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Serum Prostatic Specific Antigen Levels among Adult Male Patients Seen at Two Nigerian Tertiary Hospitals

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Authors' contributions

This work was carried out in collaboration among all authors. Author OKO conceptualized, design and wrote the draft manuscript. Authors ACC, IMF and AA analysed the samples. Author OOE analysed the data and authors AO, EFA, II and JTM were involved in the literature searches. All authors agreed on the final manuscript before submission. All authors read and approved the final manuscript.

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ABSTRACT

Background: The clinical utilization of PSA test in early detection and monitoring therapy of cancer of prostate is influenced by demographic factors like age, geographical location, metabolic factors, method of analysis and sensitivity and specificity of the test. Hence, we retrospectively compared the serum PSA levels of adult male patients seen at two Nigerian tertiary hospitals.

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Methodology: The retrospective study was conducted at two Nigerian tertiary hospitals, Federal medical centre, Yola and Makurdi between January and December 2019. Study participants were adult males with lower urinary tract symptoms presented at the Urology units and referred to the hospital chemical pathology laboratories for total PSA assay using quantitative method, Time – resolved Flourence immunoassay, Bioscience Diagnostic Technology Ltd, China. Data extracted includes,age, clinical details, and PSA levels. Descriptive analysis using SPSS version 21.0 was employed. A total of 430 data were extracted, 201 from Yola and 229 from Makurdi

Result: Significant difference was observed in the mean age, 61.67+0.09years vs 58.61+58.61years(p=0.009) and mean serum PSA level of patients21.88+3.04ng/ml vs 14.81+0.74ng/ml(p=0.041). Significant difference was observed in the mean serum PSA level(1.33+0.09ng/ml vs 1.65+0.08ng/ml)(p=0.011) of patients with PSA level (LUTS) within the range of <4ng/ml,and those with >10ng/ml(65.88+0.09 vs 40.43+3.66ng/ml)(p=0.003). 211(49.1%, 51.7 vs 46.7%)had PSA level 4ng/ml, 86(20%, 17.9% vs 21.8%)within 4-10ng/ml and 133(30.9%, 30.3 vs 31.4%) had >10ng/ml. No significant correlation was observed between PSA level and age, but increased with advancement in age. Diabetes Mellitus(DM)(0.9%) and co-existence of DM and hypertension(2.0%) were recorded as comorbidities

Conclusion: The study findings affirmed high PSA level and increase with age in suscepted cases of cancer of prostate. it serves as a baseline epidemiological template for further comprehensive study for better understanding of PSA level in clinical diagnosis and create awareness of the disease.

Keywords: Serum prostatic specific antigen; cancer of prostate; adult males with Lower Urinary Tract Symptoms(LUTS); Yola and Makurdi.

1. INTRODUCTION

As cancer of prostate incidence continued to increase, it posed a major public health problem with clinical and societal consequences. Globally, It is the second leading cause of morbidity and mortality among males, common among those aged above 50years and the risk increases with advancement in age [1] Available data had shown high prevalence among the blacks, African-American, Caucasian compared to Asian men [2].To stem down the increasing trend is dependent on early detection, monitoring therapy and the level of awareness of the disease. In Nigeria, the level of awareness of the disease and willingness of Nigerian adult males to undertake cancer of prostate screening is relatively low [3].

Prostate specific antigen(PSA) is a glycoprotein is produced by prostate luminal epithelial cells gland, with low concentration in the blood [4]. PSA is prostate –specific marker but not a good marker for cancer of prostate. While the test is a valuable test for detection of cancer of prostate, it lacks the sensitivity and specificity for accurate dectection of cancer of prostate. Elevated PSA level is not indicative of cancer of prostate as high level is also associated with prostatic infections like benign prostate hyperplasia, prostatic infection, manipulation, massage surgery and transrectal resection [5]. In 1996, the United State Food and Drug Agency approved PSA test for screening of cancer of prostate. But the PSA level prevalence varies age, geographical location, metabolic effect, Basal metabolic Index(BMI), androgen and method of analysis metabolic and hormonal factors [6,7]. In 1989, Myothe and Ivor [8] established PSA reference range of 4ng/ml based on study of 860 healthy males aged between 40 and 80years.Due to the influence of age and other factors on result outcome , there was no agreed consensus on the normal range. As most studies observed that the use of 4ng/ml cutoff under estimate the risk of cancer in younger men and sometime necessitate biopsies in older men [9] Catalona et al. [10] proposed the combination of PSA testing with digital rectal examination and transultrasound in screening for prostate cancer. Then, Oesterling et al. [11] proposed the PSA level range of 0-2.5ng/ml, which had been established in most studies in and outside Nigeria among apparently healthy adult males, which had improved the sensitivity and specificity of detection [12-15] .

In Nigeria, PSA level of 4ng/ml cutoff is still routinely used in most tertiary hospital for detection and monitoring therapy, in suspected case of cancer of prostate despite its pitfalls. Therefore, clinical utilization of PSA test in diagnosis of cancer of prostate requires detailed consideration of patient age, geographical

location and metabolic factors. Based on this consideration, we retrospectively compared the PSA level among adult males with lower urinary tract symptoms seen at two Nigerian tertiary hospitals.

2. PATIENTS AND METHODS

The retrospective, hospital –laboratory based study was carried out at two Nigerian tertiary hospitals, Federal medical Centre, Yola and Makurdi between January and December 2019.The two hospitals provides mutlispecialities services and training programme for healthcare professionals. Geographically, the two study sites are located at different locations, with different ethic population and occupational activities. FMC Yola is located in sahel savanna region, with Fulani ethic group constituted the majority tribes, while TIV ethnic group in Makurdi capital of Benue state located in guinea savannah region. Patients involved in the study were seen at urology units of the hospitals with lower urinary tract symptoms/ comorbidities, clinically reviewed by attending physician and referred to the Chemical Pathology laboratory for total PSA level analysis. The PSA assay was carried out using ELISA technique, according the manufacturer instruction. Data were extracted from hospital laboratory record includes age, associated clinical details, comorbidities and PSA level. A total of 430 PSA data were extracted, 201 from FMC Yola and 229 from FMC,Makurdi. Descriptive statistical analysis was employed using SPSS version 21.0, data expressed in means(SD), frequency and comparison of variables using student 't'test at $p<0.05$

3. RESULTS

Of 430 PSA data extracted and analyzed over the study period, significant difference was observed in the mean age61.67+0.91 vs 58.61+0.7 years($p<0.009$) and mean serum PSA level 21.88+3.04 vs 14.81+1.63ng/ml($p<0.04$)of the patients(Table 1)

The PSA level ranges as presented in Table 2, significant difference was observed in the PSA level ranges in <4ng/ml($p=0.011$) and >10ng/ml($p=0.003$). Two hundred and eleven patient (49.1%, 51.7% vs 46.7%)had PSA level range of <4ng/ml, while 219(50.9%, 48.2% vs 53.2%) had PSA level of >4ng/ml. Significant high mean serum PSA level of 1.65+0.08ng/ml was recorded among patients seen at Makurdi within <4ng/ml range compared to 1.33+0.09ng/ml at Yola($p=0.011$), while significantly higher mean PSA level of 65.88+0.09ng/ml was recorded among patient within level>10ng/ml at Yola compared to 40.43+3.66ng/ml at Makurdi($P=0.003$). No significant difference was observed in PSA level range of 4-10ng/ml at both study sites(6.68ng/ml vs 6.08+0.26ng/ml)($p=0.136$).

The distribution of mean serum PSA level according to age-group(Table 3), showed increase in the mean serum PSA level and advancement of age. The frequency of patients within age-group of <50years was 20.4% vs 25.8% while >50years was 79.6% vs 74.2%. Highest PSA level recorded among patients within age-group >71years was 37.99+7.81 vs 28.13+6.04ng/ml .No clinical records for 43.8% patients in Makurdi and 64.2% in Yola. Available records showed frequency of LUTS of, BPH (25.9 VS 18.3%), bladder outlet obstruction/BPH(9.5% vs 6.6%), retention Obstruction(5.0% vs 5.2%) and co-morbidities of diabetes mellitus and hypertension(2.0%) and DM(0.9%)

4. DISCUSSION

To the best of our knowledge, this is the first report of PSA level among adult males presented with lower urinary tract symptoms at both study sites. This study findings provides an insight into suscepted cases of cancer of prostate and mean serum PSA levels and ranges. The influence of demographic and geographical on result outcome as documented in other studies was clearly seen in the study finding [5,6]. However, the main findings of the study was the high PSA level and increasing trend with advancement in age among patient in both study sites .

In the study, significant difference was observed in the mean age(61.67+0.91years vs 58.61+0.74years)($p<0.009$) and mean PSA level(21.88+3.04ng/ml vs 14.81+1.63ng/ml($p<0.041$) of the patients in both study sites. The mean age is consistent with other studies [16-19], as suspicion of cancer of the prostate tends to be diagnose within the 5^{th} and 8^{th} decade of life[1]. The mean serum PSA level of 21.14ng/ml and 14.81 is higher than 4.7ng/ml reported in similar study in Abakalilki, Southeast Nigeria [16]. The mean serum PSA level of 14.81ng/ml reported in Makurdi was

similar to 14.8ng/ml and 13.2ng/ml among obese and non-obese Nigeria men with LUTS in Southwest Nigeria [19]. However, our PSA levels are low when compared to levels reported in studies that evaluated PSA level among cancer of prostate patients [17,18], these observed difference in PSA level may be due to the influence for geographical location ,studied population and method of analysis.

The continuous diagnostic usage of PSA 4ng/ml cutoff as normal range in most tertiary hospital for detection and monitoring therapy without considering of those factors has its pitfalls. As its potentially results in misdiagnosis of cases in younger males and unnecessary biopies among older patients [8] This necessitate the need for the establishment of local age-specific range based on apparently healthy males without LUTS, demographic variable, geographical location and metabolic factors. Several documented studies on apparently healthy individual using statistical application had established age-specific reference range of 0-2.5ng/ml [10-15], which had improved sensitivity and specificity of PSA test and early detection of cancer of the prostate.

The PSA levels are classified into 0-4ng/ml as normal, 4-10ng/ml intermediate/grey –zone and >10ng/ml high risk range. High risk of suspicion of cancer of prostate is linked with high PSA level, but differentiated from BPH by PSA density, as cancer increase serum PSA more than BPH especially in patients with serum level of 4.0ng/ml to 10ng/ml [20]. Likewise, patient with serum PSA level of <4ng/ml do not necessary exclude cancer cases [8]. Therefore, clinical utilization of these PSA level ranges requires its combination with digital rectal examination, transrectalultasound(TRUS) and histological examination to increase detection of prostate cancer [21] From this study, significant difference was observed in the PSA level range of 0-4ng/ml with mean value of 1.33+0.09ng/ml(p=0.011) vs 1.65+0.08ng/ml and >10ng/ml, 6588+0.09ng/ml vs 40.43+3.60ng/ml(p=0.03). The prevalence of patients with PSA level within 0-4ng/ml was 49.1%,while those with PSA level >4ng/ml was 50.9%. The >4ng/ml alluded to high risk of cancer of prostate due to the high mean PSA level within the range of 4-10ng/ml(6.68+0.30 vs 6.08+0.20) and >10ng/ml(65.88+0.09 vs 40.43+3.66). Using the combination of diagnostic indices with PSA level in the improvement the sensitivity and specificity was collaborated by a study conducted in Kano, northwestern Nigeria which reported 3 cancer cases was among 35 patients with PSA range of 0-4ng/ml and 5 out of 35 patient with 4-10ng/ml [22].

Table 1. Mean age(years) and PSA level(ng/ml) according to study site

	Yola	Makurdi	
	Mean(SD)	**Mean(SD)**	**p-value**
Age	61.67 ± 0.91yrs	58.61±0.74yrs	0.009
PSA	21.88 ± 3.04ng/ml	14.81 ±1.63ng/ml	0.041

Table 2. PSA level among patients according to study sites

	Yola(n=201)		Makurdi(n=229)		
	n(%)	**Mean(SD)**	**n(%)**	**Mean(SD)**	**P=value**
<4ng/ml	104(51.7)	1.33+0.09	107(46.7)	1.65+0.08	0.011
4-10ng/ml	36(17.9)	6.68+0.30	50(21.8)	6.08+0.26	0.136
>10ng/ml	61(30.3)	65.88+0.09	72(31.4)	40.43+3.66	0.003

Table 3. Mean PSA levels according to Patient age-group

	Yola		Makurdi		p=value
	n(%)	**Mean PSA(SD)**	**n(%)**	**Mean PSA(SD)**	
<40years	13(6.5)	1.65+2.33	16(7.0)	8.17+6.27	0.360
41-50	2813.9)	7.53+3.99	43(18.8)	9.23+3.13	0.736
51-60	58(28.9)	18.35+5.09	67(29.3)	10.71+2.50	0.182
61-70	51(25.4)	22.82+6.08	73(31.9)	17.83+2.85	0.460
>71	51(25.4)	37.99+7.81	30(13.1)	28.13+6.04	0.321

Correlation between mean serum PSA and age is a common pattern documented in most studies [14-18], attributable to prostate gland enlargement in size resulting in PSA production [17,18]. In this study, there was no significant difference in the mean serum PSA level and age-group of patients at both study sites,despite the fact that there was an increase in the level with age. However, we observed no difference in the mean serum PSA level among patients within aged <40years in Yola(1.65+2.33) compared to Makurdi(8.17+6.27) which may be due to clinical presentation as cases are rare in this age-group, but cases had been reported within age-group [23].While the highest PSA level was recorded among patients aged <70years which is consistent with other studies [17,18] . From our study, the comorbidities recorded was diabetes mellitus(2.0%) and coexistence of diabetes mellitus and hypertension(0.9%) among patients from Yola. This prevalence is relatively lower than level reported in other studies [17]. The findings of this retrospective study provided an insight into the clinical diagnostic perceptive of PSA in cancer of prostate in the two study sites, and also served as template for further comprehensive study. The study has limitations, as retrospective study data extracted is subject to documentation errors as majority of cases had no clinical details provided, which could have added information for observed difference in the PSA level.

5. CONCLUSION

In conclusion, the retrospective findings was consistent with similar studies conducted in Nigeria, as relate to high serum PSA level and increases with advancement in patient age. Clinical application of PSA test in diagnostic approach will required an established age-specific reference range in each locality .

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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