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Original Article

Studying the effect of type 2 diabetes mellitus on prostate-related parameters: A prospective single institutional study

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ABSTRACT

Background: To examine the effects of type 2 diabetes mellitus (DM) on the variables associated with prostatic growth including serum prostate-specific antigen (PSA), serum testosterone, and prostate volume, and to correlate these variables with the duration of diabetes treatment.

Methods: Our study was conducted over 3 months recruiting 501 men aged ≥ 55 years; of whom 207 had type 2 DM. Exclusion criteria were active urinary tract infection, suspicious rectal examination, urologic cancer, end-organ damage, and recent urological manipulations. Serum PSA and serum testosterone were measured. Prostate volume was determined by abdominal ultrasonography using an ellipsoid formula.

Results: The mean patient age was 60.21 ± 5.95 years. The mean PSA, testosterone, and prostate volume for diabetic men were 2.3 ng/mL, 3 ng/mL, and 56 g, respectively. The corresponding values for nondiabetic men were 3.5 ng/mL, 4 ng/mL, and 51 g, respectively ($P = 0.001$, $P = 0.001$, $P = 0.03$, respectively). The mean PSA density was 0.049 ± 0.043 ng/mL/cm^3 in diabetics versus 0.080 ± 0.056 ng/mL/cm^3 in nondiabetics ($P < 0.001$).

Conclusion: Type 2 DM is significantly associated with lower serum PSA and testosterone, and larger prostate volume.

1. Introduction

Diabetes mellitus (DM) is a serious problem in male health. A positive association exists between clinical markers of benign prostatic hyperplasia (BPH) and DM.[1,2] Subnormal serum free testosterone is detected in diabetic men.[3] Kasper et al suggested an inverse correlation between DM and the risk of prostate cancer.[4]

The aim of this work was to determine the effects of type 2 DM on serum total prostate-specific antigen (PSA), serum total testosterone, and prostate volume.

2. Materials and methods

The study was prospectively conducted over 3 months and recruited male patients aged ≥ 55 years who presented to our hospital with different benign urological conditions. The study included 501 men and 207 of them had type 2 DM. Exclusion criteria were patients with active urinary tract infection, urological cancer, end-organ damage, abnormal digital rectal examination findings, and recent urological manipulations.

This study was approved by the ethical committee of our institution and informed consent was obtained from participating patients.

All men were subjected to detailed history taking and physical examination. Body mass index was calculated. Six milliliters of venous blood were drawn at 8:00 AM, then serum was separated and stored at −20°C. Serum PSA and testosterone were assessed using electro-chemiluminescence immunoassay. Prostate size was calculated using abdominal ultrasonography. The ellipsoid formula was applied.

Data were analyzed using SPSS version 18.0 (SPSS, IBM Corporation, Chicago, IL, USA). The P value was assumed to be significant at ≤ 0.05.

3. Results

The mean age of patients was 60.21 ± 5.95 years (55.0–93.0 years). For diabetic patients, the mean PSA, testosterone, and prostate volume were 2.3 ng/mL, 3 ng/mL, and 56 g, respectively.

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Table 1
Comparison between the two studied groups according to PSA, testosterone, prostate volume, PSA density, and BMI.

Variable		Diabetics (207)	Nondiabetics (294)	*P* value
PSA		2.3 ± 1.5	3.5 ± 1.9	0.001
PSA	< 4	179 (86.5%)	193 (65.6%)	< 0.0001
	> 4	28 (13.5)	101 (34.4%)	
Testosterone		3 ± 1.8	4 ± 2.1	0.001
Prostate volume		56 ± 18	51 ± 23	0.03
PSA density		0.05 ± 0.04	0.08 ± 0.05	0.001
BMI		32.23 ± 5.04	29.32 ± 4.20	0.001

BMI, body mass index; PSA, prostate-specific antigen.

The corresponding values for nondiabetic individuals were 3.5 ng/mL, 4 ng/mL and 51 g, respectively. The mean body mass index (BMI) was 32.23 ± 5.04 and 29.32 ± 4.20 for diabetic patients and nondiabetic individuals, respectively (Table 1).

There was a significant positive correlation between duration of treatment of DM and mean prostate volume ($r = 0.147$, $P = 0.034$) (Fig. 1), while significant negative correlations were found between duration of DM treatment and mean serum PSA values ($r = -0.219$, $P = 0.002$) (Fig. 2), mean serum testosterone values ($r = -0.221$, $P = 0.001$) (Fig. 3), and mean PSA density values ($r = -0.203$, $P = 0.003$) (Fig. 4).

High BMI in diabetic patients was a confounding factor, therefore, multiple regression analysis was done, confirming the true significant correlation of DM with the studied parameters (Table 2).

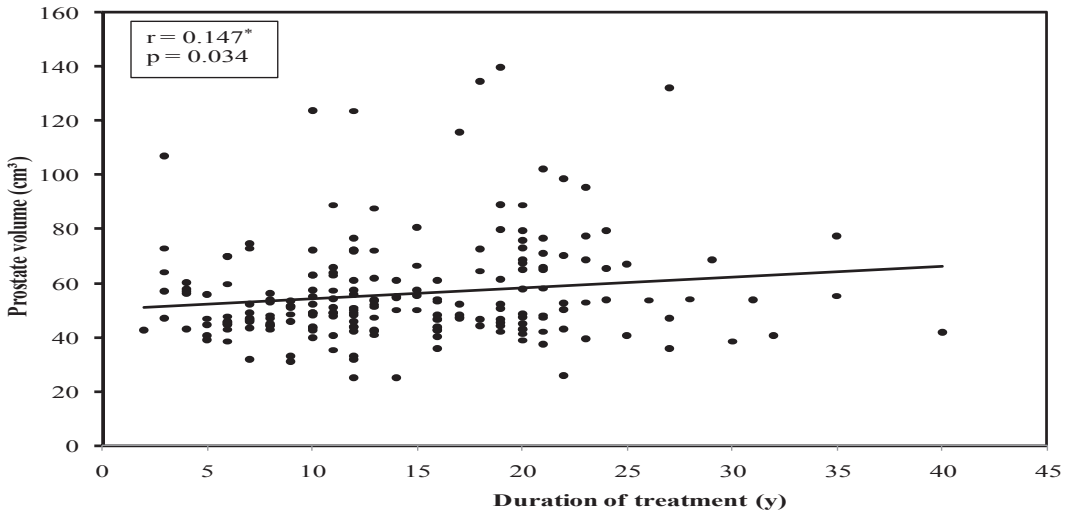

Fig. 1. Correlation between duration of treatment of diabetes mellitus with prostate volume in diabetic group.

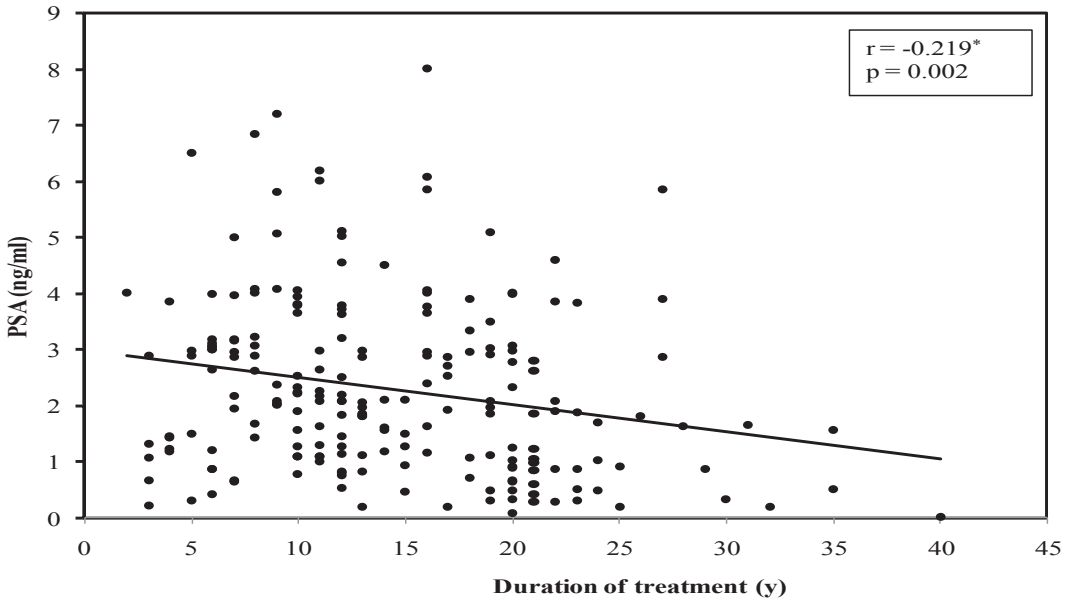

Fig. 2. Correlation between duration of treatment of diabetes mellitus with PSA in diabetic group. PSA, prostate-specific antigen.

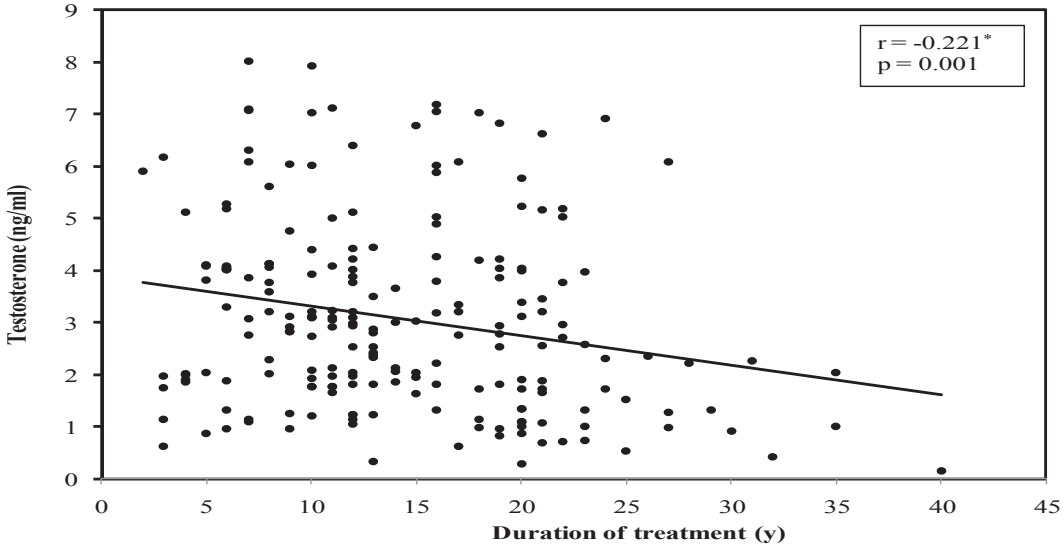

Fig. 3. Correlation between duration of treatment of diabetes mellitus with testosterone in diabetic group.

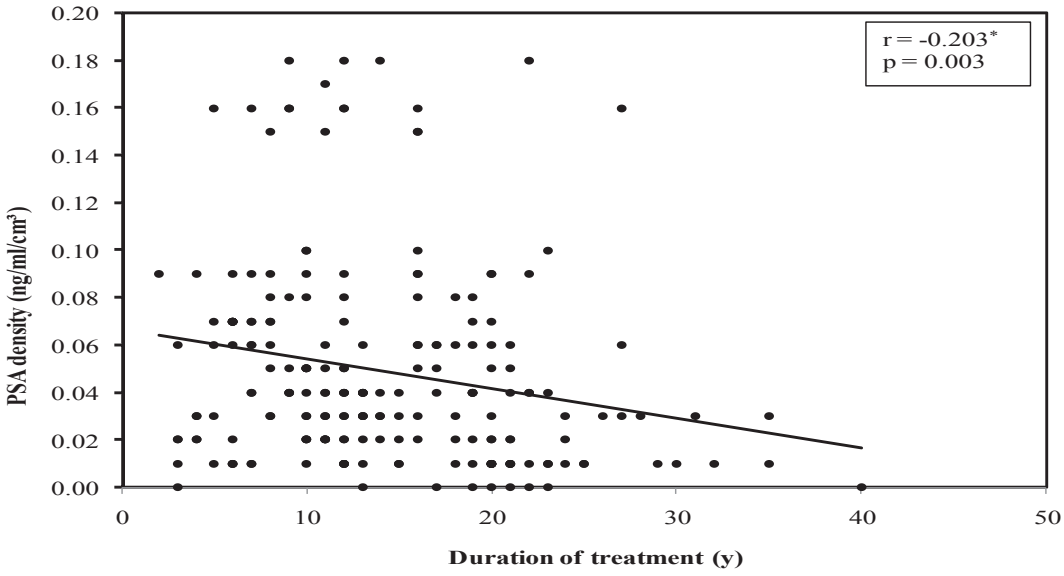

Fig. 4. Correlation between duration of treatment of diabetes mellitus with PSA density in diabetic group. PSA, prostate-specific antigen.

Table 2
Multiple regression analysis for PSA, testosterone, prostate volume and PSA density, in relation to DM, studying BMI as a confounding factor

		B	SE	t	p	95% CI	
						Lower	Upper
PSA	DM	0.743	0.155	4.795*	< 0.001	0.439	1.048
	BMI	−0.166	0.016	10.359*	< 0.001	−0.197	−0.134
$F = 87.977^*$, $P < 0.001^*$, $R = 0.511$, $R^2 = 0.261$							
Testosterone	DM	0.400	0.165	2.420*	0.016	0.075	0.724
	BMI	−0.210	0.017	12.305*	< 0.001	−0.243	−0.176
$F = 96.237^*$, $P < 0.001^*$, $R = 0.528$, $R^2 = 0.279$							
Prostate volume	DM	4.629	1.633	2.835*	0.005	1.420	7.837
	BMI	3.011	0.168	17.883*	< 0.001	2.680	3.341
$F = 136.430^*$, $P < 0.001^*$, $R = 0.629$, $R^2 = 0.396$							
PSA density	DM	0.020	0.004	4.853*	< 0.001	0.012	0.028
	BMI	−0.006	0.000	14.784*	< 0.001	−0.007	−0.005
$F = 156.697^*$, $P < 0.001^*$, $R = 0.621$, $R^2 = 0.386$							

BMI, body mass index; CI, confidence interval; PSA, prostate-specific antigen; SE, standard error.

4. Discussion

The overall mean PSA in the present study was 3.02 ± 1.89 ng/mL. Comparable levels were observed among Middle Eastern men showing higher PSA with no evidence of prostate cancer. This was attributed to increased incidence of BPH, alone or with concomitant prostatitis.[5]

Our study showed that type 2 DM is associated with a significantly lower serum total PSA, than in nondiabetic individuals; a finding that has been shown in other studies. This may be attributed to lower androgen levels found in diabetic men.[3] Muller et al[6] reported that men with elevated and highly elevated hemoglobin A1c levels had 15% and 29% lower serum PSA levels, respectively. Our results also suggested that men with type 2 DM have slower increases in serum PSA levels over time. Similarly, Parekh et al[7] reported lower prostate-cancer risk and serum PSA levels in later stages of diabetes, which are characterized by insulin resistance and lower levels of circulating insulin. Moreover, diabetes might alter PSA values through impaired kidney function.[8] Low serum PSA

in diabetic men may also be explained, in our cohort, by the significantly lower serum testosterone level in men with type 2 DM, confirming the direct role of hypogonadism in PSA values reported by many authors.[3,9,10] Accordingly, an endocrine society currently recommends the measurement of testosterone in patients with type 2 DM on a routine basis.[11]

Large prostate volume has been associated with components of metabolic syndrome.[12,13] This was consistent with our study, in which a positive correlation between the duration of diabetes treatment and prostate size was observed. In fact, both type 2 DM and BPH seem to share similar epidemiological features, possibly related to aging and diet.[14] Barnard et al[15] connected the reduction of growth of stem epithelial prostate cells with the reduction of insulin. Other possible mechanisms have been proposed to associate the development of BPH with type 2 DM, such as the increase in peripheral sympathetic nerve tone and activity of the autonomic nervous system caused by hyperinsulinemia,[16] and hypoxia caused by DM-induced vascular damage.[17]

We have previously shown that high BMI is associated with the same observed changes in prostate-related parameters.[18] However, in the present study, multiple regression analysis confirmed that type 2 DM was significantly associated with a change in prostatic parameters, independent from the effect of BMI.

We believe the importance of this study lies in studying the effect of type 2 DM on the main parameters related to prostatic growth, and being novel in correlating the effect of duration of DM on these parameters.

A meta-analysis has proved the inverse correlation between DM and prostate cancer.[4] Baradaran et al[19] studied 511 patients and concluded that longer duration of DM may be protective against prostate cancer. We did not study the association with prostate cancer as an endpoint in our study. We tried to study how DM can affect the prostate. This possibly refers to the protective effect against prostate cancer or possibly just underdiagnosis of prostate cancer in diabetic patients because of lower PSA and even larger prostate volume that affects transrectal ultrasound biopsy outcomes. Our study may extend further to hypothetically show that diabetic patients may be liable to develop early castration-resistant prostate cancer, due to larger prostate volume in the presence of lower testosterone, pointing to the role of early androgen-independent growth of the prostate. Many theories concerning prostate cancer could be understood from this study, but will need further studies to prove how practical they are.

In conclusion, patients with type 2 DM tend to have significantly lower serum total PSA, lower serum testosterone, and larger prostate volume compared to nondiabetic individuals.

Conflicts of interest

All authors have no conflict of interest to declare.

References

1. Safarinejad MR. Prevalence of benign prostatic hyperplasia in a population-based study in Iranian men 40 years old or older. Int Urol Nephrol 2008;40:921–31.
2. Sarma AV, Burke JP, Jacobson DJ, McGree ME, St Sauver J, Girman CJ, et al. Associations between diabetes and clinical markers of benign prostatic hyperplasia among community-dwelling black and white men. Diabetes Care 2008;31:476–82.
3. Rhoden EL, Ribeiro EP, Teloken C, Souto CA. Diabetes mellitus is associated with subnormal serum levels of free testosterone in men. BJU Int 2005;96:867–70.
4. Kasper JS, Giovannucci E. A meta-analysis of diabetes mellitus and the risk of prostate cancer. Cancer Epidemiol Biomarkers Prev 2006;15:2056–62.
5. Kehinde EO, Sheikh M, Mojimoniy OA, Francis I, Anim JT, Nkansa-Dwamena D, et al. High serum prostate-specific antigen levels in the absence of prostate cancer in Middle-Eastern men: the clinician's dilemma. Br J Urol 2003;91:618–22.
6. Muller H, Raum E, Rothenbacher D, Stegmaier C, Brenner H. Association of diabetes and body mass index with levels of prostate-specific antigen: implications for correction of prostate-specific antigen cutoff values? Cancer Epidemiol Biomarkers Prev 2009;18:1350–6.
7. Parekh N, Lin Y, Marcella S, Kant AK, Lu-Yao G. Associations of lifestyle and physiologic factors with prostate-specific antigen concentrations: evidence from the National Health and Nutrition Examination Survey (2001-04). Cancer Epidemiol Biomarkers Prev 2008;17:2467–72.
8. Bruun L, Ekberg H, Bjork T, Lilja H, Høglund P, Christensson A. Rapid elimination by glomerular filtration of free prostate specific antigen and human kallikrein 2 after renal transplantation. J Urol 2004;171:1432–5.
9. Corona G, Mannucci E, Petrone L, Ricca V, Balercia G, Mansani R, et al. Association of hypogonadism and type II diabetes in men attending an outpatient erectile dysfunction clinic. Int J Impot Res 2006;18:190–7.
10. Grossmann M, Thomas MC, Panagiotopoulos S, Sharpe K, Macisaac RJ, Clarke S, et al. Low testosterone levels are common and associated with insulin resistance in men with diabetes. J Clin Endocrinol Metab 2008;93:1834–40.
11. Bhasin S, Cunningham GR, Hayes FJ, Matsumoto AM, Snyder PJ, Swerdloff RS, et al. Testosterone therapy in adult men with androgen deficiency syndromes: an endocrine society clinical practice guideline. J Clin Endocrinol Metab 2006;91:1995–2010.
12. Hammarsten J, Ogstedt BH, Holthuis N, Mellstrom D. Components of the metabolic syndrome-risk factors for the development of benign prostatic hyperplasia. Prostate Cancer Prostatic Dis 1998;1:157–62.
13. Ozden C, Ozdal OL, Urgancioglu G, Koyuncu H, Gokkaya S, Memis A. The correlation between metabolic syndrome and prostatic growth in patients with benign prostatic hyperplasia. Eur Urol 2007;51:199–206.
14. Gades NM, Jacobson DJ, Girman CJ, Roberts RO, Lieber MM, Jacobsen SJ. Prevalence of conditions potentially associated with lower urinary tract symptoms in men. BJU Int 2005;95:549–53.
15. Barnard RJ, Obayashi NK, Aronson WJ. Effect of diet and exercise intervention on the growth of prostate epithelial cells. Prostate Cancer Prostatic Dis 2008;11:362–6.
16. Kasturi S, Russell S, McVary KT. Metabolic syndrome and lower urinary tract symptoms secondary to benign prostatic hyperplasia. Curr Urol Rep 2006;7:288–92.
17. Berger AP, Deibl M, Halpern EJ, Lechleitner M, Bektic J, Horninger W, et al. Vascular damage induced by type 2 diabetes mellitus as a risk factor for benign prostatic hyperplasia. Diabetologia 2005;48:784–9.
18. Elrifai A, Kotb A, Sharaki O, Abdelhady M. Correlation of body mass index with serum total PSA, total testosterone and prostatic volume in a sample of men. Polish Ann Med 2016;223:1–5.
19. Baradaran N, Ahmadi H, Salem S, Lotfi M, Jahani Y, Baradaran N, et al. The protective effect of diabetes mellitus against prostate cancer: role of sex hormones. Prostate 2009;69:1744–50.