The Clinical Significance of Tumor Biomarker (PSA) In The Diagnosis of Prostate Cancer and Its Correlation with The Stage of the Disease

Hanaa S. Khadhum¹, Azhar A. Ameen², Mahdi M. Thuwaini³ ¹Department of pathological analysis, College of science/ Basrah University, Iraq; ² Department of Biology, College of Science \Basrah University; Iraq

 3 Department of pathological analysis, College of Health and Medical Technology \backslash

Southern Technical University, Iraq.

E-mail: hanaa.kadhum@uobasrah.edu.iq

Abstract

Prostate cancer is the most frequently type of cancer which leading death in male, Prostate-specific antigen (PSA) is possibly the most commonly utilized tumor marker for prostatic carcinoma screening. The present study was conducted to assess the diagnostic efficiency of Serum PSA in identifying of prostate cancer as compared to tissue biopsy. The study was conducted in the private clinics in Basra city All of the patients in this study have been diagnosed with prostate cancer. The study was carried out from February 2018 to February 2019. In total, 49 patients took part in the trial, with 30 normal participants serving as controls. The results of the current study revealed that the mean age of prostate cancer patients was 59.68±9.04 years and that of control subjects was 52.50± 6.27 years (differences were insignificant). PSA of the patients with prostate cancer was significantly more than that of control (11.04±1.73 VS 7.3±0.87 ng/ml, P< 0.01 t- test). The percent of patients with prostate cancer with overweight was significantly more than that recorded in normal subjects (12.24 VS 10.00% %, P< 0.01 Chi square). The percent of obese among patients with prostate cancer was also more than that noted in control group (12.24 VS 3.33%, P< 0.05 Chi square). Furthermore, the percent of smokers among patients with prostate cancer (69.38%) was more than that in healthy subject (20.00%) (P<0.01 Chi square). When compared to a healthy (control), the patients with prostate cancer showed significant elevation of serum cholesterol (174± 12.01 VS 286±27.23 mg/dl, P < 0.01 t-test), LDLc (99.4±8.5 119± 7.4VS mg/dl, P < 0.01 t-test) and triglycerides (116±13.7 VS 116±13.7, P < 0.05 t-test). While the serum level of HDLc was significantly decreased in prostate cancer patients compared to healthy (controls) (38.8±1.04 VS 44.3±3.7, P < 0.05 t-test. Our data was statistically analyzed, and the results showed there was no correlation between serum PSA and the stage of prostatic cancer. However, of the total patients, 24.49% appeared with PCa, T1, 20.41% with PCa, T2, 14.29% with PCa, T3, 24.49% with PCa, T4 and 16.32% with PCa, T5. Prostate cancer was positively correlated with BMI, lipid profile and smoking, while no correlation was recorded between PSA and the stage of the disease.

Keywords: Prostate cancer, Serum PSA, Lipid profile, BMI, Stages

1. Introduction

Cancer has already placed a huge burden on public health worldwide [1]. Over the course of the twenty years that have passed, researchers have noted an increasing trend in new recorded patients and deaths appeared from different types of cancers, Especially because of different lifestyles and behaviors in low and center of countries, as well as geographic and environmental aspects that influence the occurrence of Cancer [2, 3]. One of the most famous medical diseases is prostate cancer, which affects men. It is the most common cancer diagnosed in American male population [4]. In Iraq, prostate cancer was classified as one of the top ten cancers between 1995-1997.

However, (PSA) is about a (32-34) kDa single-chain glycoprotein (68-70) consisting of 237 amino acids, molecular weight (26,079) for the peptide moiety with five disulfide inter-chain bonds. Numerous studies and research have shown that PSA is a useful tumor marker for prostate cancer, staging, and diagnosis, with continuous monitoring of the patient's response to treatment and recurring disease detection. It is normally found in low amounts in the blood, many clinical studies have shown that The PSA test's value rises with age. [5, 6].

It was recently found that tall boys have a high risk of developing prostate cancer in adulthood, and tall boys have a higher risk of developing prostate cancer in adulthood. And have proven that obesity in adults increases the risk of prostate cancer. However, the influence of body mass index is more on adults [7]. The present study was done in order to evaluate the diagnostic efficiency of Serum PSA in identifying of prostate cancer as compared to tissue biopsy.

2. Materials and Methods

The present study was included 49 patients (59.68±9.04 years) with prostate cancer, attended the private clinics in Basra city from February 2018 to February 2019. Thirty control subjects (52.50± 6.27 years) were also included for comparison. Prostate cancer patients diagnosed as a juvenile were included in this study over 40 years of age were enrolled. However, the current study was certified by the ethical commission of the South technical university /Iraq. Whole participants signed the written consent form before starting data and sample collection. BMI was measured for all participants. Participants were categorized to non-obese when their body mass index (BMI) was (19.8-24.9) kg/m2, overweight when their BMI was 30 kg/m2 or more [8].

Blood samples were taken from all study groups, patients and healthy ones, and tested for PSA levels and lipid profile using (German Roche device, Hitachi).

The disease stage was recorded according to histopathological results which performed by routine histological techniques (H and E stain). The results were analyzed statistically by using the statistical program (SPSS). A P-value of 0.05 or less was dependent as statistically significant.

3. Results

The results of the current study revealed that the mean age of patients with prostate cancer was 59.68 ± 9.04 years and that of control subjects was 52.50 ± 6.27 years (differences were insignificant). PSA of the patients with prostate cancer was significantly more than that of control (11.04 ± 1.73 VS 7.3 ± 0.87 ng/ml, P< 0.01 t- test). The percent of patients with prostate cancer with overweight was significantly more than that recorded in normal subjects (12.24 VS 10.00% %, P< 0.01 Chi square). The percent of obese among patients with prostate cancer was also more than that noted in control group (12.24 VS 3.33%, P< 0.05 Chi square). Furthermore, the percent of smokers among patients with prostate cancer (69.38%) was more than that in healthy subject (20.00%) (P< 0.01 Chi square) (Table 1).

In comparison with healthy control, the patients with prostate cancer showed significant elevation of serum cholesterol (174 \pm 12.01 VS 286 \pm 27.23 mg/dl, P < 0.01 t-test), LDLc (99.4 \pm 8.5 119 \pm 7.4VS mg/dl, P < 0.01 t-test) and triglycerides (116 \pm 13.7 VS 116 \pm 13.7, P < 0.05 t-test). however, the serum level of HDLc was significantly decreased in patients with prostate cancer compared with healthy control (38.8 \pm 1.04 VS 44.3 \pm 3.7, P < 0.05 t-test) (table 2).

The statistical analysis of our data demonstrated that there was no correlation between serum PSA and the stage of prostatic cancer. However, of the total patients, 24.49% appeared with PCa, T1, 20.41% with PCa, T2, 14.29% with PCa, T3, 24.49% with PCa, T4 and 16.32% with PCa, T5 (table 3).

Table 1: Age, PSA level, BMI and percent of smokers of men with prostate cancer in compared with healthy							
subjects.							
Variables	cases	Control		P-V	alue		
No	49	30					
Age (years)	59.68±9.04	52.50± 6.27		Not sig	gnificant		
PSA (ng/ml)	11.04±1.73	7.3±0.87		< (0.01		
BMI (km/m ²)							
Normal weight	32 (65.30%)	26 (86.66%)		< (0.01		
Overweight	11 (12.24%)	3 (10.00%)		< (0.01		
Obese	6 (12.24%)	1 (3.33%)		< (0.05		
Smokers	34 (69.38%)	6 (20.00%)		< (0.01		
Table 2: The levels of PSA and lipid profile in patients							
with prostate cancer compared with healthy control							
group.							
Groups	Healthy	ontrol Patients					

group.						
Groups parameters	Healthy control (=30)	Patients (n=49)	P-Value			
PSA (ng/ml)	7.3±0.87	11.04±1.73	< 0.01			
Cholesterol (mg/dl)	174± 12.01	286±27.23	< 0.01			
HDLc (mg/dl)	44.3±3.7	38.8±1.04	< 0.05			
LDLc (mg/dl)	99.4±8.5	119± 7.4	< 0.01			
TG (mg/dl)	116±13.7	123± 10.9	< 0.05			

according to the stage					
Staging	Number	Percent			
PCa,T1	12	(24.49%)			
PCa,T2	10	(20.41%)			
PCa,T3	7	(14.29%)			
PCa,T4	12	(24.49%)			
PCa,T5	8	(16.32%)			

PCa; prostate cancer, T1; Tumor cells could be invading sub epithelial connective tissue, T2; Tumor invades superficial muscle, T3 Tumor invades pervesicatissue (Microscopically). T4; Tumor invades muscle T5; Tumor passed beyond the muscle tissue.

4. Discussion

Cancer is a leading cause of mortality. Cancer of Prostate is now Cancer is the most frequency cancer in males and after lung cancer, the second most prevalent cause of death. Lifestyle constituents, such as smoking, poor diet, and physical inactivity were positively correlated to. Prostate cancer [9].

The current study, gave further evidence that hyperlipidemia and high BMI were significantly associated with high PSA and prostate cancer as compared to control patients. It was recognized that cholesterol played a k

ey role in prostate cancer as a precursor of androgens, the cell proliferation regulator [10]. Nevertheless, several experimental studies using laboratory models have shown that particles resemble the remnants of triglycerides-wealthy, have a role in stimulating carcinogenesis by interfering with a pathway for cellular signals such as the MEK/ERK and AKT pathways, that have a role in controlling cell growth and proliferation, apoptosis, interruption of the life cycle and biosynthesis of lipids [11]. On the other hand, high-density lipoprotein cholesterol (HDL-C) has recently gotten a lot of attention as a potential risk factor for prostate cancer growth and prognosis. The effect of low HDL can be explained by its role in the way of reducing the binding to paraoxonase-1 (PON-1), which lead to lowing PON-1 free radical scavenging capacity. In addition HDL, By preventing the production of lipid rafts, it is possible to reduce the severity of cancer, which have been related with signaling of cancer-causing cells through Caveolin-1 (Cav-1) activity [12, 13].

This study showed significant correlation between smoking and prostate cancer. The precise relationship between smoking and prostatic carcinoma remained unclear. However, there have been several possible mechanisms by which cigarette smoking may increase the risk of prostate cancer. One is the ability of cigarette smoking to increase bioavailable testosterone which leads to a decrease in bioavailable estradiol and then may alter the hormonal environment and favor a higher androgenic exposure of the prostate. The possible mechanism was that the cigarette contained carcinogens [14].As in this study, the previous studies also revealed that no correlation between PSA and the stage of the disease [15, 16].

5. Conclusion

Prostate cancer was positively correlated with BMI, lipid profile and smoking, while no correlation was recorded between PSA and the stage of the disease.

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Nil. 7. Conflicts of interest

There are no conflicts of interest References

1. Arbyn M, Castellsagué X, de Sanjosé S, Bruni L, Saraiya M, Bray F, Ferlay J. Worldwide burden of cervical cancer in 2008. Annals of oncology. 2011;22(12):2675-86. https://doi.org/10.1093/annonc/mdr015

2. Parkin DM, Bray F, Devesa S. Cancer burden in the year 2000. The global picture. European journal of cancer. 2001;37:4-66. <u>https://doi.org/10.1016/S0959-8049(01)00267-2</u>

3. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: a cancer journal for clinicians. 2018;68(6):394-424.

https://doi.org/10.3322/caac.21492

4. Surapaneni KM, Venkata GR. Lipid peroxidation and antioxidant status in patients with carcinoma of prostate. Indian J Physiol Pharmacol. 2006;50(4):350-4. Available from:

https://pubmed.ncbi.nlm.nih.gov/17402264/

5. Belanger A, Rong P, Liu S, Lavoie L, Labrie F. Characterization and measurement of prostate-specific antigen using monoclonal antibodies. Clinical and Investigative medicine Medecine Clinique et Experimentale. 1993;16(6):409-14. Available from: https://europepmc.org/article/med/7516829

6. Bonovas S, Filioussi K, Tsantes A. Diabetes mellitus and risk of prostate cancer: a meta-analysis. Diabetologia. 2004;47(6):1071-8. https://doi.org/10.1007/s00125-004-1415-6

7. MacInnis RJ, English DR. Body size and composition and prostate cancer risk: systematic review and meta-regression analysis. Cancer causes & control. 2006;17(8):989-1003. <u>https://doi.org/10.1007/s10552-006-0049-z</u>

8. Melchor I, Burgos J, Del Campo A, Aiartzaguena A, Gutiérrez J, Melchor JC. Effect of maternal obesity on pregnancy outcomes in women delivering singleton babies: a historical cohort study. Journal of perinatal medicine. 2019;47(6):625-30.

https://doi.org/10.1515/jpm-2019-0103/html

9. Presti Jr J. Neoplasms of the prostate gland. Smith's general urology. 2000:399-406. Available from: https://cir.nii.ac.jp/crid/1573950400669169536

10. Arthur R, Rodríguez-Vida A, Zadra G, Møller H, Hemelrijck MV. Serum lipids as markers of prostate cancer occurrence and prognosis? Clinical Lipidology.

2015;10(2):145-65. https://doi.org/10.2217/clp.14.69

11. Sekine Y, Koike H, Nakano T, Nakajima K, Takahashi S, Suzuki K. Remnant lipoproteins induced proliferation of human prostate cancer cell, PC-3 but not LNCaP, via low density lipoprotein receptor. Cancer epidemiology. 2009;33(1):16-23.

https://doi.org/10.1016/j.canep.2009.04.004

12. Kotani K, Sekine Y, Ishikawa S, Ikpot IZ, Suzuki K, Remaley AT. High-density lipoprotein and prostate cancer: an overview. Journal of epidemiology. 2013;23(5):313-9.

https://doi.org/10.2188/jea.JE20130006

13. Han JH, Chang IH, Ahn SH, Kwon OJ, Bang SH, Choi NY, Park SW, Myung SC, Kim HW. Association between serum prostate-specific antigen level, liver function tests and lipid profile in healthy men. BJU international. 2008;102(9):1097-101.

https://doi.org/10.1111/j.1464-410X.2008.07774.x

14. Field AE, Colditz GA, Willett WC, Longcope C, McKinlay JB. The relation of smoking, age, relative weight, and dietary intake to serum adrenal steroids, sex hormones, and sex hormone-binding globulin in middle-aged men. The journal of clinical endocrinology & metabolism. 1994;79(5):1310-6.

https://doi.org/10.1210/jcem.79.5.7962322

15. Hope TA, Goodman JZ, Allen IE, Calais J, Fendler WP, Carroll PR. Metaanalysis of 68Ga-PSMA-11 PET accuracy for the detection of prostate cancer validated by histopathology. Journal of Nuclear Medicine. 2019;60(6):786-93.

https://doi.org/10.2967/jnumed.118.219501

16. Aksenov LI, Gansler T, Sineshaw HM, Fedewa S, Yabroff KR, Jemal A, Moul J. Prevalence and correlates of non-tissue prostate cancer diagnosis in the United States. Journal of Geriatric Oncology. 2020;11(5):885-92. https://doi.org/10.1016/j.jgo.2019.11.003