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Research Article

Risk of prostate cancer and its correlation with different biochemical parameters in non diabetic men

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ABSTRACT

Background: It has been hypothesized that men with long term diabetes have a lower risk of prostate cancer then non-diabetic men. Whether diabetes influences level of biomarkers such as prostate specific antigen (PSA), which is involved in the detection of prostate cancer is, unknown. In view of the aforementioned controversial literature, it was decided to evaluate this relation-ship in non-diabetic men. We evaluated the correlation between fasting glucose, prostate specific antigen and different biochemical lipid profile parameters with serum uric acid and serum creatinine in non-diabetic male between age group 40-61 years.
Methods: Association between fasting serum glucose , different lipid parameters, serum uric acid, serum creatinine and prostate specific antigen in 83 non-diabetic males aged 40 to 61years were studied retrospectively. Glucose and lipid parameters and serum creatinine, serum uric acid were measured on fully automated analyser using standard reagent kits. Serum prostate specific antigen was measured by TOSOH-AIA-360, immunoassay method.
Results: Correlations between different biochemical parameters were determined. Prostate specific antigen were negatively correlated with HDL (r= -0.22, p= 0.03) in age group 40-61 years. At the same fasting blood sugar were correlated positively(r= 0.34, p= 0.02) with prostate specific antigen in age group 51-60 years , but not in age group 40-50 years.
Conclusion: We concluded that serum HDL (high density lipoprotein) was negatively associated and FBS (fasting blood sugar) was positively associated with risk of prostate cancer. We also suggest that in men of this age group a low HDL level should not be ignored while assessing prostate cancer risk especially if accompanied with an elevated FBS level even in the upper normal range.

Keywords: Prostate specific antigen, Diabetes, non-diabetics, Blood glucose, High density lipoprotein

INTRODUCTION

Type 2 diabetes mellitus (DM) is associated with severely acute and chronic complications that negatively impact both the quality of life and the survival of affected individuals.[1] Diabetic patients are prone to develop cancer involving pancreas, liver, breast, colorectum, bladder, and endometrium.[2,3,4] With increasing duration and severity of diabetes, chronic complications may set in and interfere with the association between diabetes and prostate cancer. Some suggested that diabetes might only convey a higher risk of more advanced prostate cancer.[2,5] Prostate cancer is the second most frequently diagnosed cancer of men (899 000 new cases, 13.6% of the total) and the fifth most common cancer.[6] The incidence of prostate cancer has increased rapidly in the last two decades in most Asian Countries.[7,8] PSA levels are influenced by a number of demographic, lifestyle, and

health characteristics, all of which deserve careful attention in the interpretation of test results.[9]

Diabetes mellitus (DM) and cancer are two common severe chronic diseases that lead to many deaths.[10] However, the association between diabetes and cancer is still in dispute, and various mechanisms have been suggested to explain the potentially causal relationship between diabetes and cancer. The former is associated with insulin resistance, relative insulin deficiency, insulin secretor defect, or both. Insulin may stimulate cell proliferation through activation of the insulin receptor or insulin-like growth factor receptor.[11]

Several studies have suggested that diabetes significantly increases the risk of different cancers, and the association between diabetes and cancer is of clear importance.[12] In contrast with various other malignancies, published data obtained from population-based studies indicate that the risk of prostate cancer may have an inverse relationship with DM.[12] An inverse relationship between diabetes and prostate cancer was found in several earlier studies.

High testosterone levels may increase the risk of prostate cancer and, therefore, low testosterone levels may actually be protective.[12,13] Similar results were found in a population-based cohort study.[12] However, A positive link between diabetes and prostate cancer is observed, which is more remarkable in the youngest age of 40–64 years.[14]

PSA (prostate specific antigen) is a most valuable cancer marker that is use for population screening, diagnosis and monitoring of patients with prostate cancer. PSA is a glycoprotein produces primarily by the epithelial cells of prostate gland and its regulation under control of androgens and progestin's. PSA is secreted in to seminal plasma at high concentration (~0.5-3 g/l), whereas lower (~10^6 times) concentrations normally found in the circulation are the result of leakage from prostate gland.[15]

There are some epidemiological studies on the relationship among, diabetes, prostate cancer risk and PSA; however, the results have often been discrepant and confusing. Identifying risk factors for prostate cancer is critically important to develop potential interventions and to expand our understanding of the biology of this disease.[16,17,18] In view of the aforementioned controversial literature, it was decided to evaluate the relation-ship in non diabetic men between risk of prostate cancer and various biochemical parameters.

METHODS

This study was conducted at the Shri Ram Murti Smarak Institute of Medical Sciences, Bareilly (North Indian city), on company employees that visit the Medicine OPD for 'health checkups' under which they are tested for various biochemical parameters, including fasting blood glucose and fasting lipid profile, in the hospital's clinical biochemistry. Eighty three such male OPD attendees between August 2012 and July 2013 who were non-diabetic and aged between 40 and 61 years were included in this retrospective study. The lipid profile, fasting blood glucose levels, serum creatinine, serum uric acid and serum prostate specific antigen of these 83 subjects obtained from our clinical biochemistry laboratory were used for the study.

Blood Sampling and Routine Biochemical Analysis

As per our clinical laboratory procedure, serum was separated from venous blood of fasting subjects and analysed within two hours of collection. Serum glucose, serum TG , serum TC , serum creatinine and serum uric acid were was analysed spectrophotometrically by GOD-PAP, GPO-PAP and CHOD-PAP, jaffey's, uricase methods respectively by employing reagent kits on a fully automated analyser of the mind ray series Serum HDL-C was measured using reagent kit (Accurex, Mumbai) on semi autoanalyser- BTR-830 (Biosystems SA, Spain). This uses the supernatant for HDL-C assay by the same enzymatic method used for TC analysis, after the other lipoproteins are precipitated by phosphotungstate and Mg^{2+}. VLDL-C and LDL-C was calculated by Friedewald's formula (Friedewald *et al*., 1972) as TG was <400 mg/dl in all the subjects. Lipid ratios (TC/HDL-C and LDL-C/HDL-C) were calculated by simple division, non-HDL-C was determined by subtracting HDL-C from TC, AIP was calculated as log (TG/HDL-C) with TG and HDL-C expressed in molar concentrations (Dobiasova& Frohlich, 2001). It has been suggested that AIP value of −0.3 to 0.1 is associated with low CAD risk, 0.1 to 0.24 medium and above 0.24 high risk (Dobiasova, 2006). Serum prostate specific antigens were measured by TOSOH-AIA-360, immunoassay method. Ranges of serum PSA (<49 year- <2.0 ng/ml, 50-59 years <3.5 mg/dl, 60-69 years <4.5 ng/ml, 70-79 years <6.5 ng/ml) used. The subjects were divided into two age groups: ≤50 years (40 to 50 years,) and ≤61years (51 to 61 years), the reason being that age of >40 years is considered to be a major risk factor in men. Exclusion criteria were diabetic or male who were suffered any other health problem.

Statically analysis

Results are presented as mean ± SD. Correlations between the serum PSA levels and other variables were examined by Pearson's correlation analysis. A p value < 0.05 was considered significant. Statistical analysis was performed using Graph Pad Prism version 5.00 for Windows (GraphPad software, San Diego California USA, www.graphpad.com).

RESULTS

The age of the study population was 40- 61 years. The mean serum PSA, fasting glucose were 0.74 ±0.76. 0.83 ± 0.61 and 99.82 ± 21.88, 110.41 ± 47.06 in age group

40-50 years and 51-61 years, respectively. Table 1 and Table 2 were represented different biochemical parameters with their mean and SD.

Table 1: Lipid profile and its derivative with PSA in non diabetic male subjects.

Parameters	40-50 years Mean ± SD	51-61 years Mean ± SD	P- value
Fasting glucose	99.82± 21.88	110.41± 47.06	0.1842
Serum Total cholesterol	177.95± 33.29	184.15± 44.65	0.4723
Serum Total triglyceride	166.98± 76.89	160.62 ± 73.12	0.7013
Serum HDL	40.23± 7.70	39.15± 8.49	0.5475
Serum LDL	103.23± 31.33	113.56± 37.15	0.1730
HDL/LDL	0.48± 0.42	0.40± 0.24	0.2861
AIP	0.22± 0.19	0.21± 0.23	0.8160
Serum PSA	0.74± 0.76	0.83± 0.61	0.5834

Table 2: Different biochemical parameters in non diabetic male subjects.

Parameters	40-50 years Mean ± SD	51-61 years Mean ± SD	P- value
Serum creatinine	0.98± 0.13	1.07± 0.22	0.0424*
Serum uric acid	5.20 ± 1.03	5.8± 0.77	0.0042*

* Significant p value

Table 2 represented statically significant p value for serum creatinine (0.042) and serum uric acid (0.004). Figure 1 was represented a significant positive correlation (r=0.3498, p=0.029) between fasting blood glucose (FBS) and prostate specific antigen (PSA) in non-diabetic men. It means when increased the concentration of blood glucose in non diabetic men at the same increased the secretion of prostate specific antigen to epithelium cell of prostate and because of this increased the risk of prostate cancer in this age group 50-61 years, while there were no correlations between age group 40-50 years.

Figure 2 was represented a negatively significant correlation (r= -0.2297, p = 0.036) between serum high density lipoprotein (HDL) and prostate specific antigen (PSA) in non diabetic men age group 40-61 years. According to this when decreased the level of serum HDL in non diabetic men at the same increased the level or concentration of prostate specific antigen, which is responsible to increasing the risk of prostate cancer in this population.

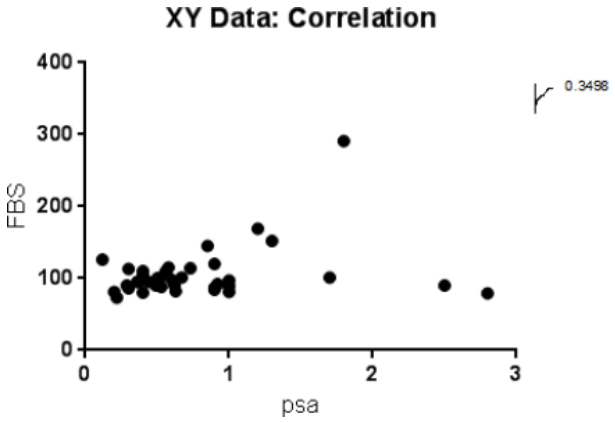

Figure 1: Positive correlation (r= 0.3498) graph between PSA (prostate specific antigen) and FBS (fasting blood glucose) in age group 50-61 years.

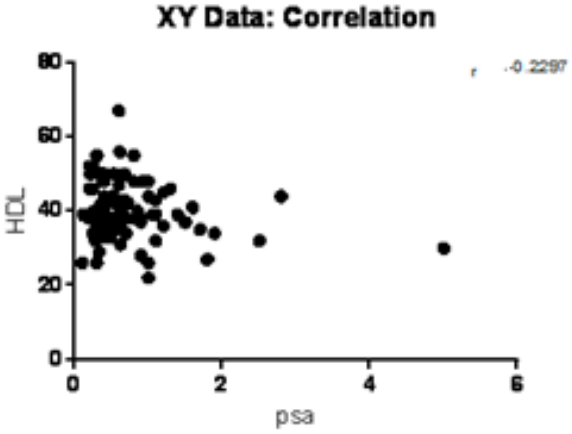

Figure 2: Negative correlation (r= -0.2297) graph between serum HDL (high density lipoprotein) and PSA (prostate specific antigen) in age group 40-61 years.

In our study, we found that there were no correlation between serum uric acid and prostate specific antigen, while these data were statically significant in both age groups. At the same there were no significant correlation was presented between serum creatinine and prostate specific antigen (PSA) in non diabetic men.

DISCUSSION

PSA in serum mostly found as a PSA-ACT (alpha-1 antichymotrypsin) complex and free PSA (representing about 10-30%) of total PSA.[19,20] Elevated serum PSA concentration are known to be connected with the three most common prostatic diseases, prostate cancer, benign prostatic hyperplasia and prostitis.[15,21,22] Serum prostate concentration is age dependent, i.e. it tends to increase with age because the prostate enlarge with years and contain more PSA- producing tissue.[23]

To the best of our knowledge, DM (diabetes mellitus) has been associated with increased risk of numerous cancers including cancers of the pancreas, liver, breast, kidney, colon, and female reproductive organs.[24,25,26] However, diabetes is also linked to lower serum PSA.[27,28] But in our study we were found that, when increased the level of fasting glucose in non diabetic subjects in age group 50-61 years, at the same time increased the concentration of PSA in serum. That means there were positive correlations between the fasting blood glucose concentration and PSA in this group, while there were no correlations found between fasting blood glucose and PSA in men with age group 40-50 years. It means that serum PSA correlated positively with age and fasting blood glucose.

Our study was correlated with the study of Xiang-Ju Long et al, according to them**,** meta-analysis strongly support that diabetes is associated with an increased risk of prostate cancer in Asians.[29] Apparently, the associations of patients with DM and prostate cancer risk in Asian and Caucasian populations are different. Several factors such as environmental factors, family history, duration of diabetes, type of diabetic medication, duration of medication use, and different genetic backgrounds might contribute to the different result, which should be clarified in further studies.

Serum creatinine is a measure of renal function, but it is also influenced by other factors and therefore not a specific or sensitive indicator of renal disease within normal ranges.[30] In addition to the glomerular filtration rate, for example, creatinine concentrations are influenced by age, sex, muscle mass, and intake and absorption of dietary creatine and creatinine, which are consumed in meat.[30,31] In our study the creatinine sensitivity was also more in these subjects.

Our study was correlated with this study; the reason for creatinine sensitivity may be due to the lymph node enlargement and around prostate area and ureters cause obstruction, even partial obstruction and back flow causes increased creatinine levels in serum. Carcinoma prostate itself leads to partial obstruction to urinary flow. Due to increased back pressure of urinary flow may result into mild increase in Serum creatinine levels.[32] With this in our study we were found that serum uric acid also significant, this finding was supported by this statement: Increased production of uric acid may be due to enhanced turnover rate of nucleic acids may be due to (i) rapidly growing malignant tissue (ii) increased tissue breakdown after treatment of malignant tumors (iii) increased tissue damage due to trauma and raised rate of catabolism.[33]

According to Jan Hammarsten and Benkt Högstedt that clinical prostate cancer is a component of the metabolic syndrome. Lipids have been found to be involved in many human diseases including cancer.[10] Many previous studies have demonstrated that obesity, DM, high insulin, and low HDL cholesterol are risk factors for the development of Benign prostatic hyperplasia (BPH).[34-36]

Our study was also supported this fact, when decreased the concentration of HDL in men between age group 40-61 at the same increased the concentration of serum PSA. However, the exact roles of different lipid fractions on prostate cancer aggressiveness should be further evaluated.

While our study has some limitations. A retrospective study, like ours, is less dependable than prospective ones when conclusions about relations between determinants and incidence of disease are to be made. A larger sample size would have given more reliable results.

CONCLUSION

Correlations between different biochemical parameters were determined. Prostate specific antigen were negatively correlated with HDL (r= -0.22, p= 0.03) in age group 40-61 years. At the same fasting blood sugar were correlated positively (r= 0.34, p= 0.02) with prostate specific antigen in age group 51-60 years, but not in age group 40-50 years.

Increasing fasting glucose level in age group 51-61 years and decreasing serum HDL level in age group 40-61 years are an independent risk factor for prostate Cancer even in non diabetic men. In the end we can concluded that decreasing HDL and increasing glucose concentrations were not only risk factors for cardiac vascular diseases but also risk factors for prostate cancer in the age group 40-61 years. We also suggest that in men of this age group a low HDL level should not be ignored while assessing prostate cancer risk especially if accompanied with an elevated FBS level even in the upper normal range.

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