The clinicopathologic patterns of prostatic diseases and prostate cancer in Saudi patients

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ABSTRACT

الأهداف: دراسة و تحديد أنماط أمراض البروستاتا وعلى و جه الخصوص مرض سرطان البروستاتا.

الطريقة: تم إجراء البحث في مستشفى مدينة جامعة الملك عبد العزيز الطبية ومستشفى الملك فيصل التخصصي في جدة – المملكة العربية السعودية خلال الفترة من شهر يونيو 2003 حتى يونيو 2008. تمت مراجعة الملفات الطبية بأثر رجعي للمرضى الذين أجريت لهم دراسة باثولوجية لأنسجة عينات البروستاتا لديهم وذلك. وتم دراسة العوامل الآتية: العمر، الفحص الشرجي، دواعي أخذ عينات البروستاتا، التشخيص الباثولوجي، ودرجة الخبث عند مرضى السرطان.

النتائج: اشتملت الدراسة على 330 مريض متوسط عمرهم 68 عاما من (100–37 عام). تكونت العينات من 233 عينة حُصِل عليها بتوجيه الموجات الصوتية الشرجية، 85 عينة استئصال البروستاتا البسيط جراحيا، 3 عينة استئصال جذري للبروستاتا، 1 عينة استئصال جذري للمثانة و البروستاتا . كانت دواعي أخذ العينات عند مرضى السرطان هي ارتفاع قيمة PSA عند 85.2%، فحص شرجي غير طبيعي في 5.5%، أو كلا السابقين عند 9.3% وجاءت نتيجة التحاليل كالآتي: السرطان 28.5%، التضخم الحميد 43.3%، التضخم مع الالتهاب 20.3%، الالتهاب فقط 4.2%. ووجد أن قيمة PSA أقل من 4ng/ml>موجودة عند 13.6% من مرضى السرطان. وكذلك وجد سرطان بالمصادفة في 15% من العينات بالمرضى الذين شخصوا اكلينيكيا ان مرضهم حميد. أما في مرضى السرطان فكان مجموع جليسون لديهم 6 أو أكثر (92.8%).

خاتمة: معدل انتشار سرطان البروستاتا في المملكة العربية السعودية منخفض مقارنة بالدول الغربية. وهذه النتيجة تأكدت بفحص العينات المأخوذة بتوجيه الموجات الصوتية الشرجية. ولكن وجد ان نسبة السرطان في العينات في ارتفاع مما يستدعي مزيدا من البحث لدراسة ذلك و الاسباب المحتملة. وهذا يعزز توصية خفض الحد الادنى المقبول لأخذ العينات من البروستاتا الى 2.5ng/ml بدلا من4ng/ml.

Objectives: To determine the clinicopathologic patterns of prostatic diseases in Saudi patients, with special emphasis on prostate cancer (PCa).

Methods: The records of patients who underwent histopathological examinations of their prostatic specimens in King Abdulaziz University Medical City and King Faisal Specialist Hospital, Jeddah, Kingdom of Saudi Arabia, between June 2003 and June 2008 were reviewed retrospectively. The age, indications for biopsy, histological diagnosis, and Gleason grading of cancer patients, were studied.

Results: The study included 330 patients aged 37-100 years (median=68). Specimens included 233 transrectal ultrasound (TRUS) biopsies, 85 transurethral resection of the prostate (TURP), 8 simple prostatectomies, 3 radical prostatectomies, and one radical cystoprostatectomy. Indications for TRUS guided biopsy in PCa patients were elevated prostate specific antigen (PSA) (85.2%), abnormal digital rectal examination (5.5%) or both (9.3%). Prostate specific antigen values <4 ng/ml were found in 13.6% of PCa patients. Among others, adenocarcinoma was found in 28.5%, benign prostatic hyperplasia (BPH) alone in 43.3%, BPH with inflammation in 20.3% and inflammation alone in 4.2%. In specimens of TURP or simple prostatectomy for apparently benign disease, incidental PCa was detected in 14/93 (15%). The Gleason sum of ≥6 was found in 92.8% of patients.

Conclusions: The incidence of prostate cancer in Saudi Arabia is low compared to the western countries. However, incidental PCa detected in presumed benign disease appears to be rising. Further future studies addressing this issue are needed to confirm the potential rising trend, and its possible etiology. Our findings support the recommendations to lower the PSA cutoff value for prostatic biopsy to 2.5 rather than 4ng/ml.

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The incidence of prostate cancer (PCa) has been reported to be low in Saudi Arabia,[1] although properly conducted population-based epidemiological studies are lacking. Whether the incidence will rise with aging of the male population, and more cancer detection with wide spread use of prostate specific antigen (PSA) and performing more prostatic transrectal ultrasound (TRUS) guided biopsies, remains to be observed. The primary objective of this retrospective study is to determine the clinicopathologic patterns of prostatic diseases in Saudi patients, with special emphasis on prostate cancer.

Methods. King Abdulaziz University Medical City (KAUMC) and King Faisal Specialist Hospital (KFSH) are tertiary care teaching hospitals located in Jeddah, Saudi Arabia. They receive patients from Jeddah, as well as from the Western, Southern, and Northern Regions, hence, the data presented here pertains to a major part of the Saudi population. The medical records of patients who underwent histopathological examinations of their prostatic specimens in both KAUMC and KFSH during the period of June 2003 to June 2008 were reviewed retrospectively. The age, PSA value, digital rectal examination (DRE) findings, indications for biopsy, histological diagnosis, and histological grading of cancer patients, were studied. The prostatic specimens examined included TRUS guided initial biopsies as well as prostatic specimens from patients with apparently benign disease who underwent either transurethral resection of the prostate (TURP) or simple prostatectomy (adenomectomy), and without previous biopsies. Radical prostatectomy and radical cystoprostatectomy prostatic specimens were also included. Repeat biopsies were excluded from the study. Similarly, in patients who ultimately underwent radical prostatectomy, only the histopathological findings of the whole prostatic specimens were considered, disregarding their initial biopsies findings. Transrectal ultrasound guided biopsy cores were obtained from various sites in the prostate according to the standard sextant technique. Prostatic specimens were stratified according to pathological features into adenocarcinoma, benign prostatic hyperplasia (BPH) alone, BPH with inflammation, inflammation alone, other pathologies or unspecified. Prostate cancers were graded and scored according to the Gleason system.

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The Institutional Ethics Committee approved the study protocol and written informed consent was obtained for each patient prior to TRUS guided biopsies.

Study data were compiled and examined with Microsoft® Office Excel® 2007 (12.0.6331.5000) SP1 MSO (12.0.6320.5000) software.

Results. The study included a cohort of 330 patients with age distribution of 37-100 years (median = 68 years). The prostatic specimens included 233 TRUS guided biopsies, 85 TURPs, 8 simple prostatectomies, 3 radical prostatectomies and one radical cystoprostatectomy. **Table 1** demonstrates the overall distribution of different prostatic diseases diagnosed according to pathological features, where adenocarcinoma of the prostate was detected in a total of 94/330 (28.5%) patients. Among the cohort of cancer patients, PSA values were accessible in 66 patients. Prostate specific antigen values ranged widely between 0.002-1535 ng/ml. Elevated PSA (>20 ng/ml) was found in 35 patients (53%) as shown in **Table 2**. On the other hand, PSA <4 ng/ml was seen in 9 patients. Out of the 233 patients, who underwent prostatic TRUS guided biopsies, 80/233 (34.3%) had evidence of PCa. Indications for biopsy were accessible in 54/80 patients. The indications for TRUS biopsy of those patients are displayed in **Table 3**. In patients with

Table 1 - Overall distribution of different prostatic disorders in prostatic specimens (N=330).

Diagnosis	n	(%)
Adenocarcinoma	94	(28.5)
Benign prostatic hyperplasia	143	(43.3)
Benign prostatic hyperplasia with inflammation	67	(20.3)
Inflammation	14	(4.2)
Others (n=12)		
Transitional cell cancer infiltration	8	(66.7)
Squamous cell cancer infiltration	1	(8.3)
Leiomyomatous nodules	1	(8.3)
Non-Hodgkin's lymphoma	1	(8.3)
Extension from colonic cancer	1	(8.3)

Table 2 - Prostate specific antigen (PSA) values among patients with prostate adenocarcinoma (N=66).

PSA (ng/ml)	n	(%)
<4	9	(13.6)
4 - <10	9	(13.6)
10 - 20	13	(20)
>20	35	(53)

Prostate specific antigen values ranged widely between 0.002-1535 ng/ml

apparently benign disease who underwent either TURP (85) or simple prostatectomy, PCa was detected in 14/93 (15%). Histologically, Gleason sum of 6 or more was found in 92.8% of cancer patients. The histological grading and Gleason scores of patients with PCa are demonstrated in **Table 4**.

Discussion. Prostate cancer is the third most common cancer in men in the world, with 543,000 new cases each year according to the World Cancer Report 2003.[2] In the 1998 cancer incidence report of the Gulf Cooperation Council Countries, published by the Gulf Center for Cancer Registration, the highest age standardized incidence rate of PCa was in Oman and Kuwait 10.6/100,000, followed by Bahrain 10.3/100,000, Qatar 8.6/100,000, and United Arab Emirates 7.1/100,000. The least was in Saudi Arabia with an age standardized incidence rate of 4.2/100,000.[3]

Other reports from Saudi Arabia had shown PCa to be of low incidence. The National Cancer Registry (NCR) in 1996 produced its first report on all cancer patients in Saudi Arabia starting from the beginning of January 1994. During 1994, there were 137 new cases of PCa among Saudis, accounting for 2.7% of all newly diagnosed cases. Prostate cancer ranked sixth for males with a crude incidence rate of 2.1 per 100,000 for that year.[4] In a study on PCa cases that had been reported between 1975 and 1996 in Saudi Arabia, a conclusion was made that in Saudi Arabia the incidence of PCa is very low compared to the western countries.[5] Another report from the Eastern region in Saudi Arabia further supported this conclusion.[6] Additional reports from Dhahran Health Center, revealed a cancer detection rate of 27.5% when combined PSA, DRE, and TRUS were used.[7] These reports attributed the low incidence rate to lacking of aged male population in Saudi Arabia, whose population is predominantly young.[4] The current study shows an overall incidence of 28.5% of PCa among all prostatic specimens, further confirming the low incidence of PCa in Saudi Arabia. Still when there is an abnormally elevated PSA, the western cancer detection rate is higher in the range of 65-80%.[8,9]

Additionally, our report demonstrated a 34.3% incidence of PCa in TRUS biopsies. In 2005, Taha and Kamal,[10] reported on TRUS guided biopsies of the prostate in 63 patients with abnormal DRE or PSA. Prostate cancer was confirmed in 14/63 (22.2%) patients.

Moreover, the low incidence of PCa in Saudi males was further confirmed by examining the rate of incidental cancer discovered in prostatic specimens removed at surgery carried out for a clinically presumed benign disease. More than a decade ago, our center (KAUMC) reported[11] a 7.2% rate of incidental PCa detected in surgical specimens removed from clinically presumed benign disease (stages T1a and T1b), compared with international rates of 10-20%.[12-16] The calculated average incidence rate of incidental PCa, from 6 Saudi centers reporting between 1993-2000, was found to be 3.3%.[1] However, contrary to the stationary incidence of PCa in TRUS biopsies, the incidence of incidental PCa in specimens of apparently clinically benign prostates appears to be surprisingly rising in our current study. The incidence in our report is 15%, compared to a 7.2% incidence reported 12 years ago.[11] Further future studies addressing this issue are needed to confirm the potential rising trend, and to evaluate the possible role of changing dietary habits and environmental risk factors.

In a report by Tayib et al[17] in 2003, out of 45 patients with high PSA abnormal DRE, or both, who underwent TRUS guided biopsy, PCa was detected in 28.8%. The cancer detection rate in patients presenting with abnormal DRE alone was 7.6%. When PSA was elevated to 4-10 ng/ml, cancer was detected in 21.4%. Elevation of PSA to10-20 ng/ml lead to cancer detection in 40% of the patients and when PSA was >20 ng/ml all cases were considered positive for cancer.[18] In our study, among the cohort of cancer patients, PSA values ranged widely between 0.002-1535 ng/ml. These findings

Table 3 - Indications for prostatic TRUS biopsy in 54 prostate cancer positive patients (N=54).

Indications	n	(%)
Elevated PSA	46	(85.2)
Abnormal DRE	3	(5.5)
Elevated PSA + abnormal DRE	5	(9.3)

PSA - prostate specific antigen, TRUS - transrectal ultrasound, DRE - digital rectal examination

Table 4 - Histological grading and Gleason score of patients with prostate cancer (N=83).

Grades	Gleason sum	n	(%)
Grade 4	10	3	(3.6)
Grade 5	10	3	(3.6)
Grade 6	10	25	(30)
Grade 7	10	23	(27.7)
Grade 8	10	18	(21.7)
Grade 9	10	9	(11)
Grade 10	10	2	(2.4)

shown in **Table 2**, denote that using the PSA cutoff value of 4 ng/ml for TRUS guided prostatic biopsy entails missing a diagnoses in 13.6% of our PCa patients.

Recently, some authors have recommended lowering the total serum PSA cutoff for prostate biopsy from 4-2.5 ng/ml.[18] They found that up to 17% of men with a PSA level below the prostate biopsy cutoff of 2.5 ng/ml may have prostate cancer.[18] In 2009, Jones et al[19] reported on the probability of finding incidental (T1a and T1b) PCa during TURP in the PSA era. Ninety-five of their patients were biopsied before TURP. Elevated PSA (using the cutoff of 4.0 ng/ml) was observed in 90 men and was the most common indication for biopsy. Of the 95 men, 5 (5.3%) were found to have unrecognized cancer in the TURP specimen, highlighting the need to lower the PSA cutoff.[20] Our findings support the recommendations to increase the cutoff value for prostatic biopsy to 2.5 rather than 4 ng/ml. Using 4 ng/ml as a cutoff could miss up to 13.6% of our cancer patients. In a pathological study in the Sultanate of Oman, a total of 1163 patients underwent prostate biopsies during a 5 year period. Cancers were seen in 10.9%. Most of the patients had high Gleason's score, with 65.6% having scores between 7 and 10 (poorly differentiated) and 24.8% with scores 5 or 6 (moderately differentiated). Only 0.08% had well differentiated carcinomas with Gleason's score between 2 and 4.

In an analysis of 126 patients of PCa from Riyadh Armed Forces Hospital (RAFH), 108 patients were Saudis, 16 were non-Saudi Arabs, and 2 were Pakistanis. Forty-seven patients had well differentiated adenocarcinoma, 34 had moderately well differentiated adenocarcinoma, and 45 patients had poorly differentiated adenocarcinoma of the prostate.[17] Notably, in our current study, the vast majority of cancers (92.8%) have Gleason sum of 6 or more, while only 3.6% had Gleason sum of 4. Hence, worth to mention, although the incidence of PCa is low in Saudi Arabia, it usually takes place as high-grade disease. The shortcomings of this study include its retrospective nature. Another limitation was the inability to access some information concerning the included patients.

In conclusion, the incidence of PCa in Saudi patients is low compared to the western countries. This finding is confirmed in our TRUS guided prostatic biopsies. However, the rate of incidental PCa detected in surgical specimens removed from clinically presumed benign disease appears to be rising. The incidence in our current report is double the incidence reported by us 12 years ago. Further future studies addressing this concern are needed to confirm the potential rising trend, and to evaluate the possible etiological factors.

Additionally, our findings question the diagnostic value of the current PSA cutoff value of 4 ng/ml for TRUS. This study supports the recommendations to lower the PSA cutoff value for prostatic biopsy to 2.5 rather than 4 ng/ml, otherwise we may miss diagnosing a considerable number of our cancer patients. Prospective larger scale cohort biopsy studies are required to better address this issue.

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