Estimation of total L-fucose, Glutathion, te stosterone and some trace elements levels in serum of prostate cancer

Nadia ahmed al-joboury

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Abstract

In this study the levels of L-fucose, Glutathion, testosterone and some trace elements in sera of patients with prostate cancer and control group were estimated for 30 samples of prostate cancer and 25 samples of control groups. The results showed there was a significant increase in the level of total L-fucose at ($p<0.001$) for blood serum of patients with prostate cancer compared with their levels in control group, while there were a significant decrease in testosterone and Glutathion at ($P \leq 0.01$) and ($P \leq 0.05$) respectively for blood serum of patients with prostate cancer compared with their level in control group. Trace elements there was a significant decrease in the level of selenium at ($p<0.001$) and a significant increase in Cadmium and Zinc at ($P \leq 0.05$) and ($P \leq 0.01$) respectively for blood serum of patients with prostate cancer compared with their level in control group.

The smoking factor at prostate cancer showed a significant decrease in glutathion and Zinc at ($P \leq 0.001$) while the results showed a significant increase in L-fucose and Cadmium at ($P \leq 0.001$) and ($P \leq 0.05$) respectively. The correlations between all parameters above for patients and control group and the correlation of all parameters with age has been obtained.

Key Word: L-Fucose, GSH, Prostate cancer.

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تقدير مستوى الفيوكوز الكلي, الكلوتاثايون, التستوستيرون وبعض العناصر النزرة في مصل دم المرضى المصابين بسرطان البروستات

نادية احمد الجبوري

الملخص

في هذا البحث تم تقدير مستويات ل-فيوكوز, الكلوتاثايون, هورمون التستوستيرون وبعض العناصرالنزرة في مصل دم المرضى المصابين بسرطان البروستات, ومجموعة السيطرة حيث تم اخذ عينات دم من 30 مريض بسرطان البروستات و25 عينة لاشخاص اصحاء كمجموعة سيطرة . بينت النتائج وجود ارتفاع معنوي في مستوى ل-فيوكوز الكلي وعند مستوى الاحتمالية ($P<0.001$) في امصال مرضى سرطان البروستات عند مقارنتها مع مجموعة السيطرة في حين لوحظ وجود انخفاض معنوي في مستوى التستوستيرون و الكلوتاثايون وعند مستوى الاحتمالية ($P<0.001$)و ($P<0.05$) على التوالي عند مقارنتها مع مجموعة السيطرة. اما بالنسبة للعناصر النزرة وجد ان هناك انخفاض معنوي في مستوى السيلينيوم عند مستوى الاحتمالية ($P<0.001$) وارتفاع معنوي في مستوى الكادميوم و الخارصين عند مستوى الاحتمالية ($P<0.05$) و ($P<0.001$) على التوالي عند مقارنتها مع مجموعة السيطرة.

عند دراسة تأثير عامل التدخين في مرضى سرطان البروستات وجد ان مستويا الكلوتاثايون والزنك منخفضان عند مستوى الاحتمالية ($P<0.001$) في حين وجد ان مستويا الفيوكوز الكلي والكادميوم مرتفعان عند مستوى الاحتمالية ($P<0.001$)و($P<0.05$) على التوالي. وتم دراسة العلاقات الترابطية بين المتغيرات المذكورة لدى المرضى والاصحاء, وكذلك وجدة العلاقات الترابطية ايضا بين المتغيرات المذكورة والعمر.

الكلمات المفتاحية: الفيكوز الكلي ، GSH، سرطان البروستات.

Introduction

Prostate is a gland in the male reproductive system. It secretes a milky or white slightly acidic fluid constituting 50%–75% of semen along with spermatozoa and seminal vesicle fluid [(1)]. This disease tends to develop in men over the age of fifty[(2)], and the presence of prostate cancer may be indicated by symptoms, physical examination, prostate-specific antigen (PSA), or biopsy. Prostate-specific antigen testing increases cancer detection but does not decrease mortality[(3)]. Androgen receptor plays essential roles in the development of male

sex organs and prostate tissues, and also plays important roles in the development, progression, and metastasis of prostate cancer [4,5,6]. The prostate gland has a sexual function , but it is unclear how important its secretions are , to human fertility. The growth of the prostate is controlled by many local and systemic hormones whose exact functions are not yet known [7].

A potential risk of testosterone therapy is an increase in the incidence of prostate cancer [8]. However, whereas androgen depletion hinders the development and clinical progression of prostate cancer [9], and exogenous testosterone may stimulate growth of metastatic prostate cancer [10]. Androgen ablation therapy is the primary treatment for metastatic prostate cancer. However, most prostate cancer patients receiving the androgen ablation therapy ultimately develop recurrent castration-resistant tumors within 1–3 years after treatment [11]. Race is another risk factor that may contribute to the increased incidence of prostate cancer at a lower age[12].

Prostate had been characterized as a tissue that possesses a low respiration. Consistent with this, the respiration are markedly lower in prostate mitochondria than those found in other cells. Several reports have identified zinc as an inhibitor of terminal oxidation in mammalian cell mitochondria. Because of the uniquely high concentration of zinc in prostate cells, we reported that physiological levels and forms of zinc inhibit the respiration and terminal oxidation of prostate mitochondria[13].

Selenium has many functions in the body. It is present in the active site of many enzymes which may encourage apoptosis of cancer cells. Lastly, selenium, at high doses can decrease the rate of tumor growth in humans[14].

This study aims to evaluate concentration of total L-fucose, Glutathion, testosterone and some trace elements levels in serum of prostate cancer.

Materials and methods

Sampling (Subjects)

In a plane tube (no anti coagulant),5 mL of venous blood placed, which was taken from the groups(25 control and 30 patients with prostate cancer), left for (15 min) at room

temperature, then centrifuged (at 3000 rpm for 10min) to get the serum, which is stored at (-20°C) unless used immediately.

Collection of blood

The samples were collected classified into two groups as follow:

1- Control group: include (25) healthy with, with no previous diseases which may interfere with the parameters analyzed in this study.
2- Prostate cancer group(tikrit hospital): include (30) patients, smokers (15) and non-smokers (15).

Estimation of testosterone in Blood Serum

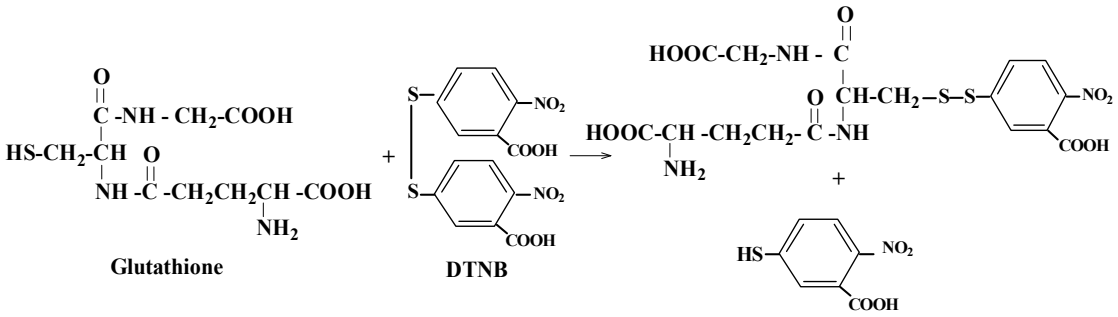
Serum testosterone was determined by using AccuBind ELISA Microwells (competitive enzyme immunoassay kit) (Monobind Inc.,USA).

The essential reagents required for an enzyme immunoassay include antibody, enzyme-antigen conjugate and native antigen. Upon mixing biotinylated antibody, enzyme-antigen conjugate and a serum containing the native antigen, a competition reaction results between the native antigen and the enzyme- antigen conjugate for a limited number of antibody binding sites. A simultaneous reaction between the biotin attached to the antibody and the streptavidin immobilized on the microwell occurs.

Determination of serum glutathione (GSH)[15]

Serum GSH was determined by using a modified procedure using Elmans reagent 5,5-dithiobis(2-nitrobenzoic acid) (DTNB), which is depend on the action of the sulfhydryl groups of the GSH.

5,5-Dithiobis(2-nitrobenzoic acid) (DTNB) is a disulfide chromogen that is readily reduced by sulfhydryl group of GSH to an intensely yellow compound .



The absorbance of the reduced chromogen is measured at 412 nm and directly proportional to the GSH concentration.

Estimation of Total L-Fucose (TF)[16]

Total L-fucose were estemated according to Dische and Sheetels Methods (Dische, 1948), This method depends on a direct reaction of concentrated sulfuric acid with serum components ; the reactants combine with cysteine , and the color product measured at (396 and 430 nm).

The differences in absorbance were directly proportional to α-L- fucose content of the solutions.

Estimation of selenium concentration in Blood serum [17]

Selenium Concentration in Blood serum was estimated by using Electrothermal atomic absorption spectrophotometer method

Estimation of zinc [13] **and cadmium**[18] **concentration in Blood Serum**

The concentration of zinc and cadmium in blood serum has been estimated by using flame atomic absorption spectrophotometer method.

Results and discussion

This study was conducted in order to find out the values of some biochemical parameters and its relationship to the disease. In addition to relations between some of these parameters in blood serum which may have an important effects in the Proceeding of the disease and to find the possibility of using such parameters as a biomarker in the diagnosis of prostate cancer patients compared to control.

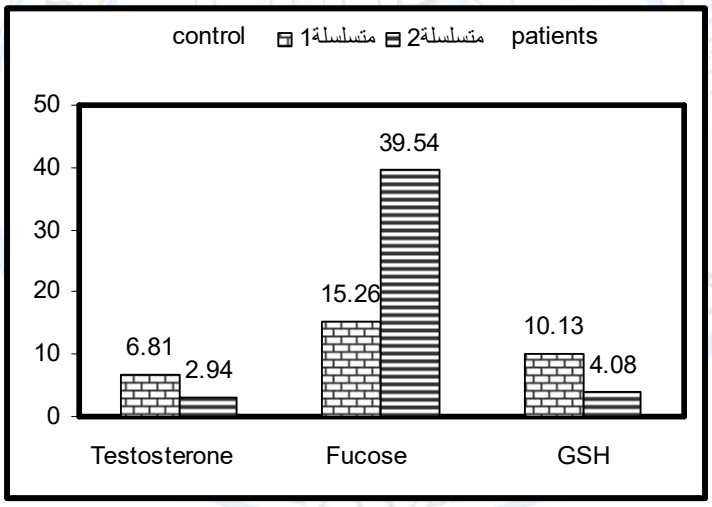
The table 1 clarifies the level of testosterone, total fucose (TF) and glutathione(GSH) in the patient group and healthy group.

It is noticed that there are a high significant decrease at the probability level (<0.001) for the testosterone, which was (6.81± 0.72) and (2.94 ± 0.03) for the control and patient groups respectively. This result compatible to that of (Hendrik I. et al., 2009)[19] .The development, differentiation, and maintenance of the prostate gland has been shown to be closely linked to the bioavailability of testosterone and other related sex hormones, so , these steroidal functions involve complex interactions of many other growth factors with different receptors affecting various cell types in the prostate[20].

The high significant decreases at the probability level (<0.001) has been obtained for the (TF) and at the probability level (<0.05) for (GSH) in the patients group in contrast to the healthy group, and the levels of (TF) were (15.26±1.08) and (39.54 ± 7.29), while the levels of (GSH) were (10.13± 0.89) and (4.08 ± 0.16) for the control and patient groups respectively. This result compatible to that of (Osama F. M. al-jebori, 2006)[12] and (D.S.L.Srivastava and R.D. Mittal, 2005)[21].

Table(1): Testosterone, L-Fucose and Glutathione in sera of control and patients (prostate cancer)

Parameters	Control Mean± SD N=25	Patients(prostate cancer) Mean± SD N=30	P-value
Testosterone(ng/ml)	6.81± 0.72	2.94 ± 0.03	<0.001
Total L-Fucose (mg/dl)	15.26 ±1.0 8	39.54 ± 7.29	<0.001
GSH (mg/dl)	10.13 ± 0.89	4.08 ± 0.16	<0.05



Figure(1): deferent levels of Tostesterone, L-fucose, GSH between control and patients groups

Fucose is a powerful immune modulator; it is distributed in macrophage , which is important to immune function, and it is also particularly active in inflammatory disease.[22]

Glutathion was significantly decreased in sera of patients with different types of cancers as a response to oxidative stress[23,24]

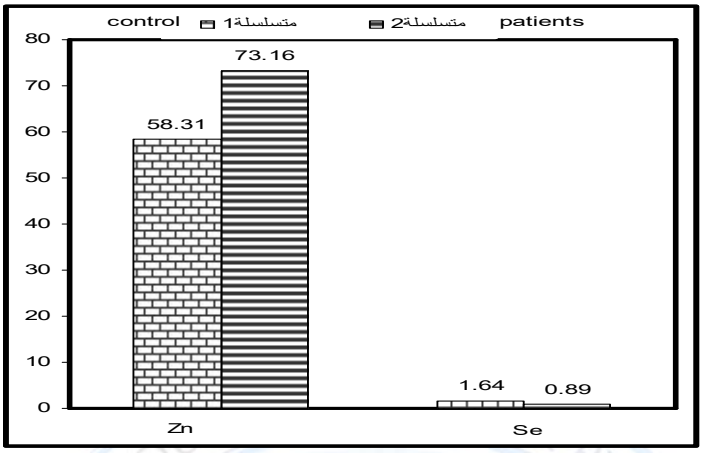
Table 2 clarifies the level of trace elements Se, Cd and Zn in the patient group and healthy group.

The results showed a significant decreases at the probability level (<0.05) for the Se and the levels were (1.64 ± 0.018) and (0.87 ± 0.01) for the control and patient groups respectively. Because oxidative stress increases with androgen exposure a putative risk factor for prostate cancer, the antioxidative activity of selenoenzymes may be particularly relevant for prevention of this disease.[25]

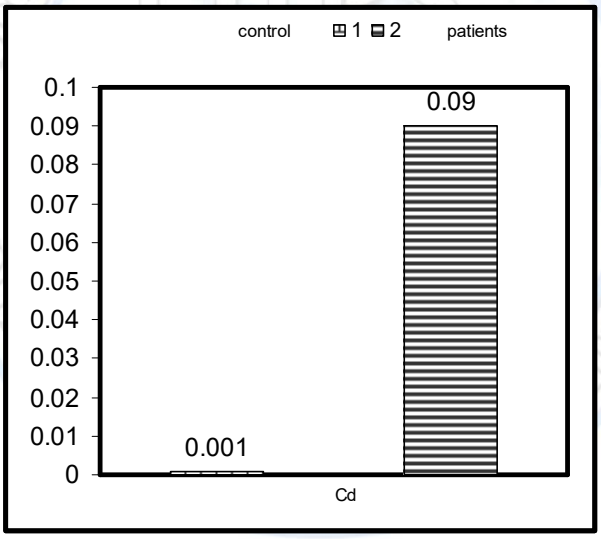
The Cd and Zn showed high significant increases at the probability level (<0.001) for each of the two elements above, and the levels of Cd were (0.001±0.00) and (0.09 ± 0.001), while the levels of Zn were (58.31± 8.85) and (73.16 ± 11.97) for the control and patient groups respectively. The cause of increasing in Zn level may be refer to amassing Zn from prostate during the disease[26].

Table(2): Seleniun, Cadmium and Zinc in sera of control and patients (prostate cancer)

Parameters	Control Mean± SD N=25	Patients(prostate cancer) Mean± SD N=30	P-value
Se (uml/L)	1.64 ± 0.018	0.87 ± 0.01	<0.05
Cd (µg/100ml)	0.001±0.00	0.09 ± 0.001	<0.001
Zn (µg/100 ml)	58.31 ±8.85	73.16 ±11.97	<0.001



Figure(2): deferent of Zn and Se between control and patients groups



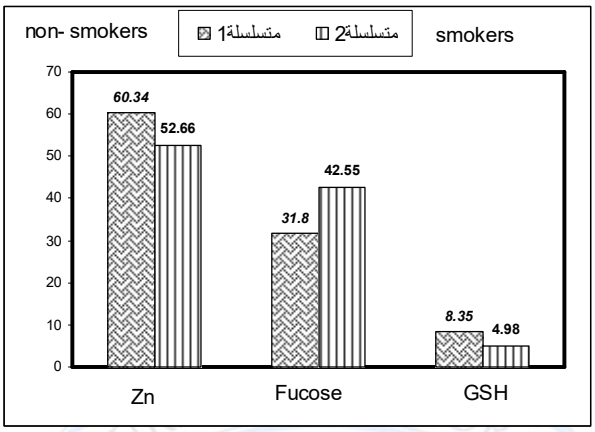
Figure(3): deferent of Cd between control and patients groups

The effect of smoking have been obtained in table (3) for (TF), (GSH), Cd and Zn. The results showed a high significant decreases at the probability level (<0.001) for each of (TF) and Cd between smokers and non-smokers, and the levels of (TF) were (42.55±7.33) and (31.8 ± 6.49). The levels of Cd were (0.13± 0.01) and (0.002 ± 0.00) for the patients (smokers and non-smokers) group respectively.

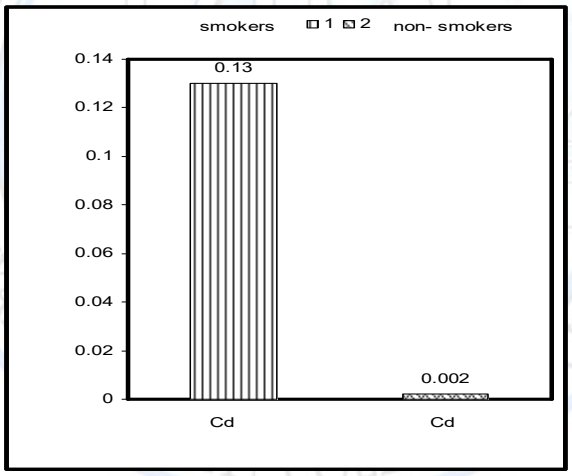
At the same table, the results showed a significant increases at the probability level (<0.05) for (GSH) between smokers and non-smokers, and the levels of (GSH) were (4.98±0.20) and (8.35 ± 0.017) for the patients (smokers and non-smokers) group respectively, and the levels were (0.13± 0.01) and (0.002 ± 0.00) for the patients (smokers and non-smokers) group respectively, while a high significant increases has been obtained at the probability level (<0.001) for Zn between smokers and non-smokers, and the levels were (52.66± 8.11) and (60.34 ±12.4) for the patients (smokers and non-smokers) group respectively.

Table(3): Total L-Fucose , Glutathione, Cadmium and Zinc in sera of patients (smokers and Non-smokers)

Parameters	smokers patient Mean± SD N=15	Non- smokers patient Mean± SD N=15	P-value
Total L-Fucose (mg/dl)	42.55± 7.33	31.8 ± 6.49	<0.001
GSH (mg/dl)	4.98± 0.20	8.35 ± 0.017	<0.05
Cd (ug/100ml)	0.13±0.01	0.002 ± 0.00	<0.001
Zn (ug/100 ml)	52.66± 8.11	60.34 ±12.41	<0.001



Figure(4): deferent of Zn, L-Fucose and GSH between smokers and non-smokers patients



Figure(5): deferent of Cd between smokers and non-smokers patients

The correlations between Cd, Zn, GSH, Total L-Fucose and Se were obtained in table (4) for control group and in table (5)for prostate cancer, and the results showed extrusive proportion for all correlations.

Table (4) showed a significant correlations between (Zn and GSH), (Zn and Se) and (GSH and L-fucose), While table (5) showed a significant correlations between (Cd and Zn), (Cd and Se), (Zn and Se) and (GSH and L-Fucose)

Table(4):correlations between Cd, Zn, GSH, Total L-Fucose and Se in sera of control group

Parameters	Zn	GSH	L-Fucose	Se
Cd	0.019	0.031	0.001	1.05
Zn		0.841*	1.26	0.49*
GSH			0.923*	1.45
L-Fucose				0.331

Table(5): correlations between Cd, Zn, GSH, Total L-Fucose and Se in sera of patients (prostate cancer)

Parameters	Zn	GSH	L-Fucose	Se
Cd	0.42*	0.01	0.011	0.82*
Zn		0.07	0.25	0.47*
GSH			0.28*	0.29
L-Fucose				0.51

The correlations between age and the obtained parameters for prostate cancer patients were expressed in figures below.

The results showed decreasing in GSH, testosterone, and Se with the increasing of age, while L-fucose, Cd and Zn were directly proportional with the age.

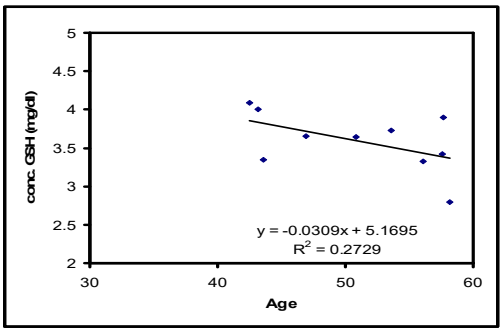


Figure (6):Correlation between GSH and age for prostate cancer

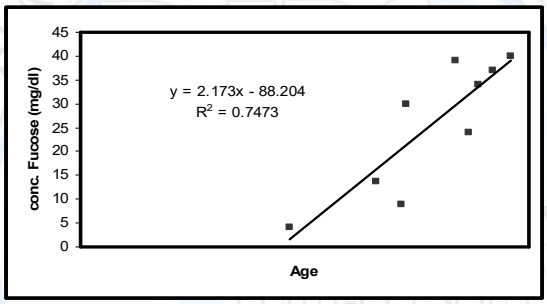


Figure (7):Correlation between total L-fucose and age for prostate cancer

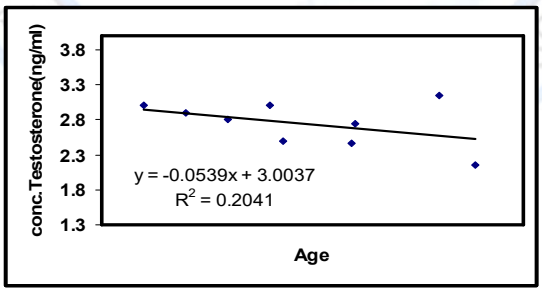


Figure (8):Correlation between Testosterone and age for prostate cancer

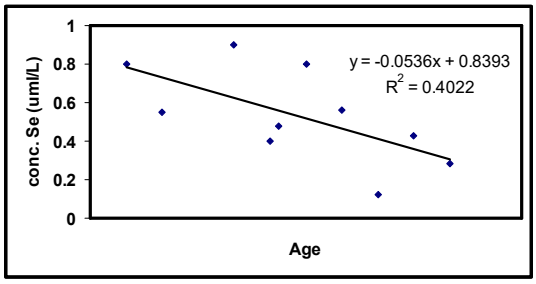


Figure (9):Correlation between Se and age for prostate cancer

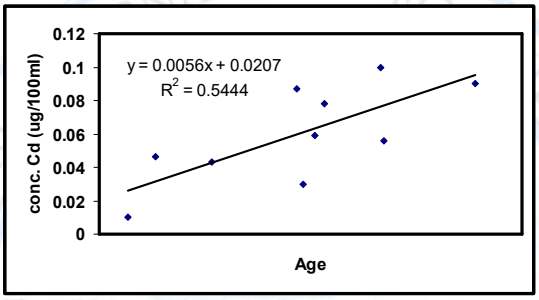


Figure (10):Correlation between Cd and age for prostate cancer

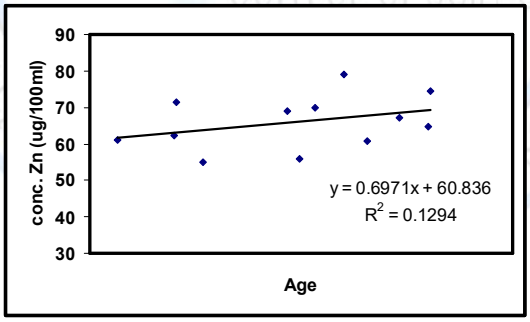


Figure (11):Correlation between Zn and age for prostate cancer

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