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The epidemiology, histopathology and screening prospective of prostate cancer in Trinidad

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SUMMARY

Background: Prostate cancer is the most prevalent carcinoma found in males as well as the most prevalent carcinoma found in the overall male population of Trinidad. According to the Pan American Health Organization, Trinidad has one of the highest incidence and mortality rates of Prostate Cancer in the region. Factors such as age, ethnicity, diet, family and drug history all play a role in Prostate Cancer epidemiology and thus was assessed in this study. Objectives: The purpose of this study is to investigate the usefulness of prostate-specific antigen (PSA) values and digital rectal examination (DRE) findings/screening findings, to determine the histopathologic features of prostate cancer and correlate with the screening findings, and evaluate the role of positive family history, dietary patterns and drug history in proven cases of prostate cancer. Method: Clinical records from the Eric Williams Medical Sciences Complex were used to identify prospective candidates for the study. Data collection sheets were then used to collect clinically based information (PSA values and DRE findings) as well as the histopathologic results from reports requested. Additionally, a questionnaire was asked via telephone to each suitable candidate in order to obtain their respective family history, dietary patterns and drug history. The data was then analyzed and appropriate correlations were made. Results: Of 130 prostate cancer patients, the majority (42.86%) were of African ethnicity. The most common age range at which patients were first diagnosed was found to be between ages 70-75, which accounted for 31.43% of the 130 patients. The median age range for diagnosis was 65-70 years old. The most common symptom experienced by the patients was a pain in the back/hip/ribs (46.7%). Most of the patients were found to have PSA values in the range 10-20 ng/ml range (22.9% of the patients) and>100 ng/ml range in 20% of the patients. 25.74% of the sample had a family history of prostate cancer, with 20.02% being first degree relatives and 5.72% being second-degree relatives. 8.58% and 5.72% of the sample with first degree and second-degree relatives respectively were diagnosed before the aforementioned median diagnostic age indicating that men with a family history of prostate cancer are more prone to developing the disease at an earlier age. Histopathologic analysis showed all of the prostatic carcinomas were of the acinar type of adenocarcinoma with 42.30% been moderately differentiated type (Gleason score of 7). Conclusion: The results suggest that attention should be given to educating men especially those of African ethnicity, about prostate cancer so as to raise awareness. Steps should be taken to reduce the symptom of back/hip/rib pain as this is the most common occurring symptom within this population. Males over the age of 40 years with first degree relatives diagnosed with prostate cancer should undergo regular (yearly) screening examinations and be educated about their risk factors. More research into the effect of diet and the increased risk of developing prostate cancer is warranted especially in Trinidad and Tobago where the local cuisine is of unique varieties.

Key words: prostate cancer, histopathologic, adenocarcinoma, intraepitleial neoplasia

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INTRODUCTION

In 2018, Prostate Carcinoma (PCa) was the second most common cancer in males. The increase in the incidence rates of PCa is attributed mainly because of the screening for Prostate-Specific Antigen (PSA) in PCa patients who are clinically unrecognized [1]. Geographically, the highest incidence rates are in North America and Western Europe, with Asia and North Africa showing the lowest incidence rates [2, 3]. Since 1990, the incidence rates in the Caribbean men have increased by 40% mainly due to the African- Americans and men exhibiting germline mutations [4, 5]. In Trinidad and Tobago (T and T), PCa is the most commonly diagnosed male malignancy [6].

METHODOLOGY

This project is a prospective study of PCa in which PSA, DRE and histopathologic findings were correlated. The sample consisted of 130 male patients who attended the PCa clinics over the period of January 2014 to January 2017 (4 years). These patients were identified as potential subjects through an examination of clinical records.

To determine the study participants, certain criteria were outlined. After conducting initial research it was found that PCa is present only in men aged 45 and over, thus the age range of 45-80 years was used. Due to the nature of this study, the inclusion criteria also comprise a proven case of PCa on histopathology and documented serum PSA values and DRE findings.

The exclusion criteria for this study consisted of men who underwent screening examination but who have no documented histopathology report and patients with missing PSA or DRE findings.

A questionnaire centered on factors contributing to PCa development such as family, dietary and drug history was formulated and employed. Data collection sheets were also

devised to facilitate accurate and efficient collection of data when perusing case files and laboratory reports. Analysis of the results obtained was done in order to achieve the objectives stated above using the Statistical Package for the Social Sciences (SPSS) software.

RESULT

Age first diagnosed with prostate cancer (years)

The greatest number of participants diagnosed with PCa were within the age of 70-75 years (31.43%) followed by the age group of 65-70 years (20.00), 2.86% were diagnosed before the age of 55 years constituting an early diagnosis. The average age of diagnosis was 65-70 years old (Figure 1).

The ethnicity of patients with prostate cancer

The highest percentage (42.86%) of patients with PCa were Africans, whilst the total percentage of patients of African descent is 60.00%. This large percentage of the sample population indicates that genetic susceptibility to developing prostate cancer exists in men of African descent. Conversely, it was found that the lowest percentage (5.71%) of patients diagnosed with PCa were Caucasians (Figure 2).

Family history

From tabulating the data, the results show that 25.74% of the sample has a family history of PCa, with 20.02% being first degree relatives and 5.72% being second-degree relatives (Table 1). 8.58% and 5.72% of the sample with first degree and second-degree relatives respectively were diagnosed before the aforementioned average diagnostic age (65-70 years) indicating that men with a family history of PCa are more prone to developing the disease at an earlier age (Figure 3).

Drug history

From the results obtained, it can be deduced that statin use for 3 years or more has the potential to reduce the risk of developing an advanced stage of PCa as the Gleason score does not rise above 7 and the sclerotic tissue is confined to the prostate (Table 2). The same is true for the use of NSAIDs (Figures 4 and 5).

Diet and gleason score

On examination of the raw data, there were 20 patients (5.4% of the total sample) who were on the exact diet of fruits and vegetables once/day or more, together with fats and oils and food from animals twice a week or less. These patients had Gleason scores of 6 and 7, and both patients had cancers which were confined to the prostate gland.

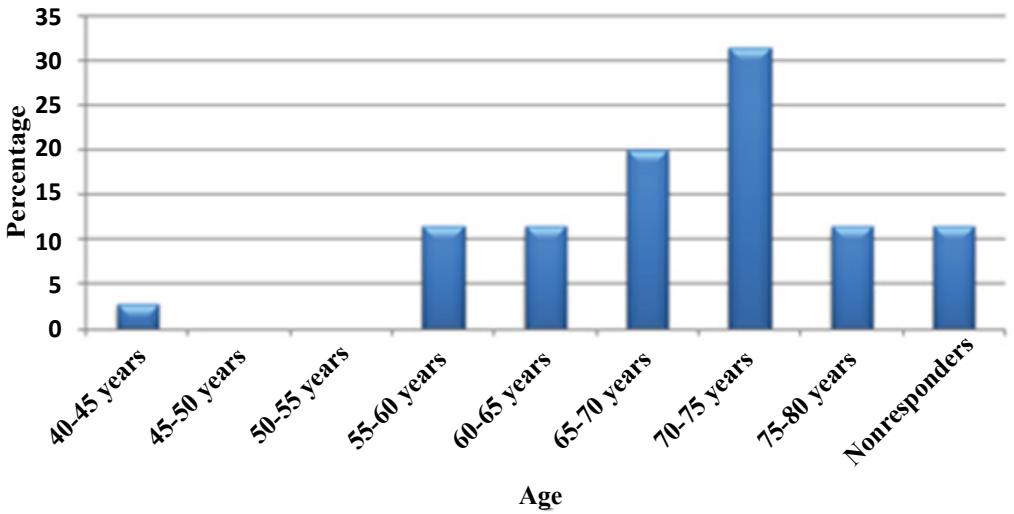

Fig. 1. Bar Chart showing the percentage of patients diagnosed in each age group with prostate cancer

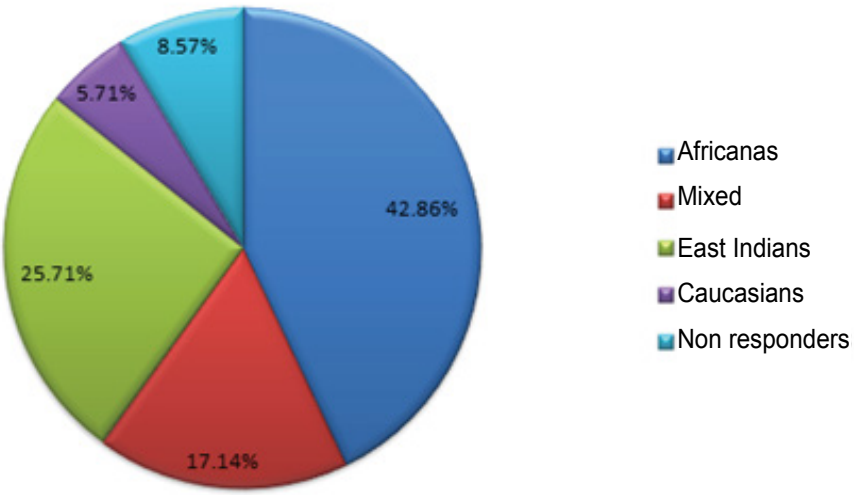

Fig. 2. Pie Chart showing the percentage of each ethnicity represented in the study

Tab. 1. Showing the patient's familial relation of prostate cancer and their age of diagnosis

Age of Diagnosis (years)	Family History (%)		
	Father	Brother	Uncle
40-45	2.86	0	0
45-50	0	0	0
50-55	0	0	0
55-60	2.86	0	2.86
60-65	2.86	0	2.86
65-70	0	0	0
70-75	2.86	5.72	0
75-80	0	2.86	0
Total	11.44	8.58	5.72

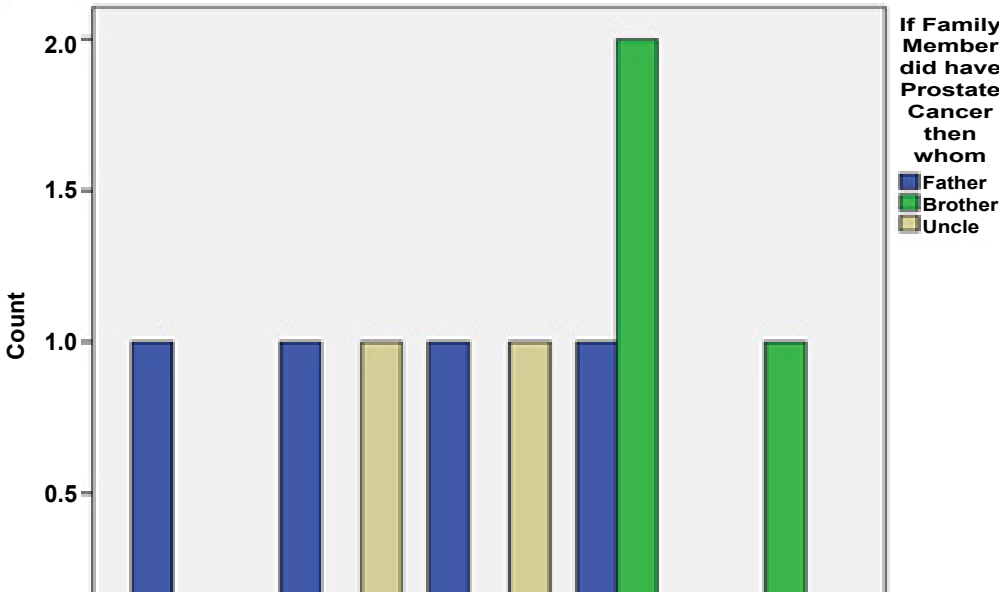

Fig. 3. Bar Graph showing the age of diagnosis of prostate cancer of the patients in the study and their corresponding family history

Tab. 2. Showing the frequency and duration of statin and NSAID use with its influence on the carcinoma

Case	Drug used	Frequency of use	Duration of use	Gleason Score	Extent of sclerosis
1	Statins	Once-daily	3 years or more	7	Confined to prostate
2	Statins	Once-daily	3 years or more	7	Confined to prostate
3	NSAIDs	Once-daily	3 years or more	7	Confined to prostate
4	NSAIDs	Once-daily	3 years or more	7	Confined to prostate
5	NSAIDs	Once-daily	3 years or more	7	Confined to prostate
6	NSAIDs	Once-daily	3 years or more	9	Confined to prostate
7	NSAIDs	Once-daily	6 months	-	Seminal vesicles
8	None	-	-	7	Beyond capsule

On examination of the raw data, there were 42 (11.4% of the total sample) patients who were on the exact diet of fruits and vegetables twice a week or less together with eating fats and oils and food from animals once/day or more. These patients had Gleason scores of 7,6,6 and 9 and all had cancers which were confined to the prostate.

On comparing these results, it was seen that there was a greater frequency (11.4%) of patients on high meats and low fruits and vegetable diet with prostate cancer as opposed to high fruits and vegetable and low fats and food from the animal diet (5.7%). The data collected did not allow for the assessment of a high-fat diet as it was non-existent in the sample population. However, the assessment of high meat and dairy, low fruit and vegetable diet was done but a clear statistical correlation could not be drawn.

The usefulness of serum PSA and DRE values in this study

The most frequent PSA values occurred in the range 10-20 ng/ml (22.9%), while the least frequent PSA values occurred within the ranges of 1-4 ng/ml and 30-40 ng/ml, both accounting for 5.7% (Tables 3 and 4).

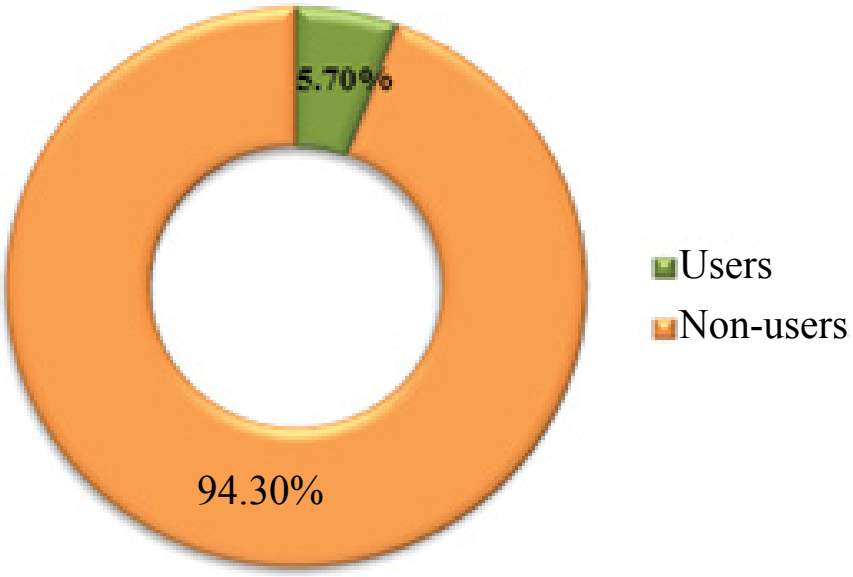

Fig. 4. Showing the percentage of Statin users and non-users.

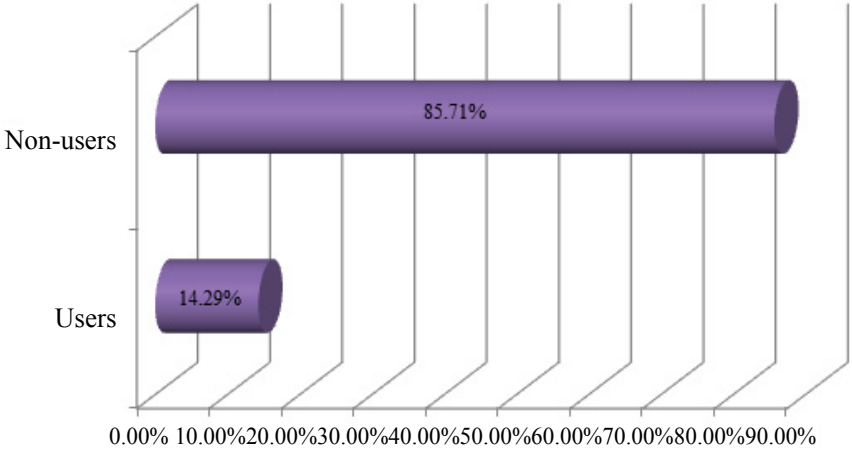

Fig. 5. Showing the percentage of NSAID users and non-users

Tab. 3. Showing the number of patients having serum values within each PSA range

PSA ng/ml	Frequency	%	Valid%	Cumulative%
01-Apr	8	5.7	6.1	6.1
04-Oct	12	8.6	9.1	15.2
Oct-20	31	22.9	24.2	39.4
20-30	12	8.6	9.1	48.5
30-40	8	5.7	6.1	54.5
40-50	12	8.6	9.1	63.6
50-100	20	14.3	15.2	78.8
>100	27	20	21.2	100
Total	130			

Tab. 4. Showing the prostate examination results for the sample population

Prostate examination Results					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Abnormal	130	100	100	100
	Normal	0	0	0	0

PROSTATE EXAMINATION (DIGITAL RECTAL EXAMINATION-DRE) RESULTS

From the study, 100% of the study population had abnormal Prostate Exam Results, while 0% had normal results.

Histopathologic analysis

During the 5-year period, 130 patient's pathologic data with histopathology report confirming PCa were identified and analysis was done. 42.3% of these cases were of Gleason grade 7, 28.4% were of Gleason Grade ≤ 6 and 29. 2% were of Gleason grade 8-10. Among 55 tumors with a Gleason score

Tab. 5. Histopathologic analysis based on Gleason pattern and score in relation to the ethnicity of the patients diagnosed with prostatic carcinoma

Gleason score	African	Mixed	East-Indian	Caucasians	Non-Responders	Total
≤ 6	9 (16.7)	8 (36.3)	9 (27.2)	5 (71.4)	6 (50)	37 (28.4)
7	28 (50)	10 (45.4)	13 (39.3)	1 (14.2)	3 (25)	55 (42.3)
08-Oct	19 (33.9)	4 (18.8)	11 (33.3)	1 (14.2)	3 (25)	38 (29.2)
Total	56 (42.8)	22 (17.1)	33 (25.7)	7 (5.7)	12 (8.5)	130

of 7, 36 tumors (65.4%) were assigned a score of 3+4, while 19 (34.5%) were assigned a score of 4+3 (Table 5).

DISCUSSION

The highest incidence of PCa in our study was in the age group of 70-75 years (31.43%). This was similar to the PCa incidence rates reported to the T and T Cancer Registry 1995-2009. In comparison with other countries, T and T fall in the same category as Netherlands, UK, Scotland, England, Denmark, Norway, Sweden, and Costa Rica which showed similar peaks of PCa in the age group of 70-75 years [7].

Based on 2012 GLOBOCAN data, the highest percentage of PCa was identified in Afro-Caribbean and Sub-Saharan African men [8]. The data in our study also indicated the same. Epidemiological data indicates the higher rates of incidence and poor prognosis of PCa among African descent men. This is mainly attributed to multifactorial reasons such as genetics, diet, high poverty, higher infectious diseases, lack of community-based screenings and health promotion programs [9, 10].

In our study, 25.74% of patients had a family history of PCa with 20.02% been first degree relatives. In the Health Professionals Follow-Up Study (HPFS) subcohort study, the results showed a strong association between family history and risk of PCa. PCa in father's and brothers showed a significant association with a higher risk of PCa in the family [11, 12]. In a study done in Mayo the clinic, 32.3% of men reported a family history of PCA [13]. Overexpression of COX-2 in human PCa tissue has been reported in the literature [14]. This attributes to the fact that prostate tissue with the presence of inflammation along with inflammatory zones of Prostatic Intraepithelial Neoplasia (PIN) was more at risk to develop PCa than those without inflammation [15, 16]. When NSAIDs are used at higher doses for their anti-inflammatory effects once daily for over 6 months to 3 years showed chemopreventive action against cancer [17]. The Epidemiological study of prostate cancer (EPICAP) study data has well established this fact.

Cholesterol-lowering drugs like statin cause dysregulation of the mevalonate pathway and inhibition of oncogenic proteins. We found that the use of statin potentially reduces the risk of developing advanced stage of PCa and confines sclerotic tissue in the prostate. This finding has been previously reported in the literature [18, 19].

Patients with a diet consisting of fruits and vegetables had a lower risk of Gleason score advancement in comparison to patients with animal diet. This was mainly attributed to the anti-inflammatory and metabolic state, the fruits and vegetables provide which is less conducive for tumor progression [20].

PCa, when detected at an early stage, enables intervenable curative treatment approach, thereby reducing the disease-specific mortality. Serum PSA is a valuable screening tool for this purpose [21]. PSA screening allows PCa detection at any stage, the detection is higher in early stages (I and II) of PCa [22]. Epidemiology showed that every year in the USA, 220,000 new cases of PCa were diagnosed by PSA screening and 30,000 deaths notified [23]. PSA screening is usually followed by biopsy and treatment intervention. Surprisingly two studies done in the US and Canada showed that higher rates of PCa diagnosis had PCa mortality rates that were not significantly lower than those in areas with less intense testing and treatment [24]. However, in the USA, the vast majority of newly diagnosed PCa cases were detected by PSA screening rather than clinical examination proving PSA still remains the most valuable available PCa screening tool [23].

Any abnormal DRE requires prostate biopsy even if the PSA levels are normal [25]. PCa detection rate varies from 3-41% when the PSA levels are normal with an abnormal DRE as reported in the literature [26, 27]. This rate further rises when PSA levels are higher and as close to 90% as seen in our study [28].

Histologic diagnosis of PCa on needle biopsies has remained the gold standard diagnostic approach. In routine, a pathology report of PCa includes histologic type, the grade of differentiation based on Gleason grading system, the number of cores involved by malignancy, qualitative percentage of tumor volume per biopsy and few also include perineural invasion [29, 30].

Increasing age of more than 70 years has been known to have an increased incidence of moderate to poorly differentiated PCa (GS 7-10) [31]. The histologic type of acinar adenocarcinoma remains the most common histologic variant compared to other rarer types such as ductal cancer [32, 33]. The study done previously in T and T and Jamaica showed that moderately differentiated PCa were most common as noted in our study [33].

CONCLUSION

Limitations encountered in our study were, firstly, this study included only PCa cases diagnosed in a single regional health authority hospital, hence restricting the results only to a particular region in the country. A further wide study inclusive of correlation of our study results with molecular genetics and the treatment-related prognostic outcome remains to be conducted.

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