Retrospective review of clinical and pathological pattern of prostatic diseases: a reminder to clinicians on an increased clinical vigilance, an experience from central, Tanzania.

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Abstract

Introduction: Prostatic diseases are a very common in men over 40 years of age and pose a significant risk in terms of morbidity and mortality. Globally, benign prostatic hyperplasia (BPH), prostatic cancer and prostatitis are the most common conditions mainly presenting with lower urinary symptoms or symptoms related to complications of urinary bladder obstruction. Despite the relatively high prevalence of prostatic diseases, there is paucity of literature on in most developing countries, East Africa inclusive. The aim of this study was therefore to conduct a retrospective review of all prostatic biopsies submitted to private histopathology laboratory in Central, Tanzania in order to understand the clinical and histological pattern of the diseases.

Methodology: This was a retrospective laboratory-based descriptive study. The study involved review of the available prostatic biopsy database for a period of one year, from February 2014 to February 2015.

Results: Benign prostatic hyperplasia (61.6%) and prostate cancer (28.3%) are the most prevalent clinical diagnoses. They often presented with lower urinary tract symptoms (45.5%) and urinary retention (41.5%), although a significant proportion of cases were missing clinical information (10.1%). Histologically, BPH was the most common prostatic disease (60%), followed by prostate cancer

(24.1%) and prostatitis (15.9%). The likelihood of making correct clinical diagnosis of BPH and cancer of prostate was consistently low (66.3% and 51.9% respectively). Despite clinical suspicion of prostatic cancer, there was high preponderance by clinicians to perform prostatectomy (80%), contrary to standard recommendation. Most histologically confirmed prostatic cancer had unfavorable scores in terms of histological extent of tumor (63.6%) and Gleason's sum (92.9%).

Conclusion: This study has demonstrated that clinical and histological patterns of prostatic diseases are similar to other studies, most of which are presenting with lower urinary tract symptoms and urinary retention. The accuracy of clinical diagnosis is low and a significant number of clinically suspected cases of prostate cancer underwent surgical operation, many of whom had unfavorable prognostic scores.

Recommendations: It is recommended that clinicians should: scale up clinical vigilance and index of suspicion in dealing with cases of prostatic diseases, provide necessary information to histopathologists, and adhere to guidelines in managing prostatic cancer. Furthermore, resources for management of prostatic diseases should be increased and more studies should be conducted.

Key words: Prostatic diseases, presenting symptoms, histology, prostatectomy, tumor extent and Gleason's sum.

Introduction

Prostatic diseases in adults are diverse, and they pose significant morbidity and mortality in men over 40 years of age with immense resource costs for research and management[1]. Many authors have reported benign prostatic hyperplasia, prostatic cancer and inflammation (prostatitis) to be the most common[2, 3, 4]. In USA, BPH has an incidence of about 50% in men older than 50 years and that the occurrence rises to about 75% as men enter their eighth decade[5]. Of these cases, 10.9 per 1000 men older than 80 years will have significant symptoms which will eventually require surgical intervention[6]. On the other hand prostate cancer is the most common cancer among men across the globe in terms of morbidity, but is a second most common cause of mortality in men after lung cancer[1]. With aging populations and increased screening using prostatic specific antigen (PSA), the incidence of prostatic cancer has doubled in many countries.[1] Mortality is higher in developing countries, especially Sub Saharan region[7]. On the other hand prostatitis is the third most frequent disease of the prostate. Recent studies suggest that globally, the prevalence of prostatitis is 5% to 9% among unselected men in the community[8], whilst histopathological literature suggests a prevalence of 18–24% [2, 3, 4.] Prostatic disease commonly presents with constellation of symptoms termed as lower urinary tract symptoms (LUTS) [9]. These symptoms are generally divided into obstructive symptoms (hesitancy, intermittency, excessive terminal dribbling and weak stream) and irritative symptoms (frequency, nocturia, urgency, urge incontinence) [10]. Patients can also present with symptoms related to complications of prostate disease, these symptoms include; urine retention, urinary tract infection, bladder stone, obstructive uropathy (hydronephroureter), urinary bladder diverticulum and renal failure in neglected cases[11]. In view of high prevalence, morbidity and mortality of prostatic diseases and the fact that there is paucity of literature in this country and East Africa, research on histological patterns is important in highlighting disease patterns and burdens in the region.

Methodology

This was a retrospective laboratory-based descriptive study, in which all prostatic specimens obtained from three levels of health service delivery centers (namely regional hospitals, district hospitals and health centers) were conveniently recruited. The study involved review of the available prostatic biopsy database for a period of one year from February 2014 to February 2015. Clinical information, histological diagnosis, extent of tumor in the sampled tissue, and Gleason's sum were recorded directly into preconstructed questionnaire and then analyzed using SPSS version 20 software program. Frequencies and cross-tabulations were done accordingly; Pearson's chi square test was used to measure the relationship of parameters, where a p value of 0.05 was considered significant, within the level of significance of 95% and

marginal error of 5%. Biopsies reported as autolysed were excluded from this study. Permission to conduct this study was obtained from the University of Dodoma ethical clearance board through College of health sciences ethical subcommittee.

Results

A total of 477 records from 477 patients were recruited in the study. The mean age in years was 72, with a range of 47 – 97 and a standard deviation of 9.8. The mean weight of submitted prostatic biopsies was 36.5 grams with a range of 0–320 and standard deviation of 32.3. The frequency of commonest symptoms, clinical diagnoses, type biopsies and histological results are presented in a **table 1** below:

Table 1: Frequency of presenting symptoms, Clinical diagnosis, type of biopsy and histological results.

Presenting symptoms	Frequency	Percent
Lower urinary tract symptoms	217	45.5
Urine retention	198	41.5
No clear history	62	13.0
Total	477	100.0
Clinical diagnosis	**Frequency**	**Percent**
BPH	294	61.6
Prostatic cancer	135	28.3
No clinical diagnosis	48	10.1
Total	477	100.0
Type of biopsy	**Frequency**	**Percent**
Open prostatectomy	242	50.7
Transurethral resection of prostate	208	43.6
Tru cut (core needle biopsy)	27	5.7
Total	477	100.0
Histology	**Frequency**	**Percent**
Benign prostate hyperplasia (BPH)	259	54.3
Prostatitis	76	15.9
Cancer of prostate	115	24.1
BPH with fibromascular hyperplasia	27	5.7

Total	477	100.0

The commonest presenting symptoms were lower urinary tract symptoms and urine retentions with a frequency of 45.5% and 41.5% respectively. There were only two diagnoses (BPH and prostatic cancer) in almost all cases (89.9%). About 50.7% of cases underwent open prostatectomy and only a minority (5.7%) had trucut done. With regard to histological results, BPH was commonest (54.3%), two histological diagnoses which didn't in clinical diagnosis becoming apparent in histological diagnosis: prostatitis and fibromuscular hyperplasia of the prostate at 15.9% and 5.7% respectively.

Table 2: Clinical diagnosis versus presenting symptoms

CLINICAL DIAGNOSIS	PRESENTING SYMPTOMS			Total
	Lower urinary tract symptoms	Urine retention	No clear history	
BPH	137(46.6)	132(44.9)	25(8.5%)	294(61.6%)
Prostatic cancer	69(51.1%)	56(41.5%)	10(7.4%)	135(28.3%)
No clinical diagnosis	11(22.9%)	10(20.8%)	27(56.3%)	48(10.1%)
Total	217(45.5%)	198(41.5%)	62(13.0%)	477
p value < 0.0001				

Majority of patients with BPH presented with lower urinary tract symptoms (46.6%); this was significantly higher in patients with a clinical diagnosis of cancer of prostate (51.1%). Twenty seven (13%) lacked both clinical history and diagnosis. After controlling for the level of health facility as a possible confounding factor, observed differences in presenting symptoms and clinical diagnosis was only seen at regional hospital and health center (See table 3 below).

Table 3: Chi-Square Tests result after controlling for the level of hospital

LEVEL OF HEALTH FACILITY		Value	Df	Asymp. Sig. (2-sided)
Regional hospital	Pearson Chi-Square	48.776[b]	4	.000
District hospital	Pearson Chi-Square	4.339[c]	4	.362
Health center	Pearson Chi-Square	44.246[d]	4	.000
Total	Pearson Chi-Square	88.831[a]	4	.000

Table 4: Clinical diagnosis versus type of biopsy procedure

CLINICAL DIAGNOSIS	TYPE OF BIOPSY			Total
	Open prostatectomy	TURP	Tru cut	
BPH	175(59.5%)	118(40.1%)	1(0.3%)	294(61.6%)
Prostatic cancer	31(23.3%)	79(58.5%)	25(18.5%)	135(28.3%)
No clinical diagnosis	36(75.0%)	11(22.9%)	1(2.1%)	48(10.1%)
Total	242(50.7%)	208(43.6%)	27(5.7%)	477

p value <0.0001, when controlled by health facility level significance was observed at regional and health center levels with p values less than 0.0001 at both levels

Over 80% of clinically diagnosed cases of cancer of prostate were operated (open prostatectomy – 23.3% and TURP – 58.5%). Open prostatectomy was the commonest procedure for BPH (59.5%), while transurethral resection of the prostate was the commonest in a prostatic cancer subgroup. Only a minority of patients had trucut biopsy.

Table 5: Clinical diagnosis versus histological diagnosis

CLINICAL DIAGNOSIS	HISTOLOGY				Total
	Benign prostate hyperplasia	Prostatitis	Cancer of prostate	BPH fibromascular	
BPH	195 (66.3%)	50(17.0%)	35(11.9%)	14(4.8%)	294(61.6%)
Prostatic cancer	41(30.4%)	16(11.9%)	70(51.9%)	8(5.9%)	135(28.3%)
No clinical diagnosis	23(47.9%)	10(20.8%)	10(20.8%)	5(10.4%)	48(10.1%)
Total	259(54.3%)	76(15.9%)	115(24.1%)	27(5.7%)	477

p value < 0.0001, when controlled by health facility level, significant difference was observed at all levels.

The prevalence of histological BPH, cancer of prostate and prostatitis is 60%, 24.1%, and 15.9% respectively. Clinical diagnosis of BPH missed 17% and 11.9% cases of prostatitis and prostatic cancer respectively, while a clinical diagnosis

of prostatic cancer missed about 48% of cases. None of the surgeons thought about chronic prostatitis and or BPH with fibromascular hyperplasia as a possible diagnosis. The actual pattern of histological results is presented in the figure1 below:

Figure 1: Pie chart showing pattern of histology

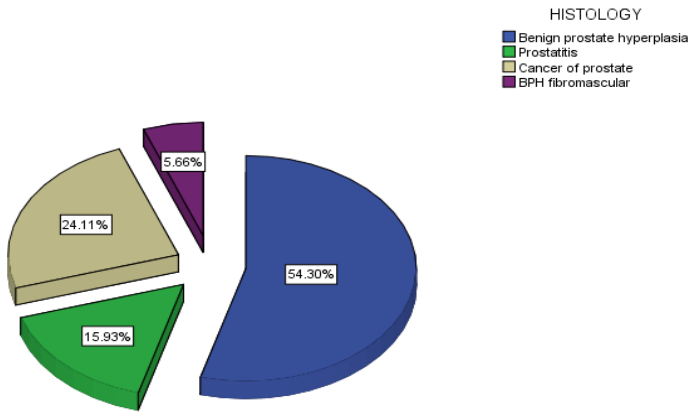
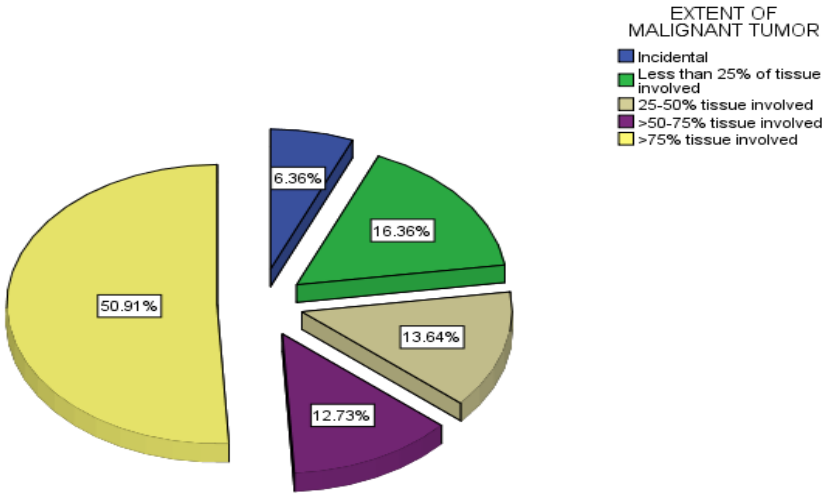
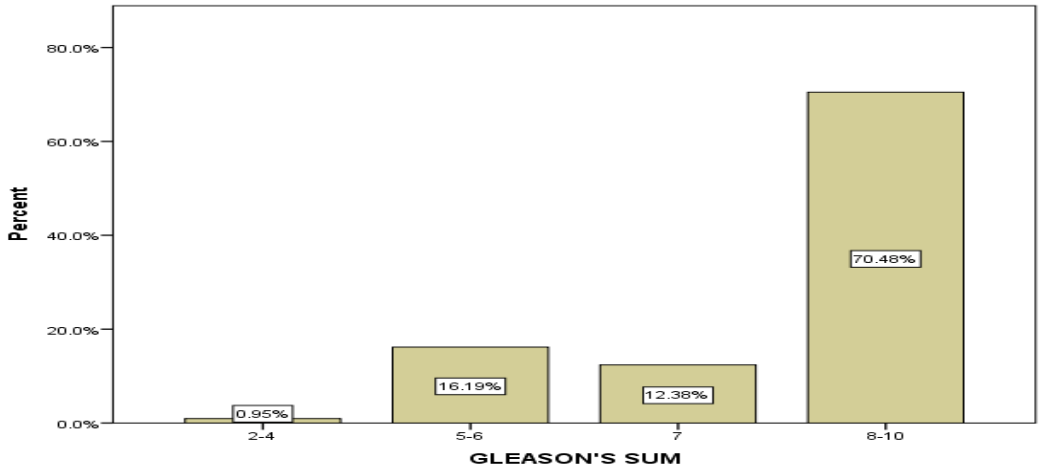


Figure 2: Pie chart showing histological extent of prostatic cancer in the various biopsies observed.



Slightly over 50% of cases had tumour spreading in more than 75% of the tissues observed; in total about 63.6% had tumor spread of more than 50%. The prevalence of incidental cancer among the biopsies is 6.36%.

Figure 3: Frequency distribution of Gleason's scores



Majority of cases had Gleason's sum of 8-10, indicating they are histologically poorly differentiated.

Only 18 cases had had Prostate specific antigen tested, and the mean value was 32 ng/dl, with a range of 3.0 – 35.7.

Discussion

In this study, a retrospective review of 477 cases of prostatic biopsies submitted to the histopathologist at a private facility located in Dodoma municipality was done. The mean age was 72 years, with a range of 47 – 97 and a standard deviation of 9.8, similar to other reports [2, 3]. The average prostatic biopsy weight of 36.5 grams was obtained from patients who underwent open or transurethral resection of the prostate; there are no comparable studies.

Lower urinary tract symptoms and urine retention were and the commonest presenting symptoms in 45.5% and 41.5% respectively, while BPH and prostatic cancer were the most common clinical diagnosis in 62% and 28% respectively. About 10% of cases had no clinical diagnosis. Similar to studies elsewhere, LUTS occurred in 46.6% of patients with BPH and in 51.1% of patients with prostatic cancer[9, 10, 11]. Urinary retention was the second commonest clinical presentation in both prostate cancer and BPH. The distribution of clinical presentation and clinical diagnoses was statistically significant, with a p value less than 0.0001, although after controlling by the level of hospital or health care center as possible confounders, the differences observed were only significant at health center and regional hospital, probably because these two are served by trained surgeons and urologists unlike district hospitals.

With regard to histological results; BPH (including fibromuscular hyperplasia) was the most common histological pattern (60%), followed by prostate cancer (24.1%) and prostatitis (15.9%). This histological pattern is similar to other

findings[2, 3, 13], but Mohamed et al reported a slight higher frequency of prostatitis at 23.6% as compared to the index study (15.9%). It should be noted further that, two histological diagnoses (which were not included or considered in clinical diagnoses): prostatitis and fibromuscular hyperplasia were found to fairly common. It appears many surgeons did not of these two conditions despite their relative high prevalence and the fact that they may have changed the mode of treatment. For example, prostatitis would have benefited from a course of antibiotics rather than surgical intervention. It is important therefore that a thorough history and physical examination should be done in every patient who presents with lower urinary tract symptoms or those suspected to have prostatic diseases.

Another finding of significance in this study is the fact that over 80% of clinically diagnosed cases of cancer of prostate were operated on. Open prostatectomy was done in 23.3% and transurethral resection of the prostate (TURP) in 58.5% of clinically suspected cases. Generally, open prostatectomy was more common among BPH cases (59.5%), while TURP was commonest in patients with cancer of prostate. Under ideal circumstances, the conventional prostatectomy is not a recommended procedure for cancer of the prostate; other treatment modalities should be considered. According to the American Urology Association (AUA) and the Canadian Urology Association (CUA) , modalities for management of prostatic cancer include: watchful waiting in selected patients [14–16], radiotherapy (brachytherapy or external beam radiation) [17, 18], nerve sparing and non nerve sparing radical prostatectomy[19], androgen deprivation in form of surgical or medical castration, cryotherapy, and high density focused ultrasound [20, 21]. The high rate of surgical treatment in Tanzania can be explained in three ways: the first is to assume that cases transurethral resected cases needed this procedure as part of symptomatic management (channel TURP) as it is one of the recommended method for advanced cancer, the second assumes inadequate knowledge on the part of assessing doctors, and the third assumes desperate decisions in limited resource settings. None of these can be verified unless another study is done to determine factors contributing to these kinds of decisions.

On the other hand and according to AUA and CUA, the gold standard surgical intervention for BPH is TURP. Other recommended procedures include: laser prostatectomy, transurethral incision of prostate, open prostatectomy, transurethral microwave therapy, and transurethral needle ablation and the use of various types of stents. [22, 23.] In this study the proportion of patients who underwent TURP for BPH was only 40.1%, almost all of them were referred from private health centers. Majority of open prostatectomy biopsies were actually coming from the regional and district hospitals. In this respect, authors assume resource limitation as the main reason for higher prevalence of open prostatectomy than TURP at the regional and district hospitals. TURP services

are only available in a few tertiary hospitals and are consistently absent in most regional hospitals in this country.

Another important finding was the fact that there was a significant mismatch between provisional diagnosis (clinical diagnosis) and confirmed diagnosis (histological findings). For example, a clinical diagnosis of benign prostatic hyperplasia was significantly more likely to be correct (66.6%) than that of cancer of prostate (52%). Of all clinically diagnosed cases of BPH, about 12% actually had cancer of prostate, and 17.0% cases had prostatitis. Furthermore, in clinically suspected cases of prostate cancer, 30% had BPH and 12% had prostatitis. None of the surgeons considered prostatitis or fibromasucular prostatic hyperplasia as a possible clinical diagnosis. When considered together with the fact that a significant number of patients with clinically suspected cancer of prostate were operated on, two reasons are speculated to explain the phenomenon: the first is probably related to limitation in resources necessary for accurate diagnosis prostatic diseases and the second is possibly related to reduced clinical vigilance and judgment among doctors when attending patients with prostatic diseases. None of them could again be verified by this study.

One of the most important prognostic factors among patients with prostate cancer is extent of the tumour spread within the sampled prostate biopsies despite their limitation in assessment of local and regional extent. The study found that slightly over 50% of cases had tumor spreading in more than 75% of the sampled tissues and about 63% had tumor spreading in more than 50%. The majority of these cases had Gleason's sum of more than 7 indicating the disease was significantly advanced at the time of diagnosis. This pattern is similar to other findings [2,3,4], but it doesn't concur with Mohammed et al all, who found that the majority of cases had well to moderate differentiation pattern[3]. The prevalence of incidental cancer among the biopsies of 6.36% is slightly higher than that reported 3% by Temi et al[2], but lower than the 15% reported by Mosli [23]. The high prevalence of advanced cancer with a low prevalence of early cancer is probably not only related to delayed hospital reporting, but also it is due to the fact that prostatic cancer is an indolence disease which without screening is unlikely to picked up by unsuspecting patient or health care provider. It is known that patients from developing countries tend to report late in hospitals and therefore present with advanced stages of disease than those in developed countries [24, 25]. Screening programs done in developed countries can also partially explain the disparity in disease pattern we see between developed and developing countries [26]. Moreover, prostate cancer is reported to affect some races (including black) more than the others and some geographic areas are more affected [27].

Conclusion

This study has demonstrated that in terms of clinical pattern of prostatic diseases, benign prostatic hyperplasia and cancer of prostate are the most prevalent, and often present with lower urinary tract symptoms and urine retention. Furthermore, a significant proportion of cases had missed clinical information to aid pathologists to make/infer diagnosis. The study has also demonstrated that BPH is still the commonest histological diagnosis followed by prostate cancer and prostatitis similar to other studies. There is significant mismatch between clinical diagnosis and histological diagnosis. It has been revealed that despite clinical suspicion of cancer of prostate, there was high preponderance for prostatectomy contrary to standard recommendation from various researchers and professional associations. In this study most histological confirmed prostatic cancer has unfavorable scores in terms of histological extent of tumor and Gleason's sum.

Recommendations include:

1. It is recommended that clinicians should scale up their clinical vigilance and index of suspicion through thorough history taking and physical examination when managing cases of prostatic diseases, and that surgeons should strive to provide necessary information to histopathologists to aid in making correct diagnosis,
2. The high prevalence of cases of prostatic cancer which have been operated on is alarming; it is recommended that surgeons should adhere to agreed proctocols in managing these cases in order to prevent unnecessary invasive treatment. Resources for management of prostatic diseases should be scaled up across Tanzania, including screening where implicated and access to non-surgical treatment modalities,
3. Further studies should be conducted to better evaluate clinical and histological patterns of prostatic diseases in Tanzanian men.

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