Original Research Paper

Volume-9 | Issue-3 | March-2019 | PRINT ISSN - 2249-555X

Biochemistry

PROSTATE SPECIFIC ANTIGEN TESTING IN A TERTIARY TEACHING HOSPITAL

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ABSTRACT

BACKGROUND: Prostate cancer is a major global health concern that disproportionately affects Blacks with increasing incidence in Afro-Caribbean men. Not surprisingly, it is the leading cause of cancer-related deaths in Jamaica. Jamaican clinicians have used prostate specific antigen (PSA) for nearly three decades to aid screening and monitoring of prostate cancer, but concerns regarding its specificity and usefulness exist.

METHOD: This study examined the pattern of total prostate specific antigen (TPSA) test requests by clinicians at a tertiary hospital, University of the West Indies (UHWI) in Jamaica during a two-year period. It also analysed the distribution of the results by age as well as the proportion of men with repeated requests. Data from 2,550 TPSA requests was extracted from the laboratory information system (LIS) and carefully analysed.

RESULTS: The audit revealed that 69.4% of TPSA requests were sent from outpatient departments (Accident and Emergency as well as clinics appointments) at UHWI. The 61-70 age-group had the most TPSA requests and was most recurring amongst patients with single request. In assessing repeated requests, complete identifying information (DOB/ age, registration number and full name) was available for 2,468 of the total requests received. Of this number, less than 20% of patients had repeated requests (11.4% had two requests and 7.9% had three or more requests). The 61-70 age group was most common when the first test was performed in patients with multiple requests (40.0% for two requests and 37.7% for three or more requests). TPSA levels showed that whilst majority of TPSA levels was normal (<4.0ng/ml), there were 92 requests with levels >400 ng/ml. TPSA levels at first request showed that 51.0% of patients with two requests had normal results. Of patients with three of more requests, only 43.5% had normal TPSA levels at the first time the test was performed.

CONCLUSION: The study provided information as to the patterns of TPSA requests at a tertiary hospital in Jamaica.

KEYWORDS : prostate specific antigen, request, cancer, hospital

INTRODUCTION

Prostate cancer is a common malignancy among men and is characterized by a slower growth progression compared with other cancers1. It has a strong ethnic propensity and men of African descent such as those in the Caribbean are disproportionately affected with higher incidence and mortality rates[2].

In the 2012 global cancer statistics, the Caribbean region has the highest deaths from prostate cancer with age-standardized prostate cancer-specific mortality rate at 29.0/100000/year3. Prostate cancer is the leading cancer affecting Jamaican men and the age-standardized incidence for the period 2003-2007 in the Kingston and St Andrew area in Jamaica was 78.1/100,0004. Blake and colleagues reported an age-standardized prostate cancer-specific mortality rate of 53.9/100,000/year making prostate cancer the leading cause of cancer-related deaths in Jamaica[5].

Prostate specific antigen (PSA) was discovered by Wang and colleagues and was introduce to Jamaica in 19896,7. It is currently used as a tumour marker for screening, diagnosis, monitoring and prognosis of prostate adenocarcinoma although there are concerns regarding its specificity8. The increase in prostate cancer incidence in Jamaica is partially due to the effect of PSA testing9. Despite the increasing use of PSA testing, approximately one-half of men with newly diagnosed prostate cancer in St. Andrew and Kingston (two urban parishes in Jamaica) presents with symptomatic, locally advanced and metastatic disease[10].

The United States Preventive Services Task Force (USPSTF) initially recommend against PSA-based screening especially in men 70 years and older as the harms from screening, diagnosis and treatment outweighs the benefits[11]. Caribbean population is predominantly blacks and the biology of prostate cancer is more antagonistic when compared with Caucasians and differences in androgen receptor genes may play a role[12]. Primary care physicians and urologist in the Caribbean practice PSA-based-screening although there is the absence of clinical trials with evidence of the benefits of such in high-risk black populations[9].

There is a divergence of opinions regarding PSA testing among medical practitioner in hospitals in Jamaica. This study examine the pattern of PSA test requests by medical practitioners in a tertiary hospital in Jamaica and the distribution of the results by age as well as the proportion of men with repeat test requests.

MATERIAL AND METHODS

Population

This study incorporated all Total PSA (TPSA) requests received by the Chemical Pathology Department, The University of the West Indies (UWI)/University Hospital of the West Indies, between 1 January 2015 and 31 December 2016. Data collection was performed by extracting information pertaining to TPSA results and patients' demographics (age, hospital number and source of requisition) from the Laboratory Information System (LIS). The patients' age and TPSA results were organised into ordinal categorical groups, and requisition source was organised into the following four categorical variables: hospital wards, clinics/outpatient departments (OPD), private sources, and miscellaneous sources. Miscellaneous sources were defined as those requests received from on-going studies during the period.

Laboratory assays

TPSA analyses were performed using the Cobas 6000 e601 analyser, (Roche Diagnostics, Kingston, United States of America). The TPSA was determined using the Roche Cobas 6000 e601. The Roche Elecsys Total PSA method is a sandwich electrochemiluminescent immunoassay which involves the PSA in the specimen (serum or plasma) reacting with both monoclonal PSA-specific antibody (mouse) labelled with a ruthenium and biotinylated monoclonal PSA-specific antibody (mouse) resulting in the formation of a sandwich complex. Streptavidin-coated micro-particles are added and the mixture aspirated into the measuring cell where the micro-particles are magnetically captured onto the surface of the electrode. Unbound substances are then removed with ProCell. Application of voltage to the electrode induces the A chemiluminescent emission is induced after the application of voltage to the electrode which is then measured against a calibration curve to determine the amount of PSA in the patient specimen. This method has been standardized against the Reference Standard/WHO 96/670[13] (Butch et al., 2001).

Laboratory quality standards were achieved during the analysis of serum samples for TPSA during the study period.

Statistical analysis
Data analysis and presentation was performed using SPSS software version 24.

RESULTS

The study included data from a total of 2,550 TPSA requests received over the two-year period spanning 1 January 2015 and 31 December 2016. Of the 2,550 requests, 1,215 (47.6%) were received in 2015 and the remaining 1,335 (52.4%) were received in 2016. This represents a 9.9% increase in TPSA request in 2016 compared with 2015.

Figure 1 shows that of the 2,550 TPSA requests, 1,770 (69.4%) were received from clinics and outpatient departments inclusive of the Accident and Emergency Department at the UHWI. Admitting wards at the UHWI accounted for the second largest requisition source with 454 (17.8%) requests. The laboratory received 197 requests (5.1%) from private sources including external medical laboratories. Miscellaneous sources provided the smallest fraction of the requests with only 129 requests (5.1%) sent over the 24-month period.

The requests were organised based on the age-group of the patients. Of the 2,550 PTSA requests, 2468 (96.8% of total requests) provided information on patients' age/ date-of-birth (DOB). As seen in figure 2, the 61-70 years age-group made up close to one-third of the requests with 773 requests (31.3%). The 71-80 years age-group was next with 617 requests (25.0%). From the 2,468 requests that provided age, 437 (17.7%) was in the 51-60 years age-group. There was only 1 request from a patient over the age of 100 years that made up less than 1% of the total age-group distribution for the 24-month period.

TPSA results extracted by the LIS were organised into groups and are displayed in Table 1. From the 2,550 requests, 1555 (61.0%) reported normal levels (0.0-3.9 ng/ml). There was TPSA levels greater than 100 ng/ml for 166 (6.5%) requests. The highest TPSA level measured for the period was 14545.0 ng/ml but a total of 92 requests (3.6%) had TPSA results >400 ng/ml.

The 2,468 requests that provided age/date of birth information include 1,747 patients with single or repeated TPSA requests. Of this number, 1,409 (80.7%) patients had only one TPSA request. Two hundred patients (11.4%) had two requests and 138 patients (7.9%) had at least three requests received during this period.

We also assessed the age and TPSA levels at the first request for these patients (Tables 2 and 3). Table 2 shows the 51-60 and 61-70 age-groups were the two most recurring amongst patients with single requests. Respectively, these groups represented 22.4% and 27.5% of the total number of patients with single requests (Table 2). For patients with two requests, the 61-70 years age-group was most common (40.0%) when the first test was performed. This age group was seconded by the 71-80 years age-group with 24.5% of the total 200 patients with two TPSA levels measured. From the 138 patients that had three or more TPSA levels measured, 37.7% were 61 to 70 years old and 36.2% were 71 to 80 years old, making up more than half the total number (Table 2).

Table 3 shows that 67.2% of patients with only one TPSA test performed had normal levels, and 15.3% had slightly elevated TPSA levels (4.0-10.0 ng/ml). For those patients with two TPSA levels measured, approximately one-half (51.0%) had normal levels at first test, and 21.5% had levels between 4.0-10.0 ng/ml. Of the 138 patients with three or more TPSA levels measured, 43.5% had normal values when first tested. This proportion was halved (21.7%) for the patients with TPSA levels 4.0-10.0 ng/ml. The patient >100 years old had a TPSA level of 885.2 ng/ml and levels > 400 ng/ml were observed in patients ≥ 54 years old. The highest TPSA level processed (14,545.0 ng/ml) in a 76-year-old patient (Table 3).

DISCUSSION

Over the past two decades there is increased incidence of prostate adenocarcinoma in many countries including Jamaica partly due to enhanced detection via the use of PSA testing11,14. Many persons including men in Jamaica access healthcare mostly through public sector clinics. However, it is found that prostate cancer screening among chronic disease patients is suboptimal15. In addition to screening for prostate cancer in the parishes of Kingston and St. Andrew, the Jamaica Cancer Society has established screening clinics for prostate cancer in rural parishes such as St. Elizabeth, Manchester and St. Ann amongst others. The Jamaica Cancer Society seeks to increase public awareness about prostate cancer and screening among high-risk men(Morrison et al., 2016)[17]. In this study the majority (approximately seven tenths) of the PSA requests were received from clinics (such as the Genitourinary Clinic) and outpatient departments at the University Hospital of the West Indies. The screening of male patients who attend these clinics provides a potential opportunity for the implementation of prostate cancer prevention programs. It is reported that approximately fifty percentages of males in Jamaica residing in Kingston and St. Andrew present to their general practitioners for medical care possesses symptoms of metastatic disease or locally advanced prostate cancer rather than on the basis of screening using the PSA test[10].

Despite its limitations and shortcomings, PSA still remains a valuable tool in diagnosis, monitoring the treatment as well as follow up of male patients with prostate-related diseases. This study showed a slight increase in the number of PSA requests over the two-year period. Collaboration between The Jamaica Cancer Society and the Jamaica Urological Society provides early detection programmes for early detection of prostate cancer[9]. PSA was introduced into Jamaica in 1989 and is reported to contribute to the already rising prostate cancer incidence curve reported by Gibson and colleagues in the period 1977 – 1992[18]. In Jamaica, men 40 years and older with at least a 10-15 year life expectancy are encouraged to have an annual PSA blood test and a digital rectal examination (DRE)[16]. It is recommended that men who presented with abnormal PSAs and DREs have confirmatory transrectal ultrasound (TRUS) guided biopsies and those diagnosed with prostate cancer referred for treatment at a urology clinic at one of the public General Hospitals16. In this study, request by general medical practitioners and consultants for TPSA blood test was primarily in the 61-70 years age-group followed by the 71-80 years age-group. Approximately one-tenth of the request for TPSA was in the 41-50 year age-group. It should be noted that request for TPSA blood test were made for a minority of male patients in the 20-30 year and 31-40 year age-groups. Thus the results are in keeping with the general trends and recommendation concerning the use of TPSA blood test in screening programs targeting men 40 years and older in Jamaica[9].

Men of African and Caribbean descent are well known to be of high risk for developing prostate cancer(Nowlader et al., 2010)[19], and incidence rates in several Caribbean islands with mostly black population are notable high(Hennis et al., 2011)[20]. The increase prostate cancer risk among men of African and Caribbean descent appears to be genetically related and there is evidence that factors such as obesity, inflammation and diet may affect these genes and alter risk(Whittemore et al. 1995; Amling 2004)[21,22]. Strategies for PSA screening among men in different countries vary according to a number of variables such as the age at which PSA testing begins and ceases, the gap between tests and the PSA threshold that warrants further investigation such as biopsy of the prostate[23,24](Bell et al., 2014 and Nair-Shalliker et al., 2018). In this study most of the requests for PSA tests were in men over 50 years, but testing of younger men was not uncommon. It is noted that almost 30% of men aged 61 - 70 years had their first PSA test request while the majority of men with two and three PSA test requests were also in this age group. In a study by Fowler and colleagues examining prostate cancer screening and beliefs about treatment efficacy among urologists and primary care physicians, the majority of the latter reported requested PSA tests during routine examination of men over 80 years of age and older and refer men with abnormal values for biopsy24. The increased PSA requests by physicians in this age group could be due to monitoring of men with prostate cancer and among those due to screening there may be increased demand for the PSA tests due to increased awareness and being worried about the disease especially among high-risked individuals25. If these older men are symptomatic then the PSA test may be diagnostic and is conducted with the intention of palliative care rather than aggressive treatment[27](McGing, 1998).

The early diagnosis of prostate adenocarcinoma and BPH is usually achieved by the combined use of serum PSA determination and digital rectal examination in the first phase and confirmation of the former in the second phase by prostate imaging, transrectal ultrasound of prostate gland and ultrasound guided biopsy of prostate in selected cases. In this study the majority of the patients with only one TPA test performed had normal levels while one-eight had values between 4.0 – 10 ng/ml. PSA values falling within the gray zone i.e. between 4- 10

ng/ml present difficulty in differentiating between BPH and early prostate adenocarcinoma[28](Perdona et al., 2011). There are a number of studies conducted in different populations that have reported varied percentage of patients with serum total PSA values in the gray zone area with values ranging from 18-46 %[29-32](Lange et al., 1989; Hudson et al., 1989; Monda et al., 1994; Martin et al., 1990). Mild elevation of PSA were observed in men with BPH and grossly elevated serum levels in untreated adenocarcinoma prostate cancer patients with the highest TPSA level of 14,545 ng/ml observed in a 76-years old man with advanced prostate adenocarcinoma. Stamey et al. 1989 reported a mean TPSA of 563 ng/ml in 35 men with untreated prostate adenocarcinoma.[33]

The main limitation of the study is that it is retrospective in nature and information regarding the reason for PSA test requests is not given. However it is noted that the majority of PSA test request is for the suspicion of prostate cancer or benign prostatic hyperplasia, as well as monitoring patients' diagnoses with prostate cancer.

In conclusion, the study provides an examination of first and total number of PSA test requests, and investigation of the pattern of PSA testing by age and source of request such as Departments and clinics at a tertiary hospital in Jamaica. The results support the implementation of prostate cancer prevention programs in all parishes in Jamaica.

Figure 1: The distribution of TPSA requests per the source of the requisition between1 January 2015 and 31 December 2016.

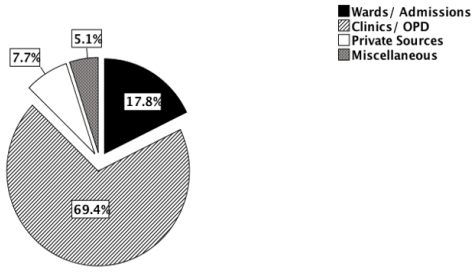

Figure 2: The distribution of age in relation to TPSA requests received.

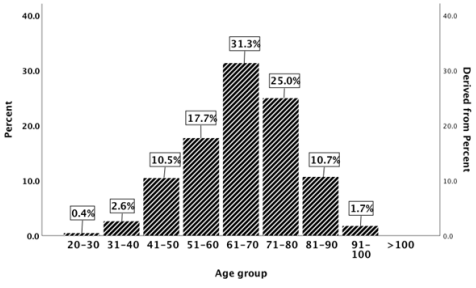

Table 1: TPSA levels of requests processed in the Chemical Pathology laboratory between 2015 and 2016.

PSA result (ng/ml) (n=2550, missing=0)	Frequency	Percent (%)
0.0-3.9	1555	61.0
4.0-10.0	436	17.1
10.1-20.0	212	8.3
20.1-50.0	128	5.0
50.1-100.0	53	2.1
100.1-400.0	74	2.9
>400	92	3.6
Total	2550	100

Table 2: Distribution of men having single or repeated test requests by age at the first test.

	Number of tests		
	1	2	≥3
Age group at first test	Proportion (%)		
20-30	0.6	0.5	0
31-40	3.6	1.0	1.4
41-50	15.3	9.0	2.2
51-60	22.4	14.5	8.7
61-70	27.5	40.0	37.7
71-80	18.7	24.5	36.2
81-90	10.2	9.5	11.6
91-100	1.6	1.0	2.2
>100	0.1	0	0

Table 3: Proportion of men having single or repeated test requests by TPSA levels at the first test.

	Number of Tests		
TPSA results at first test (ng/ml)	1	2	≥3
	Proportion (%)		
<4.0	67.2	51.0	43.5
4.0-10.0	15.3	21.5	21.7
10.0-20.0	7.5	6.0	9.4
20.1-50.0	4.5	11.0	8.0
50.1-100.0	1.8	1.0	4.3
100.1-400.0	1.9	4.5	5.8
>400.0	1.8	5.0	7.2

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