) and the frequency of these two types showed a significant increase with advanced age. An increased frequency in almost all lung types with increased age is also clear.

Our findings clearly show that adenocarcinoma is more predominant in younger age groups <40 as 64.3% out of the total lung cancer types in this age group were diagnosed with adenocarcinoma. This finding is in agreement with several other studies where adenocarcenoma is the most prominent histological type among young population (Arthur *et al.*, 2000). In our patient population, squamous cell carcinoma was represented by 16% of total cancer cases in the young age group and second to adenocarcinoma. This finding is also in agreement with that of Arthur *et al.*, 2000.

With respect to other age groups, in our patient population, the incidence of lung cancer clearly shows an increase beyond the age of 30 and

peaks at age groups over 60. In general it seems that the incidence of lung cancer in our population increases with age and is rare disease among young adults.

In our patient population, adenocarcinoma predominates among females with a frequency of 63.9% compared to the frequency of 37.6 % among males (see table 4). This finding is consistent with several reports where adenocarcinoma was reported to be the most frequent histological subtype in women (Skuladottir *et al.,* 2000 and Teppo *et al.,* 2000).

A noticeable higher frequency for squamous cell carcinoma was found among males (37.6%) compared to that among females (11.1%) population. This finding is consistent with other reports were squamous cell carcinoma is still the most predominant histological type among males (Geoffrey, 1996).

The findings of the current study also shows that 8% of the men and 20% of the women with lung cancer were below the age of 50 indicating a high prevalence among women in younger age groups. This finding is consistent with previous reports (Damuhuis and Schutte, 1996 and Olsen, 1995).

Risks for lung cancer associated with occupation exposure are described in table 5. The findings of this study show that employment in farming is associated with a significant increase in risk compared to other occupations as 49.4% of total lung cancer cases were among those in

farming occupation. This finding is consistent with the findings on lung cancer incidence in the various districts where, Jenin and Tulkarem (mainly farming areas) seems to show the highest incidence of lung cancer cases (table 1).

Data presented in table 6 represent the findings of the various histological types of lung cancer in the various districts. Variations among districts for the occurrence of the different histological types were of no statistical significance and it was difficult to link any association between the reported types and place of living. Another interesting observation in this respect is the finding of 68.4% of all carcinoma histological types in Tulkarem district were adenocarcenoma. Adenocarcinoma is well documented to be dominant among non-smokers and among those who are exposed to fine dust particles (Geoffrey, 1996). This finding may explain our previous finding on lung cancer in Tulkarem district as this district is considered to be with relatively high level of air pollution (ARIJ, 1998).

Association between histological lung cancer types and smoking is shown in table 7. The findings of this study strongly suggest that cigarette smoking is associated with all the histological types of lung cancer. This provides additional evidence for a causal relationship between smoking and all histological types of the disease.

A strong association was observed between small cell lung cancer and smoking as 84% of small cell lung cancer cases were smokers. This finding

is in agreement with most reports in is respect (Kathryn *et al.,* 2000 and Sadik, 2001).

Adenocarcenoma is the most common form of lung cancer in none smokers (Geoffrey, 1996; Sadik, 2001). Our data is consistent with previous results in this respect as 70.8% of the non smoker study population was diagnosed with adenocarcenoma.

Squamous carcinoma was the most dominant histological lung cancer type among smokers in our study population and was represented by 37.7% of total smoker's cases. This result is consistent with previous reports (Yesner, 1999).

Conclusions and Recommendations

1. The over all prevalence of lung cancer in the West Bank, excluding Jerusalem, was 18/100,000 population and the highest rates were observed among the inhabitance of both Jenin and Tulkarem districts.

2. Air pollution generated by the Israeli industrial zone (Tulkarem district) and the fumes from charcoal production process (Jenin district) in addition to farming occupation seems to constitute important risk factors for lung cancer development in our population.

3. A noticeably high prevalence rate of adenocarcinoma was found in the district of Tulkarem.

4. A specially designed educational program about the possible hazards of chemicals should be launched for those at risk with the emphasis on the importance of cessation of smoking, awareness of symptoms and signs and early registration.

5. The Ministry of Health should think about adopting new registry forms, as available protocols are inadequate.

6. Further investigation on possible links between lung cancer and use of pesticides and air pollution in the area is essential.

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جامعة النجاح الوطنية
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سرطان الرئة وعوامل الخطورة المرتبطة به في الضفة الغربية

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ملخص الدراسة

نظرا لمحدودية الدراسات المتعلقة بسرطان الرئة في فلسطين، هدفت الدراسة الحالية إلى تحديد مدى انتشار سرطان الرئة في مناطق الضفة الغربية في الفترة الواقعة بين سنة 1997-2001، حيث اعتمدت على الملفات الخاصة بالمرضى والموثقة في كل من مركزي مستشفى بيت جالا ومركز المستشفى الوطني بمدينة نابلس كمركزين معتمدين للامراض السرطانية في منطقة الضفة الغربية. شملت الدراسة 286 حالة مرضية واعتمد التحليل الإحصائي البرنامج SPSS لتحليل البيانات. تشير نتائج الدراسة ان نسبة انتشار سرطان الرئة في مناطق الضفة الغربية باستثناء القدس هي 18 لكل مائة الف وكانت اعلى النسب في كل من جنين 24.4 وطولكرم 22.9. كما لوحظ ان هناك علاقة بين الاصابة بسرطان الرئة ومهنة الزراعة، وان ارتفاع نسبة الاصابة في بلدة يعبد قضاء جنين والمشهورة باستخدام الطريقة التقليدية لانتاج الفحم، يلقي الضوء على عوامل خطورة محتملة للاصابة بسرطان الرئة. دلت الدراسة على وجود نسبة عالية من الاصابة بسرطان الرئة من النوع النسجي Adenocarcima في مدينة طولكرم مما يلقى الضوء على علاقة محتملة بين تلوث الهواء المنبعث من المنطقة الصناعية الاسرائيلية والاصابة بهذا النوع. تشير نتائج الدراسة الى ضرورة البحث عن نظام تسجيل افضل والحاجة الى دراسات مستقبلية لربط ارتفاع نسبة الاصابة بالمرض في كل من جنين وطولكرم وعوامل الخطورة.