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A PRELIMINARY STUDY OF SERUM PROSTATE SPECIFIC ANTIGEN LEVEL IN BANGLADESHI TYPE II DIABETIC MALE

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Abstract

Problem: The objective of this study was preliminary investigation of lowering PSA levels in type II diabetic patient of Bangladeshi population as reported by other researchers in different ethnic groups of different countries.In this study we compared the level of PSA in serum of type II diabetic group with non diabetic control group to investigate the possible relationships. **Experimental approach:** This study includes fifty type II diabetic male patients aged 40-70 years which were divided in two groups depending on age (<50 and >50 years of age) and fifty non diabetic male of two groups (<50 and > 50 years) aged from 33-83 years. PSA level was measured with chemiluminescent microparticle enzyme immune assay technique. These two groups are sub divided according to age (<50 and >50 years). These groups were compared by z test to find out whether any significant change occurred in PSA level and investigate linear correlation. **Major findings:** There was a negative correlation between PSA of diabetic male patients (r = 0.46; P= 0.001). **Conclusion:** Serum PSA levels were lesser in diabetic patients when compared with those in healthy male. This greatly supports the earlier observations that type 2 diabetic patients have lower level of serum prostate specific antigen.

Key words: Prostate specific antigen, Diabetes mellitus, Prostate cancer, Benign prostatic hyperplasia, Prostatitis.

Introduction

Prostate specific antigen (PSA) is known as gamma-seminoprotein or kallikrein-3 (KLK3) protein. These are glycoprotein enzyme which is encoded in human genome by the KLK3 gene. PSA is a member of the kallikrein-related peptidase family. PSA is produced and secreted by the epithelial cells of the prostate gland. Distraction of this epithelium, urinary tract infection or in the benign prostatic hyperplasia or from malignant tissue can prime diffusion of the antigen into the tissue around the epithelium. This cause the elevated blood levels of PSA in this conditions[1]. PSA is a 34-KD glycoprotein which is produced almost entirely by the prostate gland. It is an androgen regulated serine protease (EC 3.4.21.77) enzyme and gene responsible for this is located on the chromosome number 19 (19q13) in humans[2]. In the United States, the PSA test was approved as gold standard by U.S. Food and Drug Administration (FDA). Serum PSA test is done for yearly screening of prostate cancer in men of age 50 to more than 50 years and to monitor the relapse of cancer after treatment. It is required to inform patients about the dangers and benefits of testing PSA level before doing the test. Serum PSA levels between 4 to 10 ng/mL (nanograms per milliliter) are considered to be doubtful and the test supposed to be confirmed with a repeat test. Determination of prostate-specific antigen (PSA) is extensively functional for early detection of prostate cancer. Though, serum PSA levels appear to be predisposed by a number of factors such as demographic and health features. So, it deserves careful consideration to interpret the PSA test. In a current study from the United States showed there is an inverse association between diabetes and PSA levels[3], and numerous studies reported inverse associations between body mass index (BMI) and PSA levels[4, 5], while others presented lower mean[6] or median[7]PSA in higher BMI group of people. Though, the severity, period, and treatment of diabetes are yet to be explored. Recent inquiries have recommended that diabetic men are at a reduced risk for prostate cancer[8-11].Several studies have reported inverse associations of PSA level with diabetes[12-17].

In this study we have compared the values of PSA in serum of diabetic and non diabetic subjects of two age groups.

Materials and method

In order to get rid of the potential effects of high PSA values, individuals with evidence of prostate disease such as prostatitis, prostate cancer or benign prostate hypertrophy or patients whose serum PSA levels are more than 4 ng/ml, were excluded. The case group (diabetic) patients attending Popular Diagnostic Centre Ltd. during the study time were selected randomly. The control group included healthy non diabetic maleindividuals were chosen by random sampling. Type IIdiabetes mellitus was defined by American Diabetes Association [18] when both fasting plasma glucose (FPG) is equals or more than 126 mg/dl and HbA1c is equals or more than 6.5%. Fiftymen with type II diabetes aged 40-70 years (52.1±8.15) years of two groups (<50 and >50 years) and 50 non-diabetic men aged 33-83 years (55.6±11.92) as controls were included in this study. PSA was measured by microparticle enzyme immunoassay in Architect 2000i. Determination of serum Total PSA analysis is a two-step immunoassay procedure in order to determine the level of total PSA as both free PSA and bound PSA (PSA complex with alpha-1-antichymotrypsin). Determination of PSA level in human serum was done by Chemiluminescent Microparticle Immunoassay (CMIA) technology. At first, collected serum sample from patient and anti-PSA coated paramagnetic microparticles are mixed together, after that PSA present in the serum sample fixes to the anti-PSA antibody coated microparticles. Then the solution is washed and acridinium labeled anti PSA antibody conjugate is added. Then addition of pre-trigger and trigger solutions were done to the reaction mixture. Resulting chemiluminescence formed through the reaction is measured as relative light units (RLU) and straight association exist among the quantity of total PSA of the serum and the RLUs sensed by the sensor of Architect i optical system. Statistical analyses were done using Statistical Package for the Social Sciences (SPSS), Version 20 (IBM Corp., USA). Z test and linear correlation were done to contrast the values of PSA between diabetic and non-diabetic male groups and subgroups depending on age (<50 and ≥50 years of age). The results are represented in tables where continuous variables are articulated as means, median and standard deviations and P value < 0.05 was considered as statistically significant.

Results and Discussion

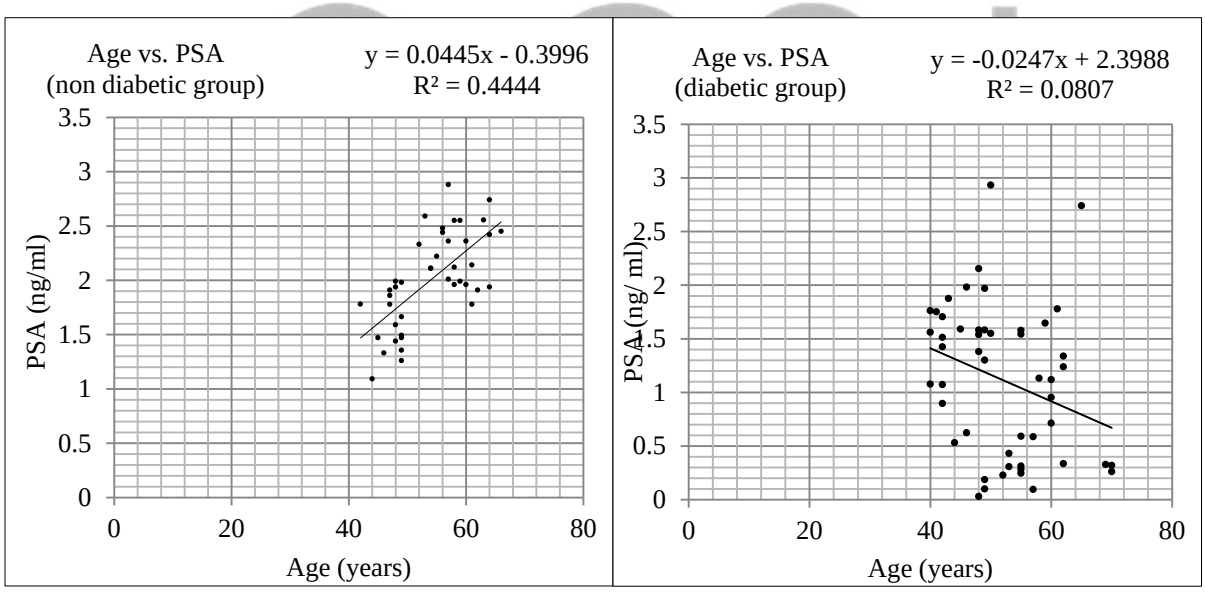
All PSA values for diabetic and non diabetic groups were within the normal range.

Table 1: Descriptive statistical data of PSA of diabetic and non diabetic group

Group	Sub group	n	Mean (ng/ml)	Standard Deviation	Median (ng/ml)	Minimum (ng/ml)	Maximum (ng/ml)
Diabetic	<50 yrs	25	1.34	0.53	1.152	0.029	2.154
	≥50 yrs	25	0.92	0.763	0.713	0.095	2.933
Non-diabetic	<50 yrs	25	1.567	0.278	1.492	1.092	1.99
	≥50 yrs	25	2.278	0.28	2.278	1.778	2.88

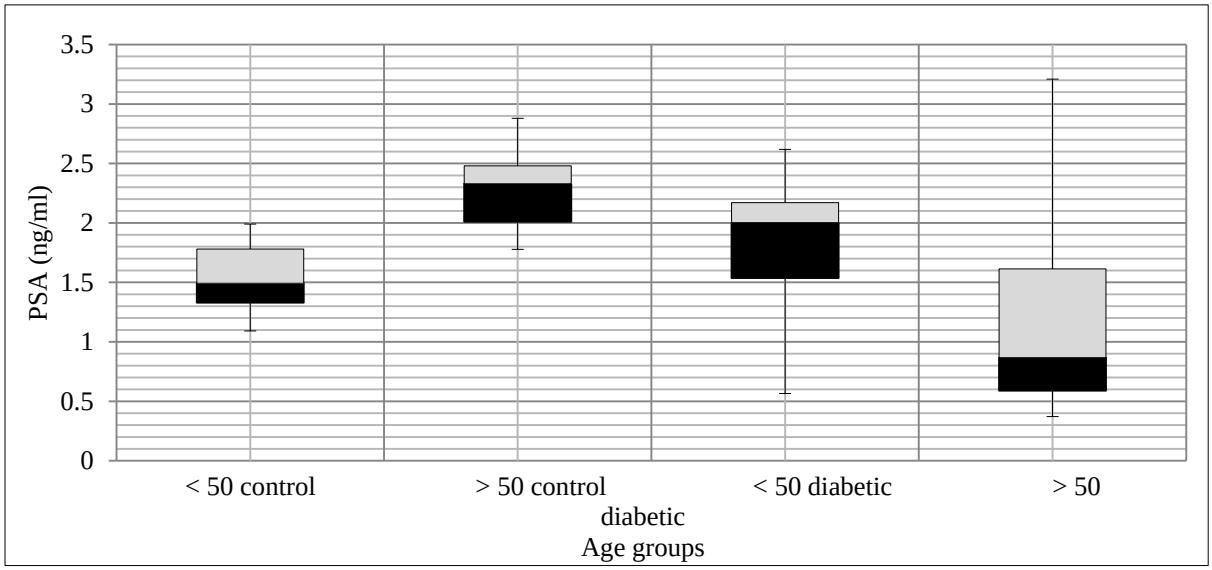
From table 1,the PSA level was significantly lower among two subgroups of diabetic group than that of non-diabetic group. Serum PSA level in <50 years group of diabetic and non diabetic are 1.30 ± 0.58 ng/ml vs. 1.57 ± 0.27 ng/ml and in > 50 years group PSA levels are 0.92 ± 0.76 ng/ml vs 2.278± 0.28 ng/ml respectively. In non-diabetic group, there is significant correlation between age and PSA level (r=0.66) and negative relationship was observed between serum PSA level and age of diabetic male patients (r= 0.28).

Figure: 1, Correlation of age vs. PSA of non diabetic and diabetic group.



Z test yielded statistical significance (P<0.001) when PSA level of both sub groups of diabetic and non diabetic were compared. In diabetic patients, median PSA level of <50 years age sub group was higher than that of >50 years age sub group. But the PSA level of both <50 and >50 years sub group of diabetic group were lower than that of both <50 and >50 years sub group of non diabetic group.

Figure: 2, Box whisker plot of control and diabetic groups



Insulin like growth factor‑1 (IGF-1) was showed to be the growth promoter of cell of Prostate gland [18] and is positively associated to PSA[19]. The low level of IGF‑1 in long term diabetes[20] as insulin production drops[21] may further explain the low level of PSA in diabetic patients. This is also reported that impaired kidney functions[22]andmedications for diabetes mainly metformin[23] or others, which are commonly used in diabetes such as statins, can also lower serum total PSA[24].It has confirmed that diabetic men have significantly lower serum testosterone than that of non diabetic males[25] and is also consistent with a possible association between succeeding diabetes and declining testosterone concentrations, which may cause lowering the risk of prostate cancer [26].A different study however reported that there are no relations between serum PSA levels and serum testosterone level[27]. Other studies[28] elucidated those diabetic men who took insulin with microvascular difficulties shows lesser risk of prostate cancer, which indicates that severity of diabetes, decreases the risk of prostate cancer. Some researchers recognized their findings to the hormonal hypothesis, which suggests that serum PSA is influenced by steroid hormone levels[29].On the other hand, some other researchers recommended a haemodilution theory, which suggests that obesity cause increase of plasma volume, which leads to the reduction of circulating PSA level[30].

Conclusion

Our study indicated that serum PSA is less age dependent in diabetic patients than in non diabetics, particularly in elderly people. In diabetic patients, PSA increased with age until age of 60 years and then decreased without significant association. While in non diabetic patients, it increased significantly with age.

Limitations and recommendations

This study encompass some limitations which are, firstly, we were unable to detect and compare serum androgen levels between non diabetic healthy male and type II diabetes mellitus male patients and correlate them with the PSA levels of respective groups. Secondly the prostate gland volume was not measured which may affect the prostate growth and PSA level. Thirdly the sample size was small, so it can be considered as a preliminary study. Additionally, some information could not be gathered such as, duration of treatment, dosage of medications etc. In spite of these limitations, the results of our study are still in accord with other published findings that serum PSA level is affected by type 2 diabetes mellitus. So, supplementary studies are required to investigate the results of this study, which mention only to a small group of men between forty and seventy years of age. And this study results are also pertinent to other populations as well for the better perceptive of the deterministic limitations of PSA level.

References

1. Leong, Anthony S-Y, Cooper, Kumarason, Leong, F Joel W-M (2003). *Manual of Diagnostic Cytology* (2nd ed.). *Greenwich Medical Media, Ltd.* ISBN 1-84110-100-1. 79–80.
2. Lilja H (2003). "Biology of prostate-specific antigen". *Urology*. **62** (5 Suppl 1), PMID 14607215, 27-33.
3. Werny DM, Saraiya M, Gregg EW. (2006). Prostate-specific antigen values in diabetic and nondiabetic US men, 2001-2002.*Am J Epidemiol*., 164, 978 –983.
4. Baillargeon J, Pollock BH, Kristal AR, et al. (2005). The association of body mass index and prostate-specific antigen in a population-based study. *Cancer*, 103, 1092 – 5.
5. Barqawi AB, Golden BK, O'Donnell C, Brawer MK, Crawford ED. (2005). Observed effect of age and body mass index on total and complexed PSA: analysis from a national screening program. *Urology*, 65, 708 – 12.
6. Hutterer G, Perrotte P, Gallina A, et al. (2007). Body mass index does not predict prostate-specific antigen or percent free prostate-specific antigen in men undergoing prostate cancer screening. *Eur J Cancer* , 43, 1180 – 7.
7. Atchison EA, Gridley G, Carreon JD, (2011). Leitzmann MF, McGlynn KA. Risk of cancer in a large cohort of U.S. veterans with diabetes. *Int J Cancer*, 128, 635–643.
8. Kasper JS, Liu Y, Giovannucci E. (2009). Diabetes mellitus and risk of prostate cancer in the health professionals follow-up study. *Int J Cancer*, 124, 1398–1403.
9. Leitzmann MF, Ahn J, Albanes D, Hsing AW, Schatzkin A, Chang SC, Huang WY, Weiss JM, Danforth KN, Grubb RL, 3rd, Andriole GL. (2008). Diabetes mellitus and prostate cancer risk in the prostate, lung, colorectal, and ovarian cancer screening trial. *Cancer Causes Control*, 19, 1267–1276.
10. Kasper JS, Giovannucci E. (2006). A meta-analysis of diabetes mellitus and the risk of prostate cancer. *Cancer Epidemiol Biomarkers Prev*., 15, 2056–2062.
11. Turner EL, Lane JA, Donovan JL, Metcalfe C, Neal DE, Hamdy FC, Martin RM. (2011). Association of diabetes mellitus with prostate cancer: nested case-control study (Prostate testing for cancer and treatment study). *Int J Cancer*, 128, 440–446.
12. Muller H, Raum E, Rothenbacher D, Stegmaier C, Brenner H. (2009). 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*., 18, 1350–1356.
13. Werny DM, Saraiya M, Gregg EW. (2006) Prostate-specific antigen values in diabetic and nondiabetic US men, 2001–2002. *Am J Epidemiol*., 164, 978–983.
14. Wallner LP, Morgenstern H, McGree ME, Jacobson DJ, Sauver JL, Jacobsen SJ, Sarma AV. (2011). The effects of type 2 diabetes and hypertension on changes in serum prostate specific antigen levels: results from the Olmsted County Study. *Urology*, 77, 137–141.
15. 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: 930–931.
16. Ando R, Nagaya T, Hashimoto Y, Suzuki S, Itoh Y, Umemoto Y, Ikeda N, Tozawa K, Kohri K, Tokudome S. (2008). Inverse relationship between obesity and serum prostate-specific antigen level in healthy Japanese men: a hospital-based cross-sectional survey, 2004–2006. *Urology*, 72, 561–565.
17. Ochiai A, Fritsche HA, Babaian RJ. (2005). Influence of anthropometric measurements, age, and prostate volume on prostate-specific antigen levels in men with a low risk of prostate cancer. *Urology*, 66, 819–823.
18. American Diabetes Association. (2016) 2. Classification and diagnosis of diabetes. *Diabetes Care*., 39 Suppl 1:S13-22.
19. Cohen P, Peehl DM, Rosenfeld RG. (1994) The IGF axis in the prostate. *Horm Metab Res*., 26, 81‐4.
20. Oliver SE, Barrass B, Gunnell DJ, Donovan JL, Peters TJ, Persad RA, *et al.* (2004). Serum insulin‐like growth factor‐I is positively associated with serum prostate‐specific antigen in middle‐aged men without evidence of prostate cancer. *Cancer Epidemiol Biomarkers Prev*., 13,163‐5.
21. Giovannucci E. (2003). Nutrition, insulin, insulin‐like growth factors and cancer. *Horm Metab Res*., 35, 694‐704.
22. Bruun L, Ekberg H, Bjørk T, Lilja H, Høglund P, Christensson A, *et al.* (2004). Rapid elimination by glomerular filtration of free prostate specificantigen and human kallikrein 2 after renal transplantation. *J Urol*., 171, 1432‐5.
23. Jayalath VH, Ireland C, Fleshner NE, Hamilton RJ, Jenkins DJ. (2016). The relationship between metformin and serum prostate‐specific antigen levels. *Prostate*; 76, 1445‐53.
24. Chang SL, Harshman LC, Presti JC Jr. (2010). Impact of common medications on serum total prostate‐specific antigen levels: Analysis of the nationalhealth and nutrition examination survey. *J Clin Oncol*; 28, 3951‐7.

25. Betancourt‐Albrecht M, Cunningham GR. (2003). Hypogonadism and diabetes. *Int J Impot Res*; 15 Suppl 4, S14‐20.

26. Barrett-Connor E, Khaw KT, Yen SS. (1990). Endogenous sex hormone levels in older adult men with diabetes mellitus. *Am J Epidemiol*.,132, 895–901.

27. Hutterer G, Perrotte P, Gallina A, Walz J, Jeldres C, Traumann M, Suardi N, Saad F, Benard F, Valiquette L, McCormack M, Graefen M, Montorsi F, Karakiewicz PI. (2007). Body mass index does not predict prostatespecific antigen or percent free prostate-specific antigen in men undergoing prostate cancer screening. *EurJ Cancer*, 43, 1180–1187.

28. Monath JR, McCullough DL, Hart LJ, Jarow JP. (1995). Physiologic variations of serum testosterone within the normal range do not affect serum prostate-specific antigen. *Urology*., 46, 58–61.

29. Velicer CM, Dublin S, White E. (2007). Diabetes and the risk of prostate cancer: the role of diabetes treatment and complications. *Prostate Cancer Prostatic Dis*., 10, 46–51.

30. Kubota Y, Seike K, Maeda S, Shinohara Y, Iwata M, Sugimoto N, *et al.* (2011). Relationship between prostate‐specific antigen and obesity in prostate cancer screening: Analysis of a large cohort in Japan. *Int J Urol*., 18. 72‐5.