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

Sharif Neaz¹, Sayeeda Monira Rahman², Md. Abul Kaiser Bhuiyan³, Md. Sohrab Alam⁴ Shahdat Hossain⁵, Ishtiaq Mahmud⁶*

¹ Lecturer, Department of Biochemistry & Molecular Biology, Tejgaon College, Dhaka-1215, Bangladesh.
² Lecturer, Department of Biochemistry & Molecular Biology, Habibullah Bahar University College, 10/A Circuit House Road, Dhaka-1000, Bangladesh.
³ Junior Consultant, Department of Biochemistry and Immunology, Popular Diagnostic Centre Ltd., Dhaka, Bangladesh.
⁴ Lab In-charge & Senior Research Officer, Molecular Genetics Laboratory, Department of Immunology, BIRDEM General Hospital, Dhaka-1000, Bangladesh.
⁵ Professor, Department of Biochemistry & Molecular Biology, Jahangirnagar University, Savar, Dhaka, Bangladesh.
⁶ Professor (Retired), Department of Biochemistry & Molecular Biology, Dhaka University, Dhaka-1000, Bangladesh. Mail address: ishtiaq51@yahoo.com

Correspondence: ishtiaq51@yahoo.com

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. 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. 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, and numerous studies reported inverse associations between body mass index (BMI) and PSA levels, while others presented lower mean or median 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. Several studies have reported inverse associations of PSA level with diabetes. 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 male individuals were chosen by random sampling. Type II diabetes mellitus was defined by American Diabetes Association when both fasting plasma glucose (FPG) is equals or more than 126 mg/dl and HbA1c is equals or more than 6.5%. Fifty men with type II diabetes aged 40-70 years (52.1±8.15) years of two groups (<50 and ≥50 years of age) 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

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

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.
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\(^{22}\) and medications 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


