CORRELATION BETWEEN PROSTATE SPECIFIC ANTIGEN, DIGITAL RECTAL EXAMINATION AND HISTOLOGY IN PATIENTS WITH PROSTATE CANCER

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ABSTRACT

Introduction: Prostate cancer remains a health concern worldwide with an increasing global incidence. In Nigerian men it is the most common diagnosed cancer. Diagnosis of prostate cancer is made through biopsy and histology which in turn is dependent on prostate specific antigen and digital rectal examination finding.

Objective: This study sought to look at the correlation between PSA , DRE and histology in patient who had prostate biopsy.

Method: It was a prospective study of all patients who presented to our clinic and had prostate biopsy. Data on age of patient, size of prostate, PSA, DRE finding of benign or suspicious for cancer of the prostate and the final histology were collated and there correlation analysed using SPSS and Microsoft Excel 2013.

Results: The mean age, prostate volume and PSA were 70.99+ 9.1years, 97.6+ 88.1ml and 70.13 + 73.2ng/ml respectively. The positive predictive value, negative predictive value and overall diagnostic accuracy are 55.61, 66.67, 55.77 respectively for PSA above 4ng/ml , 71.97, 73.68, 72.60 respectively for DRE alone and 55.59, 0.00, 55.29 respectively for a combination of PSA above 4ng/ml and DRE.

Conclusion: PSA and DRE singly or in combination have a poor PPV, NPV and ODA to help counseling of patients prior to prostate biopsy.

Keyword: PSA, DRE, biopsy histology, diagnostic accuracy

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INTRODUCTION

Prostate cancer remains a health concern worldwide, with an increasing global incidence.

It is the second most common cancer diagnosed among men and fifth most common cause of cancer deaths among men, globally.[1,2] Among Nigerian men, it is the most commonly diagnosed cancer. [3,4] While the true prevalence in Nigeria remains unknown, recent data suggest a hospital prevalence rate of 182.5 per 100,000 male admissions and 61.3 per 100,000 in the southwestern and southeastern Nigeria, respectively. [5,6,7]

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Despite being, mostly, a slow-growing cancer, thousands of men die of the disease each year. Thus, the need for early detection and intervention. Diagnosis is made through biopsy and histology. The main indications for biopsy are abnormal digital rectal examination (DRE) findings and/or elevated serum Prostate-specific antigen (PSA) level. [8,9,10]

In Nigeria, DRE and serum PSA are mostly applied in the course of assessing individuals with clinical features suggestive of the disease.[11]

Conflicting reports abound, from several studies, with respect to positive predictive value, sensitivity and specificity of PSA and DRE.[12-16]These indices were used to assess the efficacy of these screening tests.

We aim to evaluate the efficacy of serum PSA and digital rectal examination in the diagnosis of prostate cancer in our locality

METHOD

This was a 2 years prospective study of patients who underwent prostate biopsy in our centre. Inclusion criteria were all patient who had biochemical and/or clinical indication for prostate biopsy and consented to prostate biopsy. The biochemical indications were patients with PSA above 4ng/ml , while the clinical indications were findings on DRE suspicious of cancer of the prostate as reported by a senior registrar in urology and/or a consultant urologist.

Patient were counseled on the DRE procedure, placed on left lateral position, an index finger well lubricated with a water soluble gel is gently inserted into the rectum to assess the prostate and reported as benign or suspicious of malignancy. PSA was done By Elisa Method using Stat Fax-2100 microplate reader of Awareness Technology Incooperated ,Ultrasound size of the prostate was done by radiologist using Aloka Prosound SSD 3500 and histology of the prostate tissue was done by our pathologist using Haematoxylin and Eosin staining. The findings suspicious of cancer of the prostate included hard prostate, nodular prostate, fixed rectal mucosa and/or palpable seminal vesicles. Ethical clearance was sought and received from the ethical committee of our institution. We also gave routine antibiotics in the form of Tablet ciprofloxacin and metronidazole 1 hour before the procedure and then for 5 days after biopsy. We routinely did a rectal washout on the morning of the procedure.

On the day of the procedure, patients were placed in left lateral position with their hip and knees flexed to 90 degree. In this position we scrubbed the lower back and buttocks. Using 20ml of 1% lignocaine we did a caudal block for the procedure. Then with a plaster taped to the tip of our index finger (the finger that guides the biopsy needle to avoid injury to the operator) we did a Digitally guided prostate biopsy with size 18G semi-automated Trucut^{R} biopsy needle. We usually did a Sextant biopsy and biopsy of any palpable nodule or hardness. After the biopsy we gave antibiotics as above and analgesics for 5days.

We collected information on their biodata, PSA, Ultrasound size of the prostates, digital rectal examination finding and Histology results

Analysis was done using statistical package for social sciences IBM SPSS Statistics for windows, version 21.0. Armonk, NY: IBM Corp. and Microsoft Excel 2013.

RESULTS

A total of 208 patients were qualified for the study. The mean age, prostate volume and PSA were 70.99$\pm$ 9.1years, 97.6$\pm$ 88.1ml and 70.13 $\pm$ 73.2ng/ml respectively (See table 1).

Table 1: Descriptive statistics of the age, prostate volume and total PSA.

Variable	N	Range	Minimum	Maximum	Mean	Std. Deviation
Age	208	54.00	46.00	100.00	70.9856	9.10618
Prostate Volume	208	889.77	10.23	900.00	97.5937	88.06822
Total PSA	208	775.10	2.00	777.10	70.1255	73.22910

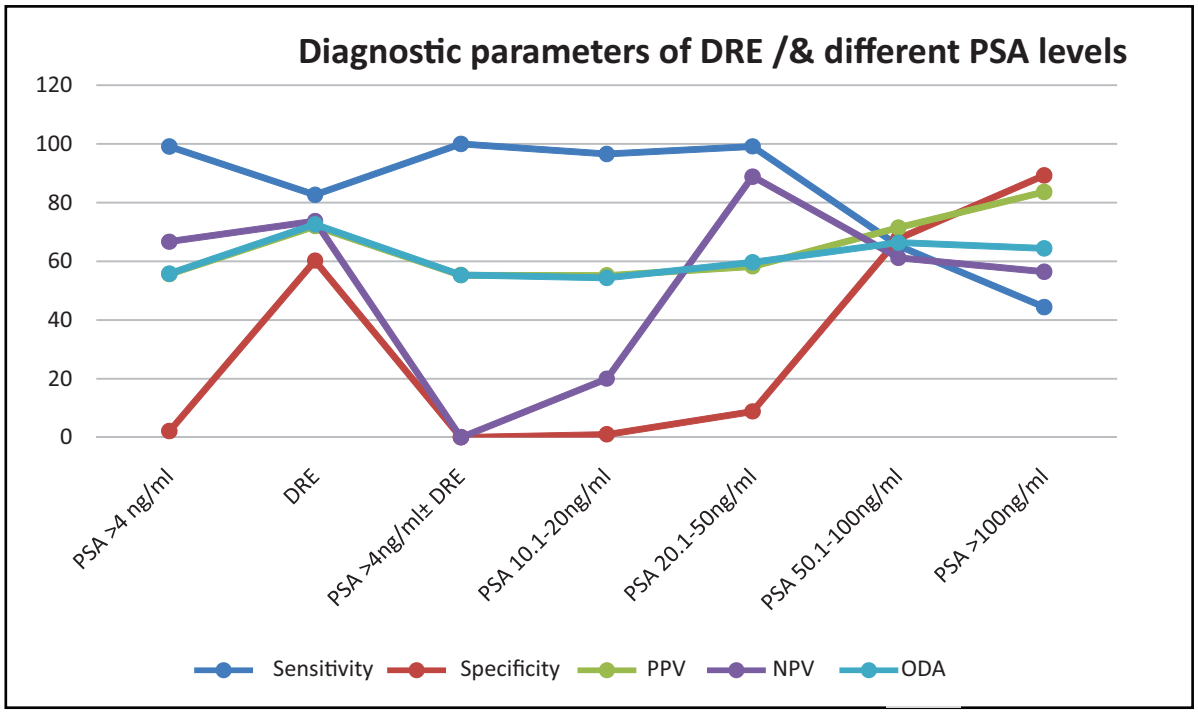
The positive predictive value, negative predictive value and overall diagnostic accuracy is 55.61, 66.67, 55.77 respectively for PSA above 4ng/ml alone, 71.97, 73.68, 72.60 respectively for DRE alone and 55.59, 0.00, 55.29 respectively for a combination of PSA above 4ng/ml and DRE.

Table 2 shows the various sensitivities, specificities, positive predictive values (PPV), negative predictive values (NPV) and overall diagnostic accuracy (ODA) for various values of the PSA and DRE separately and in combination. The Diagnostic parameter of DRE and/or different PSA levels is depicted in figure 1

Table 2: Sensitivity, Specificity, PPV, NPV, and ODA of PSA and DRE

	Sensitivity	Specificity	PPV	NPV	ODA
PSA> 4ng/ml	99.13	2.15	55.61	66.67	55.77
DRE	82.61	60.22	71.97	73.68	72.60
PSA >4ng/ml± DRE	100	-	55.29	-	55.29
PSA 10.1-20ng/ml	96.55	1.00	55.17	20	54.32
PSA 20.1-50ng/ml	99.15	8.79	58.29	88.89	59.62
PSA 50.1-100ng/ml	65.22	67.74	71.43	61.17	66.35
PSA >100ng/ml	44.35	89.25	83.61	56.46	64.42
DRE	82.61	60.22	71.97	73.68	72.60
PSA 4-10ng/ml± DRE	100	0	55.29	-	55.29
PSA 10.1-20ng/ml±DRE	98.04	7.55	50.51	80	51.92
PSA 20.1-50ng/ml±DRE	94.78	24.73	60.89	79.31	63.46
PSA 50.1-100ng/ml±DRE	88.70	43.01	65.81	75.47	68.27
PSA >100ng/ml±DRE	77.24	48.24	68.35	59.42	65.38

Figure 1: Diagnostic parameter of DRE and/or different PSA levels



DISCUSSION

Methods used to identify prostate cancer include DRE and PSA assay. The DRE, while being simple to perform, non-invasive and, relatively, inexpensive is subjective.[17,18] Also as the entirety of the prostate is not assessed, up to 25% of prostate cancers detected with biopsy after abnormal DRE findings are found in a different area than the palpable abnormality.[19] Thus, DRE often detects advanced disease.[17]

PSA is organ-specific but not cancer-specific and so other prostatic diseases, such as benign prostatic hyperplasia and prostatitis, may influence its effectiveness for cancer detection.[20] However, it is objective and cost-effective.[17]

All the patients in the present study had a transrectal digitally-guided needle biopsy of the prostate which was indicated by an abnormal DRE finding and/or abnormal serum PSA result. Diagnosis was by histology. Most of the serum PSA values were above 100ng/ml (29.3%) reflecting the high incidence of late presentation in developing countries like ours where routine screening is not being practised.[6,11] The PSA sensitivity in the present study was 99.13% at 4ng/ml cut-off while DRE was 82.6%. This is similar to the findings by De et al[21] which showed sensitivity of 95% and 60% for PSA and DRE, respectively. A high sensitivity of 94.6% for serum PSA was also observed by Ojewola et al[22] which outperformed DRE which had a sensitivity of 75.7%. Similar to our findings, Cupp et al[23] noted sensitivity to be in the ranges of 57-79% and 69-89% for PSA and DRE, respectively following results from several studies.

The highest sensitivity of PSA in our study was noticed when PSA levels were 20.1-50ng/ml with a value of 99.15%, in contrast to PSA levels of 0-3.9ng/ml with highest sensitivity of 95% noticed by De et al.[21] Their study population was 60 patients and their average total PSA was 12.09ng/ml while ours was 70.12ng/ml.

Combined, the sensitivity of DRE and PSA in our study was 100%. This is similar to the findings by other studies.[20,21,24] Several studies have actually, reported increasing sensitivity of PSA at lower cut-off values with resultant decreasing specificity. This is explainable by the fact that PSA is prostate-specific and not prostate-cancer-specific. In our study, PSA had a specificity of 2.15% at a cut-off value of 4ng/ml while DRE was 60.22%. Lower values of 20.2% and 44.7% were found for PSA and DRE respectively, by Ojewola et al.[22] Abdrabo et al [20] inferred a similar specificity result for DRE (68%) which was far higher than the 24% noted for PSA in the same study.

In contrast to the observation by Abdrabo et al [20], the combined specificity of PSA and DRE noted in our study was far less than the values for the individual PSA ranges. This is similar to the findings by Al Rumaihi et al [24]

The highest PSA specificity of 89.25%, in our study, was noticed at PSA values above 100ng/ml. This is in keeping with the 99.7% observed by Lojanapiwat et al[25] where PSA levels above 100ng/ml were also noticed to be 90.7% specific for bone metastasis.

The positive predictive value (PPV) of PSA, in our study, was noted to have progressively increased with increases in PSA levels. It was highest (83.61%) at PSA level above 100ng/ml. Using 4ng/ml as PSA cut-off the value was 55.61%. Similar progressive increase was noted by Lojanapiwat et al.[25]

The PPV of DRE, in our study, was higher than that of PSA and was 71.97%. In contrast Similarly previous studies reported a higher PPV for PSA than DRE.[12-14,26,27] This may be attributed to the late presentation as is common in our environment.[6,11] Furthermore, we found that combined PPV of DRE and PSA was 55.29% which was less than the individual values of the two

parameters. This reflects the report by De et al[21] but contrasts with several other studies where the combined values were higher than the individual values.[11-13,22,23] Thus, abnormal DRE in our environment is more likely to be associated with cancer of the prostate in symptomatic patients and should guide counselling of patients before biopsy. However, as the PSA rises, the PPV increases and gets to 83.67% at PSA above 100ng/ml.

The negative predictive value (NPV) of PSA at 4ng/ml in our study was 66.67% and that of DRE was 73.68%. In the work done by Al Rumaihi et al[24] and Lojanapiwat et al[25], they had NPV for PSA (above 4ng/ml) of 78.4% and 87.5% respectively which is higher than that recorded in our study. A progressively, decreasing NPV with increasing PSA was noticed by Lojanapiwat et al [25], similar to our own finding.
Outside PSA levels between 20.1-50ng/ml, in our study, DRE increased the NPV in all other PSA ranges. However, the low combined NPV (Zero percent) of DRE and PSA at 4ng/ml cut off in our study showed that the two parameters cannot be relied on to exclude the presence of Ca prostate in pre-biopsy patients.

The diagnostic accuracy of a test relates to the ability of the test to discriminate between the target condition and health. We found that to be 72.60% for DRE and 55.77% for PSA at a cut-off of 4ng/ml. the higher value for DRE is, possibly, due to the fact that our study population comprised, mainly, of referred patients and not unscreened population.

Similar higher detection accuracy of DRE was noticed by Ojewola et al[22] in their study with values of 58% and 53% for DRE and PSA, respectively. The detection accuracy of PSA, progressively, improved with rising PSA levels, and with similar improvements when PSA levels >20ng/ml were considered with abnormal DRE.
A comparable detection accuracy of 79.9% for DRE was observed by Akdas et al [28] which improved to 84.2% when combined with PSA and trans-rectal ultrasound.

Our study showed that neither DRE or PSA had sensitivity or specificity, enough to be of high diagnostic value.
Though combined, the sensitivity of both rose to 100%, but the reverse was observed with their specificity.

The diagnostic accuracy of PSA was noticed to be progressively increasing with increasing PSA levels and, further still, when DRE was combined with PSA above 20ng/ml. DRE had a, relatively, high detection accuracy in our study.
The efficacy of these screening tools in the diagnosis of prostate cancer is higher when both tools are applied and will increase further if transrectal ultrasound is employed.[29,30]

CONCLUSION

In conclusion, PSA and DRE singly or in combination have a poor PPV, NPV and ODA to help counseling of patients prior to prostate biopsy. However, on a scale of preference in our environment DRE with an overall diagnostic accuracy of 72.6% is better in predicting the diagnosis of carcinoma of the prostate than PSA with an overall diagnostic accuracy of 55.77%.

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