Pattern of Prostate Specific Antigen Request in a Nigeria Tertiary Health Care: A Decade Review

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Abstract

This study is a decade review of requests pattern for Prostate Specific Antigen (PSA), in a Nigerian tertiary health care. All plasma samples for PSA from January 2002-December 2011 were analysed weekly by immunoradiometric assay method. Biodata from request form were collated and analyzed. A total of 15079 requests were received for the period under review. There was a consistent and progressive yearly increase of request from inception to the last year of review but a sudden drop in 2010 only. Smoked or barbecued food, consumption of local herb and alcohol in order of importance, respectively, appears to be prominent factor in patient requested for PSA. There was an increasing trend in the proportion of requests with values outside the reference range over the years in review. This is consistent with previous report of increasing incidence of prostate cancer in Nigeria. Certain indigenous and tradition modifiable lifestyle especially, alcoholic, positive history of native herbs and smoked food consumption may play an important role in addition to underlying genetics and other previously implicated risk factor of prostate cancer in Nigeria.

Keywords: PSA; Nigeria males; Social factors; Prostate cancer

Introduction

Prostate specific antigen was first described about 34 years ago but is still in use today for screening, diagnosis, monitoring and prognosis of prostatic carcinoma in spite of its non-specificity as was widely believed. Prostate cancer is an increasingly important public health problem among adult men worldwide. Nigeria, which was formerly regarded as a low-incidence area by several authors [1-4] is now witnessing a steep rise in the occurrence of this disease. This has been suggested to be due to increasing availability of screening tests and diagnostic facilities and not necessarily because of increased incidence of the diseases [2]. Whichever, many notable Nigerians have lost their lives to this dreaded disease.

Prostate cancer is one of the commonly diagnosed cancers among Nigerian men. Early detection and screening can be done using two tests: PSA (Prostate Specific Antigen) test and DRE (Digital Rectal Examination). But none of these tests is specific for prostate cancer. Some men may be found to have prostate cancer even with "normal" result from PSA test and DRE. Elevated PSA levels is detected in patients with BPH (Benign Prostatic Hyperplasia), prostatitis, and as a result of some drugs treatment or prostate damage [5,6]. As a consequence, wide application of PSA screening led to over diagnosis of prostate cancer. In order to increase the specificity of prostate cancer some workers have compared the ratio of free to total PSA or free to complexed PSA [7,8]. Others have used plasma lipid levels [9,10], vitamin E (α and γ tocopherol) [9], trace metal- Selenium [11] and serum to urinary PSA ratio [12,13]. Other interventions to refine PSA testing for screening include PSA density, PSA velocity and age adjusted reference ranges. Most Clinician and Urologists in Nigeria however use total PSA in conjunction with other modalities in the initial biochemical investigation of the patients presenting with symptoms referable to the prostate gland. This review is aimed at assessing the frequency, the social demography and the indication for PSA requests in the last 10 years.

Materials and Methods

Request forms for PSA over the period of review from 2002 to 2011 were reviewed for indication, social demographic setting, and proportion of results within the reference interval as well as the relationship between the presenting diagnoses to the socio demographic factors were evaluated. PSA testing at this centre located at University College Hospital Ibadan in the Southwestern part of Nigeria. Tests were done on plasma sample by radio immunoassay technique with bulk reagents obtained from Skybio Ltd (Bedfordshire U.K.). However in 2010 when Skybio stopped production bulk reagents were purchased from Institute of Isotope Ltd, (Budapest, Hungary).

Principle of the assay

Briefly, this is an immunoradiometric assay in which the antibody is labeled with radioactive isotope usually ^{125}I. Antibody is first attached to a solid phase by passive adsorption. Antigen from the sample is then allowed to react with the solid phase antibody while the non specific proteins are washed off. Then the bound antigen antibody is identified by labeled antibody through a second distinct antigenic determinant. The bound count is directly proportional to the concentration of the antigen. Counting was done on Wallach gamma counter 1470 series.

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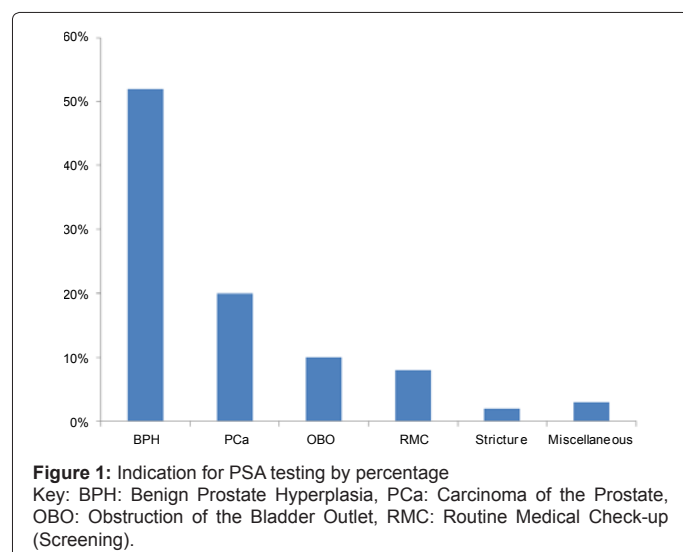
Year of Assay	Number of Tests	*Age Range of patients (%)	Positive history of smoking (%)	Positive history of Alcohol (%)	Positive history of Native herbs consumption (%)	Positive history of smoked food (%)
2002	935	1=16, 2=29, 3=30, 4=20, 5=5	2	30	51	89
2003	1086	1=10, 2=32, 3=37, 4=19, 5=2	1	33	43	95
2004	1371	1=12, 2=19, 3=39, 4=21, 5=9	4	23	30	92
2005	1443	1=14, 2=20, 3=38, 4=20, 5=8	5	15	37	72
2006	1525	1=12, 2=23, 3=40, 4=19, 5=6	2	36	48	68
2007	1669	1=10, 2=21 3=43, 4=21, 5=5	6	41	53	73
2008	1775	1=9, 2=30, 3=37, 4=20, 5=4	2	25	32	66
2009	1935	1=11, 2=22, 3=40, 4=20, 5=7	4	39	33	86
2010	1430	1=9, 2=20 3=22, 4=40, 5=9	7	29	35	93
2011	1910	1=14 2=15, 3=37, 4=24, 5=10	3	37	37	87
Total	15 079					

*Age Range: 1= 41-50, 2= 51-60, 3= 61-70. 4= 71-80, 5= >80

Table 1: Socio demographic characteristics of patients requesting PSA test over the study period.

Result Range ng/ml	No of Tests	Percentage
0-4	4590	30.4
>4.0-10	2428	16.1
>10	8061	53.5

Table 2: Percentage of PSA range over the period.

Figure 1: Indication for PSA testing by percentage
Key: BPH: Benign Prostate Hyperplasia, PCa: Carcinoma of the Prostate, OBO: Obstruction of the Bladder Outlet, RMC: Routine Medical Check-up (Screening).

Results

A total of 15079 PSA testing were carried within the period under review. The number of requests increased on a yearly basis till 2009. There was a significant drop in requests for the year 2010 and particularly worse to the extent that the number of testing recorded in 2010 were not as much in number compared to previous years (2005-2009). Table 1 shows the age range. The commonest age range of PSA test request was clearly 61-70 years, followed by the 51-60 age brackets. Prostate cancer being a problem of aged men, especially, above 50years. An insignificant proportion of the test subject had positive history of smoking cigarette or tobacco. However, higher percentage had a positive history of significant quantity of alcohol and local herbs consumption. Majority of the patients tested consumed smoked food frequently. Table 2 shows the indication for PSA testing. The commonest indication was suspicion of benign prostate hyperplasia. This was followed by

adenocarcinoma of the prostate. Interestingly, majority of the patients tested (54%) had their PSA range above the 10 ng/ml cutoff (Figure 1).

Discussion

A tumour marker is described as a biochemical substance produced by a tumour itself or by the body in response in response to the presence of tumour in higher than normal concentration. This substance can be secreted into blood, urine, other body fluid or tissues. Prostate specific antigen as a tumour marker was initially thought to be tissue and gender specific but it has been demonstrated in male and female periurethral glands, anal glands, apocrine sweat glands, apocrine breast cancers, salivary gland neoplasm and human breast milk [14,15]. Apart from this, different immunoassays show different considerable variation even in the same patient specimen which has been attributed to differences in antibody specificity, reaction kinetics and calibration [16,17]. This entity has received the attention of Scientists and kits manufacturer overtime with various modifications to confer better specificity.

Aside from all these shortcomings, PSA still remains an invaluable tool in diagnosis, monitoring the treatment and follow up of patients with prostate related diseases. Our review showed consistent and progressive increasing number of request from 2001 to 2009. However, there was a drop in the number of requests tested in 2010. This was adduced to recurrent fault in the Gamma counter used in the laboratory, resulting into inconsistence availability of the service for this period. This obviously affected the number or requests in 2010 which picked again in 2011 as soon as the situation improved. The increasing request could indicate increasing awareness among the male folk and probably increase in the incidence of prostatic carcinoma as suggested earlier [4]. The latter is supported by the findings of an increasing trend in the proportion of requests with values outside the reference range over the years in review.

The commonest indication for PSA testing in this report is suspicion of benign prostate hyperplasia. More than 50% of the tests had PSA level above 10 ng per ml. This preponderance is not however unexpected Level of total PSA in benign condition has considerable overlap with those of patients with prostate cancer. This finding is not unexpected as it has been shown that benign enlarged cell and malignant cells produce more PSA although malignant cells produce more per gram of tissue [18-20].

The positive history of consumption of smoked food has been associated with cancer. This has been associated to the fact that smoked

food contains Heterocyclic Amines (HCAs) and Polycyclic Aromatic Hydrocarbons (PAHs) chemicals formed when muscle meat, including beef, pork, fish, and poultry, is cooked using high-temperature methods, such as pan frying or grilling directly over an open flame is said to predispose to cancer generally [21]. Previous studies have reported that high consumption of well-done, fried, or barbecued meats was associated with increased risks of colorectal [22], pancreatic [23,24], and prostate [24,25] cancer. There is therefore a probability of association in our population cohort in relation to prostate cancer. Furthermore, alcoholic consumption and consumption of local herbs, apparently appears to be an important factor to the incidence of prostate cancer in our study population.

The recently published Global status report on alcohol and health analyses available evidence on alcohol consumption by WHO, provides data in over 100 individual country profiles. Analysis from 2001-2005 showed countries in the WHO Americas, European, Eastern Mediterranean and Western Pacific regions had relatively stable consumption levels during that time; but marked increases were seen in Africa and South-East Asia during the five-year period [26]. United Nation data range (1999 -2006), reported 32% of Nigerian adult males, between the ages of 15 - 85 years to be heavy episodic alcoholic drinkers with a health consequence (alcoholic disorder) of about 2% in Nigeria males [27]. Although, prostate cancer is not known to be considered as alcoholic disorder, alcohol use, and particularly heavy use, has been reported to causes cancers of the oral cavity, pharynx, larynx, esophagus, and liver [28]. Increased risks for pancreatic cancer [29] and colon tumors [30] have long been related to alcohol use in some studies. Lately, there are increasing evidences implicating alcohol in the risk of prostate cancer [31,32]. The ability of alcohol to alter the hormonal milieu and presence of chemical substances such as flavonoids (red wine), which may alter tumor cell growth was suggested as a factor that may affect prostate cancer risk [32]. We have earlier reported reduced androgen receptor polymorphism and its associated correlation to prostate cancer in similar population cohort [20]. The growth of the prostate gland depends on circulating steroid; androgens and intracellular steroid signaling pathways. The effects of this hormone; androgens are mediated through the Androgen Receptor (AR), a nuclear transcription factor encoded by the AR gene located on the X chromosome (Xq11-12). Reduced common polymorphisms, CAG and GGN repeats, in exon 1 of this gene has been reported in our study population and implicated as a risk factor in prostate cancer [20]. The ability of alcohol to alter the hormonal environment coupled with this genetic factor will obviously make our subject more vulnerable. These factors may explain the high percentage of alcohol consumption found in our cohort populated requested for PSA and may be an indication of the importance of this modifiable lifestyle as risk factor of prostate cancer.

Chemical substances such as flavonoids may alter tumor cell growth [32]. These authors also listed consumption of certain diet (intake of fat, vegetables and fruits, dairy products and certain micronutrients and vitamins) as risk factor of prostate cancer. This probably explains high percentage of positive history of herb consumption in our cohort population. Many of the local herbs consumed in our population contain flavonoids, polyphenols, heavy metals and several micronutrients. However, there are contradictory evidences that certain flavonoids and polyphenols may reduce risk of prostate cancer. Polyphenols have been shown to decrease tumor cell proliferation *in vitro* [33-35] and flavonoids have been shown to block PSA production in both breast and prostate cancer cell lines [36]. On the other hands, there appears to be no controversy on the possible involvement of certain heavy metals such as cadmium, mercury and lead, in the pathogenesis of prostate cancer [37,38].

In summary, availability of PSA screening text has not only consistently increased the request for the test but has consequently increased suspicion of increased incidence of prostate cancer in Nigeria. The commonest indication for PSA testing in this report is suspicion of benign prostate hyperplasia. Interestingly, there was an increasing trend in the proportion of requests with values outside the reference range over the years in review. This is consistent with previous report of increasing incidence of prostate cancer in Nigeria. Certain indigenous and tradition modifiable lifestyle especially, alcoholic consumption, positive history of native herbs and smoked food consumption are suggested as risk factor of prostate cancer in Nigeria.

Acknowledgement

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