World Journal of Advanced Research and Reviews, 2020, 07(03), 001–006

World Journal of Advanced Research and Reviews

e-ISSN: 2581-9615, Cross Ref DOI: 10.30574/wjarr

Journal homepage: https://www.wjarr.com

(RESEARCH ARTICLE)

Clinicopathological presentation of patients with prostate cancer at Muhimbili National Hospital in Dar es Salaam, Tanzania

Nashivai Elias Kivuyo [1], Obadia Venance Nyongole [1,*], Fransia Arda Mushi [1], Larry Onyango Akoko [1], Mucho Michael Mizinduko [2], Gabriel Francis Mtaturu [3], Ally Hamis Mwanga [1] ,Kimu Marko Njiku [3]

[1] *Department of Surgery, School of Medicine, Muhimbili University of Health and Allied Sciences, Dar es Salaam, Tanzania.*
[2] *Department of Epidemiology and Biostatistics, Muhimbili University of Health and Allied Sciences, Dar es Salaam, Tanzania.*
[3] *Department of Urology, Muhimbili National Hospital, Dar es Salaam, Tanzania.*

Publication history**:** Received on 21 August 2020; revised on 01 September 2020; accepted on 03 September 2020

Article DOI: https://doi.org/10.30574/wjarr.2020.7.3.0320

Abstract

Prostate cancer (PC) is the most common type of cancer in men and is of major public health importance worldwide. This study aimed to establish the clinicopathological presentation and its impression in disease progression like to Castrate Resistant Prostate Cancer (CRPC) of patients treated for Prostate Cancer at Muhimbili National Hospital (MNH) in Dar es Salaam.This was a retrospective descriptive hospital based study at Muhimbili National Hospital. Patients who were treated for prostate cancer were identified. Information regarding primary prostatic cancer treatment, clinical disease progression symptoms, and age of the patients were collected. A total of 293 case notes were reviewed of which 189 patients who were treated for prostatic carcinoma with androgen deprivation, 96(50.8%) met the criteria for the diagnoses of Castrate Resistant Prostate Cancer (CRPC) and their mean age was 71.23±4.2. About half of our patients 146(49.7%) presented with history of urine retention necessitating urethral catheterization but also patients had hard, nodulated, grade three prostate though 48.2% had missing documentation of Digital Rectal Examination (DRE) findings. Most of the patients had a poorly differentiated histology with PSA over 100ng/l. Almost all patients had a clinical progression signifying a metastatic disease. Majority of patients presented with symptomatic prostate cancer contrary to the natural history of prostate cancer at its early stage. Urine retention and hard nodulated grade three prostate were the commonest clinical presentation whereas poorly differentiated carcinoma of the prostate was a common pathological finding among patients with prostate cancer MNH in Dar es Salaam, Tanzania.

Keywords: Clinicopathological; Androgen deprivation therapy; Prostate cancer; Castrate Resistant Prostate cancer

1. Introduction

Prostate cancer (PC) is now the second most frequent cancer and fifth cause of cancer related mortality globally by contributing to 1.3 million cases and 359,000 deaths [1]. Hence PC is of significant public health concern to health practitioners and policy makers across the globe [2] Similarly, the outcome of PC among patients with advanced disease has been improving owing to better understanding of its biology and improvements in therapeutics [3].In Tanzania, prostate cancer is the most prevalent cancer among male and only second to cervical cancer in prevalence nationwide [4].

Despite of awareness of the public about prostate cancer, still a number of patients at MNH present with advanced prostate cancer [5]. Patients with advanced prostate cancer are initially treated with either surgical or medical Androgen Deprivation Therapy (ADT) [3]. In spite of good initial response to ADT as evidenced by dropping in the levels of Prostate Specific Antigen (PSA) after treatment, some patients will show features of disease progression after castration duration of 18 – 24 months [6-7].

* Corresponding author: Obadia Venance Nyongole

The mechanism of transition from castration-sensitive prostate cancer to castration resistant disease is still not fully understood [8]. It has been observed recently that androgen receptors remain active and continues to drive PC progression in spite of having castrate levels of testosterone [9, 10]. The existence of other biologic pathways independent of androgen signaling has also been reported to lead to CRPC (8). In the light of this, new strategies have been developed for this sub set of PC patients that progress to CRPC [11]. For this reason, practicing PC physicians need to understand the magnitude of patients who develop CRPC in their practice.

The Prostate cancer Working Group (PCWG) defined CRPC as a continuum on the basis of whether metastases are detectable (clinically or by imaging) and whether serum testosterone is in the castrate range because of a surgical orchiectomy or medical therapy [2]. CRPC carries worse prognosis, especially when associated with metastatic disease [9]. Over the past 10 years CRPC has been widely studied indicating its global burden especially related to the cost of caring for patients [2]. In Tanzania little is documented on PC in general and the burden of CRPC is unknown. This study aimed at detailing the clinicopathological presentation of Prostate Cancer and its impression on disease progression of CRPC at MNH in Dar es Salaam.

2. Methodology

A retrospective hospital based descriptive study, involving chart review, was carried out at Muhimbili National Hospital between 2018 and 2019. Muhimbili National Hospital receives patients with prostate cancer at various stages from the whole country. The hospital has capacity to diagnose and treat prostate cancer, and collaborates with a sister institution (Ocean road cancer Institute) specializing in cancer care. PC is diagnosed by a triple assessment including digital rectal examination (DRE), Serum PSA and histological evaluation of a trucut biopsy. Records for both histology and case notes are kept in the pathology registry and records department. Ethical approval was obtained from Muhimbili University of Health and Allied Sciences Institutional Review Board (MUHAS IRB) and permission to access patients records from MNH education, research and consultancy bureau.

The study included patients who had a diagnosis of PC and treated by androgen deprivation therapy (medical or surgical). Surgical androgen deprivation was by bilateral orchiectomy while medical androgen deprivation was by Subcutaneous injection of Goserelin 3.6mg as a start dose with bicalutamide 50mg once daily for 2 weeks. The patient then continues with Goserelin monotherapy once every month [18]. Testosterone levels were checked at three months to establish attainment of castrate levels, ≥0.7nmol/L. Patients with castrate resistance were considered at three months if: PSA levels remained high or continued to rise; clinical or radiological features of disease progression or onset of new symptoms related to PC. Patients who did not have testosterone levels and those who did not achieve castrate levels of testosterone were excluded from the study.

We identified medical registration numbers of patients with histological diagnosis of PC from the hospital central pathology laboratory registry. Then traced their case notes from the hospitals' records department. A structured data collection tool was used by a trained data extractor, and the following variables were extracted: patients' age, clinical presentation at follow up, Gleason score, investigations done such as serum PSA level (at baseline and at three months), abdominal-pelvic ultrasound and lumbo-sacral xrays, any co-morbidities such as diabetes mellitus and hypertension and their clinical presentation.

The collected data was checked for completeness and entered into Statistical Package for Social Scientists (SPSS) version 20 for analysis. Continuous variables were summarized as means with standard deviations while categorical variables were summarized as frequency with percentages. Bar charts and tables have been sued to summarize results as presented in the subsequent section.

3. Results

Figure 1 below represents the flow chart of patient's recruitment into the study. A total of 293 patients were treated for PC by androgen deprivation therapy (surgical and/or medical) at MNH between 2018/2019 of which 95 patients did not have testosterone levels hence were excluded. Of the remaining 198 patients with testosterone levels documented, 189 had reached castrate levels of which 96(50.8%) met the criteria for the diagnoses of CRPC and hence included in the study. The mean age of CRPC patients was 71.23±4.2 (63 – 94) years.

3.1. Recruitment of patients

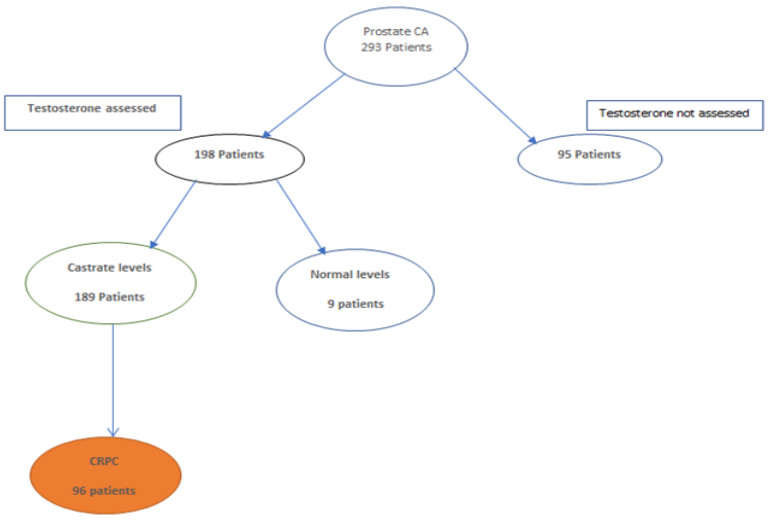

Figure 1 Is a Flow chart showing how 293 patients with PC were recruited into the study at MNH in 2018/2019.

All patients with CRPC had histology results of prostate adenocarcinoma. The most common reported Gleason score was 9 at 40(41%), which signify poorly differentiated prostate cancer. All patients had a baseline PSA of more than 50ng/mL and majority (49%) of which had a baseline PSA of more than 100ng/mL. The most common imaging done in these patients was Abdominal Pelvic Ultrasound with only 13.5% having a spine MRI. Most patients, who developed CRPC, were primarily treated by bilateral Sub capsular orchiectomy. [Table 1]

Table 1 Baseline characteristics, investigations and primary treatment of patients with prostate cancer

Variable	**Proportion, (%)**
Gleason score	
7	95 (32.3)
8	73(25)
9	122 (41.6)
10	3 (1.1)
PSA (ng/ml)	
50 – 75	45(15.6)
75 – 100	104 (35.4)
> 100	144 (49)
Radiological investigations	
Ultrasonography of AP	62 (64.6)
Lumbar-sacral X-ray	49 (51)
Chest x-ray	32 (33.3)
MR Imaging of spine	13 (13.5)
Treatment modality	
Bilateral Sub capsular orchiectomy	53 (55.2)
Medical Androgen Deprivation	17 (17.7)
Both	26 (27.1)

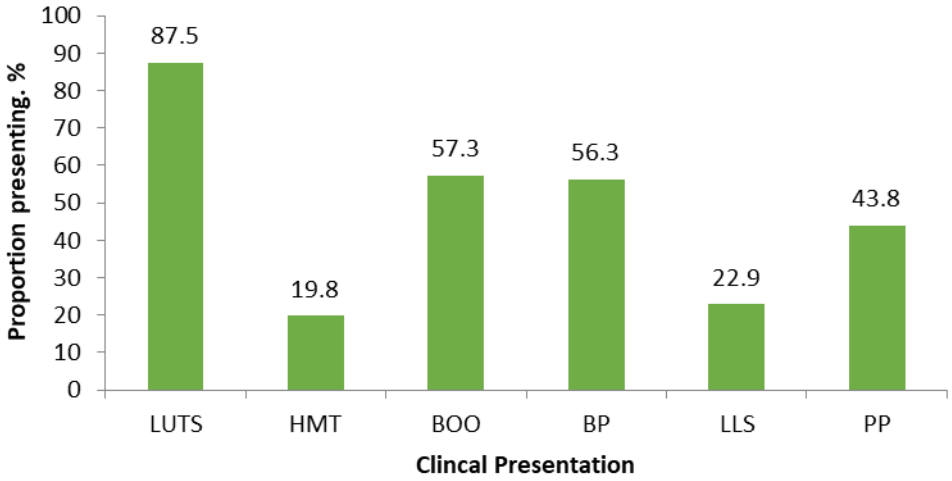

Figure 2 Clinical Presentation

Key: LUTS – Lower urinary Tract Symptoms; HMT – Hematuria; BOO – Urinary Bladder Outlet obstruction; BP – back pain; LLS – Lower Limb swelling; PP – paraplegia.

Figure 2 above represents clinical presentation among patients who developed CRPC of which Lower urinary tract symptoms was the most frequent symptom reported by 87.5% of the patients, followed by urinary bladder outlet obstruction and back pain in 57.3% and 56.3% respectively. 43.8% presented with paraplegia.

4. Discussion

Prostate cancer including CRPC is still a dilemma in low income countries given the morbidity and the cost needed to manage such patients [12]. Patients in sub-Saharan Africa have been shown to have poor access to active treatment of their CRPC [12]. It is expected that Tanzanian men, like other African men, will present with advanced stages and incurable forms of PC [13-15]. This late stage at presentation is probably reflects a weak health system in our country. It has been noted, just like in our study, that African men with advanced PC initially respond to castration before developing CRPC [16]. We report a high magnitude of CRPC with half of patients treated for advanced PC by androgen deprivation developing CRPC. This is similar to what others have reported [12]. It is important to identify patients with CRPC since there are targeted therapeutics which can improve both survival and quality of life [17-18]. While healthcare systems, in similar settings, cannot cope with screening for PC [4], it is important to detect patients with PC that progress to CRPC and these can be enrolled in clinical trials.

Androgen deprivation by bilateral orchiectomy is commonly practiced in our setting; this would imply that it is acceptable though we lack such evidence on its acceptability by patients. This has proven to be a very effective androgen deprivation strategy in settings with scarce resources [16], hence it can be advocated for widespread use in our settings along with early diagnosis strategies. There is realization that intracrine/paracrine androgen production plays a significant role in the resistance of PC cells to testosterone-suppression therapy [8]. However, there is need to study the effectiveness of castration strategy between medical and surgical options in our settings. At MNH, ~~a~~ public hospital, few patients as we saw in this study, can afford medical androgen deprivation. The most important thing is to ensure that castrate levels have been achieved by any of the strategies by checking for testosterone levels, typically at or less than 0.7nmol/L [18]. This should be done for all patients who demonstrate disease progression (new symptoms or progression of pre-existing symptoms or rising PSA levels) before declaring CRPC [19-20, 22]. Therefore, since a diagnosis of CRPC cannot be reliably made before realization of attainment of castrate levels of testosterone [18], it should therefore be a practice to have all patients check testosterone levels during routine follow up visits in Urology clinics.

Even though this study did not assess the treatment strategies offered, it should be noted that algorithms for such patients have been developed and used extensively in other settings [12, 18]. We reviewed the national cancer treatment guideline and found it lacking clear strategies and guidance on this matter. It is also important to do cost benefit analysis of what it would take to aggressively treat CRPC within our country's health care system. We therefore propose to review the current treatment strategies in patients with advanced PC and propose way forward.

Management strategies for patients with CRPC differ according to the type of presentation: biochemical without evidence of disease versus metastatic presentation [12]. Most of our patients had progression with evidence of disease hence fall in the metastatic CRPC which requires additional management strategies including: secondary hormonal manipulation, chemotherapy, radiotherapy and immunotherapy [18]. Patients need to be assigned one of the six classes for better treatment outcomes as outlined by America Urology Association [20-22]. It is important to properly investigate patients with suspected CRPC to properly assign a treatment outline [18, 22]. This study also shows the lack of uniformity in working up prostate patients and further studies are needed to establish the cause for this.

While the findings from this study have exposed the magnitude of CRPC among our patients, it has the retrospective set back of not being able to capture all the related variables needed to discuss this topic in details. There is a need to establish a PC working group at MNH and later roll it out to the entire country to standardize management strategies for PC patients since more than half will develop CRPC and bring challenges in care. Outcome data and their predictors are also lacking and not routinely collected.

5. Conclusion

Majority of patients presented with symptomatic prostate cancer contrary to the natural history of prostate cancer at its early stage. CRPC is common among patients treated by androgen deprivation therapy at MNH where by it was diagnosed in more than half of the patients. Disease progression was the main presenting symptom among patients with CRPC. Furthermore, most patients had persistently high or rising levels of PSA at initial diagnosis. More studies are needed to understand the predictors of CRPC and related treatment strategies.

Compliance with ethical standards

Acknowledgments

Thanks to MUHAS for funding our study through SIDA small grant

Disclosure of conflict of interest

The authors declare no competing interests.

Statement of informed consent

Permission to review case notes was obtained from MNH hospital management after submitting our Ethical clearance Approval from Muhimbili University of Health Allied Sciences number DA.282/298/01.C/

References

[1] Bray F, Ferlay J, Soerjomataram I, Siegel RI, 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: 394–424.

[2] Scher HI, Halabi S, Tannock I, Morris M, Sternberg C, Carducci MA et al. Design and end points of clinical trials for patients with progressive prostate cancer and castrate levels of testosterone: recommendations of the Prostate Cancer Clinical Trials Working Group. J Clin Oncol. 2008; 26: 1148–59.

[3] Brawley OW. Trends in prostate cancer in the United States. J Natl Cancer Inst Monogr. 2012; 152-156.

[4] Global Cancer Observatory. United Republic of Tanzania. GLOBOCAN 2018 report.

[5] Manyahi JP, Musau P, Mteta AK. (2009). Diagnostic values of digital rectal examination, prostate specific antigen and trans-rectal ultrasound in men with prostatism. East African Medical Journal.

[6] Rufus WO, Emanuel AJ, Kehinde HT, Moses AO, Charles OA. Clinico-pathological Correlation of Digital Rectal Examination Findings Amongs Nigerian Men with Prostatic Diseases: A prospective study of. 236.

[7] Huang Y, Jiang X, Liang X, Jiang G. Molecular and cellular mechanisms of castration resistant prostate cancer. Oncol Lett. 2018 May; 15(5): 6063-6076.

[8] Mostaghel EA, Page ST, Lin DW, Fazli L, Coleman IM, True LD et al. Intraprostatic androgens and androgen-regulated gene expression persist after testosterone suppression: therapeutic implications for castration-resistant prostate cancer. Cancer Res. 2007; 67: 5033–41.

[9] Montgomery RB, Mostaghel EA, Vessella R et al. Maintenance of intratumoral androgens in metastatic prostate cancer: a mechanism for castration-resistant tumor growth. Cancer Res. 2008; 68: 4447.

[10] Mohler JL, Titus MA, Bai S, Kennerley BJ, Lih FB, Tomer KB ,Wilson EM. Activation of the androgen receptor by intratumoral bioconversion of androstanediol to dihydrotestosterone in prostate cancer. Cancer Res. 2011; 71: 1486.

[11] Sartor AO. Progression of metastatic castrate-resistant prostate cancer: impact of therapeutic intervention in the post-docetaxel space. J Hematol Oncol. 2011 Apr 23; 4:18.

[12] Bello JO. Natural history of castration-resistant prostate cancer in sub-Saharan African black men: a single-center study of Nigerian men. Ecancermedical science. 2018; 12: 797.

[13] Odedina FT, Akinremi TO, Chinegwundoh F, Roberts R, Yu D, Reams R et al. Prostate cancer disparities in black men of African descent: a comparative literature review of prostate cancer burden among Black men in the United States, Caribbean, United Kingdom, and West Africa. Infect Agent Cancer. 2009; 4(1): S2.

[14] Tindall EA, Monare LR, Petersen DC, Smit van Zyl S, Hardie R, Segone AM et al. Clinical presentation of prostate cancer in black South Africans. Prostate. 2014; 74: 880–891.

[15] McGinley KF, Tay KJ, Moul JW. Prostate cancer in men of African origin. Nat Rev Urol. 2016; 13: 99–107.

[16] Petrylak DP. Current state of castration-resistant prostate cancer. Am J Manag Care. 2013; 19: S358–S365.

[17] Chi KN, Bjartell A, Dearnaley D, Saad F, Fritz H, Schröder FH, Sternberg C et al. Castration-resistant prostate cancer: from new pathophysiology to new treatment targets. Eur Urol. 2009; 56: 594–605.

[18] Lowrance WT, Roth BJ, Kirkby E, Murad MH, Michael S. Cookson. Castration-Resistant Prostate Cancer: AUA Guideline Amendment 2015. The Jouranl of Urology. May 2016; 195: 1444-52.

[19] Tannock IF, de Wit R, Berry WR, Horti J, Pluzanska A, Chi KN et al. Docetaxel plus prednisone or mitoxantrone plus prednisone for advanced prostate cancer. N Engl J Med. 2004; 351: 1502.

[20] Petrylak DP, Tangen CM, Hussain MHA, Lara PN Jr, Jones JA, Taplin ME et al. Docetaxel and estramustine compared with mitoxantrone and prednisone for advanced refractory prostate cancer. N Engl J Med. 2004; 351: 1513.

[21] Baade PD, Youlden DR, Krnjacki LJ. (2009). International epidemiology of prostate cancer: Geographical distribution and secular trends. Molecular Nutrition and Food Research.

[22] International Agency for Research on Cancer. (2016). Prostate Cancer Estimated Incidence, Mortality and Prevalence Worldwide in 2012. World Health Organization.