OPEN ACCESS
Saudi Journal of Biomedical Research
Abbreviated Key Title: Saudi J Biomed Res
ISSN 2518-3214 (Print) |ISSN 2518-3222 (Online)
Scholars Middle East Publishers, Dubai, United Arab Emirates
Journal homepage: https://saudijournals.com

Original Research Article

Hypertension and Type 2 Diabetes Mellitus as Risk Factors for Prostate Cancer Patients in Southern Nigerians

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DOI: 10.36348/sjbr.2022.v07i02.006 | **Received:** 08.01.2022 | **Accepted:** 15.02.2022 | **Published:** 28.02.2022

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Abstract

Background: Prostate cancer (PCa) is one of the most commonly diagnosed cancers in Nigerian men and worldwide. Some comorbidities, such as hypertension, diabetes mellitus, and cardiovascular diseases, have been investigated as potential risks for developing PCa. Hypertension and Type2 diabetes mellitus (DM) are common in the middle-aged and elderly and could be a problem during treatment. ***Aims and Objectives*****:** This study highlights prostate cancer-associated comorbidities and describes the relationship between Type 2 Diabetes Mellitus and hypertension with prostate cancer among southern Nigerian men. ***Materials and Methods:*** This was a 10-year retrospective study on all patients with histologically confirmed prostate cancer at the University of Port Harcourt and two private Urology Hospitals. The case records of the patients were retrieved, and their age, prostate-specific antigen levels, Gleason grade, comorbidities, and treatment received were analyzed. Patients with incomplete data were excluded from the study. The data were collated using Microsoft excel 2020 and analyzed using SPSS Version 20. ***Results:*** There were a hundred and fifty-two patients with histologically confirmed PCa. Sixty-four were reported with Gleason scores. Fifty-four (35.5%) of the patients had no associated comorbidity. Hypertension was the commonest associated comorbidity observed in sixty-one (40.1%) patients, followed by Type 2 Diabetes Mellitus in nineteen (12.5%). The poorly differentiated cancers were commonest among the patients with hypertension, Type 2 DM, and patients with both DM and hypertension. There was no association between Type 2 DM, hypertension, and Gleason's score. ***Conclusion:*** Diabetes and hypertension are the most frequent comorbidities associated with Prostate cancer in our patients. There was no statistically significant association between Type 2 DM and hypertension with prostate cancer and Gleason's score.

Keywords: Diabetes Mellitus, Gleason's score, Hypertension, prostate cancer

INTRODUCTION

Prostate cancer (PCa) is one of the most commonly diagnosed cancers in Nigerians [1] and all men worldwide [1,2]. Some comorbidities, such as hypertension, diabetes mellitus, and cardiovascular diseases, have been investigated as potential risks for developing PCa [3].

Hypertension and Type 2 diabetes mellitus (DM) are common in the middle-aged and elderly and could be a conundrum during treatment. Some researchers have suspected these comorbidities could even play a potential aetiological role. The result of several metanalyses have been equivocal, with some studies even suggesting Type 2 diabetes is associated with a low risk for PCa [4]. Patients with significant comorbidities who undergo aggressive treatment may not enjoy the survival advantage but suffer post-treatment complications [5]. A study in Port Harcourt 10 years ago by Sapira *et al.* found that 26% of prostate cancer patients had no comorbidity. At the same time, diabetes mellitus was more prevalent among prostate cancer patients than in the general population.

In Africa, presentation is usually late [7] with advanced disease, and these patients are more likely to receive androgen deprivation therapy. Androgen deprivation has associated complications such as vasomotor complications (hot flushes), sexual

dysfunction, gynecomastia, osteoporosis, metabolic syndrome, depression, neurocognitive deficits, and thromboembolic disease [7].

Many patients with prostate cancer ab initio had DM and hypertension [4, 5]. These comorbidities could affect treatment choices even in early diseases and are important considerations when making treatment decisions [4, 5]. This study highlights prostate cancer-associated comorbidities and describes the relationship between Type 2 Diabetes Mellitus and hypertension with prostate cancer among southern Nigerian men.

MATERIALS AND METHODS

This is a 10year retrospective study carried out from January 2012 to December 2021. All patients with histologically confirmed prostate cancer at the University of Port Harcourt and two other private urology hospitals form the study population.

The case records of the patients were retrieved, and their age, comorbidities, prostate-specific antigen levels, histology reports, and treatment received were analyzed. Patients with incomplete data were excluded from the study. The data were collated using Microsoft excel 2020. The data collected were then analyzed using SPSS version 20.

RESULTS

There were a hundred and fifty-two patients with histologically confirmed prostate cancer. Sixty-four were reported with a known Gleason score. Fifty-four (35.5%) of the patients had no associated comorbidity. Hypertension was the commonest associated comorbidity observed in sixty-one (40.1%) patients, followed by Type 2 Diabetes Mellitus in nineteen (12.5%). The poorly differentiated cancers were commonest among the patients with hypertension, Type 2 DM, and the patients with both hypertension and Type 2 DM. There was no association between Type 2 DM and hypertension, with prostate cancer and Gleason's score.

Table 1: Age distribution of prostate cancer patients

Age group	Frequency	%
40-49	3	2.0
50-59	22	14.5
60-69	54	35.5
70-79	54	35.5
80-89	15	9.9
>90	4	2.6
Total	152	100.0

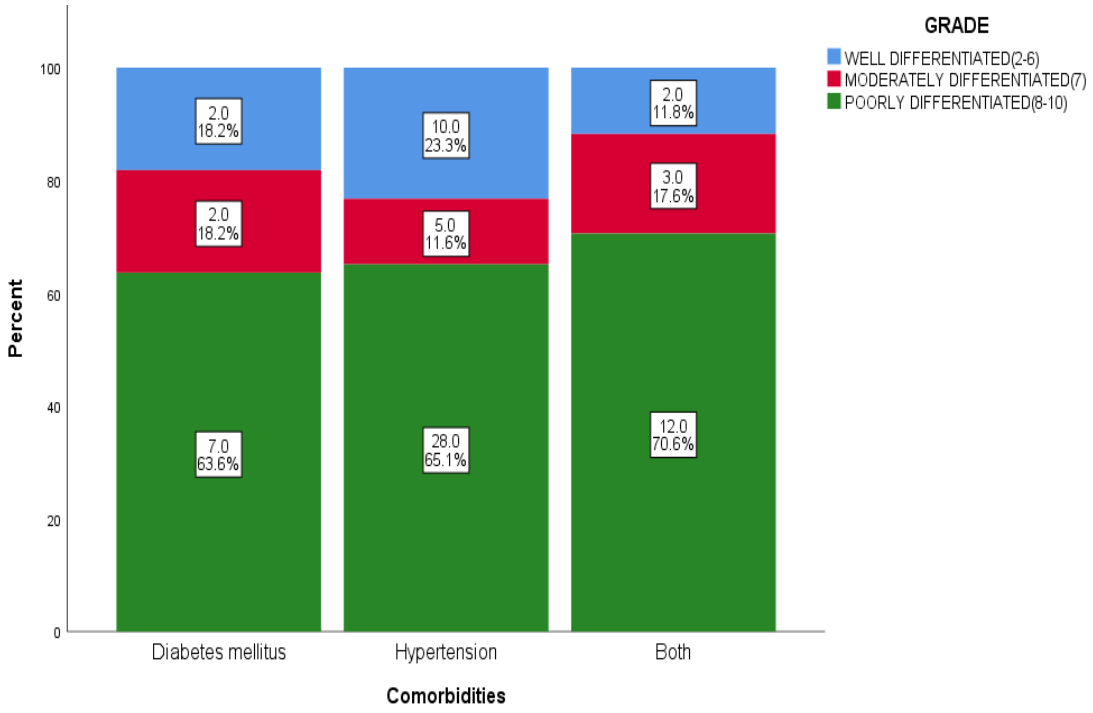

Figure 1: Distribution of Hypertension and Type 1 Diabetes and hypertension among prostate cancer patients

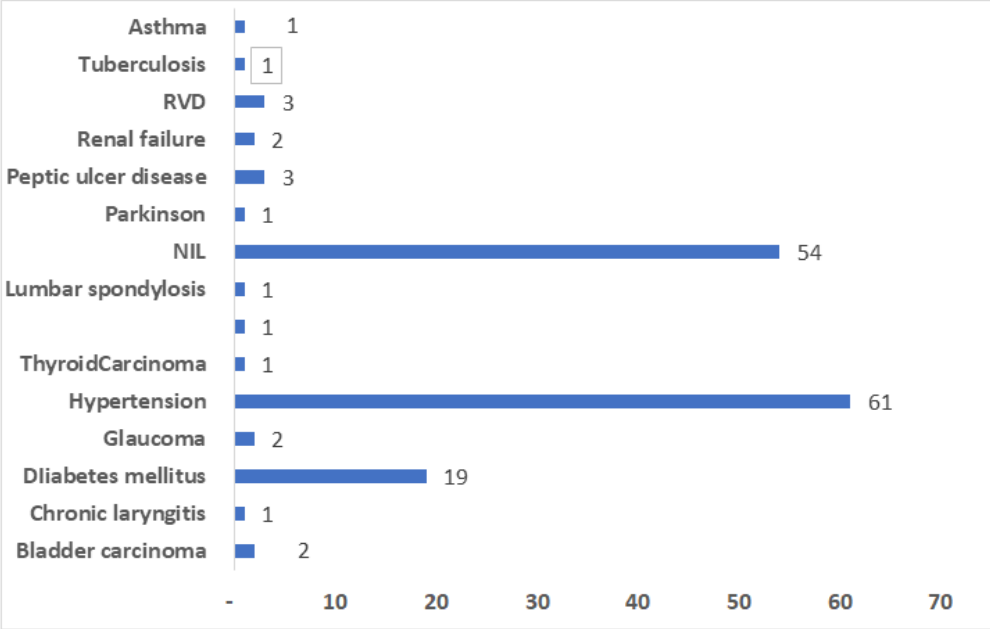

Figure 2: Associated comorbidities with prostate cancer

Table 2: Relationship between Gleason's Score with diabetes mellitus and hypertension among patients, including those with unknown Gleason's score

	Grade							
	Well-differentiated (2-6)		Moderately differentiated (7)		Poorly differentiated (8-10)		Unknown	
	N	(%)	N	(%)	N	(%)	N	(%)
Diabetes mellitus	2	(16.7)	2	(16.7)	7	(58.3)	1	(8.3)
Hypertension	10	(18.9)	5	(9.4)	28	(52.8)	10	(18.9)
Both	2	(9.5)	3	(14.3)	12	(57.1)	4	(19.0)
Total	14	(16.3)	10	(11.6)	47	(54.7)	15	(17.4)

Chi-square =2.16, p- value =0.904

Table 3: Relationship between Gleason's Score with diabetes mellitus and hypertension among patients with known Gleason's score

	Gleason's Grade					
	Well-differentiated (2-6)		Moderately differentiated (7)		Poorly differentiated (8-10)	
	N	(%)	N	(%)	N	(%)
Diabetes mellitus	2	(18.2)	2	(18.2)	7	(63.6)
Hypertension	10	(23.3)	5	(11.6)	28	(65.1)
Both	2	(11.8)	3	(17.6)	12	(70.6)
Total	14	(19.7)	10	(14.1)	47	(66.2)

Chi-square =1.36, p-value =0.850

DISCUSSION

The search for risk factors for prostate cancer is a subject of intense research interest among clinicians and scientists worldwide. There is a focus on the potential causal role that some comorbidities associated with prostate cancers could play in the carcinogenesis process. While risk factors such as advancing age, African American race, and a family history of prostate cancer have been well studied, comorbidities associated with PCa such as hypertension, obesity, and diabetes are still under a smokescreen [7].

In our study, hypertension was the most observed comorbidity seen in sixty-one (40.1%) of the patients. The prevalence of hypertension increases with age, and a study in the United States indicated that hypertension is commoner among African American men (62%) compared to white men (50%) among the 50-to-79-year age group population [8].

Wallner *et al*. [9] reported a 15-year experience of 2445 white men aged 40 to 79 years and found that hypertensive men were 1.5 times more likely to develop prostate cancer than were non-hypertensive men. This

finding was supported by a large Norwegian study [10]. A metanalysis by Esposito and colleagues [11] and Liang *et al*., [12] both drew similar conclusions of an increased association of hypertension with PCa.

The mechanism for the increased risk is not clear, but it has been observed that male rats have higher blood pressures than females [13]. Castration of the male rat leads to a fall in their blood pressure. Also, the addition of testosterone to ovariectomized female rats elevates their blood pressure [13]. Add to this, androgen could affect sodium reabsorption, as androgen receptors are located in the proximal convoluted tubules of the nephrons. Male rats are known to have higher renin-angiotensin activity compared to females [13]. Miller and colleagues [14] have documented more elevated aldosterone and higher blood pressure in men than women. Schunkert *et a*., [15] found a positive correlation between dehydroepiandrosterone sulfate, aldosterone levels, and blood pressure in hypertensive men. All the findings above suggest that hypertension could increase the risk of prostate cancer through the sympathetic nervous system activity that can lead to androgen-mediated stimulation of prostate cancer cell growth [16].

Our study did not find any statistically significant association between hypertension and the risk of PCa, even though it was the commonest comorbidity associated with the disease. More extensive randomized control trials would be required to evaluate any association of hypertension with PCa.

On the other hand, type 2 diabetes mellitus has been associated with an increased risk of several cancers. These include the pancreas, liver, breast, colorectal, urinary tract, and female reproductive organs [17, 18]. The findings with prostate cancer have been inconsistent. Nnyenwe *et l*., [19] found that the standardized prevalence of diabetes mellitus was 7.,9% and Sapira *et al.* [20] noted in an earlier 10year study, a slightly higher prevalence of diabetes among prostate cancer patients [20, 21]. A metanalysis by Bonovas *et l.,* [22] and Kasper *et a.,* [23] reported a statistically significant decrease in the risk of prostate cancer by 9% and 16%, respectively. More recent metanalysis have been inconclusive, with many suggesting a decreased risk [18, 24]; others no risk [18, 25-29], and still some found no probable association [30, 31] with prostate cancer.

The pathophysiological basis for the observed lower risk of Type 2 diabetes is also unclear. The observation of a reduced risk of PCa in diabetes may have a genetic explanation.

Meyer *et al.* [21] found a significant association between four of the thirteen Type 2 diabetes mellitus single-nucleotide polymorphisms with prostate cancer risk [21]. Another pathway that could account for the reduced risk of PCa among diabetes mellitus patient includes the change in serum level of insulin and testosterone. In their study, Pierce et al.. [33] observed that patients with increased genetic susceptibility to Type 2 diabetes had a decreased risk of prostate cancer. Insulin is a growth factor for prostatic epithelium *in vitro* [34]. It increases the replication of rat prostate cancer cell lines *in vitro* [35] and has been associated with a higher incidence and recurrent prostate cancer [36]. The insulin-resistant state in Type 2 diabetic men leads to an initially raised serum insulin level. Insulin levels may decline, [23] with cancer cell growth-inhibitory effects [37]. This is further corroborated by the findings by some researchers that the longer patients have diabetes, the less the risk of prostate cancer [23, 24, 37-40].

In addition, both animal and human studies have found lower serum testosterone in diabetes mellitus with some degree of hypogonadism [17]. High testosterone levels may be a risk factor for prostate cancer [37]. Testosterone and the more active metabolite dihydrotestosterone bind to the androgen receptor, forming a complex that binds to DNA and stimulates transcription, increasing the proliferation of normal and malignant prostate cells [41-43]. We also did not find any association between diabetes mellitus and the aggressiveness of PCa assessed by Gleason's score.

Finally, many of the patients had no associated comorbidities in our study. Different researchers have observed varying "no comorbidity rates," from 12% in geriatric patients [44] with prostate cancer to up to 79% in younger patients with localized prostate cancers [45]. The older the study population, the more likely there were associated comorbidities. In our study, fifty-four (35.5%) had no associated comorbidity. In the study by Sapira *et al*. [20] in Port Harcourt, fifty patients (26.6%) had no significant comorbidities. This could result from increased PSA testing and diagnosis at a younger age. There is a need to carry out more randomized controlled studies to effectively evaluate the risk factors for prostate cancer, especially among Africans.

CONCLUSION

Diabetes mellitus and hypertension are the commonest comorbidities associated with Prostate cancer. No statistically significant association was found between Type 2 DM and or hypertension with prostate cancer and Gleason score.

Source of funding: None

Conflict of interest: None

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