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Original Article

Comparison of serum PSA and IMPDH-2 in Predicting Aggressive Prostate Cancer: A Cross-sectional Study

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Abstract

Background: Prostate cancer is a cause of morbidity and mortality among men globally. This study compared serum Prostate-Specific Antigen (PSA) and Inosine Monophosphate Dehydrogenase-2 (IMPDH-2) in predicting aggressive prostate cancer. **Methods**: Sixty-three prostate adenocarcinoma patients were recruited for this quantitative descriptive cross-sectional study. Their serum was assayed for IMPDH-2 and PSA. Serum IMPDH-2 and PSA correlations with Gleason score and ISUP Grade Groups were determined using Spearman's rho and Kendall tau correlation coefficients, respectively. The magnitude of the correlation was assessed by calculating the coefficient of determination for the respective analysis (R2). Similarly, regression analysis and receiver operating characteristic (ROC) curve were used to assess the ability of the biomarkers to predict aggressive prostate cancer. Levels of statistical significance were set as $p < 0.05$. **Results:** The mean age was 68.6 years. The mean serum IMPDH-2 and PSA were 76.2pg/ml and 65.9ng/ml respectively. Serum IMPDH-2 did not predict aggressive prostate cancer; ($r = 0.08$, $p = 0.55$ Spearman rho), ($\tau = 0.03$, $p = 0.79$ Kendal tau). Serum PSA weakly predicted aggressive prostate cancer; ($r = 0.30$, $p = 0.02$ Spearman rho), ($\tau = 0.21$, $p = 0.04$ Kendal tau). It was responsible for 10.1 and 8.8% of Gleason score and ISUP grade group variances respectively. However, it did not significantly outperform IMPDH-2 in predicting the Gleason score ($p = 0.53$). **Conclusion:** PSA weakly predicted aggressive prostate cancer but did not statistically significantly outperform IMPDH-2. As such, none is sufficiently accurate in predicting aggressive prostate cancer when used in isolation.

Introduction

Prostate cancer is the second most common cancer among men globally and is only superseded by lung cancer.[1] In Africa, It is the most common cancer among men with an estimated 104,050 new cases based on 2022 records.[1] The true burden of prostate cancer in Nigeria is unknown due to underreporting and poor statistics.[2] However, it is reported to be the most common male cancer in Nigeria, constituting 37.5% of all newly diagnosed male cancers.[1] Furthermore, It is the most common cause of cancer deaths in Nigerian men.[1] African ethnicity is a significant risk factor for PCa and the disease tends to appear at an earlier age and is often more aggressive. Other risk factors are advanced age, family history of PCa, red meat, diet rich in fat, and dairy products.[3] Most of our patients present with locally advanced or metastatic disease. This makes prostate cancer an important public health concern in Nigeria. Prostate cancer is the fifth leading cause of mortality among men and the highest death rates have been reported among African descent.[4] The global burden of the disease is on the rise due to widespread prostate specific antigen (PSA) testing and the use of transrectal ultrasound-guided prostate biopsy.[5–7]

The use of serum prostate specific antigen has led to earlier detection of prostate cancer at the expense of overdiagnosis.[8] The greatest limitation of PSA is its poor specificity and low ability to distinguish aggressive from non-aggressive prostate cancer.[8] Identifying patients with aggressive prostate cancer is indispensable as over 80% of them will develop skeletal complications with its attendant negative effect on their quality of life.[8] The correct grading of prostate cancer is vital for management decision-making. At present, Gleason grading is used to predict the aggressive nature of prostate cancer with higher Gleason scores corresponding to more aggressive disease.[8] Hence, the Gleason score is one of the most powerful prognostic predictors of prostate cancer.[9] The Gleason grading system has undergone revisions over the years to improve on its limitations. One such revision is assigning a score of 6 as the lowest grade on prostate needle biopsy and developing a new grading system.[9] This new grading system proposed in 2013 by a group from Johns Hopkins Hospital has five grade groups. These grade groups are more accurate in predicting disease progression than the traditional Gleason grading system.9 The system was validated and proposed by the International Society

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of Urological Pathologists (ISUP) consensus. It was later adopted by the 2016 World Health Organization (WHO) classification of prostate tumors.[9,10]

Even though the Gleason score and ISUP grade group are more reliable than PSA in predicting aggressive prostate cancer, they can miss some patients with aggressive disease. This is because high-grade foci of prostate cancer can be missed during trucut needle biopsy. Furthermore, prostate biopsy is an invasive procedure with some complications. Because of these limitations, a reliable, accessible, non-invasive, and affordable screening modality for aggressive prostate cancer is required to improve diagnosis and management. This desirable biomarker will reduce the need for repeated biopsies to identify patients with aggressive disease. It will also help identify disease upgrades in patients undergoing active surveillance or watchful waiting

Serum inosine monophosphate dehydrogenase (IMPDH) may assume this role. It is a rate-limiting enzyme involved in a crucial step in the de novo pathway of purine nucleotide biosynthesis, which is essential for DNA synthesis.[11] IMPDH catalyzes the oxidation of inosine 5′—monophosphate to xanthosine 5′—monophosphate.[12] It is associated with cell growth, malignant transformation, and differentiation.[13] The enzyme exists in two isoforms, and Isoenzyme 2 is preferentially upregulated in malignant cells, including prostate, bladder, and renal cancers.[11] This enzyme was chosen in this study because high-grade aggressive cancers have higher cell replication and, hence, higher DNA requirements, which may translate to higher expression of the enzyme. Furthermore, previous reports have also found high expression of IMPDH-2 to be associated with aggressive human nasopharyngeal carcinoma.[11,13] Similarly, overexpression of IMPDH-2 in hepatocellular carcinoma (HCC) tissues was reported to be closely related to aggressive disease.[11] Likewise, a study in Poland found that serum IMPDH-2 had some usefulness in predicting aggressive prostate cancer.[14] Given the fact that the previous study was in a European population, this study aims to compare serum PSA and IMPDH-2 in predicting aggressive prostate cancer in our predominantly black population. We hypothesize that serum IMPDH-2 was better than PSA in predicting aggressive prostate cancer.

Methods

This hospital-based quantitative, descriptive cross-sectional study was conducted at the Institute of Urology and Nephrology of Usmanu Danfodiyo University/Teaching Hospital, Sokoto, Nigeria from January to December 2020. A non-randomized sampling technique was used whereby consecutive patients with adenocarcinoma of the prostate were recruited into the study. A minimum estimated sample size of 54 subjects was calculated using the formula for calculating sample size for a cross-sectional study with a quantitative outcome variable.15 Details of the calculation are contained in the supplementary file.

The inclusion criteria were all newly diagnosed patients with a histologically confirmed adenocarcinoma of the prostate who presented to the urology clinic of Usmanu Danfodiyo University Teaching Hospital, Sokoto, Nigeria. The exclusion criteria were patients on any form of treatment for prostatic diseases such as 5-alpha reductase inhibitors, androgen deprivation therapy, and radiation therapy. Patients who had any form of prostatectomy, those with any histological type of cancer other than adenocarcinoma, and those who refused to consent to be enrolled in the study were similarly excluded.

All enrolled participants were clinically evaluated through detailed history taking and physical examinations. Similarly, the participants had their routine laboratory tests that included full blood count (FBC), serum electrolytes, urea, creatinine (EUCr), urinalysis and urine microscopy, culture, and sensitivity (M/C/S). Additionally, all participants had their serum assayed for IMPDH-2 and PSA by a competent laboratory scientist at the chemical pathology department of Usmanu Danfodiyo University Teaching Hospital, Sokoto, Nigeria using the Sunlong® Biotech IMPDH-2 enzyme-linked immunosorbent assay (ELISA) kit (REF SL3371Hu) and PSA AccuBind® ELISA kit (REF 2125-300A) based on the manufacturers' instruction as contained in the instruction manual.[16,17]

For the assay of the biomarkers, the collected blood samples were allowed to clot for 30 minutes. The samples were then centrifuged at 2000 rpm for 20 minutes. The supernatant serum was collected and stored at -20oC. Any haemolyzed blood sample was discarded and a fresh blood sample was collected because it could interfere with the result. The details of the procedure are contained in the supplementary file. The diagnosis of PCa was made through a systematic prostate needle biopsy obtained via transrectal ultrasound guidance using Mindray® Diagnostic Ultrasound System DC-30. Additional targeted biopsies were obtained in subjects with suspicious nodules using a Bard® Magnum spring-loaded biopsy gun. The histopathologists at the histopathology department of Usmanu Danfodiyo University Teaching Hospital, Sokoto, Nigeria made the histological diagnosis and Gleason grading.

The patients were grouped into the five ISUP Grade groups of increasing aggressiveness of the tumor. These grade groups are 1 (Gleason score ≤ 6), 2 (Gleason score 3+4), 3 (Gleason score 4+3), 4 (Gleason score 8), and 5 (Gleason score 9 – 10). The research data were collected using structured pro-forma. At the end of the study, the data were entered into and analyzed using IBM® SPSS® statistics for Windows, version 23.0. Multiple statistical analysis was performed to assess the ability of the biomarkers to predict aggressive prostate cancer. The first was to determine the correlation of serum IMPDH-2 and PSA with the Gleason score using Spearman's rho correlation coefficient as the data were not normally distributed. The correlation with the ISUP grade group was determined using the Kendall tau correlation coefficient. The correlation was graded as very weak if r (< 0.3), weak (0.3 – 0.4), moderate (0.5 – 0.6), or strong (≥ 0.7). The magnitude of the correlation was determined by calculating the coefficient of determination for the respective analysis = (R2).[18]

The second statistical analysis was the linear regression analysis to establish a relationship between the biomarkers and the Gleason score/ISUP grade groups. Then the receiver operating characteristic (ROC) was also used to test the ability of the biomarkers to predict aggressive prostate cancer (ISUP grade group 4 and 5). A biomarker with an area under the ROC curve (AUROC) of 0.5 – 0.6 was considered to have failed, while 0.6 – 0.7 was a poor predictor of aggressive prostate cancer. A biomarker with an AUROC of 0.7 – 0.8 was considered a fair predictor, 0.8 – 0.9 as a good predictor, and 0.9 – 1.0 was considered to be a very good predictor. All levels of statistical significance were set as $p < 0.05$. The health research and ethics committee of Usmanu Danfodiyo University Teaching Hospital approved the study with reference number UDUTH/HREC/2019/No. 852

Results

The study involved sixty-three participants, whose ages ranged from 43 to 102 years, with a mean age of 68.6 years ± 8.9 and a median age of 70 years (IQR 13). Of the participants, twenty-two (34.9%) were under 65 years old, 41 (65.1%) were over 65, and just one (1.6%) was under 50. The histogram in ***Figure 1*** shows the age distribution of the participants. Every participant had symptoms; 62 (98.4%) reported lower urinary tract symptoms (LUTS), and 15 (24.2%) of them had an indwelling urethral catheter as a result of obstructive nephropathy or urine retention. In ***Table 1,*** additional typical presenting symptoms are displayed. The mean duration of symptoms before presentation was 20.4 months ±18.4. Twenty-nine (46%) participants had comorbidity as listed in ***Table 2.*** Out of the 63 participants, 5 (7.9%) exhibited benign digital rectal examination (DRE) findings and 58 (92.1%) had DRE findings suggesting prostate cancer.

In 20 (31.7%) of the participants, the urine culture yielded microorganisms as displayed in ***Table 3.*** Seven (11.1%) subjects had elevated creatinine ±urea, whereas 53 (84.1%) had normal renal function test results. The mean packed cell volume (PCV) was 31.7% ±4.7. The mean serum PSA was 65.9ng/ml ±38.6, ranging from 1.2ng/ml to 100ng/ml. Fifty-six (88.9%) participants had serum PSA above 10ng/ml while 4 (6.3%) participants had serum PSA levels in the gray zone between 4 and 10ng/ml. Interestingly, 3 (4.8%) participants had normal serum PSA <4ng/ml. Serum IMPDH-2 levels ranged from 0.25 pg/ml to 176.4 pg/ml, with a mean of 76.2 pg/ml ±55.1. The boxplot in ***Figure 2*** displays the serum biomarkers' distribution.

The prostate ranged from 14.8 to 196 ml in size, with a mean of 67.9 ml ±36.2. Of the participants, 42 (66.7%) had a breach of the prostate capsule, and 49 (78.8%) had prostatic nodules. Of those with prostatic nodules, 22 (44.9%) had hypoechoic nodules, 6 (12.2%) had isoechoic nodules, and 21 (42.9%) had mixed echoic nodules. Twenty-seven (42.9 percent) of the participants had tumor invasion of the seminal vesicles. Of the 63 participants, forty-seven (74.6%) had a Gleason score of ≥8. ***Table 4*** displays the distribution of the ISUP grade group and Gleason score.

Table 1. The Presenting Symptoms of the Study Population with Prostate Cancer.

Presenting SymptomS	Frequency	Percentage
Voiding LUTS[a]	62	98.4
Storage LUTS[a]	61	96.8
Low Back Pain	36	57.1
Lower limb Paraesthesia	28	44.4
Paraparesis/Paraplegia	14	22.2
Weight Loss	16	25.4
Body Weakness	14	22.2
Anorexia	14	22.2
Urinary Incontinence	3	4.8
Faecal Incontinence	2	3.2
Pressure Ulcer	2	3.2
Hematuria	1	1.6

Legend: [a] Lower Urinary Tract Symptoms.

Table 2. List of Comorbidities Among the Study Population with Prostate Cancer.

Co-morbidity	Frequency	Percentage
Nil	34	53.9
hypertension	21	33.3
Diabetes Mellitus	3	4.8
Hypertension & Diabetes Mellitus	2	3.2
Hypertension & CKD[a]	1	1.6
Cerebrovascular Disease	1	1.6
Cardiac Failure	1	1.6
TOTAL	**63**	**100**

Legend: [a] Chronic Kidney Disease

Table 3. List of Microorganisms Cultured in the Urine of the Study Population with Prostate Cancer.

Microorganism	Frequency	Percentage
Escherichia coli	7	11.1
Staphylococcus aureus	5	7.9
Klebsiella	3	4.8
Proteus mirabilis	2	3.2
Candida albicans	2	3.2
Pseudomona specie	1	1.6
Negative Culture	43	68.2
Total	**63**	**100**

No significant correlation was seen between serum IMPDH-2 and ISUP grade group (τ = 0.03, p = 0.79, Kendall tau) or between serum IMPDH-2 and Gleason score (r = 0.08, Spearman's rho, p = 0.55). Similarly, using linear regression analysis, serum IMPDH-2 had no relationship with the Gleason score (B=0.001, P=0.56) and ISUP grade group (B = 0.001, p = 0.78). The scatter plot in ***Figure 3*** shows the lack of a linear relationship between serum IMPDH-2 and the Gleason score. Furthermore, serum IMPDH-2 was only responsible for 0.6% (R2 = 0.006) of the Gleason score variance and 0.1% (R2=0.001) of the ISUP grade group variance.

Nonetheless, there was a positive correlation (r = 0.30, Spearman's rho, p = 0.02) between the serum PSA level and the Gleason score. However, the correlation was weak. Serum PSA also had a very weak correlation (τ = 0.21, p = 0.04, Kendall tau) with the ISUP grade group. Using linear regression analysis, PSA had a positive relationship with the Gleason score (B= 0.009, p = 0.01) and the ISUP grade group (B = 0.009, p = 0.02). It determined 10.1% (R2 = 0.101) and 8.8% (R2 = 0.088) of the Gleason score and ISUP grade group variances respectively. The weak linear relationship of the PSA and Gleason score is displayed in ***Figure 4***. Using the ROC curve, the overall ability of serum PSA in predicting aggressive PCa (ISUP grade group 4 and 5) was fair with an area under the curve of 0.74 (95% CI; 0.61 – 0.88) as shown in ***Figure 5***. However, serum IMPDH-2 failed to predict aggressive prostate cancer with an area under the curve of 0.52 (95% CI; 0.34 – 0.69) as shown in ***Figure 6.*** However, when compared, the serum PSA did not considerably outperform IMPDH-2 (p = 0.53) in predicting the Gleason score. Consequently, neither serum PSA nor IMPDH-2 can be used in isolation to predict aggressive prostate cancer.

Table 4. The Gleason Score and ISUP Grade Groups of the Study Population with Prostate Cancer.

Variable		Frequency	Percentage
Gleason Score	6	3	4.8
	7	13	20.6
	8	17	27
	9	22	34.9
	10	8	12.7
Total		**63**	**100**
ISUP[a] Grade Group	1 (GS[b] ≤6)	3	4.8
	2 (GS 3 + 4)	6	9.5
	3 (GS 4 + 3)	7	11.1
	4 (GS 8)	17	27
	5 (GS 9 & 10)	30	47.6
Total		**63**	**100**

Legend: [a] International Society of Urologic Pathologists, [b] Gleason score

Figure 1. A Histogram Showing the Age Distribution of the Study Subjects.

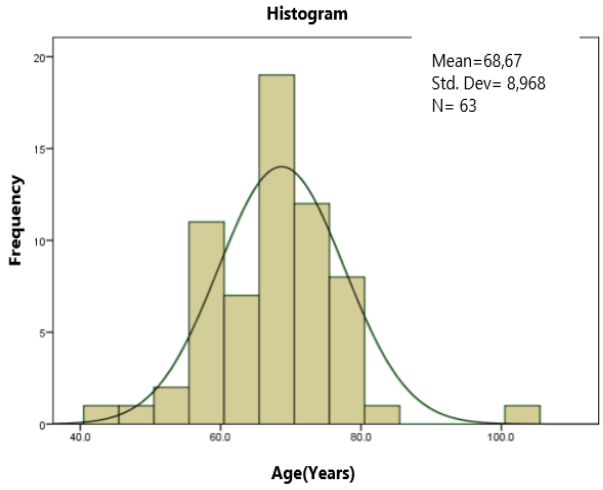


Figure 2. Boxplot Showing the Maximum, Minimum, Median, and Interquartile Range of Serum PSA and IMPDH-2.

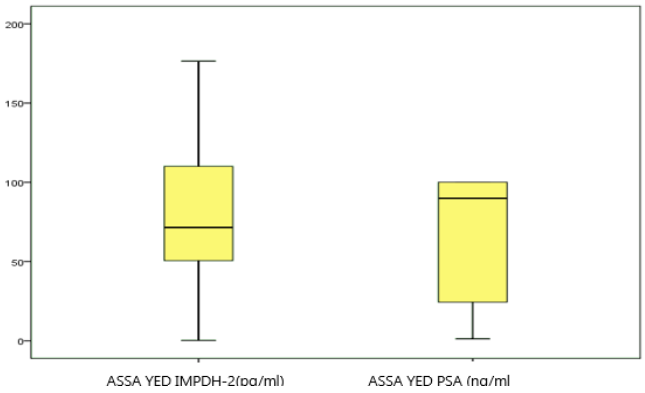


Figure 3. A Scatter Plot Showing the Absence of a Linear Relationship Between IMPDH-2 and Gleason Score.

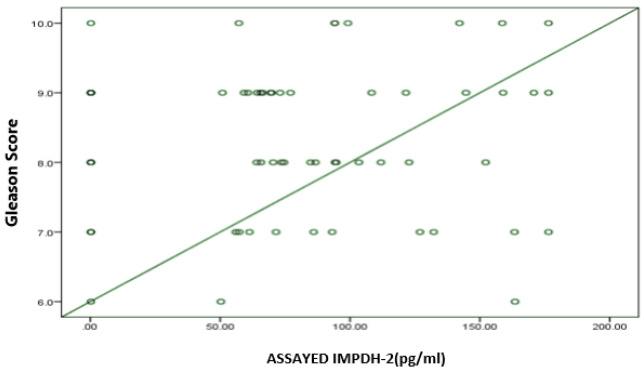
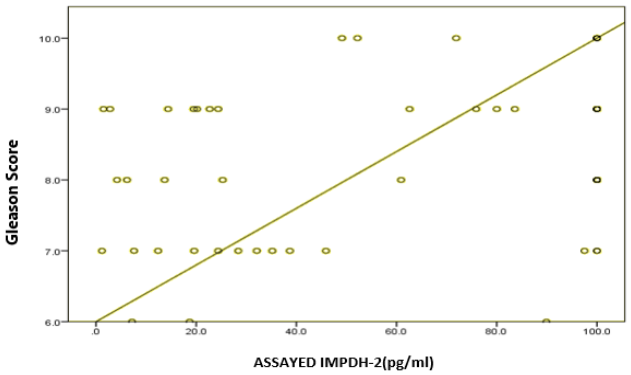


Figure 4. A Scatterplot Showing the Weak Linear Relationship Between PSA and Gleason Score.



Discussion

It is worrisome that our patients still present late with locally advanced and occasionally metastatic prostate cancer, even with the availability of PSA testing facilities. Furthermore, we frequently see patients with advanced illnesses that progress to skeletal metastasis. To make informed management decisions and lower the morbidity and death rate related to the condition,

it is essential to identify individuals with high-grade, aggressive PCa who are at risk of disease progression.

Age is a significant risk factor for prostate cancer and the majority of cases are diagnosed at 65 years or older with the risk rising after the age of 50.19 This study obtained comparable results, with a mean age of 68.6 years and most participants being older than 65. The findings by Wieczorek et al.14 in Poland and Odubanjo et al.20 in Nigeria were similar to ours reporting a mean age of 68.2 years and 68.5 years respectively. Similarly, Elabbady et al.21 in Egypt reported a mean age of 67 which is also not significantly different from ours. In Ghana, however, Egote et al.22 reported a higher mean age of 71.7 years. This may be either because their patients present late or they may have less aggressive disease and hence late onset of symptoms..

Figure 5. The ROC Curve for Serum PSA Showing some Usefulness of PSA in Diagnosing Aggressive Prostate Cancer.

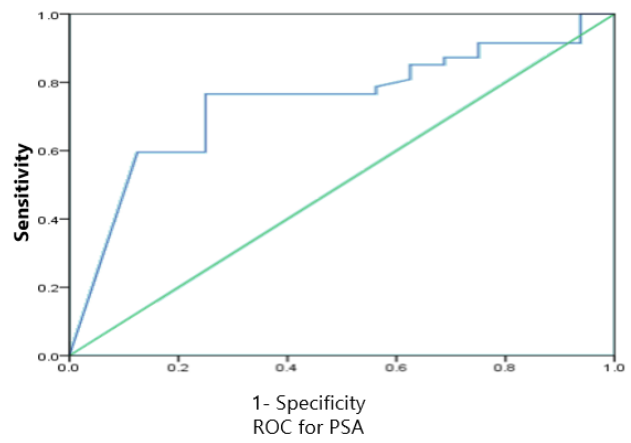
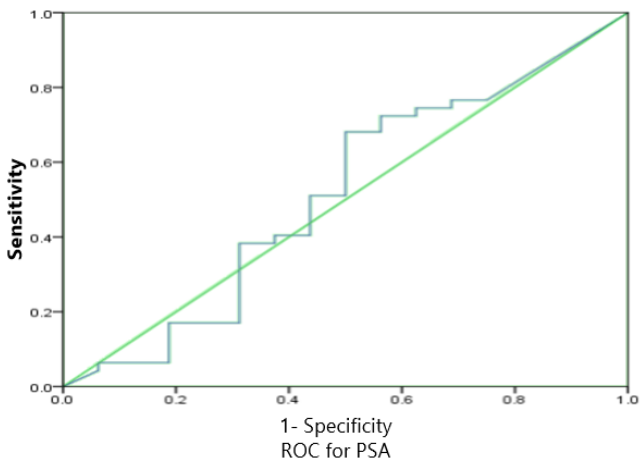


Figure 6. The ROC Curve for Serum IMPDH-2 Showing its Poor Usefulness in Diagnosing Aggressive Prostate Cancer.



Almost all our study participants had lower urinary tract symptoms (LUTS), indicating at least a locally advanced illness. This indicated inadequate PCa screening practices, which can be linked to several factors including low awareness, poverty, anxiety and fear of developing cancer, lack of urologists in primary and secondary healthcare facilities, and a dearth of PSA testing facilities in rural areas. Yahaya et al.[23] also reported LUTS as the most common form of presentation of their PCa patients. In contrast, Adewumi et al.[24] reported LUTS as the second most common complaint after bone pain. In another study, Oyibo et al.4 reported LUTS in three-quarters of their study participants. However, Elabbady et al.[21] in Egypt, reported that a quarter of their PCa patients were asymptomatic at diagnosis due to improved practice of PSA screening. In Lagos, Odubanjo et al.[20] also reported 20% of their patients being asymptomatic at diagnosis possibly due to better PCa screening awareness. According to their report, LUTS was still the most often reported form of presentation in 68.6% of their patients. Based on the aforementioned studies, LUTS is a major form of presentation of PCa patients. This may be attributed to locally advanced disease or coexisting benign prostatic hyperplasia.

Medical comorbidity affected over half of our participants; the majority had hypertension, and a small number had diabetes mellitus. The presence of a medical co-morbidity in prostate cancer patients may constitute a competing cause of mortality. This was buttressed by Stikbakke et al.[25] who reported that a systolic blood pressure of >150 mmHg among PCa patients is associated with a 49% increase in overall mortality. Also, a threefold increase in overall mortality risk was observed among prostate cancer patients with diastolic blood pressure > 90mmHg treated with curative intent.[25] The small number of diabetics among our study participants is in keeping with the findings by Kasper et al.[26] that diabetes has an inverse relationship with PCa. Ofoha et al.[19] also reported that about half of their PCa patients had comorbidity with hypertension being the commonest. The majority of participants' DRE was suspicious of PCa, supporting how late our patients presented. Oyibo et al.[4] also reported similar findings as 90% of the patients in their study had suspicious DRE. In contrast, Elabbady et al.[21] and Wieczorek et al.[14] reported less than a quarter of their study subjects with suspicious DRE which reflects an earlier diagnosis of prostate cancer in their regions. The majority of individuals with positive urine cultures were asymptomatic and had indwelling urethral catheters. According to studies, the duration of the indwelling catheter is the main determining factor of catheter-associated bacteriuria. Catheter-associated bacteriuria affects patients with an indwelling urethral catheter at a daily rate of 3 – 8%.[27]

The mean serum PSA level of our participants was 65.9ng/ml which is lower than 207.9ng/ml reported by Okolo et al.[28], 82.9ng/ml reported by Oyibo et al.[4], and 73.4ng/ml reported by Ofoha et al.[19] but higher than 37.1ng/ml reported by Egote et al.22 These variations can be a result of the biology of the cancer cells or variations in the ELISA kits used in the various studies. Even though the majority of participants had PSA levels above 10ng/ml, a few had PSA levels below 4ng/ml. This suggests that certain patients with prostate cancer may not be detected by the PSA threshold of 4ng/ml, which is why additional clinical and radiological parameters are necessary. This was also corroborated by Odubanbjo et al.[20] who reported that 3% of their PCa patients had PSA <4ng/ml. The mean serum level of IMPDH-2 in our study

was higher than the 60.[5] that Wieczorek et al.[14] The difference observed in both studies may be due to different ELISA kits, tumor biology, population characteristics, or sample size. This is because our sample size is larger than theirs and our study population is black compared to the white study population in Poland.

The mean size of the prostate was 67.9ml which is similar to 67.2ml reported by Oyibo et al.[4] also in Nigeria, but slightly higher than the 63ml reported by Elabbady et al.[21] The majority of research participants had a breached prostatic capsule, and nearly half of them had tumor invasion of one or both seminal vesicles, indicating at least a locally advanced disease. Oyibo et al.[4] likewise stated that 85% of their patients had a capsular breach. Prostatic nodules on TRUS were present in most of our research participants. These nodules were primarily hypoechoic or mixed echoic. The study by Manseck et al.[29] also reported hypoechoic lesions in 34.5% of all biopsy cores making it the most common lesion associated with PCa. The majority of the research participants had Gleason scores of 8 or above (ISUP grade group 4 and 5) which emphasizes the aggressiveness of prostate cancer in these individuals. Prior research has revealed that black and Asian individuals had germline mutations linked to high-risk prostate cancer.[30] Oyibo et al.4 reported that 52% of their study participants had Gleason scores of 8-10 which is lower than ours. Ngwu et al. 31 reported less than a quarter of their patients, 18.2% with a Gleason score of 8 – 10. Only 4.8% of our study participants had a Gleason score of 6 which is lower than the 32.5% that was reported by Oyibo et al.4 In contrast to our study Elabbady et al.[21] and Wieczorek et al.[14] reported Gleason scores of ≤7 as the most common Gleason scores in their respective studies. This shows that Arabs and Caucasians are more likely to have less aggressive prostate cancer compared to blacks.

Our research revealed that the Gleason score and ISUP Grade groups could not be predicted by serum IMPDH-2. This is in contrast to the finding of Wieczorek et al.[14] who reported a weak positive correlation between serum IMPDH-2 and ISUP grade group (τ = 0.4, p = 0.005, Kendall tau). Variances in the ELISA kits used in the two research, differences in sample size, or even variations in tumor biology related to race or ethnicity could be responsible for the disparities observed between the two studies. Serum PSA did, however, showed a very weak positive correlation with ISUP Grade groups and a weak positive correlation with the Gleason score. This further affirms PSA as a weak predictor of aggressive prostate cancer. Additionally, 10.1% of the variance in the Gleason score was dictated by serum PSA. Thus, about 80% of the Gleason score variance can be attributed to other causes. Okolo et al.[28] and Oyibo et al.[4] both in Nigeria, also reported a weak positive correlation of 0.4 between serum PSA and Gleason score. Likewise, Ngwu et al.31 reported a positive association between serum PSA and Gleason score (r = 0.6) with a moderate strength. Ngowi et al.[3] in Tanzania also reported weak ability of serum PSA in predicting aggressive PCa with an AUC of 0.71 which is not different from ours. However, in a study by Mohammed et al.[32] there was no correlation between PSA and Gleason score (p = 0.175). Most of the aforementioned studies showed that serum PSA could predict aggressive PCa. However, it is not an accurate biomarker, and therefore, at most, it should be used in combination with other markers and parameters such as Gleason score, number, and percentage of prostate biopsy core involvement among others to predict aggressive prostate cancer. Serum IMPDH-2 did not predict aggressive prostate cancer. There is a need to intensify further research into other biomarkers and advanced imaging techniques including functional imaging that may predict aggressive prostate cancer with high accuracy.

Conclusion

Serum PSA is a weak predictor of aggressive prostate cancer. It was responsible for 10.1 and 8.8% of the Gleason score and ISUP grade group variances. However, serum IMPDH-2 could not predict aggressive prostate cancer. Even though serum PSA weakly predicted aggressive prostate cancer, it was not statistically better than serum IMPDH-2. Therefore, neither of the two biomarkers can reliably predict aggressive prostate cancer, especially when used in isolation. Hence, further studies need to be done to search for better predictors of aggressive prostate cancer.

Summary – Accelerating Translation

Comparison of Serum PSA and IMPDH-2 as Predictors of Aggressive Prostate Cancer: A Cross-sectional Study

Main Problem to Solve: Prostate cancer is a major cause of morbidity and mortality globally. It is the most common male cancer among Nigerian men. Most of our patients present with locally advanced and metastatic disease. Serum PSA is not accurate in discriminating aggressive from indolent prostate cancer. Even though the Gleason score and ISUP grade group are more accurate than PSA in that regard, they require a biopsy. Prostate biopsy is an invasive procedure and foci of high-grade disease can be missed. Therefore, some patients with aggressive prostate cancer can be missed using the Gleason score and ISUP grade. Therefore, a reliable, accessible, and affordable screening modality is required to improve the diagnosis of aggressive prostate cancer.

Aim of the Study: This article aims to compare serum prostate-specific antigen and Inosine Monophosphate Dehydrogenase 2 in predicting aggressive prostate cancer.

Methodology: Sixty-three prostate adenocarcinoma patients were recruited for this quantitative descriptive cross-sectional study. Their serum was assayed for IMPDH-2 and PSA. Serum IMPDH-2 and PSA correlations with Gleason score and ISUP Grade Groups were determined using Spearman's rho and Kendall tau correlation coefficients, respectively. The magnitude of the correlation was assessed by calculating the coefficient of determination for the respective analysis (R^2). Similarly, regression analysis and receiver operating characteristic (ROC) curve were used to assess the ability of the biomarkers to predict aggressive prostate cancer. Levels of statistical significance were set as $p < 0.05$.

Results: The mean age was 68.6 years. All the recruited participants were symptomatic. The mean serum IMPDH-2 and PSA were 76.2pg/ml and 65.9ng/ml respectively. Serum IMPDH-2 did not correlate with the Gleason score (r = 0.08, p = 0.55 Spearman rho) and ISUP grade group (τ = 0.03, p = 0.79 Kendal tau). Similarly, using linear regression analysis, serum IMPDH-2 had no relationship with the Gleason score (B=0.001, P=0.56) and ISUP grade group (B = 0.001, p = 0.78). It also failed to predict aggressive prostate cancer (ISUP grade group 4 and 5) using the ROC curve with an area under the curve of 0.52 (95% CI; 0.34 – 0.69). Therefore,

IMPDH-2 is not a good predictor of aggressive prostate cancer. However, serum PSA weakly correlated with Gleason score (r = 0.30, p = 0.02 Spearman rho) and ISUP grade group (τ = 0.21, p = 0.04 Kendal tau). It was responsible for 10.1 and 8.8% of Gleason score and ISUP grade group variances respectively. Similarly, using regression analysis, there was a weak linear relationship between PSA and both the Gleason score (B= 0.009, p = 0.01) and the ISUP grade group (B = 0.009, p = 0.02). The overall ability of serum PSA in predicting aggressive PCa (ISUP grade group 4 and 5) was fair with an area under the curve of 0.74 (95% CI; 0.61 – 0.88). However, when compared, serum PSA did not significantly outperform IMPDH-2 in predicting the Gleason score (p = 0.53).

Conclusion: Serum PSA weakly predicted aggressive prostate cancer but did not statistically significantly outperform IMPDH-2. It was responsible for 10.1 and 8.8% of Gleason score and ISUP grade group variances. Therefore, neither PSA nor IMPDH-2 is sufficiently accurate in predicting aggressive prostate cancer when used in isolation.

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Conflict of Interest Statement & Funding

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Author Contributions

Conceptualization: AMU, IAM, NPA, AAA. Data Curation: AMU, EUO. Formal Analysis: AMU. Funding Acquisition: AMU. Methodology: AMU, ASM, AK. Project Administration: IAM. Resources: AMU, EUO. Software: AMU. Supervision: IAM, NPA, AAA, ASM. Validation: AMU, NPA, ASM. Visualization: AMU. Writing - Original Draft: AMU, AK, EUO. Writing - Review Editing: AMU, IAM, NPA, AAA, ASM, AK.

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