Pattern of Prostate Cancer in Karbala Province of Iraq: Data from Developing **Country**

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Background: Global patterns of prostate cancer differ with respect to environmental and demographic factors.

Objective: Our study's objective was to evaluate the prostate cancer pattern in Karbala province of Iraq, make comparisons with other populations to detect potential changes.

Methods: A retrospective descriptive research was conducted at Al-Hussein Cancer Center in Karbala, Iraq, on 265 patients found to have prostate cancer from January 2012 to December 2020 with assessment of age, presenting symptoms, pathological characteristics and stage.

Results: Median age was 70 years. The most common symptoms were irritative symptoms in 58.11% of patients, the most frequent histopathology was adenocarcinoma in 95.85% of patients, A prostate-specific antigen level (PSA) was > 20 ng/ml in more than 56% of patients. The Gleason score was ≥ 7 in (86.22%) of adenosarcomas patients. Unfortunately, more than half of our patients (51.32%) presented as stage IV.

Conclusion: This is the first statistical research about prostate cancer in Karbala province of Iraq. It can be used as a starting point to examine epidemiological characteristics, evaluate current developments, and develop therapeutic strategies.

Introduction

Prostate cancer is the second most frequent malignancy (after lung cancer) in men and the fifth leading cause of death worldwide [1]. Based on GLOBOCAN 2020 estimates, almost 1.4 million new cases and 375,000 deaths worldwide [2]. In Karbala province of Iraq it is the sixth registered cancer among males, presenting 7.1% of cancer cases [3]. Wide variation exists internationally for prostate cancer rates due to differences in detection practices, treatment, lifestyle and genetic factors [4]. The highest rates found in Northern and Western Europe, the Caribbean, Australia/New Zealand, Northern America, and Southern Africa and the lowest rates in Asia and Northern Africa

1/8

while the highest mortality rates in the Caribbean and sub-Saharan Africa [2].

For a disease as common as prostate cancer, relatively little is known about its etiology. Established risk factors are limited to advancing age, family history of this malignancy, and certain genetic mutations (eg, BRCA1 and BRCA2) and conditions (Lynch syndrome). Black men in the United States and the Caribbean have the highest incidence rates globally, supporting the role of Western African ancestry in modulating prostate cancer risk [5]. There have been few lifestyle and environmental factors identified to date for which the evidence is convincing, although this may be accumulating for smoking, excess body weight, and some nutritional factors that may increase the risk of advanced prostate cancer [2]. Prostate cancer has traditionally been diagnosed by digital rectal examination (DRE) and prostate-specific antigen (PSA) blood test, followed by transrectal ultrasound (TRUS) guided biopsy. However, considering the wide prescription of PSA tests for prostate cancer, and the development of screening programs, more than 60% of prostate cancer are diagnosed in asymptomatic patients, with normal DRE and elevated PSA [6].

Unfortunately, in developing countries, most of prostate cancer patients are not aware of the disease and as a result they do not take early urinary symptoms seriously hence they are diagnosed late with very advanced disease with incurable tumors. Late diagnosis limits treatment options, increases mortality and leads to low quality of life for patients and their families. Early diagnosis of prostate cancer may lead to early management of the disease which can lead to better treatment outcomes [7].

In fact, the majority of data about prostate cancer are from industrialized nations, and little is known about the pattern of this tumor in Iraq. For that reason, the purpose of this research was to evaluate the prostate cancer patterns in Iraq to provide real data about this cancer in our country.

Materials and Methods

Participants and study design

At Al-Hussein Cancer Center in Karbala, Iraq, this retrospective descriptive study was carried out. This center serves not just the Karbala region but also the Middle Euphrates Region of Iraq; patients are referred to this center for the treatment of solid and hematological malignancies [8-10]. In this research we registered 265 patients diagnosed as prostate cancer from January 2012 until December 2020. The eighth edition of the American Joint Commission on Cancer Staging Manual was used to record the stage at the time of the diagnosis [11]. From the patients' charts we extracted the data about clinical, demographic, and pathological features.

Inclusion/exclusion criteria

Patients with prostate cancer diagnosed between January 2012 and December 2020 were included in this study. Patients whose results were not conclusive were not included in this study.

Ethical considerations

The Ethics Committee at the Al-Hussein Cancer Center in Karbala, Iraq, provided ethical approval.

Statistical analysis

The Statistical Package for Social Sciences (SPSS) software (version 25) was used to enter and manage patients' data. The variables' descriptive statistics were presented as a number, percentage, median, and range.

Results

Incidence

In the period between 2012-2020, 265 patients of prostate cancer were registered in Karbala. The incidence rate was increased during the study period from 3.15 per 100,000 in 2012 to 6.79 per 100,000 in 2020. The percentage of prostate cases out of all diagnosed cancers ranged from 2.32% to 4.32% as shown in (Table 1, Figure 1 and 2).

Year	2012	2013	2014	2015	2016	2017	2018	2019	2020
Prostate cancer	18	24	20	20	32	38	30	39	44
All Cancers	483	555	655	861	1043	1213	1164	1256	1333
Percentage	3.73%	4.32%	3.05%	2.32%	3.07%	3.13%	2.58%	3.10%	3.30%

Table 1. Number of New Cases of Prostate Cancer and All Cancers Per Year.

Figure 1. Percentage of Prostate Cancers Out of all Cancers 2012-2020.

Figure 2. Incidence Rates of Prostate Cancer Per 100,000 Man-Year in Karbala, 2012-2020.

Age distribution

The median age of diagnosis was 70 years for all cases, patients ages were between 47 years and 95 years. The most affected age group was (61-70) years in 126 patients (47.55%) followed by (71-80) years in 81 patients (30.57%) as shown in (Table 2).

Age (year)	N (%)
≤50	5 (1.89)
51-60	27 (10.19)
61-70	126 (47.55)
71-80	81 (30.57)
81-90	24 (9.05)
>90	2 (0.75)
Total	265 (100)

Table 2. Age Distribution of 265 Patients.

Presenting symptoms

The most common presenting symptoms were: Irritative symptoms in 154 patients (58.11%), bone pain in 67 patients (25.28%), obstructive symptoms in 29 patients (10.95%) and 15 patients (5.66%) were asymptomatic as shown in (Figure 3).

Figure 3. Presentingsymptoms of 265 Patients.

Pathological subtypes

The most frequent histopathology was adenocarcinoma in 254 patients (95.85%), followed by squamous cell carcinoma in 8 patients (3.02%) and transitional cell carcinoma in 3 patients (1.13%) as shown in (Table 3).

Pathological subtypes	N (%)
Adenocarcinoma	254 (95.85)
Squamous cell carcinoma	8 (3.02)
Transitional cell carcinoma	3 (1.13)
PSA level	N (%)
< 10 ng/ml	48 (18.11)
10-20 ng/ml	66 (24.91)
> 20 ng/ml	151 (56.98)
Gleason score of adenocarcinomas	N (%)
< 7	35 (13.78)
≥7	219 (86.22)

Table 3. Histopathological Characteristics.

The mean serum total PSA was 162 ng/ml, there were 151 patients (56.98%) with PSA level > 20 ng/ml. Regarding Gleason grading of the 254 adenocarcinomas patients showed that 35 patients (13.78%) with score < 7, while 219 patients (86.22%) with score ≥ 7 (Table 3).

Stages of cancer

The most frequent stage was stage IV in 136 patients (51.32%), followed by stage III in 66 patients (24.90%), stage II in 58 patients (21.89%) and stage I in 5 patients (1.89%) as shown in the (Figure 4).

Figure 4. Presenting Stages of 265 Patients.

Discussion

Prostatic cancer incidence rates increased in nearly all countries, contributes significantly to the public health burden especially in developing countries. In Iraq, there are no enough data about prostate cancer; therefore, the exact burden remains unknown [4, 12]. In this study, the pattern of prostate cancer in Karbala province of Iraq were evaluated. Simultaneously, we made comparisons of our findings with the data from various world regions to get a better understanding of the pattern of this cancer in our country.

In Karbala province, the incidence rate of prostate cancer increased from (3.15 per 100,000) in 2012 to (6.79 per 100,000) in 2020, which remain much lower than that in developed countries such as New Zealand and Australia (111.6 per 100,000), North America (97.2 per 100,000) and European Union (70.4 per 100,000) but close to the incidence rate that reported in South Central Asia (4.5 per 100,000) and South-East Asia Region (5.5 per 100,000) [13].

This variation between developing and developed countries may be due to widespread clinical examinations, and most importantly, access to preventive services like PSA testing, and the presence of cancer registry systems in developed countries [13].

The median age of our patients was (70 years) which is close to the median age in Saudi Arabia (71 years) and Africa (69 years), but it relatively older than in India (66 years) and US (62 years). These differences were expected given the international differences in prostate cancer screening and diagnosis [14, 15].

Most of our prostate cancer cases had a lower urinary tract symptoms, and this was the main reason that their prostate cancer was uncovered. Four of these symptoms, urinary retention, frequency, hesitancy and nocturia, probably represent enlargement of the prostate gland which may be misdiagnosed as benign prostatic hyperplasia. Most cancers arise in the periphery of the prostate gland, and cause symptoms only when they have grown to compress the urethra, or invade the sphincter or neurovascular bundle leading to delay diagnosis [16, 17]. Our results revealed that the adenocarcinoma was the most frequent pathological subtype (95.85%), this result was comparable to other previous international studies [15]. While, squamous cell carcinoma of the prostate accounted for (3.02%) among total cases. Similar results have been reported in Saudia Arabia (2.7%) [18]. However, it was lower than that registered internationally with (0.5%-1%). Unfortunately, this type is described as an aggressive cancer, with a median postdiagnosis survival of 14 months only [18].

In our study, primary urothelial carcinoma of the prostate represented only (1.13%) of all cases. This subtype is a rare solid malignant tumor that exhibits highly aggressive biological behavior and has a poor prognosis. Only limited data on this malignancy have been reported [19].

PSA testing has led to changes in screening and the early diagnosis of prostate cancer, which is followed by earlier treatment. The widespread use of PSA screening had led to an increase in overall survival as more early-stage prostate cancer cases were diagnosed.

The number of prostate cancer patients with metastatic stages and comorbidities has decreased more than 25% owing to greater detection of confined tumors early [20]. The usefulness of PSA testing has been shown for assessing the response of treatment, and determining tumor progression. The general cutoff for the PSA level is 4.0 ng/mL and data showed a strong correlation of PSA level with tumor diagnosis, tumor aggressiveness, and bone metastasis [20]. In our study more than half of our patients presented with PSA more than 20ng/ml.

Unfortunately, most of them not diagnosed through surveillance programs for prostate cancer.

Most of our patients (86.22%) presented with Gleason score ≥7, this was consistent with previous studies in Oman, Africa, Malysia and Pakistan [21-24]. While the majority of patients presented with Gleason score < 7 in Greek and Jamaica [25, 26].

More than half of our patients (51.32%) presented as stage IV, which is much higher than that reported in United States (3%-6.4%) and United Kingdom (17-34%) [27, 28]. Our results even higher than that reported in Middle Eastern countries such as Syria (20%) and Lebanon (19%) [29].

The higher proportion of late-stage patients at our center can be explained by multiple factors, including: wide scale screening for prostate cancer has never been adopted in the Iraq given the lack of medical infrastructure supporting primary care interventions including cancer screening [30].

This study can be evaluated in terms of its strengths and limitations. A strength of our study is that it can help to provide basic information about prostate cancer in Iraq, comparing it to neighboring countries and the world. Moreover, to the best of our knowledge, this study is the first one to be

carried out in the Karbala province of Iraq. A limitation of our study is that it covered only Karbala province and not other regions of Iraq.

In conclusion, the incidence of prostate cancer increased during the last years in Karbala. Unfortunately, more than half of our patients presented with advance stages and significantly high PSA level & Gleason grade. These findings indicate that our patients have low level of awareness about prostate cancer risk factors, symptoms and screening methods. There should be more public awareness initiatives to educate men in Iraq about the risk factors, symptoms and screening methods for this cancer.

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Conflicts of interest

There are no conflicts of interest.

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8/8