An-Najah National University

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PREVALENCE OF PROSTATE CANCER IN WEST BANK - PALESTINE

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DEDICATION

To

My Marty Father,

My Mother,

My Wife,

My Sisters,

My Uncle

For Their Encouragement

With Love and Respect

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TABLE OF CONTENTS

List of Tables

List of Figures

ABBREVIATIONS

BPH	Benign Prostatic Hyperplasia.
DRE	Digital Rectal Examination.
HK2	Human Kallikrein 2.
NOS	Nosology.
NPV	Negative Predictive Value.
PAP	Prostatic Acid Phosphatase.
PC	Prostate Cancer
PIN	Prostatic intraepithelial neoplasia.
PPV	Positive Predictive Value.
PSA	Prostate Specific Antigen
QOL	Quality of the Life.
RR	Radical Radiotherapy.
RP	Radical Prostatectomy.
TNM	Tumer Size, Lymph Node status, Metastatic Stage.
TRUS	Transrectal Ultrasound.
TURP	Transurethral Resection of Prostate.

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Abstract

Two hundred and seventy one specimen were collected from the different northern and southern districts of West Bank – Palestine (Al-Watani Hospital and Beit Jala Hospital). All these specimen were diagnosed as having prostate cancer with different stages and different grades. In this research we examined the correlation between the grade of prostate cancer and different variables such as age, city, place, address, smoking, occupation and number of children. Also we examined the correlation between the stage of prostate cancer and the same variables. We found that there are statistically significant correlation between grade and city, grade and smoking, stage and place, stage and smoking, stage and occupation, and also between stage and number of children .Also we noticed that the incidence frequency of prostate cancer is highest in Bethlahem, followed by Nablus then Jericho, but lowest in Jerusalem.

CHAPTER ONE

Introduction

1.1 Anatomy

Prostate gland is the largest of the semen secreting glands. It secrets its products directly into the urethra through several small ducts. Prostatic fluid is thin and milky, contains anticoagulant enzymes , citrate (a sperm nutrient), and is slightly acidic (1). The prostate has three lobes, right and left lateral, and a small middle lobe. The isthmus is anterior and connects the lateral lobes. The periphral posterior region of the lateral lobes is the most common site for prostate cancer, this may be because this area is the most accessiblle from the rectum. Capsule is dense, thin, and firm fibrous muscular capsule; not easily pentrated by tumor.

1.2 Incidence

In the year 2000, as 180,400 men were diagnosed with prostate cancer in U.S.A, and approximately 31,900 men died of the disease (2) making it the second leading cause of cancer-related deaths after lung cancer in men in the U.S.A.

In the United Kingdom prostate cancer is the second most common malignancy in men with about 200,000 new cancer cases and

35,000-40,000 death each year(3) with an incidence rate of 18.6 per 100,000.

Here we have data showing the incidence rate of prostate cancer per 100,000 population in the year 1995(3):

Place	Incidence rate Per 100,000
Hawaii	59.7
Newzealand	39.8
Geneva	36.3
Finland	27.2
Israel	15.5
Japan	0.8

1.3 Epidemiology and etiology

The main known risk factors for Prostate Cancer (PC) are :-

1.3.1 Age

Prostate Cancer is the most common cancer in men over 50 years of age. It is primarily a disease of older men, the median age to onset of clinically apparent disease is 72 years and median age of death is 79 years (5). Post–mortem studies showed that the vast majority of prostate cancers never developed into clinically apparent disease, and small tumor foci are found in 30-40 % of 60 –year- old men at autopsy (5).

In most countries it has been estimated that for a 50-year-old man with a life expectancy of 25 years, there is a 42 % life time risk of having microscopic prostate cancer, 9.5 % of having clinically evident cancer, and 2.9 % of dying of prostate cancer (6, 7). Thus only a small proportion of histologically identified cases become clinically evident, and many more men die with prostate cancer than of it .

The rapid increase in incidence of prostate cancer above age 50 years is mainly due to the fact that, for this being the age to start screening for PC in most programs. The difference between the incidence and mortality curves arises because PC is often relatively indolent; many patients live with their disease for 10 years or more, but do not die from it. This has led to suggestions not to screen men ver 70 or 75 years, and to screen only those who have a live expectancy of more than 10 years (8).

1.3.2 Race

African ancestry is a significant risk factor to PC. In one screening study involving over 17,000 subjects, black Americans had a higher prevalence of clinically (but not of pathologically) advanced PC compared with white Americans (9). Black Americans have higher PSA and PSA density(10) and higher age –specific PSA concentration than white Americans(11). PC is detected more frequently in Americans with

PSA> 4 μg /L who are black (36-60%) than in those who are white (25-30%)(12). Data of this type are responsible for suggesting that black men should be screened at an earlier age (40 years).

1.3.3 Family history

A strong family history of prostate cancer is an important risk factor. A clear family history of cases in younger first-degree relatives may be associated with a specific inherited gen abnormality which may account for about 9% of PC cases (6). A 40-year old man with a father, an uncle and brother with the disease will have 30-40 % lifetime risk of developing clinically significant disease (6). About 25% of men with PC have a known family history, usually one relative. However, only about 9% have a hereditary form of the disease (13). It has been suggested that familial PC may be different disease because it has a higher rate of distant relapse, and a higher biochemical failure rate even after treatment with radical prostatectomy (RP)(39). Men who have first-degree relatives with prostate cancer have an increased risk of disease (6). Hereditary prostate cancer in which there may be a mendelian dominant or x-linked gene, is less common, accounting for only 5% of prostate cancers.

Some advocates of radical prostatectomy point out that most benefit will be gained in the treatment of younger men aged under 55 or

60 year. This is particularly the case for younger men with a strong family history of PC (15).

1.4 Severity of disease

The severity of prostate cancer ranges from non-fatal, asymptomatic. slow-growing tumors, which probably require no tretment, to aggressive. Fast growing tumors that metastasise quickly, often before symptoms are noticed (15).

Asymptomatic forms of the tumor, which never prove fatal, are common in men over the age of 60 years. Even in the fatal forms of the disease, many men remain asymptomatic until the late stages of the disease (3).

1.5 Common metastatic sites

There are cancers that are confined to the prostate in the early stages, but that well spread later; it is these tumors that screening seeks to identify (3).

About 60%of patients with prostate cancer presenting with clinically evident disease (16), and up to 40% of patients with clinically organ–confined disease (17), had metastases beyond the prostate; where cure is very unlikely in these patients. We may classify the common metastatic sites into three types:

A) Regional spread: direct extension to bladder or rectum; invasion of seminal vesicles.

B) Lymphatic spread: distant lymph nodes include cervical, scalene, supraclavicular (Virchow's or sentinel node in left supraclavicular region), common iliac, inguinal, and aortic (para-aortic, peri-aortic, lumbar) chains.

C) Hematogenous spread: bone (osteoblastic lesions), liver, kidneys, adrenal glands, and occasionlly lung and brain (18).

1.6 Signs and symptoms

Many symptoms may be used to define prostate cancer:

1- Urologic obstructive symptoms:

a- Dribbing

b- Urgency: sudden onset of necessity to void.

c- Nocturia: necessity to wake up in the middle of night to void.

d- Hesitancy: inability to initially void with a strong urinary system.

e- Tarminal hematuria: the presence of blood in the urine at the end of voiding.

f- Complete urinary obstruction requiring catheterization.

2- A symptomatic clinical findings on rectal examination:

a- nodularity or induration: palpation of lumps in the prostate; nodules are non – tender and very hard

b- prostate enlargement.

c- prostate hardness.

3- symptoms of widespread disease:

a) Weight loss.

b) Anorexia: lake of appetite.

c) Bone pain in back, pelvis, or multiple bony sites .

d) Anemia.

e) Sudden onset of incontinence and paraplegia from extradural spinal cord metastases.

Early detection is often divided into two approaches, namely case-finding (when patients have symptoms suggestive of cancer) and screening (when patients have no symptoms).

Symptoms are usually lacking in early prostate cancer, but in advanced disease symptoms of prostatism, (urine flow obstruction) may be present. However, benign prostatic hypertrophy(BPH) is more commonly associated with prostatism. Moreover, the prevalence of BPH in autopsy series is approximately 3-fold greater over all age groups than the prevalence of PC(19). Men who have symptoms of prostatism do not have an increased risk of prostate cancer, and the specificity of PSA for

prostate cancer is significantly reduced in this population of men. It has been suggested (20) that these symptoms not used to define "case finding" as opposed to "screening" but that both settings involve screening.

1.7 Screening of disease

There is considerable controversy concerning the suitability of prostate cancer for population or targeted screening, with the weight of opinion from non–urologist suggesting that there is insufficient evidence to persently recommend screening(21) .A number of criteria based on existing evidence concerning range of epidemiological and health service factors are commonly used to determine the suitability of condition for population screening for disease (22).

Screening would inevitably identify many men with cancer who would probably not benefit from treatment. It is unclear whether screening would be followed by reduction in morbidity and mortality from disease (21).

There is doubt as whether screening would be effective in identifying such tumors early enough in their natural history to alter the overall current mortality from the disease, particularly as it is not

possible to predict which microscopic lesions will develop into malignancies (3).

1.7.1 Efficiency of Screening

The sensitivity and specificity values that have emerged from various studies are influenced by several possible biases. The first bias relates to the choice for diagnosis of prostate cancer, which is usually thin core biopsy, with all of the problems associated with this technique, acommon problem are:

a- work up bias: because most studies have not carried out biopsies on patients unless at least one other test was abnormal :-

DRE (Digital Rectal Examination) or

PSA (Prostate Specific Antigen) or

TRUS (Transrectal Ultrasound).

b- Recruitment bias: some screening studies have been conducted in urology clinics, where the prevalence of prostate cancer is much greater than the general population ,and the spectrum of disease is different. Screening at a population level involves family practitioners more than urologists, and the prevalence of prostate cancer is lower in the community than the urology clinics.

c- Volunteer bias: is well documented among recruits responding to advertisements in the news media to attend screening trials(15).

1.7.2 Effects of Screening:

There are well –known effects of screening .These include :

a- lead time bias: The problem here is that if screening simply detected a tumor earlier than in its natural history, without impacting on overall life expectancy, then there would be an apparent increase in survival. This would occur because the length of time between detection and death would be increased compared with a non-screened group in whom tumours were found only after the development of symptoms.

b- Length –time bias: There is evidence from other screening studies that screening is more likely to detect a greater proportion of non-aggrassive tumors. The reason is that the more advanced ,aggressive or rapidly growing tumors are more likely to present clinically between episodes of screening (23, 24, 25).

1.7.3 Aim of Screening

The aim of screening is to detect confined tumors that can be removed, effecting a cure. Clearly,current, modes of screening are able to detect some such tumors, but they also detect both untreatable and non–fatal tumors, as well as leaving an unknown number undetected(15).

After screening there is stage migration. It is perhaps useful to note that the outcomes for patients of PSA screening can be divided into several groups (26). One group comprises patients whose cancer would have been cured by treatment even if had not been detected by screening. Their lives will not be improved by an earlier diagnosis. A second group is those patients with incurable cancer at the time of screening. These patients will die, and screening does not help them. A third group comprises patients whose cancer would not have been found without screening, but who die of causes other than prostate cancer. The quality of life (QOL) could be reduced by treatment. The main beneficiaries of screening program are those patients whose cancer would have been incurable if it had been diagnosed clinically, but is curable if found early through screening. A fifth group (and the largest) is men tested who do not have malignancy. The net harm done to this group is relatively small unless they go to biopsy, when morbidity and anxiety can be significant.

1.7.4 Levels of Evidence, Biases, and Outcomes Associated with PSA Screening

Budenholzer (27) discussed the importance of levels of evidence in the evaluation of PSA screening. He pointed out the following levels:

1- Level I: based on randomized trials of higher power and low false –positive and false –negative errors .(no PSA screening).

2- Level II: based on randomized trials with high false-positive and/ or high false –negative rates. (one publication).

3- Level III: non randomized concurrent cohort comparisons (most studies).

4- Level IV: non randomized historical cohort comparisons (most studies).

5- Level V: case series without control subject. (most Studies).

This means that tumors of an earlier stage are detected compared with non-screened or historical controls. This will result in a greater number of organ confined non- metastatic tumors being found. (23, 24).

1.7.5 Criteria for Prostate Cancer Screening

It is important to have good evidence in favor of population–based screening for prostate cancer , if screening is implemented.

There are well-established criteria for evaluating the effectiveness of a screening program. A set of five criteria that has been proposed by Hulka (28) include the magnitude of the health problem, the effectiveness of the test or procedure, the existence and identification of an early asymptomatic stage of disease, the availability of effective treatments, an accepted strategy of whom to treat and not to treat, acceptable costs of the screening program ,and the improved outcome if the disease is treated in its early stage(8).

1.8 Diagnostic studies

1.8.1 Tumor markers

1.8.1.1 Alkaline phosphatase

Also called :alk phos or alk Ø or ALP. It may be included in blood chemistry screening panel with normal range 20-90 I.U./ liter.

8.1.2 Acid phosphatase

Also called acid phos or acid Ø or acid p, tase or prostatic acid phosphatase (PAP), a test blood serum to detect specific enzyme produced by several tissues, particularly the prostate. Acid phosphatase levels are elevated in 85 % of cases with skeletal metastases, 60 % of untreated cases, and 20% of localized cases. PAP is used to measure the

acid phosphatase secreted by prostate gland specifically. So it is the primary biochemical test for prostate test before prostate specific antigen and digital rectal examination. However, numerous studies show that PAP has no added benefit once a Prostate Specific Antigen (PSA) has been measured (29).

Normal range varies according to method of processing the serum as:

King Armstrong microns /dl	1 - 4
Bodansky or Gutman microns/dl	0.5 - 2
Shinowara microns/ml	0 - 1.1
Bessy Lowry microns/nk	0.1 - 0.73

1.8.1.3 Prostate Specific Antigen

Also called PSA, excludes prostatic acid phosphatase . It is tumor marker assay of blood serum for antigen released from cells in prostate tissue. PSA (M.W30,000 dalton) is serine protease, a member of the Kallikrein family, but is expressed almost exclusively in the prostate and is secreated in the seminal fluid to increase fluidity and sperm mobility. It is strongly regulated by androgens and its concentrations in the prostate is thousands of times greater than those found in serum. Where it is partly bound to $\alpha 2$ macroglobulin ($\alpha 2M$) and a antichymotrypsin (ACT) (15). Concentrations in serum are related partly to age, and to the amount of transitional-zone benign prostatic cancer.

Hyperplasia(BPH), and partly to the amount of prostate cancer present(15). Some poorly differentiated tumors do not express PSA. Concentrations can also be increased by recent prostate surgery, biopsy of the prostate or prostatitis. The ratio of free PSA is decreased in prostate cancer. The molecular forms of PSA in serum have been discovered(30). It is known that the major immunoreactive forms of PSA in serum are PSA bound to the proteinase inhibitor α1-antichymotrypsin (about 80% of total PSA) and free PSA (about 20% of total PSA) (31).

There is a difference in the percent free PSA between patients with prostate cancer and benign prostatic hyperplasia (BPH). Prostate cancer patients have proportionally less free PSA and this difference has been proposed as a tool for the differential diagnosis between prostate cancer and benign prostatic disease, in patients with intermediate levels of PSA (32, 33).

Among the factors that seem to greatly influence the percent free PSA, apart from the diagnosis of prostate cancer and BPH are: 1) the levels of total serum PSA (33, 34).

2) volume of prostate (35).

3) age of histological characteristics of prostate cancer(36)

The mechanism by which the percent free PSA is decreased in the serum of prostate cancer patients is currently unknown; but patients whom had undergone radical prostatectomy and then relapsed, the

percent free PSA should be very low since the normal prostate tissue has been removed (34). The total PSA assay is equimolar, is based on monoclonal / polyclonal assay configuration and has a detection limit of 0.01 µg / l. The free PSA assay is based on a monoclonal / polyclonal assay configuration and has a detection limit of 0.02 µg/l. Both assays are based on detection of alkaline phosphatase activity chemiluminescence (37).

1.8.1.3.1 PSA Isoforms

The different forms of PSA have been used as ratio of free PSA (fPSA) to total PSA and the measurement of the bound form only, complexed PSA (cPSA). These tests have been reported to give better discrimination between benign and malignant disease of the prostate (38). Brawer *et al* (39) reported that fPSA ratio and cPSA identify slightly different patient groups. cPSA has much better storage stability than f PSA, both at 4 and at–20 C° (40),which could be its main advantage. The poorer stability of free PSA causes problems for laboratories wishing to measure total PSA initially, and store the sample until the physician requests the f PSA ratio at a later date.

Catalona etal (41) found that 95 % sensitivity was maintained with a fPSA ratio of 25% in both black and white men. Use of this cutoff avoided unnecessary biopsies in 20% of white and 17% of black

subjects. Higher fPSA ratio was associated with more favorable postoperative histopathologic findings for both races.

Lin *et al* (42) found a significant negative association between pre-operative percent fPSA and total post-operative PSA of patients. This may suggest that patients whose total PSA increases more rapidly post–operatively, are likely to have less percent f PSA Among all other pathological variables, including positive margins,apical margin involvement, periprostatic tissue invasion, capsular invasion, seminal vesicle invasion, bladder -neck invasion, tumor volume and clinical stage, non of them was associated significantly with percent fPSA. The variation in performance of these isoform tests from study to study may be ascribed to differences in test methodology, patient age, prostate size, and cancer prevalence (screening versus urology clinic). The PSA ratio appears to perform best for patients with prostates smaller than 60 ml(43). The principal clinical use of these isoform measurements is to improve PSA specificity, and thereby to reduce by (20-40%) the number of unnecessary negative biopsies when total PSA is borderline (4-10 µg/l) ,and at minimal (5%) risk of missing a case of cancer.

PSA is present in blood with three main forms. The most important immunoreactive form is PSA bound to α-1-antichymotrypsin (PAS-ACT). Free PSA is the other immunoreactive form present in

serum. The third form of PSA, bound to α-2-macroglopulin, which cannot be detected. (15).

1.8.1.3.2 Age Relative PSA Cutoff

For total PSA>7μg/l, fPSA ratio and cPSA were equivalent to each other, and better than total PSA .

The original cutoff of 4.0 μg/l was defined by Hypritech method as the 99th percentile of (mostly white) men under the age of 40 years without benign prostatic hyperplasia (established by lack of symptoms rather than biopsy). The test characteristics of PSA are different for black men than for white men(44). The percentage of patients with PSA> 4μg/l is age dependent because prostate size increases with age .

Computer simulation(45) suggests a 2-year screening interval starting at age 40 years leads to fewer prostate cancer deaths , fewer PSA tests and fewer biopsies per curable cancer . Lowering the cutoff even to 2.5 μg/l did not prevent more deaths from prostate cancer than a cutoff of 4.0 μg/l, but lead to more biopses.

The value of PSA taken to indicate biopsy is age -related . Even in the range of 0-4 ng /ml, a significant number of tumors can be found.(46).Given that prostate cancer is so common at autopsy, and that a tumor of volume less than 1 ml is not likely to result in raised PSA, it may be that many tumors are simply found by chance in men with raised

PSA, the concentration of PSA being related to the amount of BPH. Age –related reference ranges compensate for BPH in an indirect manner, and lead to decreased clinical sensitivity for the test in order men, and increased sensitivity in younger men(47). Some have argued that this is beneficial, since younger men need to be identified because of the possibility of grater number of life years lost , and older men have fewer life years to lose(48). However, other have pointed out that the (PPV) prostatic positive of PSA does not change with age , because sensitivity increases with age (due to the larger tumors usually detected), whereas specificity decreases with increasing age (due to increased prevalence of BPH). Using a standard cutoff of 4.0μg/l ,the overall cancer detection rate is higher than with age-adjusted cutoffs.

The target population for screening should be <75 years, and the point out that the screen interval will have little effect on men>65 years if the initial PSA is <1.0 μg/l . In other words , these men probably do not to be screened again(49). Increased cancer in men >70 years was offset by decreased yield in men aged 50-59 years(29). This suggests that screening programs need to be more targeted at younger men.

1.8.1.3.3 Importance of PSA

As we know that the prevalence and incidence of prostate cancer increase as men get older. This has led some to suggest that screening

with PSA should begin at age 50 years, unless there are other risk factors (family history or African ancestry) when age 40 yearsis suggested (8). However, there is no direct evidence that screening these two high-risk groups leads to improved life expectancy.

The main goal of PSA screening is to detect potentially curable disease in the hope of curative treatment to reduce mortality. The velocity attempts to document the rate of increase in PSA over time, based on data from specimens(50) that showed rates in the following order:- metastatic PC > localized PC > BPH > Helthy men.

Sometimes ,the approach is called PSA doubling time , the time taken for serum PSA to double in concentration. Aggressive PC usually has doubling times of less than 2 years . Both of these approaches are hampered by the significant amount of within-subject variation(51), which varies from 6% to 40 % in different studies .

The rate of progression to incurable cancer (defined as patients with initially "normal" PSA converting to PSA>5.0μg/L after 2or4 years) was rare; (49) that is the patient had an initial PSA<2.0μg/L.

Conversion was more likely for patients with initial PSA between 2.1 and 3.0 μg/l (27%) and still more likely for initial PSA between 3.1 and 4.0 μg/l (36%) (45). This confirms both a 2-years screening interval and that PSA<2.0μ/L carries a very low risk of prostate cancer progression over 4year. Little difference was found in the probability of

organ-confined cancer at PSA concentration between 2.5 and 4.0 μ/L compared with concentration between 4.0 and 6.0μg/L for men of various ages(52) However, probability of organ-confined prostate cancer was higher in younger men at all PSA ranges, concluding that for greater benefit in screening at an earlier age than there is in using lower cutoff for further testing.

With pretreatment PSA< 4.0 μg/l, there was a high probability (94%) of potentially curable cancer, most of which (69%) were small (volume<0.5 ml). For PSA in the range 4.0-5.0 μg/l , 89% of cancers were deemed curable (only 33% had volume <0.5 ml); and for PSA>5.0 μg/l, only 70 % were potentially curable (52). They interpret this data as support the cutoff of PSA>4.0μg/l for detecting potentially curable prostate cancer. In summary, PSA testing leads to an increased biopsy rate and to an increase in prostate cancer detection. The absolute increase in potentially curable prostate cancer with PSA over use of DRE is significant.

1.8.1.3.4 PSA with Other Examination

The main outcome of PSA testing is a thin core biopsy. Thin core biopsy material is stained and evaluated according to the Gleason pattern from Grad 1 (well differentiated,less aggressive in metastatic behavior) through III (poorly differntiated, more likely to metastasis). Because

more than one grade is often present, the Gleason score has developed , in which the most common pattern and the pattern of highest grade are combined to give score out of 10(8). Between 10% and 21% of patients with PSA<4 µg/l would not have prostate cancer diagnosed without a digital rectal examination (DRE), (53) unless a lower cutoff for PSA is used, it is for this reason that most screening programs advocate the use of both PSA and DRE. On the other hand, when both DRE and PSA are positive,the probability of prostate cancer quite high at about 55% (54).

Adding digital rectal examination (DRE) to measurement of serum PSA, in the context of screening asymptomatic men , does little to increase sensitivity(55). Other researchers have shown that omission of rectal examination will result in some tumors being missed. Alogistic–regression model was used to predict the number of cancers if all men were to undergo biopsy. The study found that biopsies in men with PSA<1.0 ng/l and positive DRE or TRUS would be insufficient because few tumors are detected.(55).

PSA density, volume-related PSA, and transition zone PSA all rely on an estimate of the volume of the prostate to compensate for the amount of PSA present in benign tissue in the prostate. They all suffer from operator (and method) variability estimating the volume of the prostate, usually with TRUS. They are also affected by the different ratio of epithelium to stroma in prostate tissue. This ratio varies with prostate

size, and alters the above measurements because only the epithelium produce PSA (47, 56, 57).

A promising marker is a member of the human kallikerin (HK) family, of which PSA is a member (58). HK-2 has been shown to perform better than PSA and present age free prostate specific antigen (fPSA) ratio in a number of studies (59). Unfortunately , it is not readily available, and it is true clinical utility needs further exploration (8).

In summary, PSA together with DRE is a reasonable screening approach for detection of prostate cancer. However, the true sensitivity and specifity are not known, and with the current standard cutoff of 4μg/l, a significant number of cancers is missed.

1.8.1.3.5 Problems with PSA Assay

Since Benign Prostatic Hyperplasia (BPH) is about 3- fold more prevalent than prostate cancer, this causes significant problems with PSA specificity for diagnosing prostate cancer. Many other factors can cause false–positives for the PSA test when used to screen for cancer (60), including a statistically significant increase after digital rectal examination, and a clinically significant increase after prostate biopsy necessitating a wait of 1-2 months before taking another PSA measurement. Study by Pannech *et al* (61) document increases in PSA

after strenuous bicycle riding and after ejeculation, but antiandrogen drugs like finasteride cause an average of 50 % decline in PSA concentrations after about 6 months of use to treat BPH; but the free-to-total PSA ratio is unaffected.

There have been some analytical problems with the PSA assay, some of which still persist. Most of the problems relate to existence of different isoforms of the enzyme. Agreement among PSA assays is be better that most compaines trace their calibrators either to the original hybritech method, or to the stanford "90-10" calibrator. This calibrator more closely approximates the PSA isoform composition in serum in patients with prostate cancer, where it is about 10% free (unattached to other proteins) and 90% bound (to α-1 antichymotrpsin). Use of this calibrator has been shown to reduce differences among methods (62). The differences arise in part from different incubation times; short incubation times favor binding of free PSA to the capture antibody, and bias the final result in specimens having extremes in proportions of free PSA. Alternatively, there may be recognition of different epitopes on free and bound PSA, depending on the antibody used in the assay. Methods that show a differential response towards free versus bound PSA are sometimes called "non-equimolar", because they do not give the same signal for both forms of PSA (63).

1.8.1.4 Prostate–Specific Membrane Antigen (PSMA)

Prostate–specific membrane antigen is expressed in epithelial cells of both benign and cancerous prostate tissue. It is up-regulated in hormon–resistant states, and where there is tumor invasion. Current Wisdom (64) suggests that serum PSMA can assist in the identification, staging, and monitoring of metastatic prostate cancer . It shows promise in directed imaging and therapy of recurrent prostate cancer.But its role is not yet firmly enough established to be recommended routinely. Detection of circulating prostate cancer cells by reverse transcription – polymerase chain reaction (RT-PCR) held much promise as a very sensitive approach to detect the presence of metastases. These cells are detectable in virtually all lymph node matastases.(65). However, these cells are detected in serum of patients with both localized and metastatic disease, making distinction between these two states not possible. Furthermore, there are significant analytical problems among laboratories, which preclude its routine use.

1.8.1.5 Tissue Polypeptide Antigen (TPA)

It is a non–specific to prostate cancer; elevated levels indicate presence of malignancy, also used to monitor bladder and lung cancer in males.

1.8.1.6 Other Tumor Markers

Despite the widespread use of PSA screening , derivations thereof (fPSA), and molecular marker models, such as the prostatic specific membrane antigen, prostatic acid phosphate, alkaline phosohatase. These tests do not offer optimal specificity and sensitivity required for sophisticated clinical decision making (66). It becomes increasingly apparent that the search for a single specific tumor marker for prostate cancer may have a low probability of success.(67), particularly when the model systems consist of cell lines or animal tumor models.

The variable extend to which the parameters mentioned antecedent have been found to be prognostic, has led to a number of studies of combined markers, including the use of logistic regression (68); including genetic markers. There has been considerable effort devoted to searching for genetic markers to identify patients at risk for prostate cancer, and to try to predict which cancers are likely to progress more rapidly than others. Schrader's group in Rotterdam (69) has identified chromosomal regions related to advanced tumor stage, that is, loss of 10q 24 and gain of 7 q 11.2 and/or 7 q 31 sequences. Also again of 7 pq and /or 89 was suggested to discriminate between progressors and nonprogresssors. Increased concentrations of insulin-like growth factor-1(IGF-1) are associated with high relative risk for prostate cancer (70). Low concentrations of P27 have been reported to predict for poor

disease-free survival (71), however, non of these markers has reached the point of routine clinical use.

The development of rational approaches to the diagnosis and treatment of prostate cancer may start with a basic understanding of the molecular mechanisms that underlie tumor progression. Gene sequence alone cannot predict functional consequences that are ultimately reflected in the actual protein contents within the cell (47). Normal communications between these proteins trigger signal trasduction pathways that determine whether a cell remains quiescent, proliferates, differentiates, commits programmed cell death, adapts to a differentiated state, or migrates. It is envisioned that information regarding proteins governing these processes will likely reveal new drug targets, markers for early detection, or vasccine candidates if the protein is surface expressed.

Discerning the mechanism whereby normal cells transform into premalignant cells, then into tumor cells, and finally into metastatic dissemination can best be understood if the analysis is performed in the actuall tissue itself. This is a particularly challenging problem in the study of prostate cancer because relevant cell population (i.e,normal, prostatic intraepithelial neoplasia, frankly invasive) only constitute a small frction of the whole cellular repertoire, thereby effectively limiting traditional proteomic (the analysis and characterization of global protein

modifications) investigations, such as two–dimensional electrophoresis (2D-PAGE) of homogenized prostate bulk tissue or cell lines.It is not clear whether gene or protein expression changes seen in prostate tumor progression are causal, a result of the malignancy itself, or are contributed by interpatient variability (72).

The extension of this technology to construct sensitive, specific, and reproducible protein profiles that span progressions of a variety of malignancies from microdissected samples was validated just recently (73), although a powerful technique for the discovery of novel proeins in a given disease state is laborious, time–intensive process and is not ameneable to rapidly assessing changes in protein expression in a clinical setting.

1.8.2 Physical Examination

1.8.2.1 Digital Rectal Examination (DRE)

Also it may called rectal examination, and manual examination; we can make examination of lower portion of the rectum, perineum and surrounding tissues using a gloved finger inserted into the anus to examin the presence of nodularity, induration, fixation of seminal vesicles, enlargement, firmness, lesion, neoplasm, malignancy and active

bleeding. If there is no mention of prostatic abnormality during the exam; benign prostatic hypertrophy .

As we mentioned antecedent that screening with DRE and PSA should begin at age 50 years (52). Also as we called previously that between 10% and 21% of patients with PSA<4µg/ l would not have prostate cancer diagnosed without DRE.It is for this reason that most screening programs advocate the use of both PSA and DRE.

According to American Cancer Socitey (ACS) project (74), DRE sensitivity decreased from about 48% in the first two years of screening to about 25% in the third and fourth years, wheras PSA sensitivity increased slightly during the same time period from 65% to 69%. DRE and PSA specificity remained fairly constant at 97% and 89%, respectively.

Finally, urologists tend to be better at DRE procedure, and family physicians less good at it. The large variability in performance mediates against DRE as the sole screening test for PC(8).

1.8.3 Imaging

1.8.3.1 Prostatic Ultrasound

Prostatic ultrasound may also called transrectal ultrasound (TRUS), ultrasonography, echography, sonography.

It is a recenly developed technique to locate areas of carcinoma withen the prostate and to assess whether the prostatic capsule is intact. This procedure can not assess lymph node size, but may be in guiding needle biopsies.

Most of the studied tested with PSA, DRE, and TRUS; however, the criteria of going to biopsy differred.Some screened with PSA first, and performed DRE and TRUS only if PSA was elevated (>4.0μg/l). Som (75) allowed either PSA or DRE (or both) to be positive befor performing TRUS and biopsy;other required both to be abnormal. Because a procedure by means of TRUS result in sepsis and haematuria (76, 77) TRUS is generally not regarded as a usefull screening test.brawer (78) cites 11 studies on TRUS. He documented the poor sensitivity, expressed as mean number of cancers per number of patients tested (9.7%, rang 1.7-21.6%) and the poor specificity of TRUS as a screening tool.

1.8.4 Pathology

This kind of diagnostic studies using to detection the grading,staging of prostate cancer depending on cell type, Gleason`s grade or score, exact size of lesion, number of microscopic foci (if tumor is occult), multifocal tumor, nodularity in both lobes of prostate, invasion into or through the prostatic capsule, invasion of apex of prostate , size

and number of lymph nodes involved (including micrometstases), structurs removed (ductus deferens, seminal vesicles, prostatic urethra), extension to adjacent tissues (seminal vesicles, rectum, bladder neck, floor of bladder, urethra, perineum, soft tissues) results of biopsies of distant sites or lymph nodes.

Transrectal/transperineal Needle Biopsy is a procedure performed by inserting a needle through the perineum (external) or via the rectum through the rectal wall to penetrate areas of nodularity or induration of the prostate. Fluid or tissue suitable for cytologic analysis is drawn up into the needle, which is withdrawn from the prostate. Multiple random needle biopsies may be performed to determine if tumor is multifocal (18).

1.8.4.1 Prostate Cancer Staging

Epstein *et al.* (79) compared cancers detected either by TURP (T1a) or by PSA (T1C)(in which both T1a, T1c is nonpalpabe incidental PC) to palpable T2 cases. Only 16% of T1c tumors were considered to be clinically "insignificant" (defined by volume<0.2 cm^3 organ confined, and Gleason score<7). The T1c cancers were intermediate between T1a and T2 in the various pathology attributes.

The European Screening Trial (80) divided cancers into T1c and non-T1c, and latter into groups with elevated or "normal" PSA (cutoff

4.0 μg/l). The T1c tumors were intermediate between the two PSA groups in terms of being organ-confined and the extent of positive surgical margins; there was no seminal vesicle involvement unless PSA is>4.0μg/l.

We have a brief summaries of prostate cancer staging as :

1- T0: No evidence of primary

2- T1: not palpable or visible(clinically inapparent)

T1a <5%

T1b >5%

T1c Diagnosed on needle biopsy only

3- T2: confined to prostate gland

T2a: one lobe

T2b: both lobes

4- T3: Through prostatic capsule

T3a: Extra capsular

T3b: seminal vesicle(s)

5- T4: Fixed or invading adjacent structures: bladder neck, external sphinter, rectum, levator muscle, pelvic wall.

6- N-,M-: Distant metastases

N1: Regional lymph node(s)

M1a: Non-regional lymph node(s)

M1b: Bone(s)

M1c: Other site(s)

1.8.4.2 Gleason's Score/System for Histologic Grading of Prostate Cancer

Gleason's system assigns histologic grade to predominat (primary) and lesser (secondary) pattern of tumor.

The grade number of histological grade (which is important factor for prostate cancer ranging from (1-4)) are added to Gleason pattern (ranging (1-5)) are added to obtain Gleason score (ranging (2-10)) as the following:-

1- Grade 1 (G1): well differentiated ,slight anaplasia.

Gleason's pattern 1: small,uniform gland

And2: more stroma between glangs

Gleason's score: 2,3,4

2- Grade 2 (GII): moderately differentiated ,moderate anaplasia

Gleason's pattern 3: distinctly infiltrative margins

Gleason's score 5,6,7

3- Grade 3-4(G III–IV): poorly differentiated or undifferentiated, anaplastic, marked anaplasia

Gleason's pattern4: irregular masses of neoplastic glands

Gleason's pattern5: only occasional gland formation .

Gleason's score 8,9,10

1.9 Treatment

Because prostate cancer usually develops deep in the parenchyma of the gland, complete resection of tumor is not possible through a transurethral approach, which simply cores out or scrapes away the tissue adjacent to the urethra.

Once prostate cancer has been identified, a strategy is needed to provide guidance on appropriate treatment.(76).

1.9.1 Type of treatments

There are six main treatments for localised prostate cancer:

1- Radical prostatectomy

2- Radiation therapy

3- Conservative monitoring

4- Hormonal therapy

5- Immunutherapy

6- Chemotherapy

1.9.1.1 Radical prostatectomy (RP)

Also called transurethral resection of prostate (TURP) ;in which used primarily to relieve bladder outlet obstruction symptoms and evaluate the urethral passage. It is generally not considered to be cancer-directed therapy except in very low stage disease.

Given the long natural history, and the acceptance that the possible benefits of radical local treatment may be apparent only after 15 to 20 years(5), some advocates of radical prostatectomy point out that most benefit will be gained in the treatrment of younger men aged under 55 or 60 years.

Kamoi and Babaian (57) cite radical prostatectomy data for patients identified by an increased PSA concentration (>4.0 μg/l). About 90% of these patients had tumors >0.5 ml in size, suggesting that they should be considered for treatment.

Also the resection include prostate, lymph nodes, ducts and seminal vesicles, bladder organ as testes which called orchiectomy. In cases of removing gland to change the hormonal balance of the body called hormone manipulation surgeries.

Prostate cancer incidence rose rapidly in the years when TURP rates also increased rapidly (1970s and 1980s), and subsequently declined as TRUP rates were reduced with the introduction of the drugs and minimally invasive therapies for benign prostatic disease (81.82).

1.9.1.2 Radiation Therapy (RR)

Radiation therapy is commonly used for high grade, large, or extracapsular tumors. It is also effective in treating symptoms of metastatic disease.

At present we have no high quality evidence that asseses the effectiveness and coste ffectiveness of treatments. There are some data to suggest that radical treatment of organ-confined cancer can lead to a small increase in long-term survival, but without confirmatory evidence from randomised controlled trials, such data can not be relied upon (3).

Most studies have found that there is a higher death rate (though it is small), and higher rates of impotence and urinary incontinence after prostatectomy (RP) than after radical radiotherapy (RR). RR is usually recommended if there is evidence of local spread before treatment, and may be recommended for local spread after RP (83, 84, 85).

In addition to the lack of good quality evidence on survival after radical treatment, very little research has been conducted on short-term or medium-term outcomes.

Radical treatment can clearly lead to a number of complications, some of which are likely to have a severe impact upon quality of life. One study found considerably worse sexual and urinary dysfunction among those who received radical interventions than among those treated conservatively (86).

1.9.1.3 Conservative Monitoring (Watchful Waiting)

It involves close monitoring, with active treatment if symptoms develop. Future changes may incorporate molecular markers of progression, which will allow the identification of men best treated by watchful waiting because of their low risk, and men at greater risk who might benefit from major interventions (3, 15)

Active treatments offer potential for cure, they involve iatrogenic effect, including pain, hospital admission, incontinence impotence, and occasionally death (21, 87). In some men in whom the cancer would not have caused morbidity or mortality, the patient may experience harmful side effects without benefit. On the other hand, with conservative monitoring, the patient is at risk of progression, which may be fatal in small number of cases (88).

1.9.1.4 Hormonal Therapy (HT)

There is a suggestion from a small randomised trial that early hormonal ablation in men with low-volume lymph–node metastases found at radical prostatectomy far better after such treatment (89). These data are in keeping with the randomized trial of hormonal ablation in men treated with radiotherapy, though this study did not address the question of whether hormonal ablation alone would have provided better treatment than local radiotherapy (90).

There are large number of drugs related to hormonal therapy commonly used for treating prostate cancer:

1) Estrogens: Anisene, Benezestrol, Bio-Des, chlorotrianisene, chlorotrianizen, Estrogenine.
2) Anti-androgen: Benorteron, Benoteron, Cyproterone, Flutamide.
3) Leuteinizing-hormon releasing hormon antagonists: Zoladex, Leuprolide , Lupron , Goserelin.
4)Progestins: Algestron, Anagestone, Anatropin, Amadinone.

1.9.1.5 Immunotherapy (I.T)

A number of novel treatments are now being developed, based on immunotherapy and agents active against receptor tyrosine kinases(15).

1.9.1.6 Chemotherapy (CT)

Men with low volume lymph node metastases are younger and fitter than those presenting clinically with metastatic disease, and are able to undergo more active treatments with chemotherapy and novel agents (15).

1.9.1.7 Outcomes of Treatments

The result of different types of treatment in the management of men with localised prostate cancer are difficult to interpret, because no randomized data are available. For instance,men treated by watchful waiting tend to have deen selected because they are older, with lower-grade tumors, whereas those treated by radiotherapy are more likely to have more advanced tumors (91).

The main outcomes of treatment can be viewed as life expectancy (years of survival after diagnosis), morbidity, and quality of the life(QOL).

1.9.1.71 Life Expectancy

We do not know which treatment offers the best survival in the majority of circumstances for prostate cancer. In USA, urologists are more likely to recommend radical prostatectomy, and radiation oncologists to recommend radiation therapy, for organ-confined disease (92). In Europe, watchful waiting is still the most prevalent treatment, and radical prostatectomy has been decreasing in recent years in Sweden. (93).

The difference in survival by different methods of treatment were not statistically significant, except for Grade 3 (Gleason scores 8-10) (93) However, it must be remembered that these data are not strictly comparable because patient preselection usually guides which treatment is offered, (8) and only some of the significant prognostic factors could be corrected for in the analysis. Wasson *et al* (94) found no evidence sufficiently good to support one treatment over another for localized prostate cancer.

1.9.1.7.2 Morbidity

Morbidity experianced by patients from these treatments includes impotence, urinary incontinece, and there is even a risk of death.

1.9.1.7.3 Quality of Life

More attention is now being paid to quality of life issues. At least two independent decision analytic publications on this point indicate minimal benefit for PSA screening in terms of life expectancy, and nagative benefit in terms of quality-adjusted life years (QALYs), which take into account quality in addition to quantity of life (95,96) The outcomes of these analyses are only as good as the inputs, which are far from definitive, such as natural history of disease, outcomes of treatments, morbidity, and QOL.

QOL issues were an important driving force in the choices to be made by patients, especially attitudes towards sexual function and risk–taking. The test performance characteristics of PSA and DRE were less important than these other parameters in determining benefit to the patient (8).

1.9.2 Treatment Options by Stage

There are five different stage of disease require different treatment ways there are:

1) Stage A1 (Occult):

Observation without immediate treatment .But if the patient is younger (age 50-60) immediate treatment may be considered.

2) Stage A2 (diffuse tumor):-

a) External beam radiation therapy following transurethral resection.

B) Radical prostatectomy with pelvic lymphadenectomy.

C) Interstial radioisotopes (under clinical evalution).

3) Stage B (palpable prostate tumor at diagnosis)

a) Radical prostatectomy with pelvic lymphadenectomy.

b) External beam radiation therapy following transurethral resection.

c) Intersitial radioisotopes (under clinical evaluation).

4) Stage C (extracapsular extension)

a) External beam radiation therapy transurethral resection (for cure).

B) Radical prostatectomy with pelvic lymphadenectomy in selected patients (for cure).

C) Orchiectomy for symptomatic patients .

d) Transurethral resection (for palliation).

E) Hormone therapy (leuprolide or estrogens).

F) Interstitial radioisotopes (under clinical evaluation).

5) Stage D1(regional lymph node involvement,distant metastases):-

a) Orchiectomy.

b) Hormon therapy: signal agents or combination.

c) Transurethral resection or radiation therapy (for palliation)

d) Systemic chemotherapy (under clinical evaluation).

1.10 Aim of the Study

The aim of this research is to study the correlation between the prelevence and expectency of spreading of prostate cancer in the West Bank regions and factors affecting it such as place, cities age address, smoking, occupation, and number of children.

CHAPTER TWO

Materials and Methods

2.1 Equipments and Reagents

VIDAS TPSA is an automated quantitative test for use on the VIDAS analyser, for the quantitative measurement of prostate specific antigen (PSA) levels in human serum or plasma, using the ELFA technique (Enzyme Linked Fluorescent Assay).

The VIDAS TPSA assay is an equimolar test which can detect the bound form (PSA-ACT) and the free form in the same manner. The manufacture of this kit is bioMerieux, 69280 Marcy-l'Etoile/France.

The equipments required but not provided are pipette with with disposable tip calibrated to dispense 200µl, and powderless, disposable latex gloves; as powder has been reported to cause false results for certain enzyme immunoassay test.

2.1.1 Description of the T PSA Reagent Strip

The polypropylene strip consists of 10 wells covered with a labeled, foil seal. The label comprises a bar code which indicates the type of test carried out, kit lot number and expiration date. The foil of the first well is perforated to facilitate the introduction of the sample. The last well of each strip is a cuvette in which the fluorometric reading is performed. The four wells in the center section of the strip contain the various reagents required for assay.

1- well 1: sample well

2- well 2,3,4,9: empty wells

3- well 5: conjugate: Alkaline phosphatase labeled monoclonal anti-PSA immunoglobulins (mouse)+0.9 g/lsodium azide (400 µl).

4- wells 6,7: wash buffer: Tris (0.05 mol/l,Ph 7.4) + NaCl (0.4 mol/l) + Tween (0.05%) +0.9 g/l sodium azide (600 µl).

5- well 8: Diluent: Tris (0.1 mol/l)+NaCl (0.1 mol/l)+calf serum (5%)+0.9g/l sodium azide (400 µl).

6- Well 10: Reading Cuvette with substrate :-diethanolamine DEA (0.62 mol/l or 6.6% PH 9.2) +

7- Methylumbelliferyl phosphate (0.6 mmol/l) + 1 g/l sodium azide (300 µl).

2.2 Principle

The assay principle combines a two step enzyme immunoassay sandwich method with a final fluoresent detection

(ELFA). The solid phase receptable (SPR), serres as the solid phase as well as the pipetting device for the assay in which the interior of the SPR is coated during production with monoclonal anti-PSA antibodies (mouse). Reagent for the assay are ready–to use and predispensed in the sealed reagent strips.

All of the assay steps are performed automatically by the instrument. The sample is cycled in and out of SPR several times. This operation enables the antibody fixed onto the interior wall of the SPR to capture the prostate specific antigen present in the sample. Unbound components are eliminated during the washing steps. Alkaline phosphatase labeled antibody is then incubated in the SPR where it binds with the prostate specific antigen. Unbound conjugate is then eliminated during the washing steps.

During the final detection step, the substrate (4-Methylumbellifreryl phosphate) is cycled in and out of the SPR. The conjugate enzyme catalyzed the hydrolysis of this substrate into a fluorescent product (4-Methyl umbelliferon), the fluorescence of which is measured at 450 nm. The intensity of the fluorescence is proportional to the concentration of prostate specific antigen present in the sample. At the end of the assay, results are automatically calculated by VIDAS in relation to the calibration curve stored in memory, and then printed out.

2.3 Sample Collection

Human serum or plasma collected on heparine or EDTA. It is recommended to validate collection tubes befor use as some contain substances which interfere with test result.

Samples can be stored at 2-8°C. For a maximum at 24 hours; if longer is required, freeze at–25±6 ° C. Avoid sucessive freezing and thawing. Samples containing impurities must be centrifuged befor analysis.

The following factors have not been found to significantly influence assay:-

1) hemolysis (after spiking samples with hemoglobin 0 to 300 µmol/l)

2) bilirubinemia (after spiking with bilirubin: 0 to 500 µmol/l)

3) lipemia (after spiking samples with lipids: 0 to 10 mg/ml equivalent in triglycerides)

However, it is recommended not to use clearly hemolyzed, lipmic or icteric samples, and if possible to collect a new sample.

2.4 Procedure of the Assay

1- Remove the kit from the refrigerator and allow it to come to room temprature for at least 30 minutes.

2- Remove one TPSA strip and one TPSA from the kit for each sample, control or calibrator to be tested. Make sure that storage pouch has been resealed after the required SPRs have been removed.

3- Place the TPSA strip and SPR on the VIDAS preparation/loading tray.

4- Enter the appropriate assay and patient data using the keyboard to creat code TPSA. Type "TPSA" to be run, if the calibrator should be tested, enter "S1" for the sample identification. The calibrator should be tested in duplicate if it is to be stored in memory. If the control needs to be tested, it should be identified by C1.

5- Mix the samples, the calibrator and/or the control with avortex.

6- Pipette 200 µl of sample, calibrator, or control into the sample well (NB: the samples and the control are tested singley).

7) Insert the VIDAS SPRs and strips into the positions indicated on the screen.

8) Initiate the assay processing as directed in the VIDAS operator's manual. All the assay steps are performed automatically by the instrument. Results are obtained within approximately 60 minutes.

9) After the assay is completed , dispose of the used SPRs and strips into an appropriate recipient.

2.5 Data Collection

Data were collected from files from Al-Watani Hospital in the north of West Bank and Beit-Jala Hospital in the south of West Bank.

From two hospitals we collected 270 specimen scanning all area of West Bank of Palestine including cities, villigase and camps from the year 1992- 2002. All data collected here looks for age; which is ranging up to 50 years, smoking, occupation, and number of children. Grade that can be observed ranging from grade I (well differentiate) including grade II (moderately differentiate) and grade III (poorly differentiate).

Also about the stage which can found different form as:

1- in situ

2- localized

3- regional: direct extremental (for adjacent region)

4- regional: lymph node

5- regional: lymph node and dirct extremenation

6- Distant metastasis (Nosology).

In this work we want to notice different types of treatments made in our hospitals which include surgery, radiotherapy, chemotherapy, immunotherapy and hormonal therapy.

2.6 Statistical Analysis

Statistical analysis was performed using Statistical Package for Social Sciences (SPSS) (SPSS Inc, Chicago, IL, U.S.A). Incidence frequencies (%) of the grades and stage, associated with several variables (age, city, place, address, occupation, number of children, smoking) were calculated. The Chi-Square test was used to test the significance of each of the factors that were associated with the prostate cancer. All significant tests were two sided and were considered statistically significant if the observed significance level (p value) was <0.05.

CHAPTER THREE

Result and Discussion

3.1 Grade of Prostate Cancer and Age

To examine the truth of the hypothesis which states that "there is no statistically significant correlation in the 0.05 significance level between Grade and Age variable, we applied chi-square test to the following Table (1) between the two variables .

Table 1. Frequency distribution of subjects between the variables of Grade and Age

			Age						Total
			40-50 years	51-60 years	61-70 years	71-80 years	81-90 years	91 and more	
Grade	Grade I Well diff	Count		1	5	2	5	1	14
		% within grade		7.1%	35.7%	14.3%	35.7%	7.1%	100.0 %
	Grade II mode.diff	Count		3	17	24	7	1	52
		% within grade		5.8%	32.7%	46.2%	13.5%	1.9%	100.0 %
	Grade III poorly diff	Count	1	3	8	17	4		33
		% within grade	3.0%	9.1%	24.2%	51.5%	12.1%		100.0 %
	Grade IV undiff\anapl	Count		1			1		2
		% within grade		50.0%			50.0%		100.0 %
	Killer Cell	Count			1				1
		% within grade			100.0 %				100.0 %
	Unspecified	Count	1	10	36	51	16	4	118
		% within grade	.8%	8.5%	30.5%	43.2%	13.6%	3.4%	100.0 %
Total		Count	2	18	67	94	33	6	220
		% within grade	.9%	8.2%	30.5%	42.7%	15.0%	2.7%	100.0 %

The results of the test show that the significance level (p) is 0.573 which is higher than the value given in the hypothesis i.e 0.05 ,hence we accept the truth of the hypothesis and assert that "there is no statistically significant correlation in the 0.05 significance level between Grade and Age variable.

3.2 Grade of Prostate Cancer and City

To examine the truth of the hypothesis which states that "there is no statistically significant correlation in the 0.05 significance level between the Grade and city, we applied chi-square test to the following Table (2) between the two variables .

Table 2. Frequency distribution of subjects between the variables of Grade and city

			City			Total
			North	South	Unknown	
Grade	GradeIwell diff	Count	2	11	1	14
		% within grade	14.3%	78.6%	7.1%	100.0%
	Grade II mode. diff	Count	5	40	7	52
		% within grade	9.6%	76.9%	13.5%	100.0%
	Grade III poorly diff	Count	12	19	2	33
		% within grade	36.4%	57.6%	6.1%	100.0%
	Grade IV undiff\anapl	Count	1	1		2
		% within grade	50.0%	50.0%		100.0%
	Killer Cell	Count		1		1
		% within grade		100.0%		100.0%
	Unspecified	Count	67	45	6	118
		% within grade	56.8%	38.1%	5.1%	100.0%
Total		Count	87	117	16	220
		% within grade	39.5%	53.2%	7.3%	100.0%

The results of the test show that the significance level is .000 which is less than the value given in the hypothesis i.e 0.05, hence we does not accept the truth of the hypothesis and assert that "there is statistically significant correlation in the 0.05 significance level between Grade and city.

3.3 Grade of Prostate Cancer and Palce

To examine the truth of the hypothesis which states that "there is no statistically significant correlation in the 0.05 significance level between the Grade and Place,we applied chi-square test to the following Table (3) between the two variables .

Table 3. Frequency distribution of subjects between the variables of Grade and place

			Place				Total
			city	village	Camp	Unknown	
Grade	GradeIwell diff	Count	10	3		1	14
		% within grade	71.4%	21.4%		7.1%	100.0%
	Grade II mode.diff	Count	21	24		7	52
		% within grade	40.4%	46.2%		13.5%	100.0%
	Grade III poorly diff	Count	18	13		2	33
		% within grade	54.5%	39.4%		6.1%	100.0%
	Grade IV undiff \anapl	Count	2				2
		% within grade	100.0%				100.0%
	Killer Cell	Count		1			1

		% within grade		100.0%			100.0%
	Unspecified	Count	51	57	4	6	118
		% within grade	43.2%	48.3%	3.4%	5.1%	100.0%
Total		Count	102	98	4	16	220
		% within grade	46.4%	44.5%	1.8%	7.3%	100.0%

The results of the test show that the significance level is .392 which is bigger than the value given in the hypothesis i.e 0.05, hence we accept the truth of the hypothesis and assert that "there is no statistically significant correlation in the 0.05 significance level between Grade and place.

3.4 Grade of Prostate Cancer and Address

To examine the truth of the fourth hypothesis which states that "there is no statistically significant correlation in the 0.05 significance level between the Grade and address ,we applied chi-square test to the following Table (4) between the two variables .

Table 4. Frequency distribution of subjects between the variables of Grade and address

			Address											Total
			Ramllah	Hebron	Nablus	Jenine	Jereco	B. lahem	Toalkarem	Qalqclea	Selfet	Jourslem	Unknown	
Grade	Grade I well diff	Count	1	8	2			2					1	14
		% within grade	7.1 %	57.1 %	14.3 %			14.3 %					7.1 %	100. %
	Grade II mode. diff	Count	4	28	3	1	1	6				2	7	52
		% within grade	7.7 %	53.8 %	5.8 %	1.9 %	1.9 %	11.5 %				3.8 %	13.5 %	100.0 %
	Grade III poorly diff	Count	1	12	5	1	3	7		1		1	2	33
		% within grade	3.0 %	36.4 %	15.2 %	3.0 %	9.1 %	21.2 %		3.0 %		3.0 %	6.1 %	100.0 %
	Grade IV undiff \anapl	Count		1	1									2
		% within grade		50.0 %	50.0 %									100.0 %
	Killer Cell	Count		1										1
		% within grade		100. 0%										100.0 %

	Unspecified	Count	10	24	36	17	2	12	5	2	2	2	6	118
		% within grade	8.5 %	20.3 %	30.5 %	14.4 %	1.7 %	10.2 %	4.2 %	1.7 %	1.7 %	1.7 %	5.1 %	100.0 %
Total		Count	16	74	47	19	6	27	5	3	2	5	16	220
		% within grade	7.3 %	33.6 %	21.4 %	8.6 %	2.7 %	12.3 %	2.3 %	1.4 %	.9 %	2.3 %	7.3 %	100.0 %

The results of the test show that the significance level is .123 which is bigger than the value given in the hypothesis i.e 0.05, hence we accept the truth of the hypothesis and assert that "there is no statistically significant correlation in the 0.05 significance level between Grade and adress.

3.5 Grade of Prostate Cancer and Smoking

To examine the truth of the hypothesis which states that "there is no statistically significant correlation in the 0.05 significance level between the Grade and smoke ,we applied chi-square test to the following Table (5) between the two variables.

Table 5. Frequency distribution of subjects between the variables of Grade and smoke

			Smoke				Total
			Never smoked	present smoker	past smoker	Unknown	
Grade	Grade I well diff	Count	1	4	2	7	14
		% within grade	7.1%	28.6%	14.3%	50.0%	100.0 %
	Grade II mode.diff	Count	11	12	4	24	51
		% within grade	21.6%	23.5%	7.8%	47.1%	100.0 %
	Grade III poorly diff	Count	10	2	3	17	32
		% within grade	31.3%	6.3%	9.4%	53.1%	100.0 %
	Grade IV undiff\anapl	Count			1	1	2
		% within grade			50.0%	50.0%	100.0 %
	Killer Cell	Count				1	1
		% within grade				100.0 %	100.0 %
	Unspecified	Count	8	17	8	85	118
		% within grade	6.8%	14.4%	6.8%	72.0%	100.0 %
Total		Count	30	35	18	135	218
		% within grade	13.8%	16.1%	8.3%	61.9%	100.0 %

The results of the test show that the significance level is0.011 which is less than the value given in the hypothesis i.e 0.05 ,hence we dose not accept the truth of the hypothesis and assert that "there is statistically significant correlation in the 0.05 significance level between Grade and smoking.

3.6 Grade of Prostate Cancer and Occupation

To examine the truth of the hypothesis which states that "there is no statistically significant correlation in the 0.05 significance level between the Grade and occupation, we applied chi-square test to the following Table (6) between the two variables

Table 6. Frequency distribution of subjects between the variables of Grade and occupaton

			Occupation							Total
			Clerical	Agriculture	Manufacture	unknown	worker	Without	other	
Grade	Grade I well diff	Count		3	1	8	1	1		14
		% within grade		21.4%	7.1%	57.1%	7.1%	7.1%		100.0%
	Grade II mode.diff	Count	3	8		30	6	3	1	51
		% within grade	5.9%	15.7%		58.8%	11.8%	5.9%	2.0%	100.0%
	Grade III poorly diff	Count		5	2	19	4	1	2	33
		% within grade		15.2%	6.1%	57.6%	12.1%	3.0%	6.1%	100.0%
	Grade IV undiff\anapl	Count			1	1				2
		% within grade			50.0%	50.0%				100.0%
	Killer Cell	Count				1				1
		% within grade				100.0%				100.0%
	Unspecified	Count	6	9	4	93	4		2	118
		% within grade	5.1%	7.6%	3.4%	78.8%	3.4%		1.7%	100.0%
Total		Count	9	25	8	152	15	5	5	219
		% within grade	4.1%	11.4%	3.7%	69.4%	6.8%	2.3%	2.3%	100.0%

The results of the test show that the significance level is0.096 which is bigger than the value given in the hypothesis i.e 0.05, hence we accept the truth of the hypothesis and assert that "there is no statistically significant correlation in the 0.05 significance level between Grade and occupation.

3.7 Grade of Prostate Cancer and Number of Children

To examine the truth of the hypothesis which states that "there is no statistically significant correlation in the 0.05 significance level between the Grade and number of children, we applied chi-square test to the following Table (7) between the two variables

Table 7. Frequency distribution of subjects between the variables of Grade and number of children

			Number of Children															Total
			2	3	4	5	6	7	8	9	10	11	12	13	14	15	19	
Grade	GradeI well diff	Count	1		1				1	1	1	1						6
		% within grade	16.7%		16.7%				16.7%	16.7%	16.7%	16.7%						100.0%
	Grade II mode. diff	Count		1		3	2	2	2	4	4	1	2	1	1	1	1	25

1.2%			Unspecified				Grade IV undiff\anapl				Grade III poorly diff													
	% within grade	4.7%		Count		% within grade		Count		% within grade		Count		% within grade										
		3.5%		2	5.1%				6.7%		1		4.0%											
		9.3%		1	2.6%				6.7%		1													
		11.6%		3	7.7%				13.3%		2		12.0%											
		7.0%		4	10.3%				26.7%		4		8.0%											
		16.3%		4	10.3%								8.0%											
		11.6%		9	23.1%						2		8.0%											
		18.6%		3	7.7%						2		16.0%											
		7.0%		7	17.9%			1	100.0%		3		16.0%											
		2.3%		4	10.3%								4.0%											
		2.3%											8.0%											
		1.2%		1	2.6%								4.0%											
		2.3%											4.0%											
		1.2%		1	2.6%								4.0%											
		100.0%											4.0%											
		1		39	100.0%			1	100.0%		15		100.0%											
		86																						

The results of the test show that the significance level is 0.790 which is bigger than the value given in the hypothesis i.e 0.05, hence we accept the truth of the hypothesis and assert that "there is no statistically

significant correlation in the 0.05 significance level between Grade and number of children.

3.8 State of Prostate Cancer and Age

To examine the truth of the hypothesis which states that "there is no statistically significant correlation in the 0.05 significance level between the stage and age, we applied chi-square test to the following Table (8) between the two variables

Table 8. Frequency distribution of subjects between the variables of stage and age

			Age						Total
			40-50 years	51-60 years	61-70 years	71-80 years	81-90 years	91 and more	
% Within Stage	1.6%	9.8%				1			1
		% within stage				100.0 %			100.0 %
	Localized (stage 1 for lymphoma)	Count		1	8	3	2		14
		% within stage		7.1%	57.1%	21.4%	14.3%		100.0 %
	Regional: Direct ext. (adjacent)	Count		1	8	12		2	23
		% within stage		4.3%	34.8%	52.2%		8.7%	100.0 %
	Regional: lumph node	Count					1		1
		% within stage					100.0 %		100.0 %
	Regional:dir	Count		1		1	2		4

	ect ext.& lumph node	% within stage		25.0%		25.0%	50.0%		100.0 %
	Distant metastasis nos (stage,3.4 lymphoma)	Count	1	6	22	22	10		61
					36.1%	36.1%	16.4%		100.0 %
	Unknown	Count	1	9	29	53	18	4	114
		% within stage	.9%	7.9%	25.4%	46.5%	15.8%	3.5%	100.0 %
Total		Count	2	18	67	92	33	6	218
		% within stage	.9%	8.3%	30.7%	42.2%	15.1%	2.8%	100.0 %

The results of the test show that the significance level is0.401 which is bigger than the value given in the hypothesis i.e 0.05, hence we accept the truth of the hypothesis and assert that "there is no statistically significant correlation in the 0.05 significance level between stage and age.

3.9 Stage of Prostate Cancer and City

To examine the truth of the hypothesis which states that "there is no statistically significant correlation in the 0.05 significance level between the stage and city, we applied chi-square test to the following Table (9) between the two variables

Table 9. Frequency distribution of subjects between the variables of stage and city

			City			
			North	south	unknown	Total
Stage	In Situ	Count		1		1
		% within stage		100.0%		100.0%
	Localized	Count	3	11		14
		% within stage	21.4%	78.6%		100.0%
	Regional:direct ext.(adjacent)	Count	6	17		23
		% within stage	26.1%	73.9%		100.0%
	Regional: lumph node	Count		1		1
		% within stage		100.0%		100.0%
	Regional:direct ext.& lumph node	Count	2	2		4
		% within stage	50.0%	50.0%		100.0%
	Distant metastasis (NOS)	Count	31	27	3	61
		% within stage	50.8%	44.3%	4.9%	100.0%
	Unknown	Count	44	57	13	114
		% within stage	38.6%	50.0%	11.4%	100.0%
Total		Count	86	116	16	218
		% within stage	39.4%	53.2%	7.3%	100.0%

The results of the test show that the significance level is 0.15 which is bigger than the value given in the hypothesis i.e 0.05, hence we accept the truth of the hypothesis and assert that "there is no statistically significant correlation in the 0.05 significance level between stage and city.

3.10 Stage of Prostate Cancer and Palce

To examine the truth of the hypothesis which states that "there is no statistically significant correlation in the 0.05 significance level between the stage and place, we applied chi-square test to the following Table (10) between the two variables

Table 10. Frequency distribution of subjects between the variables of stage and place

			place				Total
			City	village	camp	unknown	
Stage	In Situ	Count		1			1
		% within stage		100.0%			100.0 %
	Localized	Count	7	7			14
		% within stage	50.0 %	50.0%			100.0 %
	Regional:direct ext.(adjacent)	Count	12	10	1		23
		% within stage	52.2 %	43.5%	4.3%		100.0 %

	Regional: lumph node	Count	1				1
		% within stage	100.0%				100.0 %
	Regional:direct ext.& lumph node	Count	3	1			4
		% within stage	75.0 %	25.0%			100.0 %
	Distant metastasis (NOS)	Count	17	41		3	61
		% within stage	27.9 %	67.2%		4.9%	100.0 %
	Unknown	Count	61	37	3	13	114
		% within stage	53.5 %	32.5%	2.6%	11.4%	100.0 %
Total		Count	101	97	4	16	218
		% within stage	46.3 %	44.5%	1.8%	7.3%	100.0 %

The results of the test show that the significance level is 0.48 which is less than the value given in the hypothesis i.e 0.05, hence we dose not accept the truth of the hypothesis and assert that "there is statistically significant correlation in the 0.05 significance level between stage and place.

3.11 Stage of Prostate Cancer of Address

To examine the truth of the hypothesis which states that "there is no statistically significant correlation in the 0.05 significance level

between the stage and address, we applied chi-square test to the following Table (11) between the two variables

Table 11. Frequency distribution of subjects between the variables of stage and address

Stage			Address											
			Ramllah	Hebron	Nablus	Jenine	Jereco	B. lahem	Toalkarem	Qalqelea	Selfet	Joursiem	Unknown	Total
In Situ	Count							1						1
	% within stage							100.0%						100.0%
Localized	Count			5	1	1	1	5				1		14
	% within stage			35.7%	7.1%	7.1%	7.1%	35.7%				7.1%		100.0%
Regional:direct ext.(adjacent)	Count	2	8	2	2	1	7		1					23
	% within stage	8.7%	34.8%	8.7%	8.7%	4.3%	30.4%		4.3%					100.0%
Regional: lumph node	Count						1							1
	% within stage						100.0%							100.0%

		Unknown		distant metastasis (NOS)		Regional:direct ext.& lumph node		Total	
		Count	% within stage	Count	% within stage	Count	% within stage	Count	% within stage
Stage		16	8.8%	3	4.9%	1	25.0%	16	7.3%
		73	36.0%	18	29.5%	1	25.0%	73	33.5%
		47	23.7%	15	24.6%	2	50.0%	47	21.6%
		19	6.1%	9	14.8%			19	8.7%
		5	.9%	2	3.3%			5	2.3%
		27	7.0%	5	8.2%			27	12.4%
		5	2.6%	2	3.3%			5	2.3%
		3	1.8%					3	1.4%
		2		2	3.3%			2	.9%
		5	1.8%	2	3.3%			5	2.3%
		16	11.4%	3	4.9%			16	7.3%
Total		218	100.0%	61	100.0%	4	100.0%	218	100.0%

The results of the test show that the significance level is0.329 which is bigger than the value given in the hypothesis i.e 0.05, hence we accept the truth of the hypothesis and assert that "there is no statistically

significant correlation in the 0.05 significance level between stage and address.

3.12 Stage of Prostate Cancer and Smoking

To examine the truth of the hypothesis which states that "there is no statistically significant correlation in the 0.05 significance level between the stage and smoke, we applied chi-square test to the following Table (12) between the two variables

Table 12. Frequency distribution of subjects between the variables of stage and smoking

			Smoking				Total
			never	present	Past	Unknown	
Stage	In Situ	Count		1			1
		% within stage		100.0%			100.0 %
	Localized	Count	3	4	4	3	14
		% within stage	21.4%	28.6%	28.6%	21.4 %	100.0 %
	Regional:direct ext.(adjacent)	Count	5	7	3	8	23
		% within stage	21.7%	30.4%	13.0%	34.8 %	100.0 %
	Regional: lumph node	Count				1	1
		% within stage				100.0 %	100.0 %
	Regional:direct ext. & lumph node	Count		1	2	1	4
		% within stage		25.0%	50.0%	25.0 %	100.0 %

	Distant metastasis (NOS)	Count	13	20	7	21	61
		% within stage	21.3%	32.8%	11.5%	34.4 %	100.0 %
	Unknown	Count	9	2	2	101	114
		% within stage	7.9%	1.8%	1.8%	88.6 %	100.0 %
Total		Count	30	35	18	135	218
		% within stage	13.8%	16.1%	8.3%	61.9 %	100.0 %

The results of the test show that the significance level is0.000 which is less than the value given in the hypothesis i.e 0.05, hence we dose not accept the truth of the hypothesis and assert that "there is statistically significant correlation in the 0.05 significance level between stage and smoking.

3.13 Stage of Prosate Cancer and Occupation

To examine the truth of the hypothesis which states that "there is no statistically significant correlation in the 0.05 significance level between the stage and occupation, we applied chi-square test to the following Table (13) between the two variables

Table 13. Frequency distribution of subjects between the variables of stage and occupation

			Occupation							
			Clerical	Agriculture	manufacture	unknown	worker	without	other	Total
Stage	In Situ	Count		1						1
		% within stage		100.0%						100.0%
	Localized	Count	2	5	2	5				14
		% within stage	14.3%	35.7%	14.3%	35.7%				100.0%
	Regional:direct ext.(adjacent)	Count	1	3	1	11	4	2	1	23
		% within stage	4.3%	13.0%	4.3%	47.8%	17.4%	8.7%	4.3%	100.0%
	Regional:lumph node	Count				1				1
		% within stage				100.%				100.0%
	Regional:direct ext.& lumph node	Count		1	1	1	1			4
		% within stage		25.0%	25.0%	25.0%	25.0%			100.0%
	Distant metastasis (NOS)	Count	5	12	3	31	6	2	2	61
		% within stage	8.2%	19.7%	4.9%	50.8%	9.8%	3.3%	3.3%	100.0%
	Unknown	Count	1	3	1	103	3	1	2	114
		% within stage	.9%	2.6%	.9%	90.4%	2.6%	.9%	1.8%	100.0%
Total		Count	9	25	8	152	14	5	5	218
		% within stage	4.1%	11.5%	3.7%	69.7%	6.4%	2.3%	2.3%	100.0%

The results of the test show that the significance level is0.000 which is less than the value given in the hypothesis i.e 0.05, hence we dose not accept the truth of the hypothesis and assert that "there is statistically significant correlation in the 0.05 significance level between stage and occupation

3.14 Stage of Prostate Cancer and Number of Children

To examine the truth of the hypothesis which states that "there is no statistically significant correlation in the 0.05 significance level between the stage and number of child, we applied chi-square test to the following Table (14) between the two variables

Table 14. Frequency distribution of subjects between the variables of stage and number of children

			Number of Children															Total
			2	3	4	5	6	7	8	9	10	11	12	13	14	15	19	
Stage	Localized	Count		1		1			2	1	2	2		1				10
		% within stage		10.0%		10.0%			20.0%	10.0%	20.0%	20.0%		10.0%				100.0%
	Regional: Direct ext.(adjacent)	Count			2	2	3	2		3	2	1				2		17

		% within stage			11.8%	11.8%	17.6%	11.8%		17.6%	11.8%	5.9%				11.8%		100.0%
	Regional: Direct ext. & lumph node	Count							2		2							4
		% within stage							50.0%		50.0%							100.0%
	Distant metastasis (NOS)	Count	1	2	1	4	3	4	7	5	7	3	2	1	1		1	42
		% within stage	2.4%	4.8%	2.4%	9.5%	7.1%	9.5%	16.7%	11.9%	16.7%	7.1%	4.8%	2.4%	2.4%		2.4%	100.0%
	Unknown	Count		1		1	4		1	1	3							11
		% within stage		9.1%		9.1%	36.4%		9.1%	9.1%	27.3%							100.0%
Total		Count	1	4	3	8	10	6	12	10	16	6	2	2	1	2	1	84
		% within stage	1.2%	4.8%	3.6%	9.5%	11.9%	7.1%	14.3%	11.9%	19.0%	7.1%	2.4%	2.4%	1.2%	2.4%	1.2%	100.0%

The results of the test show that the significance level is 0.768 which is bigger than the value given in the hypothesis i.e 0.05, hence we accept the truth of the hypothesis and assert that "there is statistically no significant correlation in the 0.05 significance level between stage and number of children.

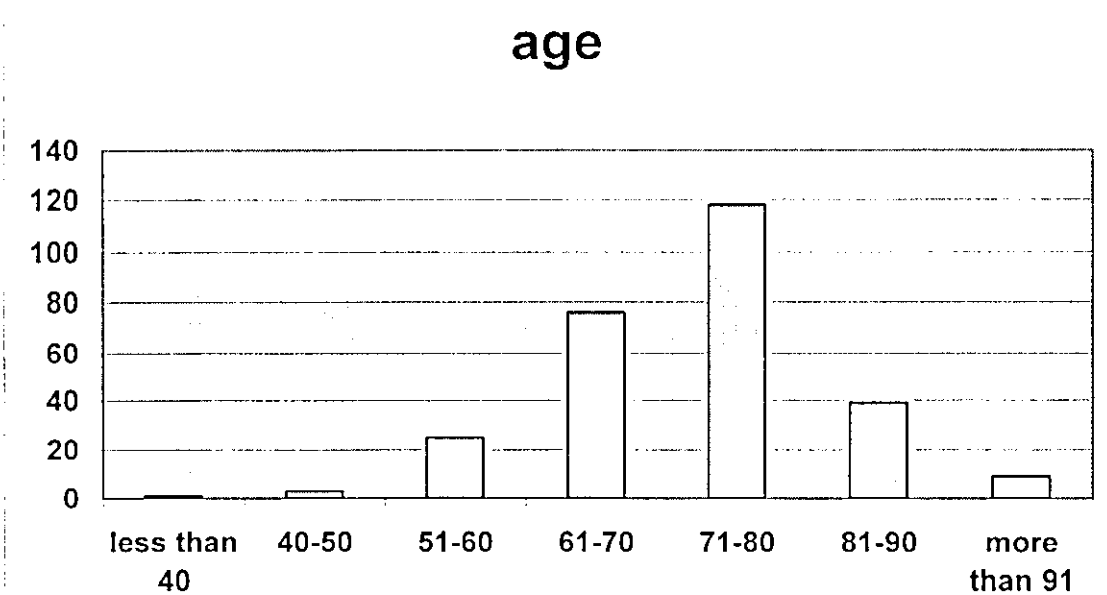
3.15 Distribution of Prosate Cancer Accordin to Age

Age is the most important risk factor for prostate cancer (Table 14 and Figure 1). Data from this table shown with remarkable consistency the incidence of prostate cancer is 118 between the age 71-80 years, 76 cases between 61-70 years, and 39 between 81-90 years, suggestion suggesting that the pathogenesis of prostate cancer may take decades, also the clinical diagnosis of prostate cancer increases directly with age. Before the age of 50, the diagnosis of prostate cancer is rare.

Table 15 Distribution of Prostate Cancer According to Age

Number	Age
1	less than 40
3	40-50
25	51-60
76	61-70
118	71-80
39	81-90
9	more than 91

Figure 1 Distribution of Prostate Cancer According to Age



3.16 Incidence of Prostate Cancer According to Place

271 cases of prostate cancer were reported from (1992-2002), For all cases of prostate cancer among Palestinian population in the west bank were 28.9 per 100.000 population. It's low rate in comparison with Jordan which is 72.9 par 100.000 (18) but high rate in comparison with Israel which is 15.5 per 100.000 (4). This is because the early detection and development of medical center which has a big role in the diagnosing g firstly infected (Table 15 and Figure 2).

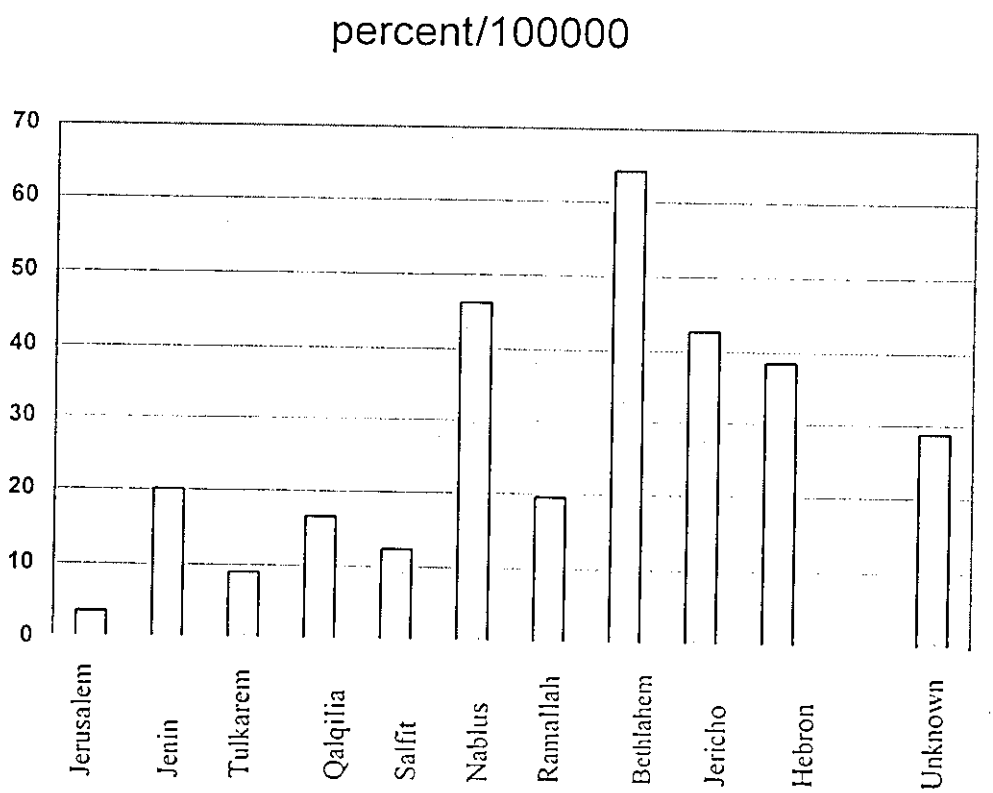
The highest incidence rates of the prostate cancer were found in Bethlahem and Nablus (46.2 and 46.1) per 100.000, followed by Jericho (42) per 100.000, hebron 38 per 100.000, where as Jerusalem is the lowest 3.5 per 100.000.

The lowest incidence in Jerusalem because u- consider part of Israel which has the same attention like other cities of Israel. But the highest incidence in Nablus and bethlahem because of the environmental factors which play some role in the geographic differences. But in Jericho and bethlahem than geographic difference the race play an important role because most its population is a black men which have high incident than weight men.

Table 16 Incidence of Prostate Cancer According to Place

Place	Number of infected	Number of mail	Percent per 100.000
Jerusalem	6	167434	3.5
Jenin	24	119280	20.1
Tulkarem	6	66766	8.9
Qalqillia	6	36049	16.6
Salfit	3	24227	12.3
Nablus	60	130071	46.1
Ramallah	21	106959	19.6
Bethlahem	44	68486	64.2
Jericho	7	16376	42.7
Hebron	78	202583	38.5
Unknown	16		
Total	271	938225	28.9

Figure 2 Incidence of Prostate Cancer According to Place



3.17 Incidence of Prostate Cancer According to Number of Children

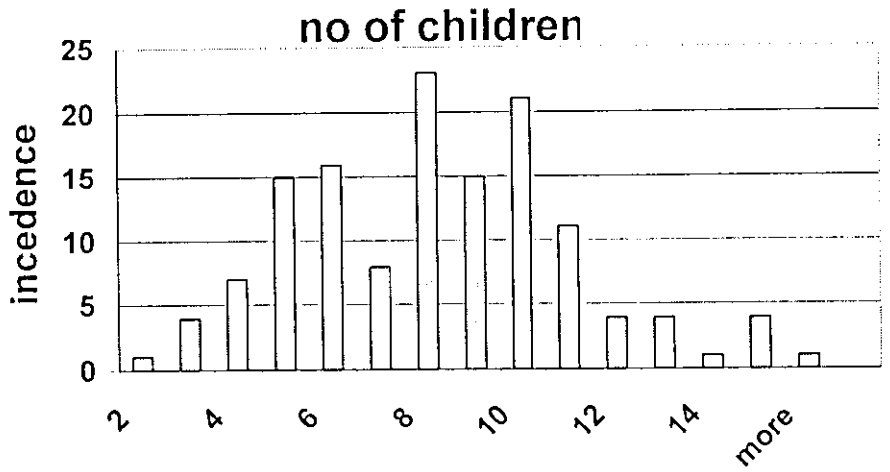
Number of children play clear role in having prostate cancer, that is men who have children from 4-11 have the highest incidence according to Table 17 and Figure 3.

There is a direct relationship between prostate cancer risk and the quartile of serum-free testosteron (97). Also, agerm- line variation in the androgen receptor gene was shown to be a significant predictor for aggressive prostate cancer in a prospective analysis, suggesting that differences in steroid hormone receptore may also play an important role in risk of prostate caner (97).

Table 17 Incidence of Prostate Cancer According to Number of Children

Number of children	Incidence
2	1
3	4
4	7
5	15
6	16
7	8
8	23
9	15
10	21
11	11
12	4
13	4
14	1
15	4
More	1

Figure 3 Incidence of Prostate Cancer According to Number of Children



3.18 Distribution of Prostate Cancer According to Occupation

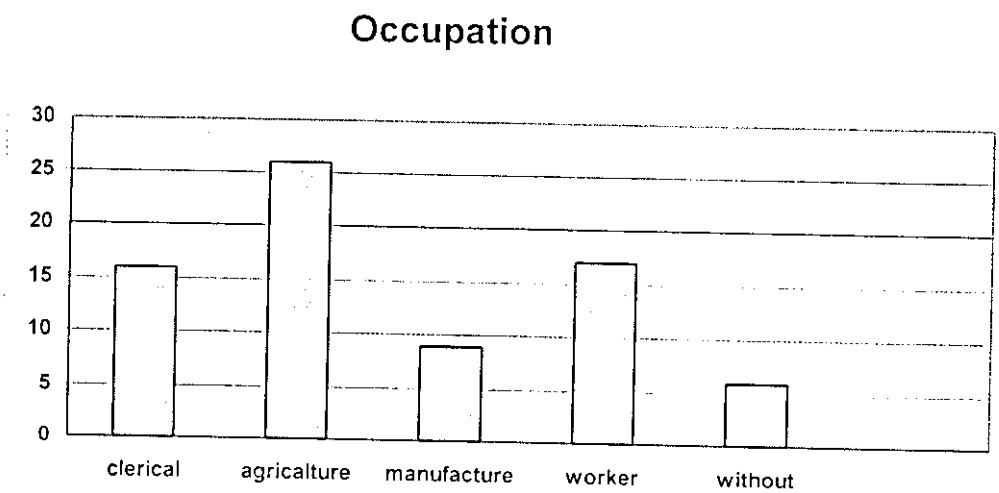
Higher rates of prostate cancer have been reborted in certain occupation. Table 18 and Figure 4 show that the agricalture have the highest incedence (26) case, I beleve that there is because agricultural men rerley make early detection. And because of using pesticide for crops.

For worker and clerical have 17 and 16 respectively which is lowest that agriculture may be due to hormonal secreation because of stress and hardworking comparison with men whom are without working.

Table 18 Distribution of Prostate Cancer According to Occupation

Occupation	Number
Clerical	16
Agriculture	26
Manufacture	9
Worker	17
Without	6

Figure 4 Distribution of Prostate Cancer According to Occupation



Conclusion

1) There is statically significant correlation between grade and city.

2) There is statically significant correlation between stage and place.

3) There is statically significant correlation between stage and smoke.

4) There is statically significant correlation between stage and occupation.

5) There are highly precent of prostate cancer in Nablus, Bethlahem, but low in Jerusalem.

6) from age 71-80 and age 61-70 have the highest incedence (76) and (39) respectively.

7) Prostate cancer in the west bank is 28.9 per 100.000 populatiom.

8) Agricultural occupation has the highest incedence.

9) Number of children play role in having prostae cancer whom have children from 4-11.

References

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توزيع سرطان البروستات في الضفة الغربية / فلسطين

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الملخص

في هذا البحث تم جمع 271 عينه من شمال وجنوب الضفة الغربية – (المستشفى الوطني ومستشفى بيت جالا) ، جميع العينات تم تشخيصها على انها مصابة بسرطان البروستات في مراحل ومستويات مختلفة.

تم فحص العلاقة بين كل من مستوى الاصابة ومرحلة الاصابة مع العمر، المدينة، الموقع، العنوان، التدخين، المهنة وعدد الأطفال.

وقد لوحظ انه هناك علاقة احصائية بين المستوى للاصابة بالمرض مع المدن ، التدخين وايضا بين مرحلة الاصابة مع المواقع ، التدخين والمهنة إضافة الى عدد الاطفال .

هذا وقد لوحظ ان نسبة الاصابة بالمرض منتشرة في بيت لحم و نابلس ومن ثم اريحا واما اقل اصابة فكانت في القدس.