Original Research Article

Age and Gleason's score in prostate cancer among Southern Nigerians: Is there any correlation?

ABSTRACT

Background: Prostate cancer(PCa) incidence and mortality are associated with age and African descent. African men are more likely to have aggressive disease, present late with complications and die from prostate cancer. Age is also an independent factor in the management of patients with PCa. The Gleason score is used both for risk classification, treatment stratification and prognostic purposes.

Aims and objectives: To determine the presence of a correlation between age and Gleason score in patients with histologically confirmed prostate cancer.

Materials and methods: This retrospective study was carried out on patients with histologically confirmed prostate cancer from August 2012 to July 2021. Their case records were retrieved, and the patient's age and Gleason grade were collated. Data collected were then analyzed using SPSS version 20. The data were collated using Microsoft excel 2016.

Results: There were 352 patients with histologically confirmed prostate cancer with a mean age of 86.88years±9.75SD, ranging from 48years to 117years. The modal age range was the 60-69year group. The commonest PCa grade is Gleason 8 {ISUP 4;27.8%(98)}, followed by Gleason 9{ISUP 5;(19.9%(70)} as shown in Figure 2. The Gleason score was an associated with

age as indicated in Table 2 p=0.001). However, Pearson's Correlation Coefficient did not establish a statistically significant relationship (r=0.045; p=0.401). The high-risk Gleason's 8-10, ISUP 4&5, was the most frequent among all the age groups. The low Gleason score cancers were commonest in the 40-49year age group.

Conclusion: There was an association between age and Gleason's score, even though it was not statistically significant. Gleason 8-10 or ISUP 4&5 PCa was associated with older patients. It is also commonest among patients 80years and above. Our study could not exclude the presence of a correlation.

Keywords: Age, correlation, Gleason score, ISUP, prostate cancer

INTRODUCTION

Prostate cancer (PCa) is the second most frequent cancer diagnosis in men and the fifth leading cause of death worldwide.[1] Evidence suggests the incidence is rising with higher reported prevalence in the developed countries.[2] Despite the absence of national prostate-specific antigen (PSA) based screening; prostate cancer is the most commonly diagnosed cancer in Nigerian men.[3,4] The incidence and mortality are associated with ageing and African descent. African men are more likely to have an aggressive disease; [1] presents late with complications and dies from prostate cancer.[5]

The original Gleason grading system was based on architectural patterns of prostate adenocarcinoma seen on haematoxylin and eosin staining on low power magnification rather

than cellular features. With Gleason pattern 1 being the least aggressive and Gleason pattern 5 being the most aggressive.[6] The International Society of Urological Pathology (ISUP) has issued guidelines for the grading of prostate cancer based on a consensus conference held in 2014. Gleason scores 6 (ISUP 1), Gleason score 3+4=7 ISUP 2), Gleason score 4+3=7 (ISUP 3), Gleason score 4+4=8 (ISUP 4), and Gleason score 9-10 (ISUP 5).[6] Treatment of Prostate cancer depends on the stage and grade of the disease at presentation, the fitness of the patient, and the facilities available. Risk stratification is essential in patient management. Patients who are fit and present early with localized disease can be offered curative treatment via radical prostatectomy or radiotherapy. Different prognostic indicators for prostate cancer have been sought to aid the treatment of prostate cancer.[7-9] The Gleason score is an essential tool in patient management.[6] Several studies on the relationship between age and Gleason score have been carried out with varying observations.[10,11,12]

AIMS

To determine the presence of a correlation between age and Gleason score in patients with histologically confirmed prostate cancer in Port Harcourt.

MATERIALS AND METHODS

A retrospective study carried out at the University of Port Harcourt Teaching Hospital, Rosivylle Clinic and Urology Centre Port Harcourt, Rivers State, Nigeria. Patients with histologically confirmed prostate cancer were evaluated from August 2012 to July 2021. Their folders were retrieved, and the patient's age and Gleason grade were collated. Data collected were then analyzed using SPSS version 20. The data were collated using Microsoft excel 2016.

RESULTS

There were 352 patients with histologically confirmed prostate cancer with a mean age of 86.88years±9.75SD, ranging from 48years to 117years. The modal age range was the 60-69year age range. The commonest PCa grade is Gleason 8 {ISUP 4;27.8%(98)}, followed by Gleason 9{ISUP 5;(19.9%(70)} as shown in Figure 2. The Gleason score was associated with age, as indicated in Table 2 (p=0.001); however, Pearson's Correlation Coefficient did not show a statistically significant relationship (r=0.045; p=0.401). The high-risk Gleason's 8-10, ISUP 4&5, was the most frequent among all the age groups. It is also commonest among patients 80years and above. The low Gleason score cancers were commonest in the 40-49year age group.

Table 1: Showing the age characteristic of the patients.

	Age (years)
N	352
Mean	68.88

Median	69.00
Mode	70.00
Std. Deviation	9.75
Variance	95.25
Youngest age	48.00
Oldest	117.00

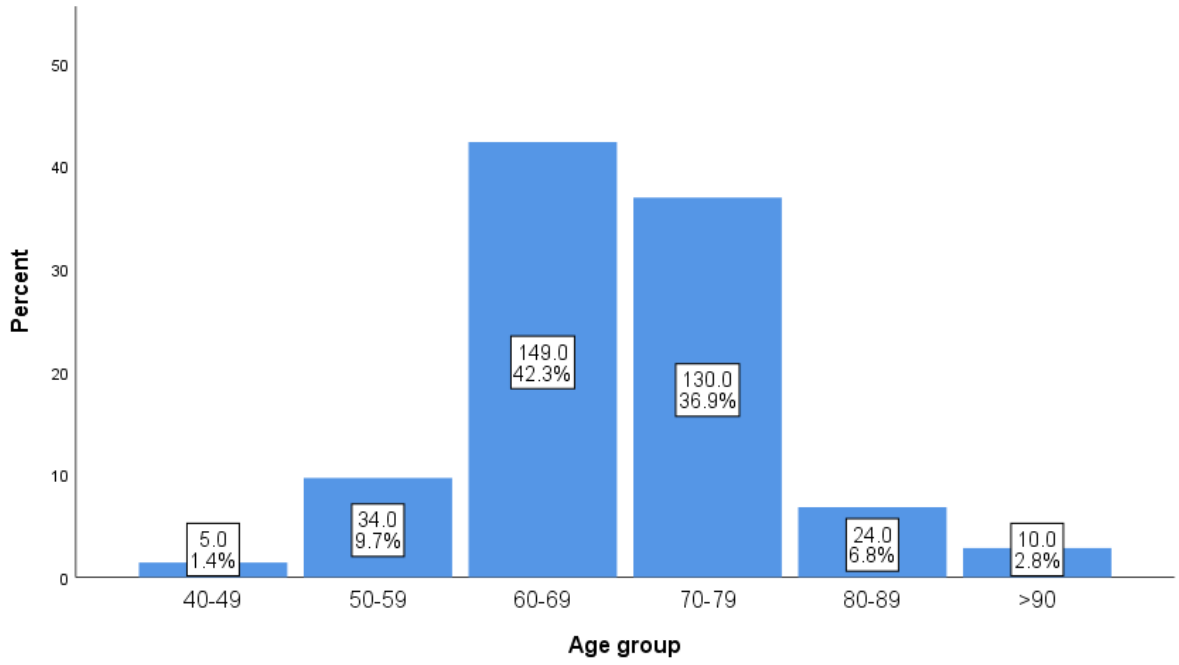

Figure 1: Showing the distribution of the patients' age groups

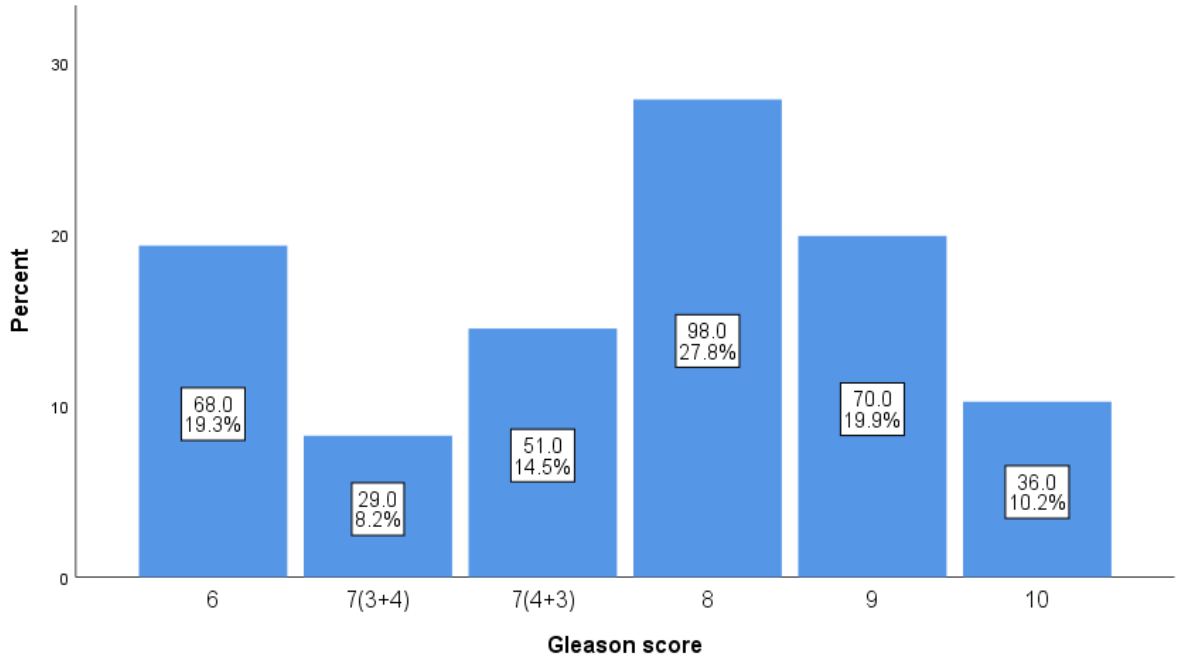

Figure 2: Showing the Gleason score distribution of the patients.

Table 2. The relationship between the age and the Gleason's score of the prostate cancer patients.

	Grading of Gleason score		
	Well differentiated (6)	Moderately differentiated (7)	Poorly differentiated (8-10)
	N (%)	N (%)	N (%)
Age group			
40-49	1 (20.0)	2 (40.0)	2 (40.0)
50-59	5 (14.7)	6 (17.6)	23 (67.6)
60-69	19 (12.8)	27 (18.1)	103 (69.1)
70-79	31 (23.8)	41 (31.5)	58 (44.6)
80-89	10 (41.7)	4 (16.7)	10 (41.7)
>90	2 (20.0)	0 (0.0)	8 (80.0)

*Chi square= 30.02, p-value= 0.001**

Table 3. Pearson correlation analysis between Age and Gleason score of the prostate cancer patients.

	Gleason score

N	352
P-value	0.401
R	0.045

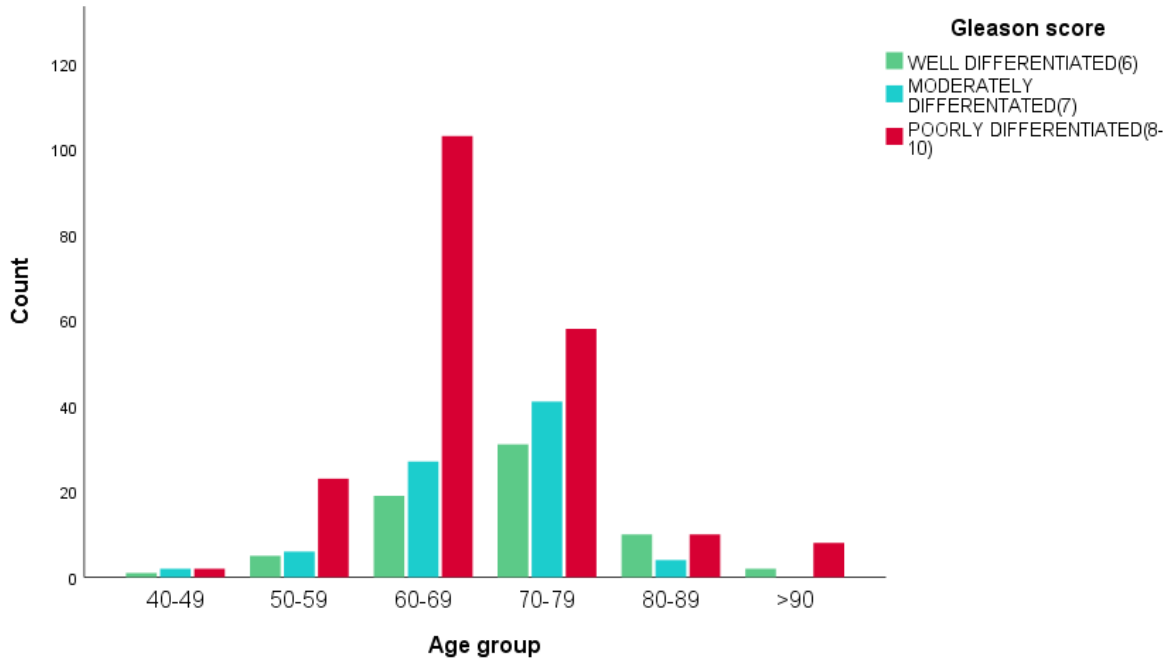

Figure 3. Gleason's score distribution among patient groups with prostate cancer.

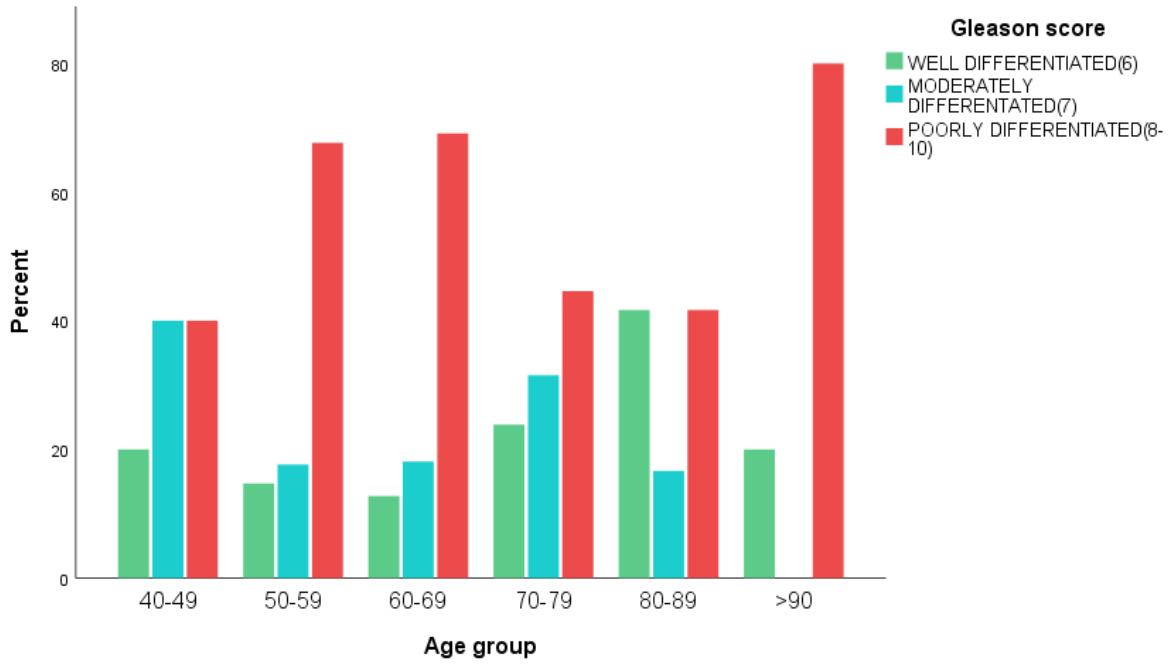

Figure 4. Percentage proportion of Gleason's score within the age groups.

Table 4. Linear regression analysis of Gleason score and age showing the model summary of the influence of age on the Gleason score

Variables	Unstandardized Coefficients	P-value	95.0% Confidence Interval for B		
	B		Lower Bound	Upper Bound	
(Constant)	8.224		7.266	9.181	$R = 0.045$
					$R^2 = 0.002$
Age	0.006	0.401	-0.020	0.008	Adjusted $R^2 = 0.001$
					$F(1,350) = 0.707$,
					$P = 0.401$

DISCUSSION

Age,[13] the black race and family history are well-established risk factors for prostate cancer.[13,14,15] In this study, the mean age was 68.88years, with the youngest 48years and the oldest 117years, as shown in Table 1. Previous studies carried out in Port Harcourt, Nigeria by Eke et al. [16] in 2002 and Ekeke et al. [17] in 2012 had a mean age of 71.6years and 69.9years, respectively. This reduced mean age at presentation over the years could be a consequence of raised awareness, and screening tends to lead to earlier diagnosis and presentation at an early stage of the disease. The mean age in Kano, Northern Nigeria, was 64.2years.[18] The mean age in Lagos (Western, Nigeria), Zaria and Benin were 68.48, 64.5 and 68years, respectively[18], while in the United Kingdom, the United States and China, it was 72.3years,[19,] 62.4years, [21]and 66.84years [21] respectively.

In developed countries with high prostate cancer awareness, most patients are diagnosed at a relatively younger age and earlier stage,22 unlike in sub-Saharan Africa, where the majority still present with an advanced stage of the disease.[5] A study in Japan found that the mean age of

patients with bone fracture secondary to prostate cancer was 77.3years.[23] The lead time bias between screen-detected cancers and the presence of symptoms may account for this difference. The lifetime risk of a 50-year-old developing latent prostate cancer is 40%; the risk is 9.5% for clinically apparent disease and 2.9% for death from prostate cancer.[24] The objective of treatment for early PCa is to achieve a cure. Treatment for localized prostate cancer includes brachytherapy, stereotactic radiotherapy, radical prostatectomy, active surveillance and watchful waiting.

In managing prostate cancer, differentiating clinically significant and potentially lethal cases from more indolent ones is crucial.[25] Gleason grade, serum PSA, and disease stage are important for treatment selection and prognostication purposes. In our study, the most common Gleason's grade was 8(ISUP-4) in 27% (98). The Gleason 9(ISUP-5) was followed with a frequency of 18.9% (70). The majority of the patient had high-risk aggressive carcinoma {57.95% (204)} with Gleason 8-10. If these patients were discovered at an early stage and fit for curative treatment.

Our study also found the poorly differentiated cancers were more abundant in all age groups except the 40-49year age group, were moderately differentiated (Gleason's 7, ISUP 2&3) and poorly differentiated carcinomas (Gleason's 8-10), (ISUP 4&5) were evenly distributed as shown in Table 2. and Figure 3&4. Several studies have shown that prostate cancer in black men may be more aggressive and likely to lead to mortality.[1] The high Gleason's score is associated with disease progression and benefits more from treatment.[1,5] Watchful waiting and active surveillance are indicated for low-grade Gleason's score of 6, ISUP 1, especially in older patients with life expectancy less than 10-15years. With younger patients, some circumspection is required because of the possibility of Gleason's score migration.

Our study revealed a weak correlation between age and Gleason's score, which was statistically significant. This entails that the higher the age, the worse the Gleason's grade and vice versa. As shown in Table 3, the model summary of the influence of age on the Gleason's score indicates a non-significant regression equation (F (1, 350) = 0.707, P = 0.401), with an adjusted R^2 of 0.002. This means that age explains 0.2% of the variance in the Gleason score. Gleason's score increased by 0.006% for every unit increase in age. Hence, age had no statistically significant impact on Gleason's score.

A retrospective study conducted by Shah et al. [12,] which included 5,100 subjects, discovered that septuagenarians with prostate cancer have a 61% frequency of GSS 7-10 prostate cancer. They concluded that screening for prostate cancer should be carried out even for men above 70years. Hunynh-Le et al. [11] carried out a cross-sectional study in 20,356 men with prostate cancer in Norway. Their ages, stage and Gleason score were collated. The percentages of men with Gleason 8 to 10 disease among men aged 55-59, 65-69, 75-79, and 85- 89 years were 16.5%, 23.4%, 37.2%, and 59.9%, respectively ($p < .001$). The older our patients, the higher the Gleason grade/ISUP grade observed among PCa patients. Shah and Huynh-Le et al. had more patients than our own. Shah had 5,100 patients, and Huynh-Le had 20,356 subjects. This high number of subjects could be a reason for the statistically significant relationship between age and Gleason score. Muralidhar et al. [26] studied 383,039 men diagnosed with prostate cancer from 2004-to 2011. They also observed that the prevalence of the high-risk Gleason score 8 to 10/ ISUP 4&5 PCa increased significantly. Because of the diversity and heterogenous presentation of PCa, the is a need for larger cohort studies to characterize further the relationship between age and Gleason's score among Africans.

Conclusion

Even though it was not statistically significant, there was an association between age and Gleason's score. Our study could not exclude the presence of a correlation. Gleason 8-10 or ISUP 4&5 PCa was associated with older patients. It is also commonest among patients 80years and above. More extensive studies are required to validate the relationship between age and Gleason's score in prostate cancer patients.

Reference

1. Rawla P. Epidemiology of prostate cancer. World journal of oncology. 2019 Apr;10(2):63.
2. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018;68(6):394–424.
3. Bosland MC, Nettey OS, Phillips AA, Anunobi CC, Akinloye O, Ekanem IO et al. Prevalence of prostate cancer at autopsy in Nigeria—A preliminary report. The Prostate. 2021 Jun;81(9):553-559.
4. Oluwole OP, Rafindadi AH, Shehu MS, Samaila MO. A ten-year study of prostate cancer specimens at Ahmadu Bello University Teaching Hospital (ABUTH), Zaria, Nigeria. African journal of urology. 2015;21(1):15-18.
5. Raphael JE, Abhulimen V. Retrospective Analysis of Complications from Prostate Cancer among Nigerians. Saudi J Med. 2022;7(2):99-104.
6. Chen N, Zhou Q. The evolving Gleason grading system. Chinese Journal of Cancer Research. 2016 Feb;28(1):58.
7. Baucknehtt M, Rebuzzi SE, Signori A, Donegani MI, Murianni V, Miceli A, Borea R, Raffa S, Damassi A, Ponzano M, Catalano F. The prognostic role of baseline

metabolic tumor burden and systemic inflammation biomarkers in metastatic castration-resistant prostate cancer patients treated with radium-223: a proof of concept study. Cancers. 2020 ;12(11):3213.

8. Stangl-Kremser J, Mari A, Suarez-Ibarrola R, D'Andrea D, Korn SM, Pones M, Kramer G, Karakiewicz P, Enikeev DV, Glybochko PV, Briganti A. Development of a prognostic model for survival time prediction in castration-resistant prostate cancer patients. InUrologic Oncology: Seminars and Original Investigations 2020 Jun 1 (Vol. 38, No. 6, pp. 600-e9). Elsevier.
9. Kreuz M, Otto DJ, Fuessel S, Blumert C, Bertram C, Bartsch S, Loeffler D, Puppel SH, Rade M, Buschmann T, Christ S. ProstaTrend—a multivariable prognostic RNA expression score for aggressive prostate cancer. European Urology. 2020 Sep 1;78(3):452-9.
10. Basiri A, Eshrati B, Zarehoroki A, Golshan S, Shakhssalim N, Khoshdel A, Kashi AH. Incidence, Gleason score and ethnicity pattern of prostate cancer in the multi-ethnicity country of Iran during 2008-2010. Urology Journal. 2020 May 4;17(6):602-6.
11. Huynh-Le MP, Myklebust TÅ, Feng CH, Karunamuni R, Johannesen TB, Dale AM, Andreassen OA, Seibert TM. Age dependence of modern clinical risk groups for localized prostate cancer—A population-based study. Cancer. 2020 Apr 15;126(8):1691-9.
12. Shah N, Ioffe V. Frequency of Gleason score 7 to 10 in 5100 elderly prostate cancer patients. Reviews in Urology. 2016;18(4):181.

13. Fapohunda A, Fakolade A, Omiye J, Afolaranmi O, Arowojolu O, Oyebamiji T, Nwogu C, Olawaiye A, Mutiu J. Cancer presentation patterns in Lagos, Nigeria: Experience from a private cancer center. Journal of public health in Africa. 2020 Dec 31;11(2).
14. Gandaglia G, Leni R, Bray F, Fleshner N, Freedland SJ, Kibel A, Stattin P, Van Poppel H, La Vecchia C. Epidemiology and prevention of prostate cancer. European urology oncology. 2021 Oct 26.
15. Oladoyinbo CA, Akinbule OO, Sobo AA, Bolajoko OO, Bassey IE, Prostate Cancer Transatlantic Consortium Members. Behavioural risk factors associated with prostate cancer: the prostate cancer transatlantic consortium (CaPTC) cohort study.
16. Eke NS, Sapira MK. Prostate cancer in Port Harcourt, Nigeria: features and outcome. Nigerian Journal of Surgical Research. 2002;4(1):34-44.
17. Ekeke ON, Amusan OE, Eke N. Management of prostate cancer in Port Harcourt, Nigeria: Changing patterns. Journal of the West African College of Surgeons. 2012 Jul;2(3):58.
18. Abdulkadir A, Alhaji SA, Sanusi HM. Pattern of urological cancers in Kano: North-western Nigeria. Sub-Saharan African Journal of Medicine. 2016 Oct 1;3(4):182.
19. Sangar VK, Ragavan N, Matanhelia SS, Watson MW, Blades RA. The economic consequences of prostate and bladder cancer in the UK. BJU international. 2005 Jan;95(1):59-63.
20.

21. Guo W, Zhang J, Zhou Y, Zhou C, Yang Y, Cong Z, Dong J, Yang D, Dai B, Wang MW. GPR160 is a potential biomarker associated with prostate cancer. Signal transduction and targeted therapy. 2021 Jun 25;6(1):1-3.
22. Shao YH, Demissie K, Shih W, Mehta AR, Stein MN, Roberts CB, DiPaola RS, Lu-Yao GL. Contemporary risk profile of prostate cancer in the United States. JNCI: Journal of the National Cancer Institute. 2009 Sep 16;101(18):1280-3.
23. Hatano T, Oishi Y, Furuta A, Iwamuro S, Tashiro K. Incidence of bone fracture in patients receiving luteinizing hormone-releasing hormone agonists for prostate cancer. BJU international. 2000 Sep;86(4):449-52.
24. Smith
25. Huynh-Le MP, Myklebust TÅ, Feng CH, Karunamuni R, Johannesen TB, Dale AM, Andreassen OA, Seibert TM. Age dependence of modern clinical risk groups for localized prostate cancer—A population-based study. Cancer. 2020 Apr 15;126(8):1691-9.
26. Muralidhar V, Ziehr DR, Mahal BA, Chen YW, Nezolosky MD, Viswanathan VB, Choueiri TK, Sweeney CJ, Trinh QD, Nguyen PL. Association between older age and increasing Gleason score. Clinical genitourinary cancer. 2015 Dec 1;13(6):525-30.