Prostate Specific Antigen (PSA), Calcium Levels and Risk of Prostatic Diseases among adult Diabetic Males on Treatment in Benin City

Adejumo B. I. G. and Ejeye B. A.
Medical Laboratory Science Department, University of Benin, Benin City, Nigeria

Abstract

Several studies have proposed possibility of less risk for long term diabetics to develop prostatic diseases, even as lots of controversies still surround the role of calcium in the pathophysiology of these diseases. The aim of this study is to determine the relationship between serum prostate specific antigen (PSA) serum calcium levels and risk of prostatic diseases among diabetic male patients undergoing treatment in a tertiary hospital in Benin City. A total of seventy four adult males aged between 35 - 68years participated in this study. They comprised of forty four, type 2 diabetics who were regular out patients of central Hospital, Benin City Edo state and thirty, healthy sex matched, non-diabetics controls. Demographic variables were obtained using questionnaires, after their informed consents were sought and medical history obtained from patients' case notes. The serum prostate specific antigen (PSA) level was determined by using enzyme-linked immunosorbent assay (ELISA) method, while the serum calcium level was determined using spectrophotometric method. Significant increase ($p<0.05$) in mean PSA level when controls was compared to diabetic group was recorded. However, calcium ion level showed a significant decrease ($p<0.05$) when control was compared to diabetic group. Meanwhile, negative correlation between age and PSA level (rs=-0.17; p=0.25) was recorded but was not significant ($p>0.05$), while age also had a non-significant positive correlation with calcium ion (rs=0.10; p=0.51) level in the diabetic group. This study suggests increased risk of prostatic diseases among the diabetic males on treatment in Benin City. Further works needs to be done especially on those who have been on treatment for a longer period of time.

***Corresponding Author**: Adejumo B.I.G.; babatunde.adejumo@uniben.edu

Introduction

Prostate specific antigen (PSA) is a 28400Da glycoprotein; comprising 237 amino acid residues (Lundwall *et al*., 1991) with five inter chain disulphide bonds and approximately 8% carbohydrate in the form of a N – linked oligosaccharide sidechain. The discovery of serum prostate specific antigen (PSA) and its extensive use over the past two decades has dramatically influenced the diagnosis and monitoring of prostate cancer before and after treatment, respectively (Dada *et al.,* 2018). In seminal plasma, PSA can be shown to exist in isoform, two biologically active and differing in the degree of glycosylation, and three biologically inactive or nicked form (Zhang *et al.,* 1999). However, recent studies showed that diabetic men showed a decreased risk of prostate cancer. It was suggested that men with long-term diabetes have a lower risk of prostate cancer than non-diabetic men, and recently diagnosed men have a higher risk (Liu *et al.*, 2015). Higher concentrations of insulin and insulin-like growth factor 1 (IGF-1) in early diabetes and the lower testosterone and IGF-1 levels and higher estrogen concentrations in long-term diabetes may explain such association (Djavan *et al.*, 2001). Patients with diabetes have been reported to be at increased risk of numerous cancers, including cancers of the pancreas, liver, and colon (Everhart and Wright, 1995; Stricker *et al.,* 2001). However, recent studies by Weiderpass *et al.* (2002); Rodriguez *et al.* (2005); Bonovas *et al.* (2004) also suggested that men with diabetes are at a decreased risk of prostate cancer.

According to Villar *et al.* (2006), calcium is the most abundant mineral, over 99% of total body calcium is found in bones and teeth, where it functions as a key

structural metabolism, serving as a signal for vital physiological processes, including vascular contraction, blood clotting, muscle contraction, and nerve transmission. Inadequate intakes of calcium have been associated with increased risks of osteoporosis, nephrolithiasis, insulin resistance, and obesity. High calcium intake suppresses the influx of calcium from outside the cells. In adipocytes, reductions in intracellular calcium inhibit fatty acid synthase and activate lipolysis, potentially leading to an anti-obesity effect Zemel (2001). In pancreatic β-cells, insulin secretion is a calcium-dependent process that will be compromised when intracellular calcium is either too high or too low Klec, (2019). An optimal range of intracellular calcium is also required for insulin-mediated activities in liver, skeletal muscle, and adipose tissues (Ojuka, 2004); Wright *et al.,* 2004; Williams *et al.,* 1990; Draznin *et al.,* 1987). Maintaining relatively low intracellular calcium levels in these target organs has favorable effects on insulin signal transduction Williams *et al.*1990; Zemel (1998) and peripheral insulin sensitivity Draznin *et al.* 1987. To the best of our knowledge, this study is the first to determine the relationship between serum prostate specific antigen (PSA), serum calcium levels and risk of prostatic diseases among diabetic male patients undergoing treatment in a tertiary hospital in Benin City, hence the justification of this work.

Materials and Methods
Study Area
This study was conducted in Benin City. Benin City is located in Edo State, Nigeria and it is located at 6.34 latitude and 5.63 longitudes. It is situated at an elevation of 88 meters above sea level. Benin City has a population of about 1,125,058 people, making it the biggest city in Edo State according national population commission. It is located in the South-South region of Nigeria. It shares boundaries with Ondo State (West), Delta State (South), and Kogi State (North). Benin City residents are mainly civil servants, bronze caster, traders while appreciable numbers are farmers. The city boasts of various staple foods but the commonest meal is carbohydrate dominated diets.

Study population: A total of seventy four participants enrolled for this study. The participants included adult diabetic (type 2) males (N=44) without any history of prostatic diseases, and adult males who had history of neither prostatic diseases nor diabetes mellitus as controls (N=30). They were recruited from Endocrinology Clinic at Central Hospital, Benin City, while the controls were recruited from different locations in Benin City. Demographic characteristics information and informed consent were obtained

from each participant after proper notification and information on the nature of the research, risks involved benefits as well as its confidentiality using structured questionnaires. Medical history as well as nature of treatment of individual patient was obtained from their case notes. Ethics and research committee of Ministry of Health, Edo State approved this work.

Sample Collection and Preservation: Five millimeters (5mls) of venous fasting blood sample was collected from the antecubital vein of each subject using a sterile needle and syringe, and dispensed into a clean dry plain container. The sample was allowed to clot undisturbed for 10minutes and centrifuged at 4000rpm for 10minutes to separate serum from the clot. The serum was dispensed into another clean and dry plain container and stored at -20°C prior to analysis.

Sample Analysis: The following investigations were carried out on the sample to ascertain the status of the participants.

Prostate Specific Antigen: Serum PSA level was determined using ELISA kits from Calibiotech ELISA PSA kit, CA 92020, USA, according to manufacturer's instructions

Calcium: Serum calcium level was determined spectrophotometrically using Randox reagent commercially purchased from Randox Limited (UK), according to manufacturer's instructions

Data analysis: Data was analysed using SPSS version 25. Data obtained were subjected to descriptive statistics for demographic variables and were presented in frequency, percentage, and tables. Inferential statistics (T-test and spearman correlation) were used to analysed hormones, PSA, and Calcium ion level, and demographic variables with these parameters; values were considered significant at $p<0.05$.

Results
Table 1 Result shows the demographic information of the participants. All the forty four respondents were married (100%), 24(54.5%) had employment, 4(9.1%), farmer 1(2.3%), businessmen/ Traders 4(9.1%), while retirees and unemployed have 5(11.4%) and 6(13.6%) respectively. The mean Age of the respondents was 53.00±7.99, with a minimum age of 44 and maximum age of 68 years.
Table 2 Result shows the comparison of prostate specific antigen and calcium ion level between controls and diabetic subjects. Significant increase ($p<0.05$) in mean PSA level was obtained when control was compared to diabetic group. Calcium ion result also showed a significant decrease ($p<0.05$) when control was compared to diabetic group.

Table 1: Demographic Characteristics Variables of Respondents

Variables	Frequency (%)	Total (%)
Marital Status		
Married	44 (100)	44 (100)
Occupation		
Retired	5 (11.4)	
Employed	24 (54.5)	
Driver	4 (9.1)	44 (100)
Farmer	1 (2.3)	
Businessman/Trader	4 (9.1)	
Unemployed	6 (13.6)	

Table 2 Comparism of Prostate Specific Antigen and Calcium ion Level between Controls and Diabetic Subjects

		MEAN	±SEM	P-VALUE	T-VALUE
Prostate Specific Antigen level (ng/mL)	Control group	0.17	±0.14	0.01*	-2.65
	Diabetic group	0.76	±0.14		
Calcium ion level (mg/dl)	Control group	8.36	±0.11	0.00*	3.24
	Diabetic group	6.44	±0.54		

Table 3 shows correlation between age of diabetic subject and PSA level and calcium ion level. There is negative correlation between age and PSA level (rs=-0.17; p=0.25) but was not significant ($p>0.05$), while Age had a non-significant positive correlation with calcium ion (rs=0.10; p=0.51) level.

Table 3: Correlation between Age of Diabetic Subject and PSA Level and Calcium ion Level

Diabetic subject		Prostate Specific Antigen level (ng/mL)	Calcium ion level (mg/dl)
Age (Years)	Pearson Correlation	-0.17	0.10
	P-Value	0.25	0.51
	Number	44	44

Discussion

Diabetes mellitus (DM) is a serious problem in male health; a positive association exists between clinical markers of benign prostatic hyperplasia (BPH) and diabetic mellitus. Recent studies have suggested an association between type 2 diabetes mellitus and lower risk of prostate cancer (Bonovas *et al.,* 2004 and Zhu *et al.,* 2004). It has also been hypothesized that men with long-term diabetes have a lower risk of prostate cancer than nondiabetic men, and recently diagnosed men have a higher risk (Rodriguez *et al.,* 2005). In this study, the serum level of PSA is higher among the diabetics compared to the controls (Table 2). The result agrees with Rodriguez *et al.* (2005) but in disagreement with Bonovas *et al.* (2004) and Zhu *et al.* (2004). Though, high level of PSA is not diagnostic of prostate cancer but an indicator and a risk factor of general prostatic diseases according to Isiwele *et al.* (2018). Questionnaires and medical history from patients' case notes showed that all the patients were diagnosed less than a year making them more at risk of prostate cancer. From this study, the level of calcium is lower in diabetics when compared with the controls. This agrees with Klec *et al.* (2019), which according to them stated that pancreatic β-cells, insulin secretion is a calcium-dependent process that will be compromised when intracellular calcium is either too high or too low. Majority of the diabetic patients in this study claimed to be on calcium supplements through the questionnaire. Though their level of compliance with the dosage of this calcium supplements was not ascertained, but it may have been responsible for the slight but not significant decrease in the calcium level among the diabetics in this work. Also, taking supplements to complement diets is not part of daily routing of people in this part of the world, hence irregularity in dosage may be responsible for this outcome. According to Oesterling *et al.* (1993) and Baillargeon *et al.* (2005), one of the factors influencing serum PSA levels in men is age, others are benign prostatic hyperplasia, prostatitis, and body mass index (BMI). This study showed a non-significant negative correlation between age and PSA level among the

diabetics, while age had a non-significant positive correlation with calcium ion level.

Conclusion

This study suggests increased risk of prostatic diseases among the diabetic males on treatment in Benin City. Further works need to be done on those patients who have been on treatment for a longer period of time.

Conflict of Interest: No conflict of interest

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