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UTILITY OF PROSTATE SPECIFIC ANTIGEN (PSA) IN THE INDIGENOUS AFRICAN MAN
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ABSTRACT

***Objectives*: To examine the great possibility that the indigenous black African man with prostate diseases requires a different diagnostic approach and strategies beyond the standard PSA reference levels generated in non-African study subjects.**
***Design:* A hospital based cross-sectional descriptive study.**
***Setting:* The Urology Outpatient Clinic and Surgical Ward of Moi Teaching and Referral Hospital, Eldoret, Kenya between 1st April 2012 to 31st March 2013.**
***Subjects*: Two hundred and nineteen patients aged 50 years and above with prostate diseases.**
***Main Outcome Measures:* The main outcome measure was the PSA levels in patients diagnosed with Acute Prostatitis, Benign Prostate Hyperplasia (BPH) and Prostate Cancer in MTRH. The secondary outcome measures were the correlates associated with elevated PSA.**
***Results:* Patients ranged in age from 50 to 96 years with a mean ± standard deviation of 65.4 ± 10.2 years. Clinical diagnosis of Acute Prostatitis, BPH and Prostate Cancer was made in 1.8, 63.9 and 34.3% of the study subjects respectively. Sixty-two patients (28.3%) had PSA in the laboratory reference range of 0-4ng/ml considered normal with an average of 1.8 ng/ml. The overall mean was 31.2 ng/ml and those with elevated PSA levels had a mean of 42.3 ng/ml. There was a positive correlate between prostate enlargement, urine retention, dysuria and family history of prostate disease and elevated PSA (all with $p<0.001$).**
***Conclusions:* The indigenous black African man has high levels of PSA even in benign prostate diseases. This together with histological findings of malignancy in some clinically diagnosed BPH with normal range PSA levels make the use of PSA in this group a bigger challenge. Studies should be conducted to not only elucidate the best use of PSA in the indigenous black African man but also his place in the new biomarkers to supplement or replace PSA in diagnosis and care.**

INTRODUCTION

While evidence points to racial and geographical differences in the presentation of prostate diseases (1), much of the available data has been gathered from European and American studies and may not comprehensively address the problem among indigenous African population (2, 3). Efforts to diversify the use of PSA in terms of density and velocity have not shown greater reliability in diagnosis or prognostication of prostate malignancy (4). Emphasis is now on age and race specific ranges, the free to total PSA ratio, Prostate Specific Membrane Antigen and use of other biomarkers that can help distinguish benign from malignant prostate conditions. The African American, the better studied of the African lineage, has been found to have 1.6 times the risk of being diagnosed with prostate cancer and 2.4 times the risk of dying of it compared to his Caucasian counterpart (4). The fate of indigenous black Africans remains known only by default in a setting of unreliable, non-disease specific PSA (5-7). It, therefore, would be of great benefit while grappling with the treacherous and controversial topic of PSA and prostate diseases to have data on the indigenous black African man as this data is sorely missing. This study shares findings that suggest a peculiar position occupied by the indigenous black African man with regard to PSA and calls for greater research and data on how best to benefit from PSA, its components and other biomarkers in the diagnosis and interventional outcomes of prostate diseases.

MATERIALS AND METHOD

Patients of indigenous black African extraction based on birth and exclusive residence in Africa presenting to the urology clinic or admitted with lower urinary tract symptoms ascribable to the prostate and diagnosed to have Acute Prostatitis, Benign Prostate Hyperplasia (BPH) or Prostate Cancer in the one year period of study (1st April 2012 to 31st March 2013) had their demographic data taken after formally consenting to participate in the study. Those with concomitant urethral strictures or considered to have other non-prostatic causes of bladder outlet obstruction were excluded. Clinical assessment included standard physical examination with a focused Digital Rectal Examination (DRE). Clinical diagnosis of Prostatitis was limited to the acute form and based on findings of a tender prostate with features of an acute inflammatory process. Benign Prostate Hyperplasia was considered where the examining urologist made findings in keeping with a benign prostate enlargement with no asymmetry or nodulations and having freely mobile overlying mucosa. Blood samples for the Prostate Specific Antigen (PSA) levels were collected at the first point of contact in the urology clinic. They were analysed in the standard laboratory procedure using Abbott IMx assay with a 0-4ng/ml normal range within 24 hours of submission of blood to the laboratory in plain specimen bottles. Patients who underwent prostate surgery or had a prostate biopsy taken on suspicion of malignancy had histological confirmation of the prostate disease. Data were ethically collected using a pre-designed data sheet, entered in a spreadsheet, confirmed for completeness, cleaned and then analysed using Statistical Package for Social Science (SPSS) version 17.0 with focus on the primary and secondary outcome measures. The findings were in descriptive terms and relied on measures of central tendency as well as measures of dispersion. Inferential statistics assumed a 95% confidence interval and statistical significance at values ≤ 0.05. The findings are presented in tables and narratives.

RESULTS

A total of 262 patients were diagnosed during the period of study to have one of the three prostate diseases namely Acute Prostatitis, BPH and Prostate Cancer. Forty-three patients with either associated urethral strictures independent of prostatic stenosis or suspected neurogenic bladder besides prostate enlargement were excluded from the study.

The 219 patients recruited into the study were 163 inpatients (74.4%) and 56 outpatients. The age range was between 50 and 96 years with a mean ± standard deviation of 65.4 ± 10.2 years. Table 1.

Table 1
Demographic features of the patients

Variable	Frequency	Percentage
Age in years		
50-59	63	28.80
60-69	49	22.40
70-79	65	29.70
Above 79	72	19.20
Marital status		
Married	172	78.50
Single	9	4.10
Divorced	3	1.40
Widowed	35	16.00
Recruitment areas		
Inpatient	163	74.40
Outpatient	56	25.60

As of the time of presentation, 149 patients (68%) had had a history of urine retention. One hundred had a history of urethral catheterisation but only 45 had indwelling catheters as of the time of admission to the ward.

On digital rectal examination, 157 patients (71.7%) had abnormal findings characterised by enlargement of the prostate, hardness, nodularity, tenderness or immobility of the overlying mucosa. Clinical diagnosis of Acute Prostatitis was made in four, BPH in 140 and prostate cancer in 75 patients, giving disease prevalence of 1.8%, 63.9% and 34.3% respectively.

Sixty patients underwent surgery for obstructive prostate, 41 of whom had Trans-Urethral Resection of Prostate (TURP) while the rest had retro-pubic prostatectomy.

The 219 study subjects had a mean PSA level of 31.2ng/ml. Only 62 patients (28.3%) had PSA within the laboratory-referenced normal range of 0-4ng/ml. These patients had an average of 1.8 ng/ml. Those with elevated PSA levels had a mean of 42.3ng/ml. Table 2.

Table 2
Distribution of PSA levels among prostate diseases

Disease	PSA≤4ng/ml	PSA>4ng/ml	Total
Ca Prostate	14(18.7%)	61(81.3%)	75
BPH	46(32.9%)	94(67.1%)	140
Prostatitis	2(50%)	2(50%)	4
Total	62(41.6%)	157(58.4%)	219

In the two diseases of surgical significance namely BPH and Prostate Cancer, BPH predominated in both categories of ≤4ng/ml and >4ng/ml in ratios of 3.3:1 and 1.5:1 respectively. It, however, had PSA levels between 2 and 15 ng/ml. The odd ratio for BPH to be in the normal range was 2.0 while cancer of the prostate had a 1.7 odd ratio for elevated PSA. Seven patients clinically diagnosed as BPH had histological findings of malignancy and two of them had PSA in the given normal range of 0-4 ng/ml.

Gross prostate enlargement on DRE was found to positively correlate with elevated PSA levels ($p<0.001$) as did a rise in age ($p=0.041$) with the highest levels being seen in the aged 70-79 years. Patients younger than 70 years had PSA in the range of 2-40ng/ml and histologically had 65.2% of BPH findings. Those older than 70 years predominated PSA levels in excess of 20 ng/ml and had 80% of the Prostate Cancer on histology. Urine retention, burning sensation on urination and family history of prostate disease all had highly significant correlations with elevated PSA ($p<0.001$). On multivariate analysis, urine retention and family history were found to be independent predictors of elevated PSA at $p=0.002$ and 0.004 respectively.

DISCUSSION

The use of PSA in testing prostate diseases has been since 1987 but its usefulness in determining diagnosis, level of care and prognosis has remained controversial with up to 75% false positives and no single cut off point separating men with prostate cancer and benign pathologies (5, 8). African men have up to 15% higher PSA levels (9) and this has nothing to do with size or weight of his prostate (10). Depressingly, there is literary no data on the indigenous black African and how he fits in the mix. This study makes efforts to utilise clinical and laboratory data to gain a glimpse into the magnitude of the challenge. In keeping with data on the African American, the PSA levels are significantly high with only 28.3% fitting in the normal range of 0-4 ng/ml. It was also evident that our PSA levels are significantly higher with clinically diagnosed BPH having PSA in excess of 10 ng/ml. This scenario is complicated by the finding that up to 5% of those considered benign clinically turned out to have malignancy on histology; a figure higher than that in studies done in America that have a range of 2-4% (4). The overall mean of 31.2 ng/ml is in the realm of metastatic disease in most of the literature. This suggests, and is evident in the study findings, that even for the benign conditions, the indigenous black African man has significantly high levels of PSA.

There has existed a concern that reliance on PSA has led to unacceptable high level of over-diagnosed prostate cancer (11). This gets more complicated when, as in our study, some men in the range considered to be normal are found histologically to have malignancy. Ganna *et al* found Prostate Intraepithelial Neoplasia (PIN) to be a risk factor for malignancy independent of PSA 12 and since it precedes the disease by five to ten years, this has been considered a plausible explanation for the normal PSA with prostate cancer. The indigenous experience with this phenomenon is yet to fully unfold and remains an area in need of research.

The variability of PSA makes it difficult to draw conclusions on disease conditions and efforts have been made to diversify into its density and velocity but these additions are no better than total PSA in diagnosis and prognosis (4). The use of other kallikreins like human kallikrein peptidase (hK2) and cytokines like Interleukin-6(IL-6) and Transforming Growth Factor-beta1 (TGF-β1) have been billed as possible enhancers of the diagnostic and prognostic values of PSA (8). We have no data on studies contacted in indigenous black Africans with regard to this new endeavour aimed at enhancing diagnosis and prognosis of prostate malignancy and it would be important if research in this aspect is done.

Inflammation is a key factor in prostate diseases (1) and this can explain our finding that patients with history of urine retention and dysuria tended to have higher PSA levels. A family history of prostate malignancy is an established risk factor for prostate cancer (5-7) and our finding it to be an independent predictor of higher PSA levels can be seen in this perspective.

The findings on the rise in PSA with an increase in age is in keeping with studies done elsewhere (7-9) and affords us the understanding that even among the indigenous black African men , this concept obtains but with higher figures. For a group of people yet to get a footing on how their prostate problems relate to PSA, this can be a good starting point.

In conclusion, the indigenous black African man has high levels of PSA even in benign prostate diseases. This together with histological findings of malignancy in some clinically diagnosed BPH with normal range PSA levels make the use of PSA in this group a bigger challenge. We recommend that, studies should be conducted to not only elucidate the best use of PSA in the indigenous black African man but also his place

in the new biomarkers to supplement or replace PSA in diagnosis and care.

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