Relationship between Diabetes Mellitus and prostate cancer in some Iraqi patients

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Abstruct

Background: Diabetes and cancer are common diseases with tremendous impact on health worldwide. Epidemiologic evidence suggests that people with diabetes are at significantly higher risk for many forms of cancer . The aim of this study is to find the association between diabetic and prostate cancer in diabetes mellitus patients

Methods and patients : A (100) male were divided into (50) patients with type 2 diabetes mellitus(T2DM), (25) patients with type1 diabetes mellitus(T1DM) and (25) apparently healthy person were taken from different sites of wassit governorate – Al hay city. Those patients were selected by systematic random sampling . Fasting plasma sugar (FPS), glycated hemoglobin(HbA1C) ,Prostate specific antigen (PSA), Testosterone(T) levels were determined for both patient and control subjects. Testosterone and prostate specific antigen was measured by ELISA. (Enzyme-linked immunosorbent assay).While, enzymatic and colorimetric methods were used for glucose test and glycated hemoglobin.

Results : Their age ranged between (21-78) years, the result recorded that the mean age of the men (51.12± 13.05) was among T1DM and most of patients (64%) were less than 50 years of life whereas the mean age (50.88 ±9.06) among T2DM and most of patients (62%) were more than 50 years. Serum PSA levels (normal range <4.0 ng/ ml) were measured with Enzyme-linked immunosorbent assay (ELIZA) .Serum PSA levels were lower (1.81± 1.41) in patients with T1DM when compared with T2DM (2±2.60) and with the healthy control group (1.32± 0.63). The mean levels of testosterone among diabetic (T1DM, T2DM) and non- diabetic groups were estimated. The results of the mean levels of testosterone were similar for the diabetic patient's (T1DM: 6.72±2.74 and T2DM: 6.46±2.48)when compared with non diabetic groups (7.27± 2.55). Only 10% of T2DM having elevated testosterone levels with normal PSA, while 10% of those patients with elevated PSA and normal testosterone. In addition, 16% of T1DM having elevated PSA levels have normal testosterone whereas, 16% of those patients having elevated testosterone and normal PSA .

Conclusion :There were inverse correlation between prostate specific antigen (PSA) levels and diabetes mellitus . Serum PSA was lower in T1DM in comparison with T2DM.

*Recommendations : Study other tumor markers for prostate cancer in Diabetes mellitus. Increase the sample number, Diabetic mellitus patients, patient control and healthy control , as well as choosing different governorate and villages to screen different geographical areas comprehensively***.**

I. INTRODUCTION

Diabetes mellitus (DM) comprises a group of common metabolic disorders that share the phenotype of hyperglycemia.(1)

There are some epidemiologic studies on the relation among diabetes, prostate cancer risk, and PSA, however, the results have often been discrepant and confusing (17,18).

The relationship between diabetes and prostate cancer is suspected to be causal due to evidence of decreasing prostate cancer risk with increasing diabetes duration and lack of evidence for any confounding of this association. Hypothesized mechanisms for decreased prostate cancer risk among diabetics include [a]decreased levels of hormones and other cancer- related growth factors among diabetics, [b] the impact of diabetes on detection- related factors, such

as prostate size, circulating prostate specific antigen (PSA), and health- care seeking behaviors,[c] protective effects of diabetes medications, and [d] a protective effect of diabetes- include vascular damage in the prostate (2).

Testosterone is the key male hormone. It regulates a man's libido (sex drive) and the development of secondary male sex characteristics, such as facial and body hair, the testes and the penis. Testosterone also protects the health of bone and muscle tissues. Testosterone deficiency is associated with many chronic health conditions, including T2DM and other metabolic disorders (3).

Significantly, there is also a strong association between testosterone deficiency and diabetes. A study in the United Kingdom found that 42% of men with T2DM also had low or borderline levels of testosterone. There is also a link between low testosterone levels and insulin resistance in men with T1DM (3). Aims of the study are determination of prevalence of PSA among diabetes mellitus patients and estimation of testosterone in the sera of studied groups. In addition , determination of the relationship among different parameters for diabetic and non diabetic groups.

II. MATERIAL AND METHODS

Subjects (Patient and control): A study was conducted on the following groups during the period between July- October/ 2012.

Patients group: The study included fifty patients with type 2 diabetes mellitus (T2DM) and 25 patients with type 1diabetes mellitus (T1DM) . The sera were collected from those subjects attending private laboratories in Wasit city referred from doctors in which DM is diagnosis on clinical ground. All patients were selected due to revised criteria for diagnosis of DM as defined by the American Diabetes Association (ADA)(1997).

Healthy Control group: Twenty five apparently healthy persons, with age range between (21-78) years and whose ethnic back ground, age, sex matched the patients group were selected as a control group. Their fasting plasma sugar (FPS) was within the normal range (70-105mg/dl) and HbA1C was normal between (4.2-6.2%).

Sample collection: Venous blood samples (5 ml) were collected from each patient and control ; (2.5 ml) placed in plain test tube and left to clot at room temperature and then separated by centrifugation (3000 rpm for about 5 min) to obtain sera and transferred into another plane tube. All sera were immediately frozen at(-20C0) until they were used. The second part (2.5 ml) of blood was placed in EDTA tube, to evaluate HbA1C immediately after collection. All tests were carried out for patients as well as the control group according to the study protocol.

Fasting plasma sugar (FPS), glycated hemoglobin(HbA1C) ,Prostate specific antigen (PSA), Testosterone(T) levels were determined for both patient and control subjects. Testosterone and prostate specific antigen was measured by ELISA. (Enzyme-linked immunosorbent assay).While, enzymatic and colorimetric methods were used for glucose test and glycated hemoglobin.

Statistical analysis: Data were revised, coded, and analyzed using the computer program, "SPSS version 18.0". The 0.05 level was used as the cut-off value for statistical significance, and the following statistical measures were used: Discriptive statistical (The Frequency distribution-Tables-mean, standard and standard error) Chi-square test (X2), Monte carol (MCP). The correlation coefficient.

III. RESULTS

Descriptive data for diabetic (T1DM,T2DM) and non- diabetic subjects (Healthy control group) ages are presented in table (1).Their age ranged between (21-78)years, the result recorded that the mean age of the men

(51.12± 13.05) was among T1DM and most of patients (64%) were less than 50 years of life whereas the mean age (50.88 ±9.06) among T2DM and most of patients (62%) were more than 50 years. (Table 1)

Table 1: Distribution of diabetic groups(T1DM,T2DM) and non-diabetic patients according to the age.

Age groups	T1DM		T2DM		c Healthy control group H	
	NO.	%	NO.	%	NO.	%
> 50	16	64.0	19	38.0	21	84.0
< 50	9	36.0	31	62.0	4	16.0
Total	25	100.0	50	100.0	25	100.0
Mean age(y)	51.12±13.05		50.88±9.06		±±±37.52±9.65659.6537	

P <0.001 (HS)

Percent study indicated that the mean age for T1DM patients was (51.12±13.05) which was in agreement with the Iraqi and Egyptian studies, that indicated the mean age of patient was (14.37±8.462), (13.4±4.24) respectively. These studies suggested that most patients were young people (4).The disease increase can occur at any age, but develop in adult before the age of 30 years (5,6). The explanation of higher incidence of this age group may be related to physiological changes occurring at this age .These variation may reflect the interaction of both genetic and environmental factors in different social, racial, and geographical areas in the world as well as hormonal changes or increased insulin secretion(7,8).

The current study revealed that the mean age for T2DM patients was (50.88±9.06) years which was confirmed by the Asian-Indian study, that indicated the mean age of the patient was (54±12.9) (9). As well as ,Cvitkovic et al (10) ,showed age of creation patients (56±9) years. While, Tomar et al (2009) suggested that the individuals were exposed to the T2DM at the fourth decade(11) .

The mean of fasting plasma sugar was highly significantly altered among the patients group (T1DM:178.2± 12.47 mg/dl ; T2DM: 210.55± 14.50 mg/dl) in comparison with the control group (93± 2.22 mg/dl) as shown in table (4.2). It is clear from this table that there was a highly significant difference in FPS level among Diabetic patients in comparison with non-diabetic subjects .(Table 2)

Table 2: Levels of FPS among diabetic patients (T1DM, T2DM)and Healthy control group.

FPS (mg/dl)	T1DM	T2DM	Healthy control group
Mean	178.20	210.55	93.95
Std. Error of Mean	12.47	14.50	2.22
Std. Deviation	63.60	102.57	11.10
Range	79.50-346.80	75.02-500.00	64.62-112.00

P< 0.001 (HS)

The current study showed higher results than that of kamath et al (12) , who stated the mean of FPS in T2DM was (162.54±58.84 mg/dl). In addition, the finding of the present study were similar to a previous study (13) which showed that levels of FPS were highly significant in the diabetic as compared with normal subjects (p<0.001).

Prostate specific antigen for both diabetic and non- diabetic subjects were estimated table(4.6).Mean levels in the diabetic patients were (T1DM: 1.81 ± 1.41,T2DM: 2± 2.60) and non diabetic subjects were (1.32±0.63).

Indeed, inverse associations between PSA levels and diabetes have been reported in recent studies (14). Serum PSA levels (normal range <4.0 ng/ml) were measured by ELISA .Serum PSA levels were lower (1.81± 1.41) in patients with T1DM in comparison with T2DM(2± 2.60) and when compared with Healthy control group (1.32+0.63).These results do not agree with waters et al (15), who found significant lower difference in diabetics than in non diabetics(mean PSA1.07 and 1.28, respectively, (p=0.003).(Table3)

Table(3): Mean of PSA of diabetic and non- diabetic groups

PSA(ng/ml)	T1DM	T2DM	Healthy control group
Mean	1.81	2.00	1.32
Std. Error of Mean	0.27	0.36	0.12
Std. Deviation	1.41	2.60	0.63
Range	0.53-5.52	0.20 - 17.70	0.71- 3.50

Most , but not all, studies have shown that, on average diabetes subjects have lower PSA levels than do those without diabetes (16-18).In our multiethnic sample, PSA levels were lower in diabetic men. However, what this indicates is not clear. Lower PSA levels in diabetics may signal a lower prevalence of prostate cancer and an indication of a biologic effect of T1DM status on prostate growth and development. The mean levels of testosterone of diabetic (T1DM, T2DM) and non- diabetic groups are shown in Table(4.7).The similarities in the mean levels of testosterone that were present for (T1DM: 6.72±2.74 and T2DM: 6.46±2.48)when compared with non- diabetic groups (7.27± 2.55).(Table4)

Table 4 : Mean of testosterone of diabetic, non diabetic and healthy control groups

Testosterone (ng/dl)	T1DM	T2DM	Health control group
Mean	6.72	6.46	7.27
Std. Error of Mean	0.53	0.35	0.51
Std. Deviation	2.74	2.48	2.55
Range	2.21-11.16	1.85-11.37	2.40-11.72

The results was disagreed with the finding of a recent study about the mean of serum testosterone (12.14± 6.04) for Asian– Indian male T2DM (19). Prostate specific antigen was measured with ELISA assay ,the values of PSA in two groups subdivided according to age (<50 and > 50 years) as noted in table (5).

Table (5) The comparison PSA levels in T1DM and T2DM patients and healthy control group

PSA Level of T2DM	Age groups of T2DM		Total	P –value
	<50	>50		
Normal	22(44%)	23 (46%)	45 (90%)	
Elevated	1 (2%)	4 (8%)	5 (10%)	p>0.05 (NS)
PSA Level of T1DM	Age groups of T1DM			

		<50	>50		
	Normal	9(36%)	12(48%)	21 (84%)	
	Elevated	1(4%)	3(12%)	4(16%)	p< 0.01(HS)
PSA Level of	Healthy	Age groups of healthy group			
	Groups	<50	>50		
	Normal	23(92%)	2(8%)	25(100%)	P<0.01 (HS)
	Elevated	0	0		

Two percent (one patient) of T2DM less than 50 years had PSA level more than 4 ng/ml , while eight percent (four patients) of T2DM more than 50 years had elevated PSA more than 4 ng/ml (p >0.05 NS).In comparison with T1DM, four percent (one patient) had elevated PSA level with <50 years while twelve percent (three patients) of TIDM had elevated PSA > 50 years (p<0.01).

Several studies found a lower serum PSAlevel among those with diabetes; Muller et al.(20) analyzed data from a large population- based cohort study in Germany, in which the participants were aged 50 to 74 years and had a 17% prevalence of diabetes. They reported that more severe forms of diabetes were associated with lower PSA levels.

Only 10% of T2DM having elevated testosterone levels with normal PSA, while 10% of those patients with elevated PSA and normal testosterone table (6).

Table(6) : Association between PSA and Testosterone in T2DM patients

		P.S.A Level of T2DM			p. value
		Normal	Elevated	Total	
Testosterone Level of T2DM	Normal	40 (80.0%)	5 (10.0%)	45 (90.0%)	P>0.05 (NS)
	Elevated	5 (10.0%)	0 (0.0%)	5 (10.0%)	
		P.S.A Level of healthy			
		Normal	Elevat		
Testosterone Level of healthy groups	Normal	23(92%)	0	23(92	p<0.01 (HS)
	Elevatec	2(8%)	0	2(8%)	

In addition, 16% of T1DM having elevated PSA levels have normal testosterone whereas, 16% of those patients having elevated testosterone and normal PSA as shown in table (7).

Table (7) Association between PSA and Testosterone in T1DM patients

Testosterone Level ofT1DM		P.S.A Level of T1DM			
		Normal	Elevated	Total	

	Normal	17 (68%)	4 (16%)	21 (84%)	P<0.01 (HS)
	Elevated	4 (16%)	0 (0.0%)	4 (16%)	
Testosterone Level of healthy groups		P.S.A Level of healthy		Total	p<0.01 (HS)
		Normal	Elevated		
	Normal	23(92%)	0	23(92%)	
	Elevated	2 (8%)	0	2 (8%)	

IV. CONCLUSIONS

Serum PSA was lower in T1DM in comparison with T2DM.

Anon significant correlation was observed between (PSA and age) among T2DM subjects.

Low number of Diabetic patients (T1DM: 4% ,T2DM: 6%) had low level of testosterone.

A highly significant correlation was observed between testosterone and age among T1DM ,while non significant correlation among T2DM subjects.

5.Thirty six percent of T1DM were classified as obese , while thirty eight of T2DM were considered as overweight and obese.

V. RECOMMENDATIONS

Study other tumor markers for prostate cancer in Diabetes mellitus

Increase the sample number, Diabetic mellitus patients, patient control and healthy control , as well as choosing different governorate and villages to screen different geographical areas comprehensively.

Further studies to be done on un controlled diet DM patients.

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