In vitro: prevalence of the prostate cancer in the western Libya

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الخلاصة :

سرطان البروستاتا من الإمراض التي تصيب غدة البروستاتا غالبا في الأعمار الأكبر من 50 سنة ويعتبر من الامراض التي بدون اعراض؛ كما انه خامس الإمراض الأكثر شيوعا بين الرجال، وتهدف هذه الدراسة إلى معرفة مدى انتشار سرطان البروستاتا في المنطقة الغربية من ليبيا وعلاقته بمجموعة من العوامل مثل العمر والغذاء والوراثة.

تم تجميع 500 عينة دم من الذكور الذين تتراوح أعمارهم من (45 – 90) سنة في المركز القومي لعلاج الأورام بصبراتة ؛ وتم تحليلها للتأكد من ايجابية النتائج بواسطة نظام (الاليزا) (Axsym) Automated ELISA system Abbott وجمعت كل المعلومات عن الحالات من خلال نماذج استبيان شامل لكل ما هو مطلوب من معلومات ذات العلاقة بالبحث.

أظهرت هذه الدراسة أن نسبة الإصابة بسرطان البروستاتا تزداد بزيادة العمر حيث بلغت (65.6%) فيما بين الفئة العمرية (60 - 79) سنة في حين بلغت (77.7 %) لدى الفئة العمرية (90 - 80) سبة عند PSA > 4ng/ml ولكن النتائج السالبة عندPSA > 4 ng/ml ولدى نفس الفئات العمرية (34.4%)، (22.3%) كما بينت النتائج الإحصائية وجود فروق دالة إحصائيا بين الإصابة والنظام الغذائي حيث ازدادت بزيادة تناول اللحوم الحمراء(74.3 %) عند PSA > 4ng / ml ؛وتقل بانخفاض التناول الى (32.3%)عندما PSA > 4 ml / ng،وتنخفض لدى مستهلكي اللحوم البيضاء بنسبة (56.8%)، وأشارت إلى ارتفاع معدلات الإصابة لدى الأشخاص متناولي الألبان ومشتقاتها (75.4 %) مما يدل على وجود فروق معنوية (P = 0.000)، وكذلك إلى وجود علاقة بين الإصابة وتناول الخضراوات والفواكه فتقل نسبة الإصابة بمعدل (32.9 %) لذا بينت النتائج الإحصائية وجود فروق دالة إحصائيا بين الإصابة وهذا العامل (P= 0.000)وعوامل اخرى مثل تناول الاسماك.

كما وجد في هذه الدراسة ارتباط العامل الوراثي بمشكلة سرطان البروستاتا فكانت نسبة الاصابة (69.4%) حالة لديهم تاريخ وراثي عند PSA < 4ng / ml.

ABSTRACT:

   Prostate cancer is a disease that affects the prostate gland with age among people over 50 years , without symptoms and is the fifth most common malignant disease among men,. The aim of this study was to investigate the prevalence of prostate cancer in the western region of Libya and several other factors as age, diets and Family history

500 blood samples were collected from males aged (45 - 90) years At National Institute for Oncology Sabratha for the treatment of tumors, the analysis by automated ELISA system Abbott (Axsym). This study showed that the incidence of prostate cancer increases with age, it showed that (65.6 %) of (60 – 79 year) and (77.7%) of the age (80 – 90) year were suffering from prostate cancer at PSA > 4ng / ml, but (34.4 %) and (22.3 %) at PSA < 4 ng / ml for the same category of age .

The statistical results showed that there are significant differences between the risk and the diet where it increases with increasing consumption of red meat (74.3%) and decrease by low intake (32. 3%) at PSA > 4ng / ml but PSA < 4ng / ml. Decrease for lower consumers of white meat (56. 8%), and pointed out the highest rates of infection among person's drinker milk and dairy products (75.4%),by statistical results there are significant differences between the risk and eating vegetables (P = 0.000) where the study pointed out that the percent of incidence (32. 9 %) among those more consumption of vegetables, in addition, other factors as eating fish. And this study show the relation between prostate cancer and screened cases with previous family history. Where it showed that the percent was (69.4%)with PSA > 4 ng / ml. There are significant differences between the risk and family history (P = 0.860) .

INTRODUCTION :

   Cancer is made up of cells that do not grow normally cause death may affect lung or brain or glandes as prostate gland (Mary and Hagstad, 2009). The prostate gland starts to develop before birth and continues to grow until reaches the size of a marble, then undergoes rapid growth spurts during puberty and reaches the size of a walnut in adolescence (William, 1991). Prostate cancer is made up of cells that do not grow normally the cells divide and create new cells that the body does not need, forming a mass of tissue called a tumor. Tumor divided into two types malignant and benign.

In fact , autopsy studies have shown that many older men and even some younger men who died of other diseases also have had prostate cancer that never affected them during their lives, in previous studies, it has been shown that 70 % to 90 % of the men had cancer in their prostate by age 80, but in many cases neither they nor their doctors even knew they had it, prostate cancer begins with a pre-cancerous condition called prostatic intraepithelial neoplasia (PIN), (Dan Theodorescu and Krupski, 2009).

In older men, the average age when Benign prostatic hyperplasia BPH is diagnosed 67 or over the age of 50, the inner part of the prostate (around the urethra) often keeps growing leading to a common condition called benign prostatic hypertrophy (BPH), or enlarged prostate and it can press on the urethra, leading to problems passing urine although BPH can be a serious medical problem; it is not a cancer (Berges *et al.,* 2000). The growth is fueled by male hormones called (androgens) in the body; essentially all men with circulating androgens will develop microscopic prostate cancer if they live long enough (Bostwick *et al.,* 2004).

The main androgen, testosterone, is a tumor promoter and would predict, that prostate cancer risk should be increased in men with higher levels of testosterone (Shirai *et al.,* 2002). Prostate specific antigen (PSA) is a protein serine protease produced by the prostate gland that may be present at elevated levels in patients with cancer or other diseases of prostate, it has been estimated that each gram of prostate cancer tissue elevates PSA by about 3.5 ng/ ml in serum, but normal value of PSA was 4 ng / ml (Harry and Stephen, 2001).

The previous studies have shown different incidence in the different countries.

In U.S.A. most incidence rates were 20 - 30 % although some variation exist the positive value of PSA ranged from 6 % for those aged 40 to 49 years to 59 % for those aged 70 to 79 years (Muta *et al.,* 2006).

Cancer is most common in older men, in U.K. less than 30 % of cases in men under 50 year and 70 % over 85 year (Searl *et al.,* 2006).

In Libya, prostate cancer is the fifth most common cancer in men (El-Mistiri *et al.,* 2003). The first report from Benghazi Cancer Registry, provides data on cancer incidence in eastern Libya.

From National Institute for Oncology Sabratha (Buhmeida *et al.,* 2006) showed that 86 % of all cases occur in patients aged more than 60 years.

Prostate cancer is the most common cancer and the second leading cause of cancer deaths in men. The incidence of prostate cancer continues to rise. Roughly 220,800 men were expected to be newly diagnosed with prostate cancer by (Siegel *et al*., 2015). As the population ages and overall life expectancy increases, prostate cancer is likely to become a growing health care burden, especially because prostate cancer is primarily a disease of elderly males. Prostate cancer incidence and mortality rates are strongly related to the age with the highest incidence being seen in elderly men (> 65 years of age). (Bray *et al.,* 2018).

Age-standardized incidence rates of PCa had also increased from about 9 per 100,000 in 1999 to over 25 per 100,000 in 2011 In patients over old, PCa incidence has continuously increased. Nearly 80% of PCa patients were over 65 years old in 2014. The incidence and prevalence of PCa have continuously increased (Hyun *et al.,* 2019). Incidence for regional- and distant-stage disease increased in both age groups during the study period. For example, distant-stage incidence in men aged 75 years and older increased by 5.2% (95% CI = 4.2 % to 6.1%) per year from 2010 to 2016 (Ahmedin *et al. ,* 2020).

It is widely known that the incidence of and mortality from prostate cancer increases with age and prostate cancer is the second leading cause of death from cancer for men in their eighties , Of the 116,796 men in the study,18.7% died of prostate cancer.

The median age of death from prostate cancer was 79.5 years (Miller *et al.,* 2022).

Growing research also showed the correlation between diet and the occurrence of prostate cancer, study in Italy indicates that the benefit correlate with eating of white meat as 1.7 % for 166 cases by (Talamini *et al.,* 1986).

Also study in Sweden showed that low intake of vegetables and fruits were associated with a 50% increased risk of prostate cancer (Chan *et al.,* 1999).

But other study in Palestine showed that the higher prevalence of prostate cancer was observed during(1992 - 2002) 28.9 % in a study of 51.000 cases, a positive association was seen between the of advanced prostate cancer and intake of red meat and animal fat (Sharaf, *et al.,* 2006) A consumption of red meat was increased the risk by 28 % incidence - 35 % in Washington (Jeanine and Anita 2007).

Other study in University of California, conducted among 10,313 prostate cancer patients, of whom 1102 patients were advanced and 419 were diagnosed with fatal disease, showed that participants who consumed more than 66.1 g of red meat per 1000 kcal had an increased (by 12%) risk of all prostate cancer compared to patients who reported red meat intake below 11.6 g/1000 kcal (multivariate HR = 1.12, 95 % CI = 1.04 - 1.21). The association was stronger for advanced disease, with a more than 30% higher risk observed among men consuming meat at significant amounts compared to those consuming small amounts (multivariate HR = 1.31, 95 % CI = 1.05 - 1.65) (Michał *et al.,* 2021). In previous study low consumption of fish increase risk of prostate cancer by 69 % in California (Li-Qiang *et al.,* 2007). Dairy foods was also linked to prostate cancer, in Chicago high consuming of milk has elevating the risk of aggressive prostate cancer by 63 % , this due to high content of fat (Smith, 2009). Numerous cohort and case-control studies report that increased dietary fat intake is associated with PCa risk, although other studies showed no association.

Additionally, the relationship between total fat consumption and PCa is controversial. A population-based case-control study of 1,300 men aged < 60 years in the United Kingdom reported that the risk of PCa increased among those with higher lipid intake as compared with those with lower lipid intake. By contrast, basic research studies repeatedly show that fat consumption induces PCa growth, with several mechanisms identified as promoters of PCa development and progression in subjects fed a high-fat diet (HFD) (Makoto *et al.,* 2020).

Study shows that an unhealthy dietary pattern was associated with increased risk of prostate cancer. The association between fat intake and prostate cancer risk has been extensively studied for many years and still remains controversial.

Dietary fat intake, depending on its quality and quantity, can result in a two-fold increase in the risk of individual stages of prostate cancer. Study, which enrolled 288,268 men and 23,281 prostate cancer cases with an observation period of nine years, found that a high intake of SFAs (at least 13.3% of total energy intake) compared with individuals consuming SFAs at the lowest level (below 5.8% of total energy) were characterized by a higher risk of advanced or fatal prostate cancer cases

(Michał *et al.,* 2021). Other study in U.S.A.(University of Texas) show that, among 2,381 participants with available dietary data, 82 reported a diagnosis of cancer. Participants who met recommendations of 5 or more servings of fruit and vegetable per day had a significantly 86% lower risk for reported cancer compared with those who did not meet recommendations, after adjusting for other covariates. Every portion increment of total fruit and vegetable intake was significantly associated with the reduced cancer risk by 11% with the adjustment of other covariates (Shenghui *et al.,* 2019). In Copenhagen, Denmark 1690 prostate cancer cases were identified through 2012. Of these, 1042 had a Gleason score of 7 or above and 498 had a Gleason score of 8 or above at the time of diagnosis; 364 died (n=228 from prostate cancer) during follow-up through 2013. Cox proportional hazard models were used for the statistical analyses. No association between any type of fish intake and risk of total prostate cancer or high-grade prostate cancer (Gleason score≥7 or ≥8) was found. For all-cause mortality, we found no association for any type of fish intake. For prostate cancer-specific mortality, only a higher intake of fatty fish was associated with a higher mortality (Outzen, *et al.,* 2018).

The risk of prostate cancer may also increase in men who inherited a faulty gene of breast cancer from their mothers (Chen and Parmigiani, 2007).

Risk of prostate cancer increase for men with a positive family history, especially if any first degree relative have been affected(Bruner et al., 2003)

Family history was defined as either positive or negative; 920 of the 5519 men (16.7%) had a family history of prostate cancer, it is clear that any family history of prostate cancer places a man at increased risk of developing the disease himself (Sun J. *et al .,* 2010) .

Prostate cancer is among the most heritable cancers, and twin studies estimate that 57% of the variation in risk can be attributed to genetic factors. Men with a brother or father diagnosed with prostate cancer have 2 to 4 - fold greater risk of developing prostate cancer (Lauren *et al .,* 2018).

Positive FH of PC was associated with increased tumor aggressiveness in black men of 1,225 men,323 had a FH of PC and 652 men were diagnosed with PC on biopsy, FH was associated with increased odds of high-grade PC (Kimberly *et al .,* 2020).

During 20 years of follow-up, 1,915 prostate cancer and 166 fatal prostate cancer events were observed. Men in the top PRS (Polygenic risk scores) quartile with a family history of prostate or breast cancer had the highest rate of prostate cancer. Compared with men at lowest genetic risk (Anna Plym *et al* ., 2020).

Materials and Methods:

Study design and Site:

Blood samples were randomly collected from patients at National Institute for Oncology, Sabratha Libya, from 2021 to 2022, sample about 3 ml of venous blood were taken by venipuncture in serum - separated tube or gel tube and centrifuge for obtained serum.

Preparation of sample for analyses:

1 -Human sample of blood collected in special tube called serum separator tubes.

2- After formation of complete clot before centrifugation, the range for clotting time from 4 - 10 minutes, some specimen from patient who receives anticoagulant drugs may exhibit it increase - clotting time.

3- For a good result, specimens should be free of fibrin, red blood cells.than stored into labeled sterile tubes and frozen at(-20°C) until analyzed. Serological analysis was performed by automated close ELISA system Abbott (Axsym) which is capable of processing 100 test at once and it consists of two sampling center and processing center in which steps of analyses occur.

The statistical analysis:

Data were analyzed using SPSS version 15.0 (statistical package for social science) program, statistical significance for all data were calculated by chi - square test ,the P - value of $< 0.05$was considered to be significant.

Questionnaire and consent:

The data and case history was attained through interviewing the patients more information was obtained through a constructed questionnaire, which contain personal information for adult males including Age, Diet, Family history.

Results :

Among 500 samples, collected there were 344 samples positive with PSA (68.8%)when PSA>4ng /ml. Whereas negative samples156 cases (31.2%) at PSA <

4ng / ml. In this study age groups divide into three categories, as in tables (1), and the percent of high positive PSA (66.7%),(65.6%) and a much higher percentage of positivity were detected among the older age group was(77.7%). The statistical analyses of data correlating the age with PSA levels which carried out by using Chi - square (x^2) test,(P-value = 0.039) then it was significant difference.

This study revealed high level of PSA among patients usually consuming large quantities of red meat (74.3 %) in contrast, patients of low consumption only (32.3%) with positive level of PSA as in table (2) By Chi - square (x^2) test, there was significant difference (P-value = 0. 000) Moreover (56.8 %) of high white meat consumers and positive level of PSA > 4ng /ml، but low white meat consumption (76. 7%) as in table (3).

By Chi - square (x^2) test, there was significant difference (P-value =0. 000)

In correlation between PSA levels and fish consumption among screened population it has been found that high consumers of fish (33.5%) showing low level of PSA, but low consumers were showing high level of PSA in their blood samples (73 .1%) as in table (4).There was no significant correlation by Chi- square (x^2) test,(P-value =0. 124).

Of those consuming more milk quantities (75.4%) of patients showed positive level of PSA > 4ng /ml، however، (39.3%) of the low quantities consumers decrease level of PSA < 4ng / ml as in table (5). But by Chi - square (x^2) test, of ،(P-value =0. 000) there was significant correlation between dairy product and PSA.

Low vegetables consumption and level of the PSA among the screened patients، was (74.9%) showed high level of PSA، but of high vegetables consumers (32.9%) low level of PSA as in table (6). Chi – square analyses of data studying the relationship between PSA، and consumption of vegetables was found to be significant، and (P - value = 0. 000). The results, which study relation between PSA and screened cases with previous family history then the percent was 30.6 %,of 41/134 cases with low level of PSA< 4ng /ml and 69.4% of 93/134 cases with PSA > 4 ng / ml. However, the case showed that no past family history 251 / 366 cases (68.6 %) among cases showing high levels of PSA and 115 / 366 cases (31.4 %) at low level of PSA as in a table (7). The statistical analyses of data correlating the history factor with the value of PSA was carried out by the Chi - square (x^2) test، (P- value = 0.860) there was no

significant relationship between PSA & past family history. This study was conducted to identify the prevalence of prostate cancer in the western Libya¸ since the results may be useful to other working in this field.

Table (1) showed the PSA level in relation to age.

PSA*Age Cross tabulation (1)

PSA = ng /ml	Groups			Total
	45-59	**60-79**	**80-90**	
PSA< 4 Count% within	9 33.3%	118 34.4%	29 22.3%	156 31.2%
PSA > 4 Count% within	18 66.7 %	225 65.6%	101 77.7%	344 68.8%
% Of the total samples	27 100%	343 100%	130 100%	500 100%

p-Value =0.039

Table (2) showed the PSA level in relation to red meat .
PSA*Red meat Cross tabulation (2)

PSA=ng/ml	Red meat		Total
	Low	**More**	
PSA< 4 Count%	44 67.7%	112 25.7%	156 31.2%
PSA > 4Count%	21 32.3%	323 74.3%	344 68.8%
% Of the total samples	65 100%	435 100%	500 100%

P- Value = 0.000

Table (3) showed the PSA level in relation to white meat
PSA* white meat Cross tabulation(4)

PSA = ng/ml	white meat		Total
	Low	**More**	
PSA< 4 Count%	70 23. 3 %	86 43.2 %	156 31.2%
PSA > 4Count%	231 76.7%	113 56.8%	344 68.8%
% Of the total samples	301 100%	199 100%	500 100%

P- Value = 0.000

Table (4) showed the PSA level in relation to Fish.

PSA* Fish Cross tabulation(4)

PSA = ng/ml	Fish		Total
	Yes	No	
PSA< 4 Count%	47 26. 9 %	109 33. 5%	156 31.2%
PSA > 4Count%	128 73.1%	216 66.5%	344 68.8%
% Of the total samples	175 100%	325 100%	500 100%

P- Value = 0.124

Table (5) showed the PSA level in relation to Milk.

PSA* Milk Cross tabulation (5)

PSA = ng /ml	Milk		Total
	Low	More	
PSA< 4 Count%	88 39. 3 %	68 24. 6%	156 31.2%
PSA > 4Count%	136 60.7%	208 75.4%	344 68.8%
% Of the total samples	224 100%	276 100%	500 100%

P- Value = 0.00

Table (6) showed the PSA level in relation to Vegetable.

PSA* Vegetable Cross tabulation (6)

PSA = ng/ml	Vegetable		Total
	Low	More	
PSA< 4 Count%	107 25.1 %	49 67. 1%	156 31.2%
PSA > 4Count%	320 74.9%	24 32.9 %	344 68.8%
% Of the total samples	427 100%	73 100%	500 100%

P- Value = 0.00

Table (7) showed the PSA level in relation to Family history

PSA* Family history Cross tabulation (7)

PSA =ng/ml	History		Total
	Yes	No	
PSA< 4 Count%	41 30.6%	115 31.4%	156 31.2%
PSA>4 Count%	93 69.4%	251 68.6%	344 68.8%
% Of the total samples	134 26.8%	366 73.2%	500 100%

P- Value = 0.860

DISSCUTION:

According to the information available in previous studies regarding the extent of spread of prostate cancer and the role of many factors in the west area of Libya as some studies carried out previously in the eastern part was recorded in Benghazi hospital and its environs (El - Mistiri *et al.,* 2003).

Age:

The current study showed that the prevalence of the prostate cancer was (68.8%) for the number of 344/500 cases PSA > 4 ng / ml of all age categories from (45 - 59), 66.7% for 18/27 cases, (60- 79) 65.6% for 225/343 cases and (80 - 90) 77.7% for 101/130 cases, but PSA lower than 4 ng/ml 31.2% for the number of 156/500 cases for all age categories from (45 - 59) 33.3% for 9/27 cases, (60 - 79) 34.4% for 118/343 cases and (80 - 90) 22.3% for 29/130 cases.

This studies showed that the incidence of prostate cancer was very high, and not compatible with the rates recorded earlier in other studies at the study area. As well as in the western region recordings from National Institute for Oncology, Sabratha Libya, (Buhmeida *et al.,* 2006) showed that 86 % of all cases occur in patients aged more than 60 years; compatible with this study.

Indeed it was the first study in Libya performed to find the prevalence of the problem described and compared PSA with the level of seriousness of the problem related with factors as regarding the prevalence according to age, There are other studies reported similar rates and different in some other countries.

In Tunisia (33%) for 29 cases, age over 50 years, PSA< 4ng/ml agrees with this study by (Khouaja, K. *et al.,* 2005).

In Palestine age from (40 - 59) 15.4 %,(60 - 70) 26.9 % and more than (70) 57.7% by (Sharaf *et al.,* 2006) disagree with this study.

In U.K. cancer is most common in older men, 70% in men aged over 85year and less than 30% for men under 50 (Searl *et al.,* 2006) compatible with this study.

In United States the positive value of PSA ranged from 6% for those aged (40 - 49) years to 59% for those aged (70 - 79) years by (Muta *et al.,* 2006) agree with this study.

Other study in U.K. Prostate cancer incidence and mortality rates are strongly related to the age with the highest incidence being seen in elderly men (> 65 years of age) agree with this study (Bray *et al.,* 2018).

In South Korea nearly 80% of PCa patients were over 65 years old in 2014. The incidence and prevalence of PCa have continuously increased compatible with this study (Hyun *et al.,* 2019).

In United States, incidence for regional- and distant-stage disease increased in both age groups during the study period. For example, distant-stage incidence in men aged 75 years and older increased by 5.2% (95% CI = 4.2% to 6.1%) per year from 2010 to 2016 disagree with this study (Ahmedin *et al.,* 2020).

In; U.K. Scardino reported that almost 30% of men over 50 years of age, who died for causes other than prostate cancer, were found with histological evidence of prostate cancer at the moment of autopsy disagree with this study (Orzechowska *et al.,* 2022)

Red & white meat & fish and dairy products :

Red and white meat this study show increase risk by high intake of red meat (74.3%) however, decrease risk by low intake (32.3%) at positive level of PSA, while for white meat decrease risk by more consumption and increase by low intake respectively (56.8%) (76.7%).

In this study correlation between PSA levels and fish consumption were low consumers of fish, of which 216/325 case (66.5 %) and 128/175case (73.1%) showing positive level of PSA. In contrast, 109 / 325 case (33.5 %) were negative level of PSA group and 175 / 500 case (35 %) of patients were shown to be high consumers.

Milk and dairy products in this study the risk decrease by low consumption (60.7%)and increase by about (75.4%) by high consumption.

In Palestine study showed that high prevalence of prostate cancer was 28.9 % due to high intake of red meat, and animal fat (Sharaf *et al.,* 2006) not agree with this study.

A study indicates that the risk decrease with eating of white meat as in Italy 1.7% by (Talamini *et al.,* 1986) disagree with this study.

In Japan study showed 2% by (Mishina *et al.,* 1985) due to consumption of red meat not compatible with this study.

Other study in University of California, conducted among 10,313 prostate cancer patients, of whom 1102 patients were advanced and 419 were diagnosed with fatal disease, showed that participants who consumed more than 66.1 g of red meat per 1000 kcal had an increased (by 12%) risk of all prostate cancer compared to patients who reported red meat intake below 11.6 g/1000 kcal (multivariate HR = 1.12, 95% CI = 1.04–1.21). The association was stronger for advanced disease, with a more than 30% higher risk observed among men consuming meat at significant amounts compared to those consuming small amounts (multivariate HR = 1.31, 95% CI = 1.05–1.65) disagree with this study (Michał   et al., 2021).

In previous study low consumption of fish increase risk of prostate cancer by 69% in California (Li - Qiang et al., 2007) agree with this study which show elevate and decrease rate of disease by (73.1%) , (35 %) respectively.

Recently, a study in Japan found that the highest intake of fish had lower risk of prostate cancer by 29 % (Victoria   et al., 2009) no agreement with this study.

In Danish; 1042 had a Gleason score of 7 or above and 498 had a Gleason score of 8 or above at the time of diagnosis; 364 died (n=228 from prostate cancer) during follow-up through 2013. Cox proportional hazard models were used for the statistical analyses. No association between any type of fish intake and risk of total prostate cancer or high-grade prostate cancer (Gleason score≥7 or ≥8) was found. For all-cause mortality, only a higher intake of fatty fish was associated with a higher mortality (per daily 25 g) increment in intake (mortality rate؛ ratio=1.27; 95% confidence interval [1.04–1.55; P=0.02)] compatible with this study (Outzen et al., 2018).

In Chicago study showed that high consumption of milk elevate the risk of aggressive prostate cancer by 63 % (Smith, 2009) there were compatibility between two studies.

High consumption of dairy products was associated with a 50 % increased risk of prostate cancer in Sweden by (Chan et al., 1999) nearly close to this study.

By contrast, basic research studies repeatedly show that fat consumption induces P.Ca growth, with several mechanisms identified as promoters of P.Ca development and progression in subjects fed a high-fat diet (HFD). (Makoto Matsushita et al., 2020).

In U.S.A.study show that 288,268 men and 23,281 prostate cancer cases with an observation period of nine years, found that a high intake of SFAs (at least 13.3% of

total energy intake) compared with individuals consuming SFAs at the lowest level (below 5.8% of total energy) were characterized by a higher risk of advanced or fatal prostate cancer cases disagree with this study (Michal *et al.,* 2021).

Vegetables and Fruit :

This study show correlation between vegetables consumption and levels of the PSA among the screened patients, it has been found that most patients were low vegetables consumers (74.9 %) showed positive level of PSA and (32.9 %) when PSA more than 4ng / ml.

In Taiwan, this study shows increase risk by (74.9%) of low intake, but high consumption decrease by (32.9%). And indicates that high consumption of vegetables decrease risk by 32.2% compatible with this study. (Sung, et al., 1999)

In previous study low consumption of vegetables increase risk of prostate cancer by 80% from California closes to this study (Li - Qiang *et al.,* 2007).

University of Texas, participants who reported 5 or more servings of fruit and vegetable per day had a significantly 86% cancer compared with those who did not meet recommendations, after adjusting for other covariates. Every portion increment of total fruit and vegetable intake was significantly associated with the reduced cancer risk by 11% with the adjustment of other covariates agree with this study (Shenghui *et al.,* 2019).

Family history :

Family history of prostate cancer is one of the strongest known risk factors for this disease, the current study showed that 93/134 cases (69.4%) have a family history, while 251/366 cases (68.6%) have no family history in the studied samples for positive PSA. However; percent of PSA at negative level (30.6%) 41/134 cases (31.4%) 115/366 with and without family history respectively.

In Palestine has been found the highest percent of prostate cancers observed in study of families were 14.1 % of (78) cases with first - degree relatives not agree with this study (Sharaf *et al.,* 2006) due to difference in assessment.

In study of (139) first - degree relatives of men with prostate cancer, of 105 men who knew about their familial risk, only 62% believed that they were at higher risk in California (Bloom *et al.,* 2010) compatible with this study may be they use the same techniques.

In U. K. study of Prostate cancer is among the most heritable cancers, and twin studies estimate that 57% of the variation in risk can be attributed to genetic factors. Men with a brother or father diagnosed with prostate cancer have 2 to 4 - fold greater risk of developing prostate cancer agree with this study (Lauren Barber *et al.,* 2018).

Other study show that; Positive FH of PC was associated with increased tumor aggressiveness of 1,225 men 323 had a FH of PC with 26.46 % and 652 men were diagnosed with PC on biopsy, FH was associated with increased odds of high-grade P.C. agree with this study at negative level (Kimberly *et al.,* 2021).

Conclusion:

The finding of this and other studies showed a significant association between the increase prevalence of the prostate cancer and it's prognosis and several cofactors including age, diet, family history.

References:

1 - Michał Oczkowski,* Katarzyna Dziendzikowska, Anna Pasternak-Winiarska, Dariusz Włodarek, and Joanna Gromadzka-Ostrowska : Nutrients. 2021 Feb; 13(2): 496. Published online 2021 Feb. Dietary Factors and Prostate Cancer Development, Progression, and Reduction.

2 - Lauren Barber,1,2 Travis Gerke,1,3 Sarah C. Markt,1 Samuel F. Peisch,1 Kathryn M. Wilson,1,4 Thomas Ahearn,1,5 Edward Giovannucci,1,4,6 Giovanni Parmigiani,1,7,8 and Lorelei A.Mucci1,4

Clin Cancer Res. 2018 Dec 1; 24(23): 5910–5917. Published online 2018 Aug 6. Family history of breast or prostate cancer and prostate cancer risk

3-Bostwick, D. G.; Burke, H. B.; Djakiew, D.; Euling, S.; Landolph, J.;Morrison,H.;Sonawane,B.;Shifflett,T.;Waters,D. J. & Timms, B. (2004): Human prostate cancer risk factors, 101 *Suppl.* (10): 2371 - 490.

4- Buhmeida, A.; Pyrhönen, S.; Laato, M & Collan,Y. (2006): Prognostic factors in prostate cancer. *Diagn. Pathol.* 3:1 - 4.

5 - Chan, J. M.; Stampfer, M. J.; Ma, J.; Rimm, E. B.;Willett, W. C. & Giovannucci, E. L. (1999): Supplemental vitamin *E* intake and prostate cancer risk in a large cohort of men in the *United States*, *Cancer Epi. Bio. Prev.* 8:893 – 9.

6 - Sun J, Kader AK, Hsu FC et al - Inherited genetic markers discovered to date are able to identify a significant number of men at considerably elevated risk for prostate cancer ahead of print]. DOI: Pup 2010.

7 - El - Mistiri, M.; Verdecchia, A.; Rashid, I.; El - Sahli, N.; El - Mangush, M. & Federico, M. (2003): Cancer incidence in eastern Libya, the first report from the Benghazi Cancer Registry, *vol. Issue* 120 (2): 392 – 397.

8 - Harry, P.; Stephen, B. S. (2001): The Clinical Stage, its Definition and Importance in Prostate Cancer, *Vol.* 3: *Pp.*1.

9 - Jeanine, M.; G. & Anita, K. (2007): Meat Consumption and Cancer Risk, *Vol. Issue* 4 (12): 345 - 46.

10 - Khouaja, K.; Ben-Sorba, N.; Bouslama, A.; Youssef, A. &Taher, M. A. (2005): an experience of individual and early diagnosis of prostate cancer in a Tunisian centre, *vol. issue* 15 (2):Pp. 255 - 9.

11 - Li-Qiang, Q.; Jia-Ying, Xu.; Pei-Yu, W.; Jian, T. & Kazuhiko, H. (2007): Milk consumption is a risk factor for prostate cancer in Western countries, evidence from cohort studies, Asia. *Pac. J. Clin. Nutr.* 16 (3):467 - 476.

12 - Mary, B. & Hagstad, R. N. (2009):Prostate Cancer Awareness, *C.N.S.* 40:349 - 6685.

13 - Makoto Matsushita, Kazutoshi Fujita,* and Norio Nonomura

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PMC Disclaimer Published online 2020 Feb 20. doi: 10.3390/ijms21041447

Influence of Diet and Nutrition on =Prostate Cancer

14- Mishina, T.; Watanabe, H.; Araki, H. & Nakao, M. (1985): Epidemiological study of prostatic cancer by matched - pair analysis, *vol.* 6:423 - 36.

15 - Muta, M. I.; Witoldzasada, k.; jhon, A. H.; john, A. P.; Chad, W. M. R. & Michael, G. (2006): The value of DRE as predictor of *P.C.*diagnoses among united state, *Vol.* issue 30(3): 269 - 275.

16 - Searl, l. A.; Habib, F. K. & Cowie, H. (2006): Literature review of prostate cancer and pesticide exposure, Exp. Biol. Med. (233)1608 – 1614.

17-Sharaf, M.; Bowirrat, A.; Yahia, F. & Yosef, F. (2006): Epidemiology of prostate cancer in North West bank palastine, *Pp.* 72 – 79.

18 - Shirai, T.; Asamoto, M.; Takahashi, S. & Imaida, K. (2002): Diet and prostate cancer, *Vol.* 181-182: 89 - 94.

19 - Smith, M. W. (2009): Fatty Fish May Cut Prostate Cancer Risk, *Eur. J. Cancer Prev.* 13(3):219 - 23.

20 - Miller, K.D.; Nogueira, L.; Devasia, T.; Mariotto, A.B.; Yabroff, K.R.; Jemal, A.; Kramer, J.; Siegel, R.L. Cancer treatment and survivorship statistics, 2022. CA Cancer J. Clin. 2022. The Effect of Age on Prostate Cancer Survival .

21 - Sung, J. F. C.; Lin, R. S.; Pu, Y. S.; Chen, Yi-C.; Chang, H. C. & Lai,M - K. (1999): Risk Factors for Prostate Carcinoma in Taiwan A Case - Control Study in a Chinese Population in Taiwan, *Vol.* (12). 604 - 609.

22 - Talamini, R.; La - Vecchia, C.; Decarli, A.; Negri, E. & Franceschi, S. (1986): Nutrition, social factors and prostatic cancer in a Northern Italian population 53(6): 817- 821.

23 - Victoria, J.; Drake, J. W. A. (2009): Oregon State Foods from the legume family, *Vol.* 24: 2311-2315.

24 - William, G. J. (1991): The role of chemotherapy in refractory prostate cancer, *vol. Iss.* 1 :(1).

25 - Dan Theodorescu, M. and Krupski,T. L. (2009): Prostate Cancer - Biology, Diagnosis, Pathology, Staging, and Natural History, *Vol.* 351:1802 – 1803.

26-Berges, R. R.; Kassen, A. & Senge, T. (2000): Treatment symptomatic benign prostatic hyperplasia with beta-sitosterol, *B. J. U. Int.* 85: 842 - 6.

27 - Chen, S. & Parmigiani, G. (2007): Meta-analysis of *BRCA1* and *BRCA2* penetrance, *J. Clin. Oncol.* 25(11): 1329 - 33.

28- Siegel RL, Miller KD, Jemal A. Cancer statistics, 2015. CA Cancer J Clin. 2015;65(1):5–29.

29- Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018;68(6):394–424. doi: 10.3322/caac.21492.

30-Hyun Young Lee, MD1 Do Kyoung Kim, MD1 Seung Whan Doo, MD, PhD1 Won Jae Yang, MD, PhD1 Yun Seob Song, MD, PhD1 Bora Lee, MS2 Jae Heon Kim, MD, PhD1:Time Trends for Prostate Cancer Incidence from 2003 to 2013 in South Korea: An Age-Period-Cohort Analysis (Published Online August 1, 2019).

31- Ahmedin Jemal, DVM, PhD, MaryBeth B Culp, MPH, Jiemin Ma, PhD, Farhad Prostate Cancer Incidence 5 Years :Islami, MD, PhD, and Stacey A Fedewa, PhD After US Preventive Services Task Force Recommendations Against Screening Published online 2020 May 20 United States.

32- Kimberly R. Jenkins1 · Taofik Oyekunle1,2 · Lauren E. Howard1,2 · Emily K.Wiggins1 · Stephen J. Freedland1,3 ·Emma H. Allott4,5
   Family history of prostate cancer and prostate tumor aggressiveness in black and non-black men ;results from an equal access biopsy study
   Received: 6 May 2020 / Accepted: 29 December 2020 The Author(s) 2021.

33- Anna Plym ,Yiwen Zhang ,Konrad H. Stopsack ,Yon Ho Jee ,Fredrik Wiklund Adam S. Kibel ,Peter Kraft ,Edward Giovannucci ,Kathryn L. Penney ,Lorelei A. Mucci ؛ Family History of Prostate and Breast Cancer Integrated with a Polygenic Risk Score Identifies Men at Highest Risk of Dying from Prostate Cancer before Age 75 Years- UK Clin Cancer Res (2022) 28 (22): 4926–4933. https://doi.org/10.1158/1078-0432.CCR-22-1723.

34-Outzen, Malene; Tjønneland, Anne; Christensen, Jane; Olsen, Anja Fish consumption and prostate cancer risk and mortality in a Danish cohort study Source: European Journal of Cancer Prevention, Volume 27, Number 4, July 2018, pp. 355-360(6).

35- Shenghui Wu1, Susan P. Fisher-Hoch2, Belinda Reininger3, Miryoung Lee4, Joseph B. McCormick2 Fruit and Vegetable Intake Is Inversely Associated with Cancer Risk in Mexican-Americans : Nutr Cancer. 2019 ; 71(8): 1254–1262.

36- Orzechowska MJ, Anusewicz D, Bednarek AK. Int J Mol ; Age- and Stage-Dependent Prostate Cancer Aggressiveness Associated with Differential Notch Signaling. Sci. 2022 Dec 22;24(1):164. doi: 10.3390/ijms24010164. PMID: 36613607 .

37-Bloom,J. R.;Stewart,S. L.;Oakley-Girvans, I.;Banks,J.P.&Subo - Chang,S. (2010) : Perceived Risk, and Prostate Cancer Screening among, African American Men, *Int. J. Radiat. Oncol. Biol. Phys. Vol.* 57(5):1292 - 6.

38- Bruner, D. W.; Moore, D.; Parlanti, J.;Engstr, P. (2003) :Relative risk of prostate cancer for men with affected relatives ; systemic review and meta – analysis, *Int. J. cancer* 107 : 797 – 803.

References:

1- Ahmedin Jemal, DVM, PhD, Mary Beth B Culp, MPH, Jiemin Ma, PhD, Farhad Islami, MD, PhD, and Stacey A Fedewa, PhD : Prostate Cancer Incidence 5 Years After US Preventive Services Task Force Recommendations Against Screening Published online 2020 May 20 United States.

2 - Anna Plym ,Yiwen Zhang ,Konrad H. Stopsack ,Yon Ho Jee ,Fredrik Wiklund Adam S. Kibel ,Peter Kraft ,Edward Giovannucci ,Kathryn L. Penney ,Lorelei A. Mucci ؛ Family History of Prostate and Breast Cancer Integrated with a Polygenic Risk Score Identifies Men at Highest Risk of Dying from Prostate Cancer before Age 75 Years- U K. Clin. Cancer Res (2022).

3- Berges, R. R.; Kassen, A. & Senge, T. (2000): Treatment symptomatic benign prostatic hyperplasia with beta-sitosterol.

4 - Bostwick, D. G.; Burke, H. B.; Djakiew, D.; Euling, S.; Landolph, J.;Morrison,H.;Sonawane,B.;Shifflett,T.;Waters,D. J. & Timms, B. (2004): Human prostate cancer risk factors.

5- Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics (2018).

6 - Buhmeida, A.; Pyrhönen, S.; Laato, M & Collan,Y. (2006): Prognostic factors in prostate cancer.

7- Bloom,J. R.;Stewart,S. L.;Oakley-Girvans, I.;Banks,J.P.&Subo - Chang,S. (2010) : Perceived Risk, and Prostate Cancer Screening among, African American Men, *Oncol. Biol. Phys.*

8- Chan, J. M.; Stampfer, M. J.; Ma, J.; Rimm, E. B.;Willett, W. C. & Giovannucci, E. L. (1999): Supplemental vitamin *E* intake and prostate cancer risk in a large cohort of men in the *United States*, *Cancer Epi. Bio.*

9- Chen, S. & Parmigiani, G. (2007): Meta-analysis of BRCA1 and BRCA2 penetrance, *J. Clin. Oncol*.

10- Dan Theodorescu, M. and Krupski,T. L. (2009): Prostate Cancer - Biology, Diagnosis, Pathology, Staging, and Natural History.

11- El - Mistiri, M.; Verdecchia, A.; Rashid, I.; El - Sahli, N.; El - Mangush, M. & Federico, M. (2003): Cancer incidence in eastern Libya, the first report from the Benghazi Cancer Registry.

12 - Harry, P.; Stephen, B. S. (2001): The Clinical Stage, its Definition and Importance in Prostate Cancer.

13 - Hyun Young Lee, MD1 Do Kyoung Kim, MD1 Seung Whan Doo, MD, PhD1 Won Jae Yang, MD, PhD1 Yun Seob Song, MD, PhD1 Bora Lee, MS2 Jae Heon Kim, MD, PhD1:Time Trends for Prostate Cancer Incidence from 2003 to 2013 in South Korea: An Age-Period-Cohort Analysis (Published Online August 1, 2019).

14- Jeanine, M.; G. & Anita, K. (2007): Meat Consumption and Cancer Risk.

15 - Khouaja, K.; Ben-Sorba, N.; Bouslama, A.; Youssef, A. &Taher, M. A. (2005): an experience of individual and early diagnosis of prostate cancer in a Tunisian centre.

16- Kimberly R. Jenkins1 · Taofik Oyekunle1,2 · Lauren E. Howard1,2 · Emily K.Wiggins1 · Stephen J. Freedland1,3 ·Emma H. Allott4,5

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17 - Lauren Barber,1,2 Travis Gerke,1,3 Sarah C. Markt,1 Samuel F. Peisch,1 Kathryn M. Wilson,1,4 Thomas Ahearn,1,5 Edward Giovannucci,1,4,6 Giovanni Parmigiani,1,7,8 and Lorelei A.Mucci1,4 Clin. Cancer Res. 2018 . Published online 2018 Aug. Family history of breast or prostate cancer and prostate cancer risk.

18- Li-Qiang, Q.; Jia-Ying, Xu.; Pei-Yu, W.; Jian, T. & Kazuhiko, H. (2007): Milk consumption is a risk factor for prostate cancer in Western countries, evidence from cohort studies, Asia.

19- Mary, B. & Hagstad, R. N. (2009):Prostate Cancer Awareness, *C.N.S.*

20- Makoto Matsushita, Kazutoshi Fujita,* and Norio Nonomura. Author information Article notes Copyright and License information ,PMC Disclaimer Published online 2020 Feb 20 Influence of Diet and Nutrition on =Prostate Cancer.

21-Michał Oczkowski,* Katarzyna Dziendzikowska, Anna Pasternak-Winiarska, Dariusz Włodarek, and Joanna Gromadzka-Ostrowska : Nutrients. 2021 Feb; Dietary Factors and Prostate Cancer Development, Progression, and Reduction

22-Miller, K.D.; Nogueira, L.; Devasia, T.; Mariotto, A.B.; Yabroff, K.R.; Jemal, A.; Kramer, J.; Siegel, R.L. Cancer treatment and survivorship statistics, 2022. CA Cancer J. Clin. 2022. The Effect of Age on Prostate Cancer Survival

23 - Mishina, T.; Watanabe, H.; Araki, H. & Nakao, M. (1985): Epidemiological study of prostatic cancer by matched - pair analysis.

24 - Muta, M. I.; Witoldzasada, k.; jhon, A. H.; john, A. P.; Chad, W. M. R. & Michael, G. (2006): The value of DRE as predictor of *P.C.*diagnoses among united state.

25 - Orzechowska MJ, Anusewicz D, Bednarek AK. Int J Mol ; Age- and Stage-Dependent Prostate Cancer Aggressiveness Associated with Differential Notch Signaling. Sci. 2022 Dec.

26 - Outzen, Malene; Tjønneland, Anne; Christensen, Jane; Olsen, Anja
 Fish consumption and prostate cancer risk and mortality in a Danish cohort study of Cancer Prevention, July 2018.

27 - Searl, l. A.; Habib, F. K. & Cowie, H. (2006): Literature review of prostate cancer and pesticide exposure, Exp. Biol. Med.

28 - Sharaf, M.; Bowirrat, A.; Yahia, F. & Yosef, F. (2006): Epidemiology of prostate cancer in North West bank palastine.

29 - Shenghui Wu1, Susan P. Fisher-Hoch2, Belinda Reininger3, Miryoung Lee4, Joseph B. McCormick 2. Fruit and Vegetable Intake Is Inversely Associated with Cancer Risk in Mexican-Americans : Nutr Cancer. 2019.

30 - Shirai, T.; Asamoto, M.; Takahashi, S. & Imaida, K. (2002): Diet and prostate cancer.

31 - Siegel RL, Miller KD, Jemal A. Cancer statistics, 2015. C. A Cancer Clin.

32 - Smith, M. W. (2009): Fatty Fish May Cut Prostate Cancer Risk, *Prev.*

33 - Sung, J. F. C.; Lin, R. S.; Pu, Y. S.; Chen, Yi-C.; Chang, H. C. & Lai ,M - K. (1999): Risk Factors for Prostate Carcinoma in Taiwan A Case - Control Study in a Chinese Population in Taiwan.

34 - Sun J, Kader AK, Hsu FC et al - Inherited genetic markers discovered to date are able to identify a significant number of men at considerably elevated risk for prostate cancer a head of print]. DOI: Pup 2010

35 - Talamini, R.; La - Vecchia, C.; Decarli, A.; Negri, E. & Franceschi, S. (1986): Nutrition, social factors and prostatic cancer in a Northern Italian population.

36 -Victoria, J.; Drake, J. W. A. (2009): Oregon State Foods from the legume family.

37 - William, G. J. (1991): The role of chemotherapy in refractory prostate cancer.