EARLY DETECTION OF PROSTATE CANCER: EVALUATING THE DIAGNOSTIC PERFORMANCE OF PROSTATE SPECIFIC ANTIGEN BY COMPARING WITH HISTOLOGICAL TECHNIQUE AMONG AFRICANS

M.A. Emokpae*, S.C. Das*, T. Orok*, A.Z. Mohammed and S. Al Hassan*****

Dept. of Chemical Pathology, **Dept of Pathology, *Dept of Surgery, Aminu Kano Teaching Hospital, Kano, Nigeria.*

ABSTRACT

This study was conducted to investigate the diagnostic performance characteristics of prostate specific antigen (PSA) by comparing serum PSA value with histological findings in patients suspected of having prostate cancer in Aminu Kano Teaching Hospital, Nigeria. Clinical and Laboratory records were examined and collated for serum PSA values, together with histological findings of biopsy specimen, clinical diagnosis, age of patients, and mode of presentation. The serum PSA values were determined by ELECSYS 1010 autoanalysers Roche, Germany based on electrochemiluminescence immunoassay technique. The results show that serum PSA values increase with age in the asymptomatic non-cancer patients who came for medical check up but were within normal limit. In prostatic disease conditions PSA values were raised in benign prostatic hyperplasia 35.957 ± 4.0315 ng/ml, in undifferentiated carcinoma 56.22 ± 4.295 ng/ml and adenocarcinoma >100 ng/ml as compared to the normal range (0-4 ng/ml). These cases were confirmed by histological diagnosis. It is concluded that PSA evaluations is a sensitive marker for prostate cancer but because of various other conditions that affect serum PSA concentration, other methods of investigations such as Digital Rectal examination, Trans Urethral Ultra-Sonography and histological examination should be combined to confirm diagnosis. Prognosis of patients will be better if early diagnosis is made.

KEY WORDS

Prostate specific antigen, Africans

INTRODUCTION

The advent of prostate specific antigen (PSA) has made prostate cancer the most common malignancy in men above 50 years and the third most common cause of cancer death in the United State of American (1-3). The prognosis of patients with prostate cancer is dependent on the stage and grade of the tumour at the time of diagnosis. Many patients who are diagnosed by PSA assay have no palpable prostatic nodules and cancer documented by means of ultrasound guided or blind biopsies (4). Prostate cancer causes significant morbidity and mortality in African men (5). There is a need for health education about the early detection of the disease. Clinically the diagnosis of prostate cancer is strongly suggested by a hard irregular prostate or by an elevated PSA, but diagnosis is confirmed by histological examinations of biopsy, transurethral prostate resection chip specimen or by

aspiration cytology (6). Advocates of prostate cancer screening argue that PSA measurement would help to select an at risk group while transurethral ultrasonography (TRUS) and biopsy would identify clinically occult early tumours in this group (6).

This article evaluates the performance of serum PSA measurement in patients suspected of having prostate cancer and comparing with histological examination of prostate biopsy specimens.

PATIENTS AND METHODS

A retrospective study of all patients who were referred to the Chemical Pathology department of Aminu Kano Teaching Hospital, Kano, Nigeria for serum PSA was included in the study. The histopathology Laboratory records and medical records were searched for the patient who's serum PSA Level was determined between December 2000 and August 2002. The hospital records were searched for diagnosis, age of the patients on presentation and mode of presentation. The histopathology records were searched for microscopic diagnosis which was compared with PSA levels to determine the sensitivity and specificity of PSA assay. The PSA assay was carried out using ELECSYS 1010 ANALYSER, Roche, Germany, based on

Author for Correspondence:

Prof. S. C. Das MBBS, MD, MD

Head, Dept., of Chemical Pathology
Aminu Kano Teaching Hospital
PMB 3452
Kano 700001
Nigeria.

electrochemiluminescence immunoassay technique. Statistical analysis was done by ANOVA diskette using Compaq micro computer of the hospital.

RESULTS

A total of one hundred and forty five (145) patients were referred to the department for PSA determination. (Table 1) The age ranged from 43 years to 98 years with the mean age of 67.9 years. The PSA values obtained were stratified to different PSA groups (0-4ng/ml; 4.1-20ng/ml;20.1-99ng/ml;and 99.1->100ng/ml respectively) and age groups (table1). Forty of them came for routine PSA check, thirty seven patients were younger than 60 years of age and twelve patients were older than 61 years. The hospital records of fifty of the patients who were admitted and treated in the hospital were traced (Table 2). The age of the patients range from 43 years to 98 years. The mode of presentation include urine frequency, terminal dribbling, suprapubic pain and urine retention (24), paraplegia and in ability to walk (20) lower back pain and abdominal pain (4) and haematuria (2). The number of patients with moderately and well differentiated prostatic adenocarcinoma were 27, two of the patients were aged 48-50 years, four were 51-60 years; ten were 61-70 years eight were 71-80 years and three were 81-98 years. Those with poorly differentiated carcinoma were 10 and three of them were aged 46-50 years, six were 71-80 years and one was 81-96 years old. While those with benign prostatic hyperplasia were 13. Twelve of them were aged 61-70 years while 2 were aged 51-60 years (table 3).

DISCUSSION

Detection of prostate cancer by screening for elevated level of PSA is increasingly popular in this centre. The most common prostate cancer screening tools are Digital rectal examination (DRE), Transrectal ultrasonography (TRUS) and PSA assay. PSA is the most clinically useful tumour marker for diagnosis of prostate cancer. Although specific for prostatic tissue, it is not prostate cancer specific(7). It has been reported that Ig of benign hyperplastic tissue (benign prostatic hyperplasia (BPH) gives rise to 0.2-0.3ng/ml of PSA in the serum (1, 8-10). Similarly serum PSA concentration directly correlated with patient's age and prostatic volume, in other word, as men grow older their prostate glands enlarge and PSA concentration increases. Table 1 in this study shows that serum PSA values increased with age in the 0-4ng/ml column. Within the age range of 40-49 the PSA value was 1.133 ± 0.29 ng/ml; 50-59 years (1.238 ± 0.233 ng/ml); 60-69 years (1.607 ± 0.517 ng/ml) and 70-79 years 1.808 ± 0.408 ng/ml (Figure 1). Apart from prostatic volume, other factors contributing to increase in PSA as men age include episodes of subclinical or clinical prostatitis, intermittent bouts of prostatic ischemia, infarction and the presence of prostate cancer that cannot be detected by currently available methods. Furthermore, as men grow older, their prostate glands may become more "leaky". The normal physiological barriers that keep PSA in the prostate duct system may become more permeable and allow serum PSA to enter the general circulation via the capillaries and lymphatics(11).

Table 1: Distribution of serum PSA values and age groups in the present investigation

Serum PSA levels (in ng/ml express in mean $\pm$ SEM)

Age (years)	0-4.0 ng/ml	4.1-20 ng/ml	20.1-99 ng/ml	99.1 - >100 ng/ml
40-50	1.1333 ± 0.296 n =10	5.557 ± 1.166 n=3	68.287 ± 7.456 n=3	>100 n=1
51-60	1.238 ± 0.233 n=27	10.016 ± 1.165 n=12	44.05 ± 12.722 n=5	>100 ± 0.0
61-70	1.607 ± 0.517 n=3	8.936 ± 0.883 n=12	37.835 ± 3.845 n=14	>100 ± 0.0 n=10
71-80	1.808 ± 0.408 n=9	7.652 ± 1.372 n=4	50.71 ± 6.342 n=4	92.44 ± 7.553 n=8
81-100	-	5.58 ± 0.0 n=1	62.47 ± 0.0 n=1	>100 ± 0.0 n=3
Total (n)	49	42	27	27

Table 2: Age Group distribution of PSA values in health and different prostatic disease conditions (Mean $\pm$ SEM and ranges)

Age Group Years	Non-Cancer patients	Benign Prostatic hyperplasia	Poorly differentiated Carcinoma	Well and moderately differentiated Carcinoma
40-49 Mean (ng/ml) Range	(n = 12) 0.455 $\pm$ 0.016 0.027- 0.795		(n = 1) 31.95	(n=1) >100
50-59 Mean (ng/ml) Range	(n = 6) 1.287 $\pm$ 0.432 0.419 – 3.56	(n = 3) 43.077 $\pm$ 20.69 15.22 – 93.69	(n=3) 63.767 $\pm$ 8.553 47.29 – 83.20	(n = 5) >100
60-69 Mean(ng/ml) Range	(n = 14) 1.586 $\pm$ 0.265 0.112 – 3.80	(n = 6) 31.667 $\pm$ 1.876 23.26 – 37.14	(n = 3) 50.033 $\pm$ 7.175 33.16 – 62.73	(n=15) >100
70-79 Mean(ng/ml) Range	(n=8) 2.552 $\pm$ 0.361 0.901 – 3.89	(n = 3) 45.57 $\pm$ 7.010 34.98 – 62.47	(n=1) 45.21	(n = 5) > 100
80-89 Mean(ng/ml) Range	-	(n = 1) 62.47	(n = 2) 72.23 $\pm$ 6.795 62.62 – 81.84	-
90-100 Mean(ng/ml) Range	-	-	-	(n = 1) > 100
Total (n)	40	13	10	27

Fig. 1: Histogram of PSA values in apparently healthy individuals of different age groups in decades

If all the records were found it would have been interesting to know the causes of the rise in the 4.1-20-ng/ml column (Table 1). However, it might be unconnected with the factors enumerated above. Five patients were discharged on financial plea or against medical advice before further investigations were carried out. From table 3, thirteen of the patients had BPH and their PSA mean value was 35.957 ± 4.035 ng/ml. This was confirmed by histological microscopy. Ten had undifferentiated carcinoma and mean serum PSA value of 56.22 ± 4.295 ng/ml while twenty seven had adenocarcinoma with mean PSA value >100 ng/ml. These also were confirmed by histological microscopy.

The reference range of serum PSA use in this centre is 0-4 ng/ml. A PSA value above 4 ng/ml signals the need for further investigations. It is important to state that in men with normal size prostate, a PSA value above 2 ng/ml may raise concerns for prostate cancer. The percent free PSA will be helpful for men with PSA values less than 10 ng/ml to enable definitive diagnosis to be made (12). There may be indication for prostate cancer when percent free PSA reading of 25% in men with a PSA value of 4.1-10 ng/ml is recorded or 15% with PSA of 2.5 – 4 ng/ml. There was one patient whose

PSA was within normal limit but cancer detected at autopsy. Some men's prostate (cancer) tissue does not secrete much PSA even in the presen of prostate cancer (12).

PSA is also very important in treatment monitoring. The steepness of the rate of fall in PSA down to undetectable levels following adequate treatment provides information on the success of therapy (13).

In summary, the finding of this investigation indicates that the serum PSA is effective in the diagnosis of prostate cancer. BPH can lead to considerable rise in PSA levels. Nevertheless, a mild to moderate rise in serum PSA level alone (without having any other concurrent diagnostic procedure) may prove inadequate in the diagnosis and confirmation of prostate cancer, and this may even lead to a false and misleading conclusion by a clinician.

To obtain good performance from PSA evaluation, blood samples for PSA should be taken first before any physical manipulation of the prostate gland. When PSA is combined with other methods of diagnosis of this all important cancer, early diagnosis will be made possible. And prognosis of patients will be better.

Table 3: Serum PSA values in different Prostatic disease conditions and in apparently healthy individuals.

Disease condition	No of cases (n)	Age range (in years)	PSA value (ng/ml) Mean $\pm$ SEM	P value
Apparently health non-cancer patients	40	40-75	1.446 $\pm$ 0.325	
Patients with Benign Prostatic hyperplasia	13	51-70	35.957 $\pm$ 4.0315	<0.001
Poorly differentiated carcinoma of prostate	10	46-96	56.22 $\pm$ 4.295	<0.001
Adenocarcinoma of the prostate (Well and moderately differentiated)	27	48-98	>100	<0.001
TOTAL	90			

REFERENCES

- Sagalowsky, A.I. and Wilson, J.D. Hyperplasia and carcinoma of the prostate in Harrison's principles of internal medicine eds Fanci AS, Brannwald, E.J.K., Isselbacher, J.D. Wilson *et al*, McGraw-Hill. Health professions division 14th Edition 1998, 596-602.
- Hass, G.P. and Sakr, W.A. (1997) Epidemiology of prostate cancer. *Cancer. J. Clin.* 273-277.
- Boring, C.C., Squires, T.S. and Tong, T. (1993) Cancer statistics. *Cancer J. Clin.* 43, 7-26.
- Ilhde, C.N. and Longe, D.L. Manifestations of cancer in Harrison's principles of internal medicine Eds. Fanci, A.S., Braunwald, E., Isselbacher, J.D., Wilson *et al* McGraw-Hill Health Professions division 14th edition 1998, 360-364.
- Dawan, D., Rafindadi, A.H. and Kalayi, G.D. (2000) Benign prostatic hyperplasia and prostatic carcinoma in native Africans. *BJU international* 85, 1074-1077.
- Alan, P.D. and Timothy, J.C. (1996) Diagnosis and Treatment of Urological malignancy: The prostate. *Brit. J. Hosp. Med.* 3, 104-124.
- Oesterling, J.E., Jacobson, S.T. and Chute, C.G., *et al* (1993) Serum prostate-specific antigen in a community-Based population of healthy men: Establishment of Age-specific Reference Ranges. *JAMA* 270, 860-864.
- Oesterling, J.E., (1991) Prostate-specific antigen: a critical assessment of the most useful tumour marker for adenocarcinoma of the prostate. *J. Urol.* 145, 907-923.
- Robles, J.M., Morell, A.R., Redorta, J.P., de Torres, Matoes, J.A. and Rosello, A.S. (1988) clinical behaviour of prostatic specific antigen and prostatic acid phosphatase: a comparative study. *Eur. Urol.* 14, 360-366.
- Christenson, A., Bjork, T. and Nilsson, O. *et al* (1993) Serum prostatic specific antigen compared to alpha 1-antichymotrypsin as an indicator of prostate cancer. *J. Urol.* 150, 100-105.
- Oesterling, J.E., Bilhartz, D.C. and Tindall, D.J. (1991) Clinically useful serum markers for adenocarcinoma of the prostate, II: prostate – specific antigen *Am. Urol. Assoc. Update Ser.* 10, 137-144.
- Information on prostate cancer. Radiotherapy clinic of Georgia (2002) A Centre of Excellence for Prostate Cancer Researches and Treatment <http://www.rcog.net/pages/info.html>.
- Patin, A.W., Pound, C.R., Clemans, J.Q., Epstein, I.I. and Walsh, P.C. (1993) Serum PSA after anatomical radical prostatectomy. The Hopkins experience after 10 years. *Urol. Clin. North Am.* 20, 713-725.