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 non-diabetic 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/cm³ in diabetics versus 0.080 ± 0.056 ng/mL/cm³ in non-diabetics (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. Subnormal serum free testosterone is detected in diabetic men. Kasper et al suggested an inverse correlation between DM and the risk of prostate cancer. 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.
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).

**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           |                 |                     |         |
| < 4           | 2.3 ± 1.5       | 3.5 ± 1.9           | 0.001   |
| > 4           | 179 (86.5%)     | 193 (65.6%)         | < 0.0001|
| Testosterone  | 28 (13.5)       | 101 (34.4%)         |         |
| Prostate volume | 3 ± 1.8       | 4 ± 2.1             | 0.001   |
| PSA density   | 56 ± 18         | 51 ± 23             | 0.03    |
| BMI           | 0.05 ± 0.04     | 0.08 ± 0.05         | 0.001   |
| BMI, body mass index; PSA, prostate-specific antigen.

![Fig. 1](image1.png)  
Fig. 1. Correlation between duration of treatment of diabetes mellitus with prostate volume in diabetic group.

![Fig. 2](image2.png)  
Fig. 2. Correlation between duration of treatment of diabetes mellitus with PSA in diabetic group. PSA, prostate-specific antigen.
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 al6 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 al7 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

### Table 2

|                         | B     | SE    | t      | p       | 95% CI Lower | 95% CI Upper |
|-------------------------|-------|-------|--------|---------|--------------|--------------|
| PSA                     | DM    | 0.743 | 0.155  | 4.795*  | < 0.001      | 0.439        | 1.048        |
| F = 87.977*, P < 0.001*, R² = 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*, R² = 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*, R² = 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*, R² = 0.386 |        |       |        |         |              |              |

BMI, body mass index; CI, confidence interval; PSA, prostate-specific antigen; SE, standard error.
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 al15 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.19 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 al19 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.

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