

The Relationship between Body Mass Index and Diabetes with Serum Prostate-Specific Antigen Levels in the Elderly

A. Ghasemi ¹, A. Akbarzadeh Pasha (MD)², S.R. Hosseini (MD)*³, E. Asadollahi ¹, A. Bijani (MD)³,
H. Shafi (MD)²

1. Babol University of Medical Sciences, Babol, Babol, I.R. Iran

2. Department of Kidney and Urinary Tract Surgery, Babol University of Medical Sciences, Babol, I.R. Iran

3. Social Determinants of Health (SDH) Research Centre, Babol University of Medical Sciences, Babol, I.R. Iran

Received: Jan 7th 2015, Revised: Feb 4th 2015, Accepted: May 6th 2015

ABSTRACT

BACKGROUND AND OBJECTIVE: Prostate-specific antigen (PSA) is the most practical screening test for prostate cancer. Given the importance of screening for cancer detection, determining a specific threshold for abnormal PSA levels has special significance in this disease. Because the threshold can be changed by factors such as diabetes and obesity, this study aimed to determine the association between PSA levels with BMI and diabetes.

METHODS: This was a cross-sectional study and part of the health status evaluation plan of the elderly in Amirkola, Mazandaran, Iran (AHAP=Amirkola Health and Ageing Project), which was conducted on all 60 year and older men in Amirkola from 2011 to 2012. Data was collected through questionnaires, examination and blood sampling. The levels of PSA and testosterone were measured by ELISA. Body mass index (BMI) was calculated for all patients and diabetes was determined based on the previous history of the disease or FBS $\geq$ 126 mg/dl, on two occasions.

FINDINGS: This study included 792 elders with an average age of 69.76 $\pm$ 7.62 (age range 60–90 years) with a mean PSA of 1.88 $\pm$ 2.98, testosterone of 4.77 $\pm$ 4.10, fasting blood sugar of 112.92 $\pm$ 40.08, and BMI of 26.04 $\pm$ 4.01. There was a significant association between PSA and BMI (p=0.001) so that the group BMI $\geq$ 30 showed lower values of PSA compared to the BMI<25, but there was no correlation between PSA levels and diabetes.

CONCLUSION: Based on findings of this study, the levels of PSA should be interpreted with caution in screening for prostate cancer in obese patients and further investigation is needed in this area.

KEY WORDS: Prostate-Specific Antigen, BMI, Diabetes Screening, Amirkola Health and Ageing Project.

Please cite this article as follows:

Ghasemi A, Akbarzadeh Pasha A, Hosseini SR, Asadollahi E, Bijani A, Shafi H. The Relationship between Body Mass Index and Diabetes with Serum Prostate-Specific Antigen Levels in the Elderly J Babol Univ Med Sci. 2015;17(6): 7-12.

*Corresponding Author: S.R. Hosseini (MD)

Address: Infectious Diseases & Tropical Medicine Research Center, Babol University of Medical Sciences, Babol, I.R. Iran

Tel: +98 11 32199596

Email: hosseinim46@yahoo.com

Introduction

Prostate cancer is one of the most common cancers and the second prevalent lethal cancer in men. From each six men, one will develop this cancer (1, 2). In general, to screen for prostate cancer, digital rectal examination, serum PSA and transrectal ultrasound biopsy, are used.

The first-line of screening for prostate cancer is the combination of PSA and rectal examination by finger; but measuring the PSA is the most useful available tumor marker for the diagnosis of prostate cancer (3). PSA index can be affected as a result of certain factors including body mass index (BMI), considering that obese men compared with non-obese men, after unification of age and race, showed lower PSA. Several epidemiological studies have evaluated the relationship between BMI and risk of prostate cancer.

Cancer prevention studies and analysis of the preventive trial of prostate cancer suggest that obesity is positively associated with prostate cancer risk and is negatively correlated with low-risk diseases (4).

Studies have shown that obese men have larger prostates and low PSA levels, and it seems that average PSA after correction for prostate volume should be low in these individuals (5).

Considering the lower PSA for these people, and more aggressive pathological and clinical demonstration, the question raised is: should PSA screening be corrected based on rate of BMI? But as long as one study does not show worse cancer-specific mortality in a screened and treated group, this change is not recommended in clinical practice.

However the relationship between BMI and PSA needs to be assessed in order to use the findings of prostate cancer prognosis.

One of the other factors which affect the levels of PSA is diabetes, although the risk of cancers such as pancreatic, liver and colon cancers is higher in patients with diabetes, but some studies have shown that men with diabetes have lower risk for prostate cancer and lower PSA, however, this relationship is not true in all age groups (6), therefore, this study investigated the relationship between diabetes and BMI with PSA.

Methods

This was a cross-sectional study and part of the health status evaluation of the elderly in Amirkola, Mazandaran, Iran (AHAP = Amirkola Health and Ageing Project), which was conducted on all 60 year olds and older in Amirkola from 2011 to 2012 (7). Demographic data were collected using a questionnaire. Men who had a history of prostate cancer were excluded. Body mass index (BMI) was calculated based on the BMI (kg/m^2) = Weight (kg) ÷ Height² (m^2) formula.

According to the WHO criteria, BMI < 18 is underweight, 20 to 24.9 is normal, 25 to 29.9 is overweight and 30 or more is considered obese (8). Diabetes was determined based on the previous history of the disease or FBS $\geq$ 126 mg/dl, on two occasions (9).

Measurement of PSA in the elderly men was performed by the ELISA method, using the German made Diametra kits, in Babol University of Medical Sciences at the Research Center of Molecular Cell Biology, and normal threshold was considered 4 ng/dl (10).

Total testosterone levels were measured by the ELISA method using Diametra kits, based on ng/ml, and the normal range was considered 8.1 to 9. Patients were sampled in the morning fasting state. Data were analyzed by SPSS18 software and statistical tests such as Pearson correlation with the significant level of $p=0.01$, chi-square, T-Test, one-way, Mann-Whitney, and Kruskal-Wallis analysis; $p=0.05$ was considered significant.

Results

This study was performed on 792 elderly men (aged 60–92 years) with a mean age of 69.76 ± 7.62 . One case with prostate cancer was excluded from the study. The mean PSA was 1.88 ± 2.98 (0–35), mean testosterone was 4.77 ± 4.10 (0.04–34.90), mean fasting blood sugar was 112.92 ± 40.08 (60–395), and mean BMI was 26.04 ± 4.01 (15.43–38.47). 199 patients (25.1%) had diabetes; 512 patients (64.9%) had metabolic syndromes (Table 1). In this study, there was a reverse relationship

between patient age and fasting blood sugar ($p=0.008$). Also, there was an inverse relationship with BMI and direct association with PSA ($p<0.01$), and fasting blood sugar directly correlated with BMI ($p<0.01$). In this study, BMI of patients was inversely associated with testosterone levels ($p=0.003$), (fig 1)

Table 1. Distribution of frequency and age-group percentages, and body mass index in studied individuals

Variable	N(%)
age	
64-60	273(34.5)
69-65	154(19.4)
74-70	143(18.1)
79-75	129(16.3)
84-80	57(7.2)
99-84	36(4.5)
Total	792(100)
(BMI)Body mass index	
25<	323(40.8)
29. 9-25	349(44.1)
30≥	120(15.2)
Total	792(100)

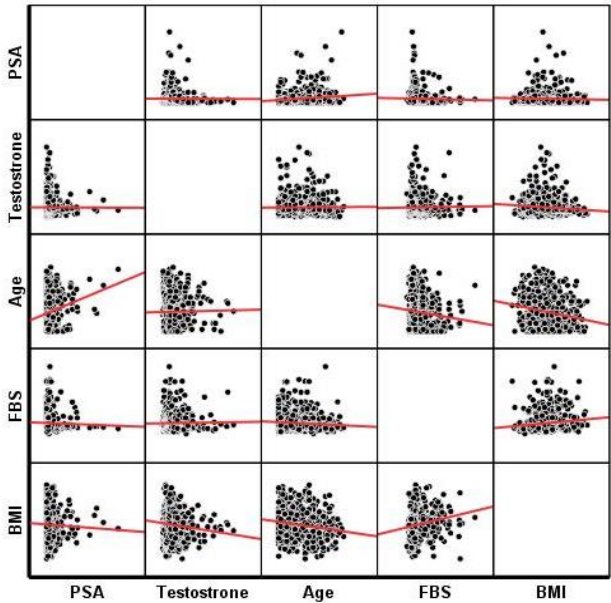


Figure 1. Correlation between the studied variables

Among diabetic patients, 181(91%) patients had serum PSA levels greater than or equal to 4, and in 18 (9%) cases it was less than 4. Among the non-diabetic patients, 531 (89.5%) had PSA greater than or equal to 4, and in 62 (10.5%) patients it was less than 4; there was no significant relationship between diabetes and serum PSA levels ($p>0.05$).

In patients with diabetes, 126 (91.3%) cases had PSA levels greater than or equal to 4. in 12 (8.7%) patients it was less than 4, in patients with undiagnosed diabetes, 55 cases (90.2%) had PSA levels greater than or equal to 4, and in 6 (9.8%) individuals it was less than 4; the association was not statistically significant.

The mean age of patients who had diabetes (199) was 68.95 ± 7.55 and the mean age of non-diabetic patients (593), was 70.03 ± 7.63 .

The means of PSA, testosterone and BMI in patients who had diabetes were 1.74 ± 2.48 , 4.65 ± 4.09 and 3.84 ± 27.08 and in non-diabetic patients they were, 1.93 ± 3.13 , 4.81 ± 4.11 and 25.70 ± 4.01 , respectively; except for BMI and diabetes ($p<0.05$), there was no significant correlation between diabetes and age, PSA and testosterone.

Average grade of PSA in the group with diabetes (199) was 383.29, and in the group without diabetes (593 patients), it was 400.93, although this association was not statistically significant.

Regarding testosterone, the average rating was 385.38 in the group with diabetes and in non-diabetics it was 400.23, but the difference was not significant. Average grade of PSA in the BMI<25 group (323 patients), the BMI between 25 and 29.99 group (349 patients) and the BMI≥30 group (120 patients), was 428.59, 377.85 and 364.37, respectively, such that the BMI≥30 group showed serum PSA levels less than the BMI <25 group, and this difference was statistically significant ($p=0.001$).

The mean levels of testosterone in the groups with BMI of less than 25, 25–29.99 and greater than or equal to 30, were 377.85, 428.59 and 364.37, respectively;

such that the BMI $\geq$ 30 group showed lower serum testosterone levels compared to the BMI <25 group ($p=0.004$) (Figure 2).

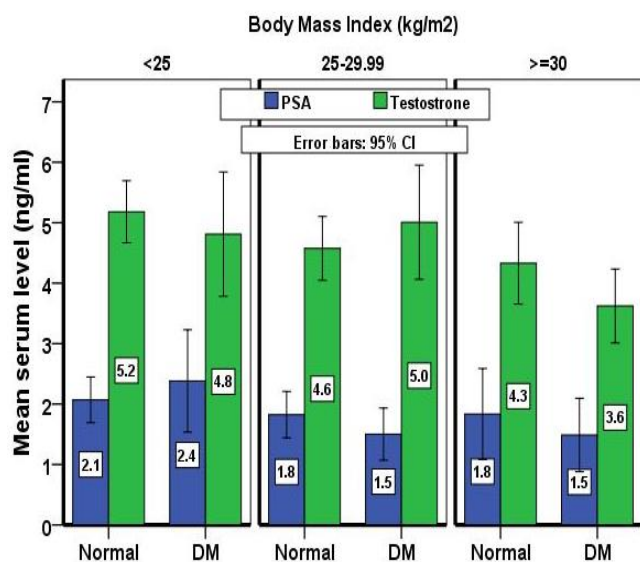


Figure 2. PSA and testosterone levels in the BMI groups and in individuals with and without diabetes

Discussion

In this study, PSA levels and BMI were inversely related. The amount of PSA in a group with a BMI of less than 25 was higher. In Naito and colleagues' study, the association between PSA and BMI in diabetic patients was not clear or significant, and the mean of PSA levels in diabetic males was clearly less than non-diabetic men in the 60 years and older age group; it was concluded that the levels of PSA in the overweight group was higher than other weight groups and it was lowest in the diabetic elderly (11).

In Yang's study, the mean age was 50 years and the average level of PSA was 0.69 ng/ml. Between BMI and serum PSA levels no correlation was found in those with a BMI of less than 23 kg/m², which confirms our research findings, but no association was found between BMI and PSA levels in the elderly group (60-79 years), which contradicts our study, performed exclusively on the elderly.

It seems this disparity may be due to genetic and racial differences. Our analysis of the relationship

between PSA and age concludes that there is a significant correlation between these two variables (12). In another study conducted by Yang et al, confirming our findings on the relationship between BMI and PSA, the probability of high serum PSA levels greater than or equal to 2.5 or 4 ng/ml, considering obesity in the Korean population, was investigated to assess the effect of PSA reduction on screening for prostate cancer in the obese.

After age unification, with increasing BMI, the probability of PSA $\geq$ 2.5 was clearly reduced, such that in obese men compared to normal BMI men, this probability was 18% lower.

Obese men were 82% as likely to have PSA $\geq$ 2.5 ng/ml compared to normal BMI men. These results may affect PSA screening for prostate cancer (13). In Liu's and colleagues study, serum PSA levels in a multiple linear regression analysis positively correlated with age, and negative association was observed between levels of BMI and PSA and the triglyceride level (TG).

Liu's study showed that age, BMI and TG affect PSA levels in men under 50 (14). Also, Abdolhosseini and colleagues in their study concluded that there was inverse and non-significant correlation between PSA and BMI.

In the above study it was shown that there was no significant relationship between PSA and BMI, while in most previous studies, the relationship between these two factors was significant, which might be due to PSA levels above 10, and uncertainty over whether better observation of probable relationship between these indicators in high levels of PSA would result (15).

Fukui et al reported that the PSA levels in diabetic men compared with non-diabetics was lower except in the 40-49 age group. However, in our study, there was no association between PSA and diabetes (16). The present study concluded that in obese patients, the PSA levels must be interpreted more cautiously. In addition diabetes has no effect on PSA levels, and it seems that PSA level changes in diabetics are not due to high blood sugar. It is worth noting that specific age group, as well

as non-normal distribution are among the limitations of the present study; hence, considering these factors in future studies, more specific results would be achieved for diagnostic and therapeutic procedures.

Acknowledgement

We thank the Deputy for Research and Technology of Babol University of Medical Sciences for funding this study.

References

1. Carter HB, Partin AW. Diagnosis and staging of prostate cancer. Campbell, s urology. 8th ed. Sydney: Elsevier science publishers; 2002.
2. Jemal A, Murray T, Ward E, Samuels A, Tiwari RC, Ghafoor A, et al. Cancer statistics, 2005. *CA Cancer J Clin*. 2005;55(1):10-30.
3. Stephan C, XU C, Cammann H, Graefen M, Haese A, Huland H, et al. Assay-specific artificial neural networks for five different PSA assays and populations with PSA 2-10 in 4,48 men. *World J Urol*. 2007; 25(1):95-103.
4. Tulloch-Reid MK, Aiken WD, Morrison BF, Tulloch TT, Mayhew R. Body mass index and prostate specific antigen levels in Jamaican men. *West Indian Med J*. 2011;60(3):316-21.
5. Cox Ansley K, Holliday Ramahi E, Swanson GP, Basler JW, Fei Du. The effects of body mass index on pretreatment characteristics, treatment choice, and response to treatment of intermediate- and high-grade prostate cancer. *J Clin Oncol*. 2012;30(Supple 5): Abstr 142.
6. Waters KM, Henderson BE, Stram DO, Wan P, Kolonel LN, Haiman CA. Association of diabetes with prostate cancer risk in the multiethnic cohort. *Am J Epidemiol*. 2009;169(8):937-45.
7. Hosseini SR, Cumming RG, Kheirkhah F, Nooreddini H, Baiani MA, Mikaniki E, et al. Cohort profile: the Amirkola Health and Aging Project(AHAP). *Int J Epidemiol*. 2014;43(5):1393-400.
8. WHO Expert consultation. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. *Lancet*. 2004;363:157-63.
9. Mirzapour A, Hosseini SR, Hosseini SM, Hezarkhani Sh, Bijani A. The relationship between serum uric acid and blood sugar levels in the elderly diabetic patients of amirkola city. *J Babol Univ Med Sci*. 2015;17(2):15-20. [In Persian]
10. Thompson IM, Pauler DK, Goodman PJ, Tangen CM, Lucia MS, Parnes HL, et al. Prevalence of prostate cancer among men with a prostate-specific antigen level ≤ 4 ng per milliliter. *N Engl J Med*. 2004;350(22):2239-46.
11. Naito M, Asai Y, Mori A, Fukada Y, Kuwabara A, Katase S, et al. Association of obesity and diabetes mellitus with serum prostate specific antigen level in Japanese men. *Nagoya J Med Sci*. 2012;74(3-4):285-92.
12. Yang WJ, Cheon SH, Kim YS, Kim DJ, Seong H, Song YS, et al. Relationship between prostate-specific antigen and body mass index according to age: lower prostate-specific antigen in middle-aged overweight and obese Korean men. *Urol Int*. 2010; 85(2):143-6
13. Yang WJ. The likelihood of having a serum PSA level of ≥ 2.5 or ≥ 4.0 ng ml⁻¹ according to obesity in a screened Korean population. *Asian J Androl*. 2013;15(6):770-2.
14. Liu M, Wang J, Zhu L, Wan G. Body mass index and serum lipid profile influence serum prostate-specific antigen in Chinese men younger than 50 years of age. *Asian J Androl*. 2011;13(4):640-43.
15. Abdolhosseini A, Totonchi Saraf K, Izanloo A, Jafari Moghadam N. Evaluation the Relationship between PSA and Prostate Size and also PSA and BMI in People referring to the Check- up Clinic of Razavi Hospital. *Med J Mashhad Univ Med Sci*. 2013;56(1):26-30. [In Persian]
16. Fukui M, Tanaka M, Kadono M, Imai S, Hasegawa G, Yoshikawa T, Nakamura N. Serum prostate-specific antigen levels in men with type 2 diabetes. *Diabetes care*. 2008;31(5):930-1.