

### **PROSTATE SPECIFIC ANTIGEN LEVEL IN DIABETIC MEN AT BINGHAM UNIVERSITY TEACHING HOSPITAL JOS PLATEAU STATE NIGERIA**

#### **Abstract**

Prostate specific antigen is one of the commonly used clinical tumor markers in prostatic pathology. Previous studies reported that diabetic patients are at higher risk of developing specific malignancies compared to non-diabetics. The focus of this study is to evaluate the impact of Diabetes on PSA level in relation to their demographic characteristics. The study was conducted among 63 male subjects attending Bingham University Teaching Hospital (BHUTH). Subjects were classified into diabetic and non-diabetic groups (control group). The subjects who met the inclusion criteria were randomly selected and 3mls of blood was collected for PSA analysis using ELISA technique. In diabetic group, there was no significant difference in PSA level in each of the demographic parameters studied,  $p\text{-value} > 0.05$ . In non-diabetic group, there was a significant difference in PSA level among the groups in Educational status,  $p\text{-value} = 0.011$  while other demographics did not report any significant change,  $p\text{-value} > 0.05$ . There was no significant difference in PSA level between diabetic and non-diabetic groups,  $p\text{-value} > 0.05$ . This study has shown Diabetes and demographic presentations have no effect on PSA level but educational status impacts on PSA level in normal individuals.

**Keywords:** *Demographic, diabetes, prostate specific antigen*

#### **Introduction**

Prostate Specific Antigen (PSA) is a biomarker widely used for early detection of prostate cancer. PSA levels in blood have been shown to be influenced by a number of demographic, life-style, and health characteristics, which might deserve careful attention in the interpretation of test results. Prostate specific antigen is one of the commonly used clinical tumor markers in prostatic pathology. For some reasons, it has been found to be organ specific and used as an immunohistochemical and also serological marker [1]. The blood level of PSA is often elevated in men with prostate cancer, and the PSA test was originally approved by the FDA in 1986 to monitor the progression of prostate cancer in men who had already been diagnosed with the disease. In 1994, the FDA approved the use of the PSA test in conjunction with a digital rectal exam (DRE) to test asymptomatic men for prostate cancer. Men who report prostate symptoms often undergo PSA testing (along with a DRE) to help doctors determine the nature of the problem [2]. PSA is the most valuable prostatic cancer marker that is used for population screening, diagnosis, and monitoring of patients with prostate cancer. There are some epidemiologic studies on the relationship among diabetes, prostate cancer risk, and PSA; however, the results have often been discrepant and confusing [3].

Diabetes mellitus is a complex group of metabolic disorders which is associated with an elevated glucose level in the blood. this could be chronic or severe. It is a heterogeneous group of disease

entity in which by several mechanisms hyperglycemia results. Hyperglycemia results from the inability of the body to utilize glucose which may be due to cells resistance to circulating insulin and could also result from an absolute or a relative deficiency in the secretion of insulin [4]. Diabetes mellitus in recent years has posed as a major risk factor to other diseases bringing about several complications such as retinopathy, neuropathy, nephropathy, cancer, coronary artery disease and death. Many studies reported that diabetic patients are at higher risk of developing specific malignancies such as cancers of the pancreas, colon and liver compared to non-diabetics.

One possible reason for such increased risk is hyperglycemia. However, recent studies showed that diabetic men showed a decreased risk of prostate cancer [4].

The focus of this study is to evaluate the impact of Diabetes on PSA level in relation to their demographic characteristics.

## **Materials and Methods**

### **Study area**

This study was a hospital based study which was carried out among diabetic patients attending Bingham University Teaching Hospital (BHUTH). BHUTH is a tertiary healthcare institution located in Jos, the capital city of Plateau state, Nigeria.

### **Study population**

The study was conducted among diabetic men attending Bingham University Teaching Hospital. Control subjects were non-diabetic individual in the hospital. The diabetic status of these subjects was confirmed from their clinical folder.

### **Eligibility criteria**

#### **Inclusion criteria**

This study included asymptomatic and symptomatic men of 20 years and above with confirmed cases of diabetes mellitus attending diabetic clinic in Bingham University Teaching Hospital, Jos.

#### **Exclusion criteria**

The study excluded female diabetic patients. Male subjects below 20 years old attending diabetic clinic at Bingham University Teaching Hospital, Jos. Diabetic patients not registered with the hospital were also not included.

### **Sample size**

The sample size formula as described by Frankline [5] was used to obtain the sample size for this project.

$$n = \frac{(1.96)^2 \times P_{exp} (1-P_{exp})}{d^2}$$

Where: n= sample size

p = expected prevalence

d = the desired absolute precision of 5%

$P_{exp} = 4.3\%$

$$n = \frac{(1.96)^2 \times 4.3\% \times (1-4.3\%)}{(5\%)^2}$$

$$n = \frac{3.8416 \times 0.043 \times 0.957}{0.0025}$$

$$n = \frac{0.1580856816}{0.0025}$$

n = 63 subjects

### Sampling Method

Subjects were recruited into the study via simple random sampling method using a numbering system described by Fyneface *et al.* [6,7] where participants were to pick numbers ranging from 0-1. All participants who picked “1” were included in the study while those that picked “0” were excluded.

### Sample collection and processing

Blood samples were collected from the Diabetic clinic, from the Medical Outpatient Department (MOPD) and General Outpatient Department (GOPD) of BHUTH.

A random three milliliters (3ml) of venous whole blood was collected via venipuncture from the antecubital vein of each man (Diabetic patient). The venous whole blood was transferred immediately into a well-labeled plain specimen tube and allowed to clot for at least 60minutes undisturbed at room temperature.

The blood samples were centrifuged at 2500 rpm for 15minutes and separated supernatant (serum) transferred into another well-labeled plain specimen tubes using Pasteur’s pipettes.

The separated serum was stored frozen at  $-20^{\circ}\text{C}$  to  $-24^{\circ}\text{C}$  and temperature validated using external digital freezer thermometer and monitored daily until analysis was done.

## Principle of Test

The PSA ELISA test is a solid phase two-site immunoassay. Rabbit anti-PSA is coated on the surface of the microtiter wells and another anti-PSA monoclonal antibody labeled with horseradish peroxidase is used as the detection antibody. The PSA molecules present in the standard solution or serum are “sandwiched” between the two antibodies. Following the formation of the coated antibody-antigen-antibody- enzyme complex, the unbound antibody-enzyme tracers are removed by washing. The horseradish peroxidase activity bound in the wells is then assayed by a colorimetric reaction. The intensity of the colored formed is proportional to the concentration of PSA present in the sample.

## Test Procedure

The desired number of coated wells in the holder was secured. Then 25ul of standard, specimens and controls were dispensed into appropriate wells. Then 100ul of Enzyme conjugate was dispensed into each well and was mixed gently for 5 seconds. The mixture was incubated at room temperature for 45 minutes. The incubated mixture was removed by emptying the plate contents into a waste container. The microtiter wells were rinsed and emptied 5 times with washing buffer(1X). The wells were stroked sharply onto absorbent paper and residual water droplets were removed. Then 100ul TMB solution was dispensed into each well and mixed gently for 5 seconds. The mixture was incubated at room temperature for 15 minutes. Then 100ul of stop solution was added to each well to stop the reaction. The mixture was gently mixed for 30 seconds until the blue color completely changed to yellow. The optical density was read at 450nm using a microtiter plate reader within 15 minutes.

## Statistical analysis

All data obtained were analyzed using **SPSS** (Statistical Package for Social Sciences). The results were presented in Tables. Mean, standard deviation (SD) and percentages were calculated while T-test and ANOVA was analyzed, p-value<0.05 was considered significant.

## Results

**Table 1: Demographic characteristics of study participants**

---

Demographic characteristics	Number (%)
-----------------------------	------------

---

---

<b>Age group</b>	
20-29	0(0.0)
30-39	5(7.9)
40-49	5(7.9)
50-59	25(39.7)
≥60	28(44.4)
<b>Gender</b>	
Male	63(100.0)
<b>Settlement</b>	
Urban	59(93.7)
Rural	4(6.3)
<b>Educational level</b>	
Informal	8(12.7)
Primary	13(20.6)
Secondary	13(20.6)
Tertiary	29(46.0)
<b>Occupation</b>	
Civil servant	8(12.7)
Business	24(38.1)
Artisan	9(14.3)
Retired	13(20.6)
Others	9(14.3)
<b>Knowledge of PCR</b>	
Yes	23(36.5)
No	40(63.5)
<b>Family history of diabetes</b>	
Yes	33(52.4)
No	30(47.6)
<b>Years of diabetes</b>	
1-5	35(55.6)
6-10	20(31.7)
>10	8(12.7)
<b>Medication</b>	
Yes	56(88.9)
No	7(11.1)

---

Key PCR: prostate cancer

The result presented in table 2 shows the comparison of PSA levels in each demographic parameter among diabetics. The result shows that there was no significant difference ( $p$ -value>0.05) in PSA levels in each of the studied demographic parameters which included, age group, settlement, educational level, occupation, knowledge of PCR, family history of diabetes, years of diabetes and medication.

**Table 2: Mean level of prostate specific antigen (PSA) in diabetic men according to demographic characteristics**

Demographic characteristics	Mean (ng/ml)	SD	F/t-test	P
<b>Age group</b>				
20-29	0.00	0.00	1.757	0.165
30-39	0.64	0.11		
40-49	0.61	0.16		
50-59	1.82	0.98		
≥60	6.09	2.07		
<b>Settlement</b>				
Urban	3.36	1.06	0.637	0.525
Rural	6.08	4.49		
<b>Educational level</b>				
Informal	1.30	0.24	0.612	0.610
Primary	5.22	3.85		
Secondary	5.04	2.15		
Tertiary	2.71	1.11		
<b>Occupation</b>				
Civil servant	7.03	6.31	0.486	0.746
Business	2.59	1.23		
Artisan	2.52	1.34		
Retired	4.14	1.84		
Others	3.03	2.06		
<b>Knowledge of PCR</b>				
Yes	3.13	1.28	0.293	0.771
No	3.76	1.46		
<b>Family history of diabetes</b>				
Yes	2.61	0.98	0.931	0.355
No	4.54	1.88		
<b>Years of diabetes</b>				
1-5	2.60	0.92	0.515	0.600
6-10	4.88	2.67		
>10	4.21	2.59		
<b>Medication</b>				
Yes	3.65	1.14	0.332	0.741
No	2.55	1.77		

P-value<0.05

Key PCR: prostate cancer.

The result presented in table 3 shows the comparison of PSA levels in each demographic parameter among non-diabetics. The result shows that there was no significant difference (p-value>0.05) in PSA levels in each of the studied demographic parameters which included, age group, settlement, occupation, knowledge of PCR, family history of diabetes, years of diabetes

and medication except in education level. There was a significant difference (p-value<0.05) in PSA levels among different education levels.

**Table 3: Mean level of prostate specific antigen (PSA) in non-diabetic men according to demographic characteristics**

Demographic characteristics	Mean (ng/ml)	SD	F/t-test	P
<b><i>Age group</i></b>				
20-29	0.64	0.09	2.077	0.122
30-39	0.78	0.12		
40-49	0.77	0.31		
50-59	1.01	0.22		
≥60	1.71	0.50		
<b><i>Settlement</i></b>				
Urban	1.02	0.15	-	-
<b><i>Educational level</i></b>				
Informal	0.83	0.00	4.774	0.011
Primary	1.98	0.53		
Secondary	0.74	0.14		
Tertiary	0.84	0.11		
<b><i>Occupation</i></b>				
Civil servant	0.76	0.19	1.458	0.252
Business	1.62	0.49		
Artisan	0.82	0.27		
Retired	1.39	0.00		
Others	0.78	0.08		
<b><i>Knowledge of PCR</i></b>				
Yes	0.88	0.12	0.870	0.393
No	1.15	0.27		

P-value<0.05

Key PCR: prostate cancer

**Table 4: Comparison of mean level of prostate specific antigen (PSA) in diabetic and non-diabetic men based on demography.**

Demographic characteristics	Diabetics PSA (ng/ml)	Non-diabetics PSA (ng/ml)
<b>Age group</b>		
20-29	0.00	0.64
30-39	0.64	0.78
40-49	0.61	0.77
50-59	1.82	1.01
≥60	6.09	1.71
<b>Settlement</b>		
Urban	3.36	1.02
Rural	6.08	
<b>Educational level</b>		
Informal	1.30	0.83
Primary	5.22	1.98
Secondary	5.04	0.74
Tertiary	2.71	0.84
<b>Occupation</b>		
Civil servant	7.03	0.76
Business	2.59	1.62
Artisan	2.52	0.82
Retired	4.14	1.39
Others	3.03	0.78
<b>Knowledge of PCR</b>		
Yes	3.13	0.88
No	3.76	1.15

The result presented in table 5 shows the comparison of PSA level between diabetic and non-diabetic subjects. The finding shows that there is no significant difference in PSA level between diabetics (3.53ng/ml) and non-diabetics (1.02ng/ml), p-value=0.131.

**Table 5: Comparison of mean level of prostate specific antigen (PSA) in diabetic and non-diabetic men.**

Subjects	Mean (ng/ml)	SD	t-test	P
Diabetic	3.53	1.03	1.524	0.131
Non-diabetic	1.02	0.15		
Total	2.81	0.75		

P-value<0.05

## Discussion

The study was conducted to determine the level of prostate specific antigen (PSA) among diabetic men attending Bingham University Teaching Hospital.

Prostate specific antigen screening is a fundamental step in the identification of early prostate cancer, PSA screening is also being used for the monitoring of prostate cancer treatment. This has been of great importance in reducing the growing burden of prostate cancer in developed and developing countries. The result from this study showed increasing pattern of PSA level in men with increasing age, just as documented by American Cancer Society (ACS), [8]. This pattern was consistent with both diabetic and non-diabetic subjects. However, the descriptive pattern was not significantly different. Prostate volume has been observed to increase as men age and with these, increase in size of the gland results in more PSA released into the systemic circulation. This expansion in prostate size has been more pronounced in blacks than the Caucasian, therefore, contributing to the reason why black men seem to have higher total PSA concentrations than their Caucasian, Chinese and Japanese counterparts [8,9].

Results obtained from diabetic men attending Bingham University Teaching Hospital showed a high level of prostate specific antigen in diabetic men in all demographic characteristics and a low level of prostate specific antigen in non- diabetic men in all demographic characteristics. The descriptive rise in PSA level may be due to age. As reported by ACS and Amadi [9] respectively in the previous paragraph, it was noted that PSA level increases with age. Most of the subjects recruited in this study were from 50 years and above (84.1%). This age group would capture more diabetic subjects than the younger age group. It is true that diabetes is now a growing concern in younger adults but the association between diabetes and age is a known fact and a vital health concern in geriatric clinic, therefore, the rise in PSA level in diabetics may be primary due to age factor and not the disease itself.

Generally, there was no significant difference or impact of demography on PSA level in diabetics and non-diabetes except on educational level. Educational level was reported to have key impact of PSA level among non-diabetic subjects. This finding is in consonance with the work of same authors of this current study is an unpublished literature. It was concluded that the more subjects were improved in their level of education, the lesser the PSA value. There was a significant difference in PSA level among various educational status as seen in this current work.

From the work done and within the limits of experimental errors, to determine if there is any significant difference between the serums prostate specific antigen (PSA) level in diabetic and non-diabetic men, it was observed from this study that there was no significant difference in the mean PSA level between diabetic and non-diabetic men. Diabetic men had a mean PSA level of 3.53ng/ml which was higher than that of non-diabetic men with mean PSA level of 1.02 ng/ml. It has been hypothesized 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. In biologic models proposed to

explain this association, researchers noted 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 [10], though the result obtained from this work contradicts the work of David *et al.* as the finding from this study showed high level of PSA in men with long-term diabetes and a low level of PSA in men recently diagnosed with diabetes.

## Conclusion

This study has revealed that demography and diabetes did not have any profound effect on PSA level among subjects attending Bingham University Teaching Hospital (BHUTH). However, level of education has a key role on PSA level among non-diabetics.

## References

1. Al-Asadi, J. N., Al-Naama, L. M., Abdul-Kareem, M. M., Mashkoor, F. C. (2017) *Nigeria Postgraduate Medical Journal*. 24(4):240-244. doi: 10.4103/npmj.npmj\_174\_17.
2. Tsodikov, A., Gulati, R., de Carvalho, T. M., Heijnsdijk, E. A. M., Hunter-Merrill, R. A., Mariotto, A. B., de Koning, H. J., Etzioni, R. (2017) Is prostate cancer different in black men? Answers from 3 natural history models. *Cancer*. 15;123(12):2312-2319. doi: 10.1002/cncr.30687.
3. Diamandis, E. P., Sardana, G., Jung, K., Stephan C. (2000) Proteomic analysis of conditioned media from the PC3, LNCaP, and 22Rv1 prostate cancer cell lines: Discovery and validation of candidate prostate cancer biomarkers. *J. Proteome Res.*7:3329–3338
4. Cheekurthy, A. J. P., Rambabu, C., Kumar, A. (2015) Biochemical Biomarkers-Independent Predictors of Type 2 Diabetes Mellitus. *J Bioanal Biomed* 7:035-039. doi: 10.4172/1948-593X.1000121
5. Frankline, K. (2021). How to Determine Sample Size for a Research Study. <https://www.geopoll.com/blog/sample-size-research/> Accessed August 1, 2022
6. Fyneyface, C. A., Emeji, R., Osere, H. and Nwisah, L. (2018). Concentrations of Nickel in Sediment and Periwinkle of Eagle Island River, Port Harcourt. *Asian Journal of Fisheries and Aquatic Research*, 1(4), 1-5.
7. Faith, D., Biambo, K. G., Nyebuchi, J., Amadi, C. F., & Konne, F. E. (2021). Comparative Study of Heavy Metals in Breast Milk of Breast Feeding Mothers in Urban and Sub-urban Subjects in Rivers State. *Journal of Applied Life Sciences International*, 24(8), 31-36.
8. American cancer Society(ACS), (2016). Prostate Cancer Risk Factors. *Prostate Cancer Causes, Risk Factors*,, www.cancer.org.
9. Amadi, C., & Odum, A. P. (2018). Age-Adjusted Serum Prostatic Specific Antigen Reference Ranges among Healthy Men in Port-Harcourt, Nigeria: A Retrospective Hospital-Based Study. *Int. J. Res Med Sci.*, 6(2): 417-421

10 David, B., & Yudkin, J. S. (2006). Diabetes care in sub-Saharan Africa. *Lancet*. 368(9548):1689-95. doi: 10.1016/S0140-6736(06)69704-3. PMID: 17098088.

UNDER PEER REVIEW