IBOM MEDICAL JOURNAL
Vol.15 No.1 January, 2022. Pages 62 - 67
www.ibommedicaljournal.org

Evaluation of serum prostatic-specific antigen levels in diabetic and non-diabetic men diagnosed with benign prostatic hyperplasia

Elijah Asuquo Udoh[1], *Anthony Joseph Usoro*[2], *Oto-Obong Okpoho Peter*[1]

[1]*Urology Firm, Department of surgery, University of Uyo Teaching Hospital, Uyo, Akwa Ibom State, Nigeria.*
[2]*Department of Chemical Pathology, University of Uyo, Akwa Ibom State, Nigeria.*

Abstract

Background: Serum prostate-specific antigen (PSA) has been noted to be lower in type 2 diabetes mellitus than in non-diabetic men. There seems to be a link between diabetes and benign prostatic hyperplasia (BPH). Many researchers have implicated high insulin levels in diabetics as contributing to the underlying aetiology in the development of BPH. We aimed at evaluating serum PSA levels in diabetic and non-diabetic men with a diagnosis of BPH.
Patients and Methods: This is a retrospective study of patients who presented in the urology clinic of our facility for follow-up review between April 2021 and August 2021. One hundred and two patients were included in the study and relevant data extracted from their case notes.
Results: Mean age of all patients was 64.25±10.26 years ranging from 41 to 97 years. 22.5% of the men were diabetic while 77.5% were non-diabetic. Diabetic men were older than non-diabetics and serum PSA was lower in diabetics than non-diabetics (P-value >0.05). Also more diabetic men had PSA in the region of 0-4ng/ml while more non-diabetic men had PSA ranging from >4 to 10.0ng/ml.
Conclusion: Diabetics have lower serum PSA than normal men. This should be taken into consideration when evaluating men with prostatic symptoms as serum PSA alone may be misleading in predicting or directing further assessments. Other factors that could influence serum PSA should be considered.

Key Words: Prostate-Specific Antigen, diabetes mellitus, benign prostatic hyperplasia

Introduction

Benign prostatic hyperplasia (BPH) is a histological diagnosis of non-malignant unregulated, androgen driven hyperplasia of both stroma and epithelial prostatic cells.[1] It afflicts men mostly in their 7th decade of life.[2-5] BPH usually manifests with symptoms of bladder outlet obstruction characterized by both voiding and storage symptoms. It represents one of the commonest causes of bladder outlet obstruction.[6,7]
Diabetes mellitus (DM) is a metabolic disorder of chronic hyperglycaemia characterized by disturbances to carbohydrate, protein and fat metabolism resulting from absolute or relative insulin deficiency with dysfunction in organ systems.[8] The connection between DM and BPH was first documented by Bourke and Graffin,[9] who suggested a similar aetiology when men who presented for BPH surgery had a higher prevalence of DM. Both disease entities usually manifest with similar Symptomatology and BPH progression and diabetes also occur in similar ages.[10] Many authors[11,12] have implicated high insulin levels in DM as contributing to the underlying aetiology in the development of BPH.
PSA is a glycoprotein produced by the epithelial cells of the prostate and was first identified and purified by Wang et al in 1979.[13] Several studies have reported an inverse association between

Corresponding Author: Dr. Elijah Asuquo Udoh

Urology Firm, Department of Surgery,
University of Uyo Teaching Hospital,
Uyo, Akwa Ibom State, Nigeria. POSTAL CODE: 520261
elijah_udoh@yahoo.com, Phone: +2348136276827

diabetes and PSA levels[14,15] even though other factors such as demographics, lifestyle and health status should be considered in such associations.[16] The aim of this study was to evaluate serum PSA levels in type 2 diabetic and non-diabetic men diagnosed with BPH in our facility.

Patients and Methods:

The study was conducted in the Urology Clinic of the University of Uyo Teaching Hospital in the South-South geopolitical zone of Nigeria between April 2021 and August 2021. Folders of all patients who attended follow-up Clinic visits were used for data collection and such case notes coded to avoid duplication of information. Information retrieved included bio-data, history of lower urinary tract symptoms and history of DM. Duration of illness was not well addressed by patients and so it was omitted to avoid distorted information. Information on general physical examination and digital rectal examination (DRE) of the prostate were recorded, laboratory results namely fasting blood sugar (FBS), PSA, Full Blood count (FBC), renal function test and urine cultures were noted. Result of imaging studies included abdomino-pelvic ultrasound scan and trans-rectal ultrasound scan examination of the prostate. BPH was diagnosed clinically and by histology of prostate tissues taken when PSA was > 4.0ng/ml or a suspicious area was felt on DRE to rule out prostate cancer. Diagnosis of DM was defined according to American Diabetes Association[17] as the presence of both fasting plasma glucose of > 126mg/dl and HbAIc of > 6.5% or a positive medical history. Based on these criteria, patients were grouped into diabetic and non-diabetic. PSA values were also grouped into those with values <4.0ng/ml in group 1 and > 4-10.0ng/ml in group 2. Age of patients was categorized at intervals of 10 into groups 1 – 6 represented as 40 – 49 years, 50 – 59 years, 60 – 69 years, 70 – 79 years, 80 – 89 years, 90 years and above respectively. Relevant data were entered into pro-forma sheets designed for this study and analyzed using statistical package for social sciences (SPSS) version 20.0 and results used for discussion.

Exclusion Criteria included those patients with diagnosis of prostate cancer, prostatitis, bladder and urethral cancers, age less than forty (40) years, those with incomplete clinical, laboratory and imaging information and patients receiving 5α-reductase inhibitors.

Statistical Analysis: Frequency and percentages of categorical variables were calculated. Continuous variables were expressed as means and standard deviations. Statistical differences were assessed using students t-test. Cross tabulations between PSA, DM and non-DM groupings were done and statistical differences assessed using chi-squared. P-value < 0.05 was considered statistically significant.

Results

We evaluated one hundred and two (102) men diagnosed with BPH who were either diabetic or non-diabetic. The mean age was 64.25 + 10.26 years ranging from 41 to 97 years. Twenty three (22.5%) patients were diabetic while 79 (77.5%) of them were non-diabetic. Mean age in the diabetic group was 66.22 + 9.15 years while non-diabetic had a

Table 1: Means and standard deviation for continuous variables and students t-test:

Variable	Mean	Standard deviation (SD)
Age (years)	64.25	10.26
PSA (ng/ml)	3.69	2.68
FBS (mmol/l)	5.27	1.37
Age of Diabetics (years)	66.22	9.15
Age of Non diabetics (years)	63.68	10.55
PSA of Diabetics (ng/ml)	3.25	2.90
PSA of Non diabetics (ng/ml)	3.82	2.62
FBS of Diabetics (mmol/l)	6.95	1.53
FBS of Non diabetics (mmol/l)	4.71	0.71
		t(100)=1.04, P>0.05*

*No statistical significant difference in the mean of variables between diabetics and non-diabetics.

Table 2: Frequency of variables:

Variable	Frequency (n)	Percent (%)	Cumulative percent (%)
(i) Age (years)			
40 – 49	7	6.9	6.9
50 – 59	24	23.5	30.4
60 – 69	43	42.2	72.5
70 – 79	19	18.6	91.2
80 – 89	7	6.9	98.0
90 and above	2	2.0	100.0
Total	102	100.0	
(ii) PSA(ng/ml)			
0 -4	64	63.4	63.4
> 4 – 10	37	36.6	100.0
Total	102	100.0	
(iii) Diabetics/Non diabetics			
Diabetics	23	22.5	22.5
Non-Diabetics	79	77.5	100.0
Total	102	100.0	

Table 3: PSA and Diabetics: Cross tabulation of variables:

		Diabetics	Non diabetics	Total
PSA 0-4ng/ml	Counts	16	49	65
	% within PSA	24.6	75.4	100.0
	% within diabetics	69.6	62.0	63.7
	% of total	15.7	48.0	63.7
PSA >4-10	Counts	7	30	37
	% within PSA	18.9	81.1	100.0
	% within Diabetes	30.4	38.0	36.3
	% of total	6.9	29.4	36.3
Total	Count	23	79	102
	% within PSA	22.5	77.5	100.0
	% within Diabetes	100.0	100.0	100.0
	% of Total	22.5	77.5	100.0

Chi-Squared Statistics: X^2 (1, N = 102) = 0.438, P>0.05 No statistical significant difference.

mean age of 63.68±10.55 years. Diabetics had a lower mean PSA (3.25±2.90ng/ml) than non-diabetics (3.82±2.62ng/ml). There was no statistically significant difference between the means [t (100) = 1.04, P>.05]. Most patients (42.2%) were in their 7th decade of life (Table 2(i)). More diabetics had PSA between 0–4 ng/ml, while more non-diabetics had higher PSA values (Table 2(ii). In Table 3, more diabetics (69.6%) had PSA in the range of 0 – 4 ng/ml as against 62.0% in the non-

diabetic arm, while more normal men (38.0%) had PSA in the region of 4 – 10ng/ml as against 30.4% for diabetics. Chi-square showed no statistical significant difference between the two groups; X^2 (1, N=102) = 0.438, P>.05.

Discussion

Serum level of prostate specific antigen has been reported to be lower in diabetic than in non-diabetic patients.[14,15] In this study, we aimed at evaluating serum level of PSA in diabetic and non-diabetic patients with BPH Symptomatology. The mean age of all patients was 64.25 + 10.26 years ranging from 41 to 97 years. Majority of them were in their 7th decade of life. Similar reports have been made in other studies.[2-5] Diabetics were older than non-diabetics, although the difference was not statistically significant (P>0.05). Other authors documented same findings.[16,18] This could have been due to chance. Mean serum PSA levels were lower in diabetics, this had been previously reported by many authors including Fukui et al[19] and Werny et al.[20] Diabetics have been associated with low serum levels of testosterone.[21,23] PSA has been known to be androgen regulated[23] and both correlate positively in type 2 diabetic patients.[21] Insulin and insulin-like growth factor-1 (IGF-1) had been known as prostate cell growth promoters and also known to correlate positively with serum PSA.[24,25] There is low serum level of IGF-1 in long term T2DM patients[26] as insulin synthesis by the exhausted β-cells of the pancreas drops[27] giving an hypothetical causal relationship with lower serum PSA levels since insulin and IGF-1 correlates with PSA in T2DM patients. Aside from the mean serum PSA that was lower in diabetics, further analysis showed that more diabetic men (69.6%) had PSA in the region of 0 – 4ng/ml than non-diabetics (62.0%) [table 3]. Higher PSA values (>4 – 10ng/ml) were recorded in non-diabetics (38.0%) than in diabetics (30.4%) P>0.05. Although no statistical significance difference was observed, we think that other confounding variables not collaborated in this study would have been responsible, for instance, duration of illness and level of glycaemic control.

Duration of diabetics[20] and use of hypoglycaemic medications e.g metformin[28] and statin intake[29] have been well documented to affect serum PSA levels by researchers. Here, we were limited by a mix of poor recall of duration of disease and adherence to medications by these men. This will be addressed in future in a longitudinal prospective study. Al-Asadi et al[18] documented lower serum PSA in diabetics who used anti-diabetic medications whether oral or insulin than in non-diabetics. In another study aimed at investigating the association between diabetic men and risk of prostate cancer, it was inferred that the use of metformin was associated with both lower serum PSA and reduced prostate cancer risk.[30]

Limitation: Although none of the diabetic men was less than 65 years, because of poor recall of duration of illness, we could not altogether rule out type 1 diabetes whose serum profile may be different from type 2 diabetes. The strength of this study is that, we have been able to document this important information in black population as all cited studies were done on Caucasians.

Conclusion

In this study, PSA in diabetic men was lower than in non-diabetics and more diabetics had PSA within reference range whereas more non-diabetics had higher PSA values. These results should however be interpreted with caution as confounders must be born in mind. In light of this current knowledge, it may not be realistic to set a different PSA cut-off value for diabetics, instead diabetic men undergoing evaluation for prostate diseases should be carefully screened since serum PSA levels alone may be misleading.

Authors Contribution:

EAU: Substantial contributions to conception and design, Acquisition of data, Drafting the article, revising it critically for important intellectual content, data analysis and Final approval of the version to be published.

AJU: Substantial contributions to conception and design, revising it critically for important intellectual content and final approval of the version to be published.

OOP: Substantial contributions to conception and design, revising it critically for important intellectual content and final approval of the version to be published.

Authors declare no conflict of interest.

References

1. Mongiu Ak, MCvary KT. Lower urinary tract symptoms, benign prostatic hyperplasia and obesity. Urol Rep 2009; 10: 247 – 53.
2. Udoh EA, Eyo AE, David DE. Correlation between prostate volume and prostate-specific antigen in patients diagnosed with Benign prostatic hyperplasia. Ibom Medical Journal 2020; 13 (3): 193 – 9.
3. Ibinaiye PO, Adeyinka AO, Obajimi MO. Comparative evaluation of prostate volume by trans-abdominal and transrectal ultrasonography in patients with prostatic hypertrophy in Ibadan. Eur J. Sci Res 2005; 10:6 – 14.
4. Damir A, Munira H, Alden P, Benjamin P, Osman H. Which is a better indicator of bladder outlet obstruction in patients with benign prostatic enlargement- intravesical protrusion of prostate or bladder wall thickness. Med Arch 2012; 66 (5): 324 – 26.
5. Badmus TA, Asaleye CM, Badmus SA, Takure AO, Ibrahim MH, Arowolo OA. Benign Prostatic hyperplasia. Average volume in South-Western Nigerians and correlation with anthropometrics. Niger Postgrad Med J. 2013; 20:72 – 5.
6. Udoh EA, Ukpong A. Causes of bladder outlet obstruction in adult males, relative frequency and mean age at diagnosis. SAS J. Surg 2016; 2(4): 156 – 160.
7. Mbibu NH, Nwofor AME, Khalid L. Spectrum of Urology diseases in the West African Sub-region. Anals of African Medicine . 2002, 1(1): 44-52.
8. WHO definition, diagnosis and classification of diabetes mellitus and its complications part 1. Geneva: WHO; 1999.
9. Bourke JB, Griffin JP. Hypertension, diabetes mellitus and blood groups in benign prostatic hypertrophy. Br. J. Urol. 1966; 38:18 – 23.
10. Boon TA, Van Venrooij GE, Eckhardt MD. Effect of diabetes mellitus on lower urinary tract symptoms and dysfunction in patients with benign prostatic hyperplasia. Curr Urol Rep. 2001; 2:297 – 301.
11. Nandeesha H, Koner BC, Dorairajan Sen Sk. Hyperinsulinaemia and dyslipidemia in non-diabetic benign prostatic hyperplasia. Clin chim Acta 2006; 370: 89 – 93.
12. Hammarstan J, Damber JE, Karlsson M. Insulin and free oestradiol are independent risk factors for benign prostatic hyperplasia. Prostate cancer prostatic Dis. 2009; 12: 160 – 5.
13. Wang MC, Valenzuela LA, Murphy GP. Purification of a human prostate specific antigen. Invest. Urol 1979; 17: 159 – 63.
14. Kasper JS, Liu Y, Giovannucci E. Diabetes mellitus and risk of prostate cancer in the health professionals follow-up study. Int J. cancer. 2009; 124: 1398 – 1403.
15. Turner EL, Lane JA, Donovan JL, Metcalfe C, Neal DE, Hamdy FC et al. Association of diabetes mellitus with prostate cancer: nested case-control study (prostate testing for cancer and treatment study). Int J cancer. 2011; 128; 440 – 6.
16. Muller H, Raum E, Rothenbacher D, Stegmaier C, Brenner H. 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 2009; 18:1350 – 6.
17. American Diabetes Association 2. Classification and diagnosis of diabetes mellitus care 2016; 39 suppl 1: S13 - 22.
18. Al-Asadi JN, Al-Naama LM, Abdul-Kareem MM, Mashkoor FC. Serum level of prostate-specific antigen in diabetic patients in Basrah, Iraq. Niger Postgrad Med J. 2017; 24: 240- 4.
19. Fukui M, Tanaka M, Kadono M, Imai S, Hasegawa G, Yoshikawa T. et al. Serum prostate specific antigen levels in men with type diabetes. Diabetes care 2008; 31: 930 – 1.
20. Werny DM, Saraiya M, Gregg EW. Prostate Specific antigen values in diabetes and non-diabetic US Men. AM J. Epidemiol 2006; 164: 978 – 83.
21. Mattack N, Devi R, Kutum T, Patgiri D. The evaluation of serum levels of testosterone in type 2 diabetic men and its relation with lipid profile. J clin Diagn Res 2015; 9: BCO 4-7.
22. Kapoor D, Malkin CJ, channer KS. Androgens, insulin resistance and vascular disease in men. Clin Edocrinol (Oxf). 2005; 63:239-50.
23. Balk SP, KO YJ, Bubley GJ. Biology of prostate specific antigen. J. Clin Oncol 2003; 21:383 –

91.
24. Oliver SE, Barrass B, Gunnell DJ, Donovan JL, Peters TJ, Persad RA et al. Serum insulin like growth factor-1 is positively associated with serum prostate specific antigen in middle-aged men without evidence of prostate cancer. Cancer epidemiol Biomarkers Prev 2004; 13:163 – 5.
25. Cohen P, Peehl DM, Rosenfeld RG. The IGF axis in the prostate. Horm metab Res 1994; 26: 81 – 4.
26. Betancourt- Albrecht M, Cunningham GR. Hypogonadism and diabetes. Int J. Impot Res 2003; 15 Suppl 4: S14 – 20.
27. Giovannucci E. Nutrition, Insulin, Insulin-like growth factors and cancer. Horm metab Res 2003; 35:694 – 704.
28. Jayalath VH, Ireland C, Fleshner NE, Hamilton RJ, Jenkins DJ. The relationship between metformin and Serum prostate-specific antigen levels. Prostate 2016; 76: 1445 – 53.
29. Chang SL, Harshman IC, Presti JC Jr. Impact of common medications on serum total prostate-specific antigen levels; Analysis of the national/health and nutrition examination survey. J. Clin Oncol 2010; 28: 3951 – 7.
30. Haring A, Murtola T, Talala K, Taari K, Tammela T. Antidiabetic drug use and prostate cancer risk in the Finnish Randomized study of screening for prostate cancer. Scand. J. Urol 2017; 51:5-12.