

# Prostate hyperplasia in St Mary's Hospital Lacor: utility of prostate specific antigen in screening for prostate malignancy

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## Abstract

**Introduction:** Prostate cancer is the second commonest cancer in men worldwide. At present, every patient with lower urinary tract symptoms (LUTS) in St. Mary's Hospital Lacor is undergoing prostate biopsy regardless of the prostate specific antigen (PSA) level. We sought to determine the association between PSA and malignant prostate histology.

**Methods:** This was a retrospective study. Data on age, PSA, prostate volume and prostate histology reported between Jan 2012 and Dec 2019 were retrieved from St. Mary's Hospital Lacor archive and analyzed using STATA SE/13.0.

**Results:** Records of 97 patients with LUTS was analyzed. The median (range) age of the patients was 71 (43-100) years. Median (range) of prostate volume was 91.8 (8.0-360.0) cc. Overall, PSA ranged from 0.21 to 399.2 ng/ml. Prostate histology showed 3.1% acinar adenocarcinoma, 24.7% adenocarcinoma and 72.2% benign prostatic hyperplasia. The median PSA amongst patients with malignant and non-malignant prostates were 15.8 ng/ml and 6.07 ng/ml respectively. Serum PSA level was significantly higher in patients with malignant prostate histology (Difference of mean= 9.7; p=0.001).

**Conclusion:** Patients with LUTS and PSA levels of 15ng/ml or more were more likely to have malignant prostate histology.

**Keywords:** Prostate specific antigen, Prostate cancer.

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## Background

Globally, prostate cancer was diagnosed in 7.1 % (1,276,106) of the world's population and contributed to 3.8% (358,989) of all cancer deaths in 2018 and it's the second commonest cancer diagnosed in men<sup>1,2</sup> The incidence of prostate cancer may be lower in low-middle income countries (LMIC) However, mortality has been on the rise<sup>3</sup>. In Uganda, the age-standardized mortality rate from prostate cancer has been recorded at 32.5/100,000 population<sup>4</sup>.

There are various risk factors for developing prostate cancer though age is a very strong risk factor with approxi-

mately 85% of all cases diagnosed in those aged over 65 years and an estimated incidence of only 0.1% in those below the age of 50 years<sup>5</sup>. Familial predisposition to prostate cancer has been demonstrated in approximately 5-10 % of cases<sup>6</sup>.

Prostate volume has been shown to increase with age. Anatomically, a prostate volume more than 20 cc is considered benign prostatic hyperplasia (BPH) with obstructive symptoms appearing in prostate size more than 50 cc<sup>7</sup>.

The diagnosis of prostate cancer entails the measurement of tumour biomarkers. Currently, several assays are available to measure serum prostate specific antigen (PSA), although the exact value that is considered "abnormal" is highly controversial with historical concentration above 4.0 ng/ml considered abnormal<sup>8,9</sup>. Therefore, PSA is a sensitive serum marker for prostate cancer but its specificity is limited by a high frequency of falsely elevated values in men with BPH, and prostatitis<sup>10</sup>.

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Screening for prostate cancer with PSA in the developed areas has contributed to the increasing diagnosis of prostate cancer in its early stage when confined to the prostate<sup>11</sup>. However, 15% of men with a PSA value less than 4.0 ng/ml have prostate cancer and 15% of these cancers are of high grade<sup>12</sup>. Therefore, evaluation for prostate biopsy by using Prostate health index has shown great help in determining men who don't need prostate biopsy in comparison to other biomarkers at a sensitivity of 91%<sup>13</sup> as most often, prostate histology will show benign prostatic hyperplasia in 70 % of sample analysed<sup>14</sup>.

Gleason grading of prostatic adenocarcinoma is one of the most powerful predictors of biological behaviour and one of the most influential factors used to determine treatment for prostate cancer<sup>15</sup>. Typical Gleason score range from 6-10, the higher the Gleason scores, the more likely that cancer will grow and spread quickly. Scores of 6 or less describe cancer cells that look similar to normal cells and suggest the cancer is likely to grow slowly, score of 7 suggests an intermediate risk for aggressive cancer and scores of 8 or higher describes cancers that are likely to spread more rapidly, these cancers are poorly differentiated<sup>16</sup>.

Currently, a prostate biopsy is being performed on every patient with Lower urinary tract symptoms regardless of the PSA level based on previous research recommendations. This study was aimed at determining whether a high prostate specific antigen test, age, prostate volume were associated with malignant prostate and this could help to make a revised recommendation on biopsy protocol.

## Methods

### Study design

This was a retrospective review of patients' medical record of patient age, prostate volume, prostate-specific antigen, and prostate histology reports. Data collected included patient age, PSA, prostate volume, histology diagnosis and Gleason score.

**Study site:** St Mary's Hospital Lacor is a missionary Catholic faith-based hospital in northern Uganda, a private-not-for-profit health facility with a 483-bed capacity.

### Study period

This study included data on all patients who had a prostate biopsy over the last 8 years (April 2012 - March 2019).

### Inclusion and exclusion criteria

We included data of all patients who had a prostate biopsy and excluded patients' data with missing entries of prostate-specific antigen.

### Data collection methods

Data were retrieved from the electronic storage computer archive of the hospital histopathology laboratory.

### Statistical analysis

The analysis was performed using STATA SE/13. Data are presented in tables, independent T-test was used to determine association between age and prostate histology and Mann-Whitney U test (Wilcoxon rank sum test) to determine the association between prostate volume, prostate specific antigen and prostate histology. The level of significance was set at  $p=0.05$

### Ethical consideration

The Lacor Hospital Institutional Research & Ethics Committee (LHIREC) approved the study and was a review of archived data. It waived the requirement to obtain individual informed consent.

### Results

A total of 97 eligible histopathological reports constituted this study. The median age of the participants was 71.0 years old, ranging between (43.0 – 100.0) years.

The median serum PSA level was 8.8 ng/ml, ranged (0.214 – 399.2) ng/ml. Among the PSA categories, 27.8% (n=27) had PSA up to 4.0 ng/ml, 30.9% (n=30) had PSA ranged between 4 and 10 ng/ml, and 41.2 (n=40)% had PSA above 10.0 ng/ml. Therefore, an abnormal PSA level was found in 72.2% (n=70) of the patients.

The median prostate volume was 91.8 cc, range (8.0 - 360.0) cc. Enlarged prostate volume was seen in 94.9% (75/97) of the sample analysed.

**Table 1:** Baseline characteristics

Variable	n	(%)
Age (years)		
Up to 50	4	( 4.12)
Above 50	93	(95.88)
Prostate specific antigen		
0 - 4 ng/ml	27	(27.84)
4 - 10 ng/ml	30	(30.93)
< 10 ng/ml	40	(41.24)
Prostate volume		
< 20 cc	4	( 5.06)
> 20 cc	75	(94.94)
Histology		
Prostate adenocarcinoma	27	(27.84)
Benign Prostatic Hyperplasia	70	(72.16)
Gleason score		
Well differentiation	11	(42.31)
Moderate differentiation	12	(46.15)
Poor differentiation	3	(11.54)

Amongst the prostate biopsies, 27.87 % (27/97) of the tissues were malignant and there was no malignant prostate tissue for men up to 50 years of age. Samples from men with normal PSA value, only 7.4% (2) were found to be malignant and for abnormal elevated PSA, 36.0% (25) were malignant tissues.

Prostate histology showed 3.1% acinar adenocarcinoma, 24.7% adenocarcinoma and 72.2% benign prostatic hyperplasia.

The Gleason score had a median of 7 (6 – 9), 42.3% were well differentiated (Gleason 6), 46.2% moderately differentiated (Gleason 7) and 11.5 % poorly differentiated (Gleason 9)

**Table 2:** Comparing age, prostate volume and prostate-specific antigen with histological characteristics.

	Malignant prostate histology	Non-Malignant prostate histology	<i>p-value</i>
Age (Completed years) Median, Range	73.0, 57.0 – 93.0	71.0, 43.0 – 100.0	0.140
Prostate Volume (cc) Median, Range	110.0, 10.0 - 360.0	83.7, 8.0 - 239.9	0.125
Prostate specific Antigen (ng/ml) Median, Range	15.8, 0.21 - 399.2	6.07, 0.4 - 341.2	0.001

## Discussion

In this 8-year retrospective study, trucut prostate histopathology reports of 97 patients were retrieved from the archive and analysed. The majority, 94.7% (93/97) comprised of the elderly men above the age of 50 years old with a median age of 71.2 and range (43 – 100) years. This similar age representation was also shown in previous studies indicating the occurrence of symptoms in the elderly population<sup>17–19</sup> In this study, prostate histology showed malignancy in 27.8%. Amongst the prostate adenocarcinoma observed in samples from patients with a normal PSA, 50% (n=1) has moderate differentiation which contrasted with 15% being high-grade cancers in the united states<sup>12</sup>.

In this study, malignant histology amongst the normal PSA patients was at 7.4%. Other studies also found malignant histology in normal PSA patients as well however with a higher rate of 15.4%<sup>12,17</sup> As most often, prostate histology will show benign prostatic hyperplasia in 70 % of the sample analysed<sup>14</sup>, this study revealed a similar finding of histological benign prostatic hyperplasia in 72.2% of the samples and amongst the samples from patients with increased PSA, 60% of the sample had benign prostate histology signifying the low specificity of Prostate-specific antigen in cancer detection<sup>10</sup>. This exposes patients to unnecessary prostate biopsy with all its potential risks. There are studies done on use Prostate Health Index (PHI) to predict the chances of malignancy in patients with PSA between 4 – 10 ng/ml. Thus, reducing the rates of unnecessarily performing prostate biopsy by 30%<sup>20,21</sup>. Abnormal level of PSA was found to be associated with malignant histology (p=0.001), whereas the patient's age or prostate volume were not associated with a malignant histological (p= 0.140 and p=0.125 respectively). A similar finding was also shown Irrespective of prostate size, PSA levels was found to be a strong predictor of tumour size than prostate volume<sup>22</sup>. PSA is a sensitive serum marker for prostate cancer but its specificity is limited by a high frequency of falsely elevated values in men with benign prostatic hyperplasia, and prostatitis<sup>10</sup>. However, This has contrasted with a previous study done in St Mary's Hospital Lacor who showed a non-statistical significant correlation between PSA value and prostate malignancy<sup>17</sup>. Okuku et al (2016) found majority, 66.7% of prostate cancer attending care at Uganda Cancer Institute had Gleason score of 9 or 10, and this study revealed the majority had a Gleason of 6 and 7. Only 11.5% 4

had poorly differentiated adenocarcinoma with a Gleason score of 9. This contrasted greatly with the above study indicating at least a good number of prostate cancer patients are seen at an earlier stage of the disease.

## Conclusion

In our setting, in one-third of men with LUTS, more than half of whom had serum PSA levels above 15.0 ng/ml had prostatic carcinoma. We demonstrated a very high association between PSA and malignant prostate histology.

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## Authors contributions

Dr Ogwang David Martin and Dr Vanusa Da Consolação Sambo contributed significantly in writing the literature, Dr Okidi Ronald contributed significantly in research writing and data analysis, Dr Opira Cyprian contributed in prostate volume measurement using ultrasound technique, and Dr Achola Caroline contributed in prostate sample histology reading.

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