ORIGINAL RESEARCH

Prostate Cancer: Burden and Correlation with Prostate Specific Antigen Among Screened African Men in Tanzania

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Background: Serum prostate-specific antigen (PSA) is a widely used maker for prostate cancer (PCa) screening. However, its correlation with PCa varies, partly due to ethnic differences. This study investigated the correlation between PSA and PCa diagnosis as well as the burden of the disease in the Tanzanian community.

Methods: This community-based PCa screening took place in Northern Tanzania from May 2022 to September 2022, where men aged ≥40 years were involved. Each participant provided 5 milliliters of venous blood for PSA determination. Those with PSA levels >4 ng/mL underwent prostate biopsy. Two pathologists independently evaluated the biopsies. The correlation between PSA and biopsy results was assessed using STATA version 17.0.

Results: The study included 6164 African men with a mean age of 60±11 years. Of these, 912 (14.8%) had PSA >4 ng/mL, and hence 581 (63.7%) underwent prostate biopsy. A total of 179 men (30.8%) were histologically diagnosed with prostatic adenocarcinoma, whereby 46 (25.7%) had Gleason scores 8–9. Among participants with PSA >20 ng/mL, over 2/3 (64.7%) had PCa, rising to nearly 100% at PSA >100 ng/mL. A positive correlation between PSA levels and PCa/aggressive disease was observed. PSA sensitivity decreased with rising levels, hitting 78.2% at >10ng/mL and 24.6% at >100ng/mL, while specificity increased, peaking at 99.8% for >100ng/mL from 73.9% at >10ng/mL. The optimal PSA cut point was >10ng/mL. PSA demonstrated an 84% overall ability to predict PCa and a 71% ability to predict aggressive disease.

Conclusion: This study found a notable presence of intermediate-high grade PCa within the community, suggesting the need for regular screening and management. Moreover, PSA demonstrated clinically useful ability in predicting PCa among African men aged 40 years and older.

Keywords: correlation, PSA and prostate cancer

Introduction

Prostate cancer (PCa) ranks as the second most common cancer among men around the globe.[1] In developing countries, like African countries, the burden is projected to surge by 50% in the near future.[1] African ethnicity is one of the important risk factors for PCa where the disease tends to present at an earlier age with more aggressive features as compared to other racial groups.[2,3] Other common risk factors include increased age and family history of PCa, diet rich in fat, red meat or dairy products.[4] Furthermore, there is strong association between breast cancer and Pca whereby men with family history of breast cancer, especially carriers of the breast cancer gene 2 mutation, have heightened risk of developing PCa.[4,5]

PCa screening among at-risk men plays an important role in early diagnosis, treatment, and survival.[6,7] PSA is the most widely used screening test with a critical cutoff value of 4 ng/mL, which determines the need for a prostate

biopsy.[8,9] However, PSA has poor specificity for cancer detection, where at the level of 4–10 ng/mL, (gray zone), the cancer detection rates range from 4.7% to 22%[10–12] which increases to 98.5% when PSA exceeds 100 ng/mL.[11] Some studies have reported a weak or no correlation between PSA and PCa diagnosis as well as Gleason score/aggressiveness.[8,13] These differences could partly be due to racial disparities, with African Americans having a higher normal PSA level compared to Caucasians and others.[14,15] This results in an unnecessary biopsy, which is associated with both psychological and physical complications.[16–19]

Most of the studies that looked at the performance of PSA in predicting Pca as well as disease aggressiveness were done among non-native Africans and some included patients, hence limiting their generalizability. Despite its limitations, PSA remains the most commonly used primary marker for PCa screening globally,[8,9] including Tanzania, where the disease is prevalent and often diagnosed late.[20–22] The study aimed at assessing the correlation between PSA and PCa among Tanzanian male community dwellers, with the findings expected to provide valuable insights and recommendations for an appropriate cutoff point for prostate biopsies among African men.

Materials and Methods

This community-based screening took place at the time of a PCa survey, which aimed at assessing community knowledge and perceived barriers for PCa screening in Northern Tanzania. The detailed methodology of the survey that was conducted in Northern Tanzania from May to September 2022 is available elsewhere.[23]

The current study, which is a sub-study of the parent study,[23] focused on the PCa burden and its correlation with PSA. It involved men aged ≥ 40 years,[24,25] who resided in Kilimanjaro, Arusha, Manyara, or Tanga regions. All eligible men who resided in the six districts of the Kilimanjaro regions were included in this study, while for the other regions, only men who resided in the three randomly selected districts from each regions were studied. The reason for studying all the districts in the Kilimanjaro region was due to the fact that according to our local record, the majority (>80%) of PCa cases are coming from this region.

Men who had previous history of being diagnosed with PCa, on five alpha reductase inhibitors, or with lower urinary tract symptoms were all excluded. Five milliliters of venous blood were collected in non-EDTA tubes from each eligible participant for PSA determination. The blood samples from Kilimanjaro region were transported to the Kilimanjaro Clinical Research Institute's (KCRI) biotechnology laboratory in biohazard containers at room temperature within 7 hours of collection. Samples collected from Tanga, Arusha, and Manyara were stored at 2–8 °C before shipment to the KCRI biotechnology laboratory.

Investigators communicated the PSA results to participants via phone calls within 7–8 working days after sample collection. Individuals with a PSA of >4 ng/mL were asked to return to the local health facility (the sample collection site) for result discussion and counseling for prostate biopsy.[25,26] Finger guided prostate biopsy procedures were conducted as outpatient, and a total of 12 core biopsies were obtained from each participant. Tissue samples were preserved in containers with 10% buffered formalin and transported to the KCMC pathology laboratory, where hematoxylin and eosin glass slides were prepared.

Two independent pathologists read the biopsy slides (in a blind fashion), and in cases of inconsistencies between their reports, they reviewed the slides and reached a consensus final diagnosis. Participants with a histological diagnosis of PCa were referred to the KCMC cancer care center for management. Negative biopsy results (benign prostate) were communicated to participants via phone calls.

Data Analysis

Statistical analysis was done with STATA version 17.0. The analysis of the diagnostic performance of PSA included participants who had biopsy results only. Continuous variables were summarized using the mean and their standard deviation, while categorical variables were summarized using frequency and percentage.

The PSA levels were categorized as >4-10, >10-20, >20-50, 50–100, and >100ng/mL, to examine how well PSA in various categories predict presence of PCa. The sensitivity, specificity, positive predictive value, and negative predictive value were computed.

To determine the precision of PSA in predicting PCa as well as aggressive disease, sensitivity and (1-specificity) at different PSA cutoff values were plotted on receiver operating characteristic (ROC) curves.

Results
Characteristics of Study Participants

A total of 6205 men attended the PCa screening sites. Of these, 41 (0.7%) were not eligible because they were not ≥ 40 years old, had previously been diagnosed with PCa, or had lower urinary tract symptoms. Of the 6164 (99.3%) men who were screened, their mean age was 60±11 years, with the majority being from the Kilimanjaro region (3206 (52.0%)). Sixty-five percent of the participants (379 (65.2%)) had primary education, and 268 (46.1%) were peasants (Table 1).

Table 1 Characteristics of Screened Men (N=6164)

Variable	n	%
Age (Years)		
40–50	1267	20.6
51–60	1930	31.3
61–70	1880	30.5
71–80	846	13.7
81–90	214	3.5
91+	27	0.4
Mean (±SD)	60(±11)	
Residence		
Kilimanjaro	3206	52.0
Arusha	1152	18.7
Tanga	979	15.9
Manyara	827	13.4
Marital status (n=6161)		
Single/never married	194	3.2
Married	5540	89.9
Divorced/Separated	180	2.9
Widowed	247	4.0
Education level (n=6160)		
None formal	154	2.5
Primary	3898	63.3
Secondary	1118	18.2
University/College	990	16.0
Occupation (n=6162)		
None	231	3.8
Business	883	14.3
Employed	729	11.8
Peasant	2652	43.0
Retired	713	11.6
Casual work	954	15.5
Health insurance (n=6160)		
Yes	2233	36.3
No	3927	63.7
Known HTN (n=6161)		
No	4763	77.3
Yes	1398	22.7
Known DM (n=6161)		
No	5601	90.9
Yes	560	9.1

Prevalence of PCa Among Men Aged ≥40 Years in Northern Zone

Of the 6164 participants who were screened for PCa, 912 (14.8%) were invited for prostate biopsy due to an elevated PSA of >4 ng/mL. Of these, 581 (63.7%) successfully underwent prostate biopsy, where PCa was detected in 179/581 (30.8%) of biopsy with an overall prevalence of 179/6164 (2.9%). All PCa cases were adenocarcinoma-type (Figure 1).

Characteristics of Participants with PCa Aged ≥40 Years

The proportion of PCa increased with the increase in age of the study participants, with the majority being between the ages of 71–80 years. The majority of PCa cases had PSA >20 ng/mL with levels between 4–10 ng/mL accounting for 39 (21.8%) of cases. Further analysis showed high grade/aggressive disease (Gleason scores 8 and 9) to account for 46 (25.7%) of cases (Table 2).
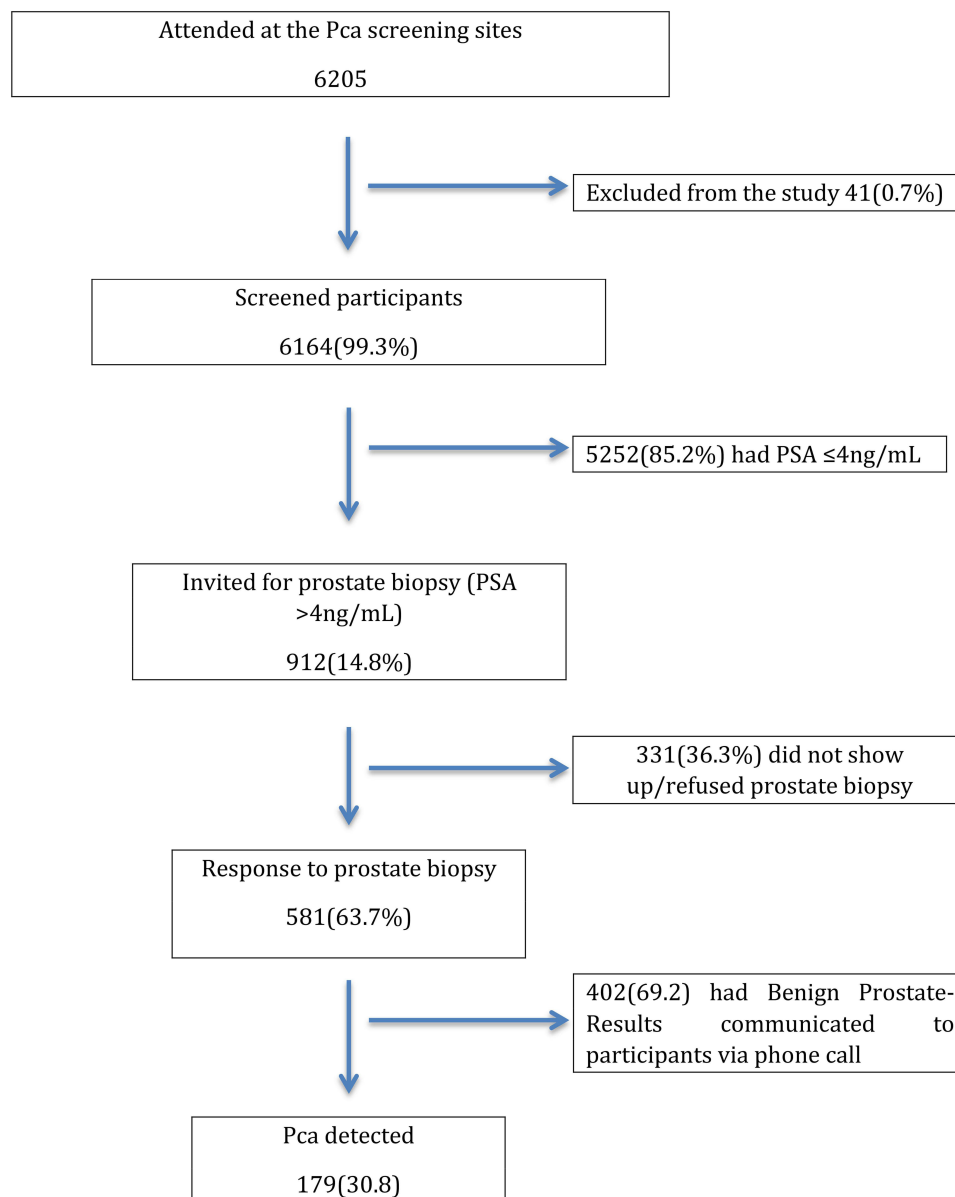

Figure I Prevalence of PCa among men aged ≥40 years (N=6164).

Table 2 Characteristics of PCa Among Screened Men Aged ≥40 Years (N=179)

Variable	n	%
Age (Years)		
40–50	2	1.1
51–60	17	9.5
61–70	62	34.6
71–80	75	41.9
81–90	19	10.6
91+	4	2.2
Mean age (±SD)	71.5(±9.0)	
Residence		
Kilimanjaro	103	57.5
Arusha	20	11.2
Tanga	40	22.3
Manyara	16	8.9
PSA Categories (ng/mL)		
>4_10	39	21.8
>10_20	34	19
>20_50	44	24.6
>50_100	18	10.1
>100	44	24.6
Mean (SD)	94(±13.45)	
Gleason score		
≤ 6	49	27.4
7	84	46.9
8–9	46	26.4

Diagnostic Correlation Between Serum PSA, PCa and Aggressive Disease

There was a positive correlation between PSA and PCa diagnosis as well as a high Gleason score (aggressive disease), with a high PSA having a higher PCa detection rate and higher Gleason score. At a PSA of > 20 ng/mL, the PCa detection rate was >60%, which increased to almost 100% at a level of >100 ng/mL (Figure 2).
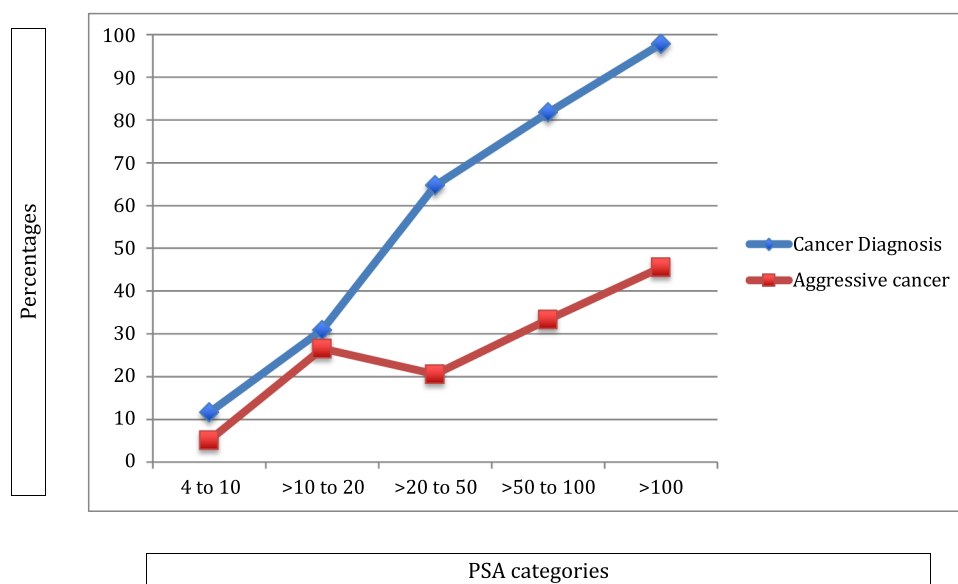
Figure 2 Correlation of PSA and PCa diagnosis and high Gleason score.

Performance of Each PSA Cutoff Point in Detection of PCa and Aggressive Disease

For PCa detection, the sensitivity of PSA decreased with an increase in PSA level; the highest sensitivity of 78.2% was achieved at a PSA of >10 ng/mL and the lowest (24.6%) at a PSA of >100 ng/mL. For the specificity, it increased with an increase in PSA level and reached a maximum of 99.8% at the cutoff point of >100 ng/mL from 73.9% for PSA of >10 ng/mL. The optimal cutoff point of PSA was >10 ng/mL. The positive predictive (PPV) values for PSA of >10ng/mL and >20 ng/mL in diagnosis PCa were 57.1 and 78.5, respectively. The positive likelihood ratio (LHR+) was >8 for PSA of >20 ng/mL (Table 3).

With regard to disease aggressiveness, at the PSA of >10ng/mL the specificity of PSA was 62.4% which increased to 95.3% for cutoff point of >100ng/mL. The PPV increased with increase of PSA and reached 44.4% at the cutoff point of >100ng/mL. At the PSA cutoff point of >50ng/mL, the LHR+ was >7.4 (Table 4).

Overall Ability of PSA in Predicting PCa and Aggressive Disease

The overall ability of PSA to predict PCa and aggressive disease (Gleason score 8 and 9) was 0.84 (95% CI; 0.80–0.88) and 0.71 (95% CI; 0.62–0.80), respectively (Figures 3 and 4).

Discussion

This community-based PCa screening has found a high proportion of PCa and confirms PSA to be a clinically useful marker for screening with an optimal cut point of >10 ng/mL. The overall PCa detection rate among biopsied men was lower than the prevalence of 40% and 39% from Northern and Northwest zonal referral hospitals in the same country, Tanzania, respectively.[22,27] In contrast, Ogbetere et al in Nigeria reported a much higher prevalence of 65%.[28] These differences may be attributed to the fact that all the other studies were hospital-based, involving symptomatic patients who are more likely to have a higher proportion of PCa compared to community-dwelling men in the current study.

Moreover, only part of eligible participants underwent prostate biopsy, which may have a negative effect on the prevalence of PCa. Despite this limitation, the overall prevalence of PCa in the current study is three times the prevalence of 1.04% reported from a similar community screening among Nigerian men who had a 78% response rate.[12] Tanzanian men are a relatively unscreened population, and therefore, we expected the burden of the disease to be much higher compared to the population practicing routine PCa screening.

The majority of PCa cases were detected among older men, which is consistent with findings from other studies.[10,20,28] The PCa detection rate demonstrated an upward trend with increasing age, solidifying the existing evidence that PCa is primarily affecting elderly men,[29,30] where age serves as an important risk factor.[28]

**Table 3** Diagnostic Value of Each PSA Cutoff Point for PCa (N=581)

PSA (ng/mL)	Sensitivity	Specificity	PPV	NPV	LHR+	LHR-	ROC
>10	78.2(71.4–84.0)	73.9(69.3–78.1)	57.1(50.7–63.4)	88.4(84.5–91.6)	2.9(2.5–3.6)	0.3(0.2–0.4)	0.8(0.7–0.8)
>20	59.2(51.6–66.5)	92.8(89.8–95.1)	78.5(70.6–85.1)	83.6(79.9–86.9)	8.2(5.7–11.9)	0.4(0.4–0.5)	0.8(0.7–0.8)
>50	34.6(27.7–41.1)	98.8(97.1–99.6)	92.5(83.4–97.5)	77.2(73.4–80.8)	27.9(10.4–68.1)	0.7(0.6–0.7)	0.7(0.6–0.7)
>100	24.6(18.5–31.6)	99.8(98.6–100)	97.8(88.2–99.9)	74.8(70.9–78.4)	98.8(13.7–711.6)	0.8(0.7–0.8)	0.6(0.6–0.7)

Table 4 Diagnostic Value of Each PSA Cutoff Point for PCa Aggressiveness (N=581)

PSA Level	Sensitivity	Specificity	PPV	NPV	LHR+	LHR-	ROC
>10	95.7(85.2–99.5)	62.4(58.2–66.5)	18.0(13.4–23.3)	99.4(97.9–99.9)	2.6(2.3–2.9)	0.1(0.0–0.3)	0.8(0.8–0.8)
>20	76.1(61.2–87.4)	81.3(77.7–84.5)	25.9(18.8–34.2)	97.5(95.6–98.8)	4.1(3.2–5.2)	0.3(0.2–0.5)	0.8(0.7–0.9)
>50	56.5(41.10–71.1)	92.3(89.7–94.4)	38.8(27.1–51.5)	96.1(94.1–97.6)	7.4(5.0–10.9)	0.5(0.3–0.7)	0.7(0.7–0.8)
>100	43.5(28.9–58.9)	95.3(93.2–97.0)	44.4(29.6–60.0)	95.1(93.0–96.8)	9.3(5.6–15.4)	0.6(0.5–0.8)	0.7(0.6–0.8)
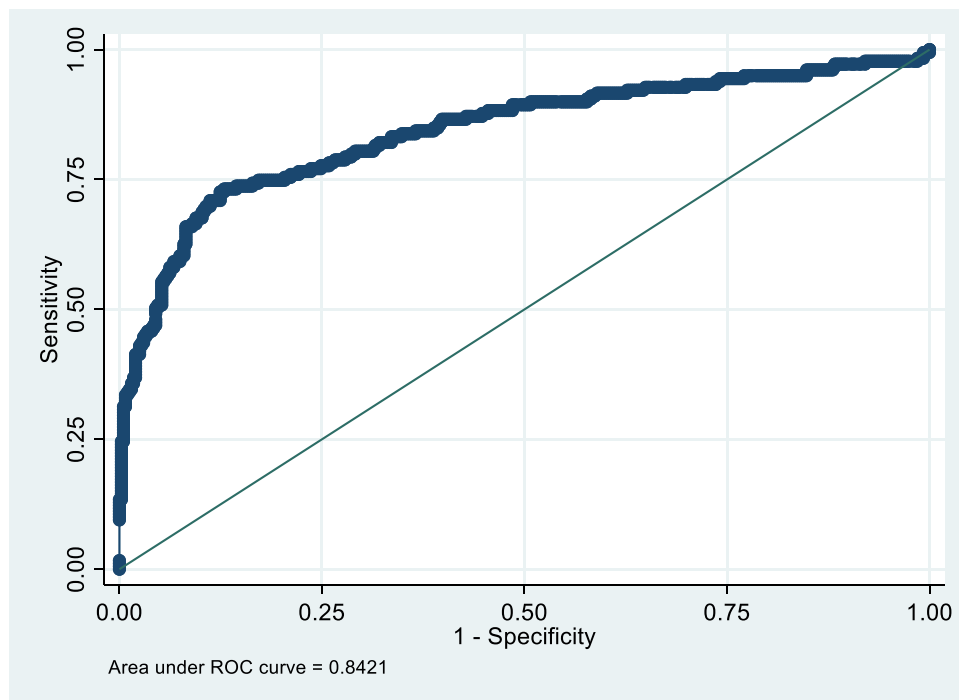
Figure 3 Area under the ROC curve of serum prostate specific antigen in the prediction of prostate cancer (N=581).
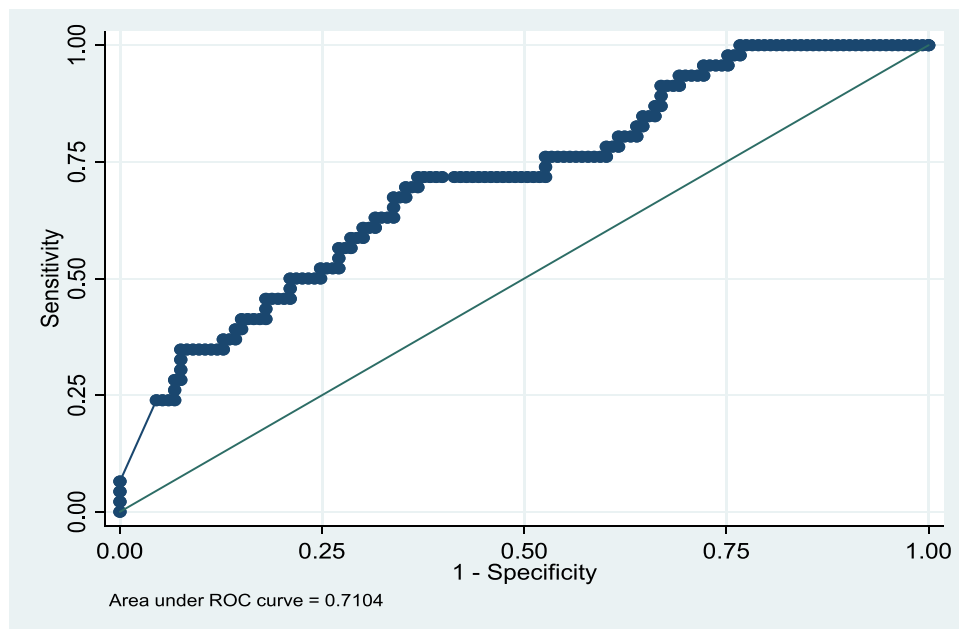
Figure 4 Area under the ROC curve of serum prostate specific antigen in the prediction of disease aggressiveness (N=179).

In addition, the majority of PCa cases in the current study exhibited intermediate to high-grade disease, closely aligning with a reported proportion of 34% for a Gleason score of 7 and 57% for a Gleason score of 8–10 in hospital-based data from Tanzania.[20] Concordantly, Ikuerowo et al in Nigeria reported that 74% of PCa cases had a Gleason score ≥7.[12] A significant challenge in PCa screening lies in the overdiagnosis of clinically insignificant cancer, contributing to an increased prevalence

of PCa without a corresponding impact on disease-specific mortality.[31] In the African setting, the detection of significant PCa among screened men is not uncommon,[12] and this may be attributed to poor screening behavior.

PSA is acknowledged for having a heightened detection rate for PCa in American men compared to black men and even other racial groups.[32] For instance, in this study, within the PSA range of 4-<10 ng/mL, commonly known as the gray zone, the PCa detection rate was 11.6%, much lower than the 26% reported by Pelzer et al among White men.[32] Similarly, Thailand and China reported detection rates of 16%.[10,11] The low detection rate among black men may be attributed to an elevated baseline PSA level in black men without PCa compared to White men.[33] Other factors that can cause elevated PSA include age, prostate volume, ejaculation within 24 hours of sample collection, prostatitis and prostate manipulation.[11] Some of these factors, together with sampling error, might have contributed to the elevated PSA in our cohort and ultimately the low detection rate. We posit that employing ultrasound or MRI-guided systematic biopsy could have enhanced the detection rate in the current study.[10]

Serum PSA serves as a crucial marker for PCa detection,[34] exhibiting a positive correlation with cancer diagnosis in the current study. The PCa detection rate increased tremendously with an increase in PSA level, where at a PSA of > 100 ng/mL, almost all patients were confirmed to have PCa, except for one case. This outlier, who declined a biopsy after obtaining only three cores, introduced a potential source of sampling error related to the number of core biopsies.[35] Similarly, results were reported by Lojanapiwat et al in Thailand, with a PSA of >100 ng/mL having a PCa detection rate of 99% and PSA correlating positively with cancer diagnosis.[11] Also, Vinit et al reported a strong correlation between PSA and PCa diagnosis.[36] The overall ability of PSA in predicting PCa in this study is consistent with those of Lojanapiwat et al, who reported an area under ROC of 82.1%.[11] The current study revealed that, the specificity of PSA increases with increased PSA level. Similar results were reported by other investigators,[11,37] suggesting that higher PSA levels tend to be more specific for PCa.

Contrarily to our findings, Patwardhan et al, reported higher optimal cutoff point of PSA of >9.7 ng/mL.[37] A much higher cutoff point of >20 ng/mL was reported in Thailand by Lojanapiwat et al.[11] Previous studies included hospital cases with potentially different characteristics, leading to different optimal cutoff points. The use of a cutoff point of >10 ng/mL is likely to reduce unnecessary biopsies, which are not without complications; however, it may miss 39 (11.6%) of cancer cases, resulting in false-negative results.

In this study, PSA demonstrated an overall positive correlation with aggressive disease, similar to other reports.[2,38] However, it has limited clinical utility in predicting disease aggressiveness offering a ≥1 in 4 chance of detecting aggressive cancer when PSA exceeds 20 ng/mL. This result aligns with other study findings.[11]

There is a strong correlation between serum PSA and bone metastasis,[11] wherein, at a serum PSA of ≥ 20 ng/mL, ≥ 95% of PCa cases have bone metastasis.[39] Consequently, a serum PSA ≥ 20 ng/mL is deemed indicative of a bone scan, while levels below this threshold offer limited advantage.[40] Although metastatic workup was not performed in the current study, 222 (24%) of the study population had PSA levels > 20 ng/mL, suggesting a significant proportion of metastatic disease might be present. The suspected high likelihood of metastatic disease in this population may be attributed to the unscreened nature of the community.

Limitation

The prostate biopsy was performed under finger guidance, which may have led to the missing of some PCa cases, leading to an underestimation of the proportion of the disease. Similarly, some participants who were screened and found to have higher PSA levels did not consent to prostate biopsy, potentially contributing to underestimation of the burden of the disease in the community. We recommend future studies investigate the barriers to accepting prostate biopsy so that these barriers can be addressed accordingly.

Conclusions and Recommendations

In the Northern Tanzania community, a notable prevalence of clinically significant PCa underscores the imperative for the development and enactment of control measures, notably screening.

PSA exhibited clinically usefully ability to predict PCa among African men aged ≥ 40 years. Thus, it is a valuable screening tool for this population, with a critical cutoff point of >4 ng/mL indicating the need for prostate biopsy.

Notable cases with PSA exceeding 100 ng/mL were consistently confirmed to have PCa. Therefore, in the absence of prostate biopsy feasibility, if indicated, androgen deprivation therapy can be innitiated for individuals >70 years of age exhibiting such an elevated PSA level.

Data Sharing Statement

Research data is available from corresponding author (email: baltonnic@yahoo.com) of the article upon reasonable request.

Ethics Approval and Consent to Participate

The College Research Ethics Review Committee (CRERC) of the Kilimanjaro Christian Medical University College (KCMUCo) approved the study (No. 2530). The National Institute for Medical Research (NIMR), (NIMR/HQ/R.8a/Vol. IX/3946). Permission was obtained from the Tanzanian local government and from regional medical officers and district medical officers of the respective regions and districts. All participants signed informed consent before enrollment in the study. Participant identifiers were not used during data collection instead research ID numbers were used. The study complies with the Declaration of Helsinki.

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Disclosure

The authors declare that they have no competing interest.

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