RESEARCH Open Access



# Prostate cancer presentation and management in the Middle East

Mutlay Sayan<sup>1,13\*</sup>, Astrid Langoe<sup>2</sup>, Ozlem Aynaci<sup>3</sup>, Ayfer Ay Eren<sup>4</sup>, Mehmet Fuat Eren<sup>5</sup>, Ilke Onur Kazaz<sup>3</sup>, Zainab Ibrahim<sup>6</sup>, Omar Tama Al-Akelie<sup>7</sup>, Loma Al-Mansouri<sup>8</sup>, Ramiz Abu-Hijlih<sup>9</sup>, Shalini Moningi<sup>1</sup>, Elia Abou Chawareb<sup>10</sup>, Albert El Hajj<sup>10</sup>, Peter F. Orio<sup>1</sup> and Layth Mula-Hussain<sup>11,12</sup>

## **Abstract**

**Background** Although prostate cancer is a prevalent malignancy worldwide, its clinical presentation and management in the Middle East are not well-documented. This study aims to provide insights into the initial clinical presentation and management of prostate cancer in this region.

**Methods** A retrospective review was conducted on seven institutional databases from six Middle Eastern countries, including Türkiye, Lebanon, Iraq, Syria, Bahrain, and Jordan, to identify patients diagnosed with prostate cancer in 2021. Descriptive analysis was performed on the collected data to provide an overview of the demographic, clinical, and treatment variables.

**Results** A total of 1,136 patients were identified with a median age of 70 (range, 50-84). Most patients (78%) received their prostate cancer diagnosis after presenting with symptoms, as opposed to routine PSA screening. At the time of diagnosis, 35% of men had clinical T3 or T4 disease, 54% with Stage IV disease and 50% with Gleason score  $\geq 8$ . Regarding treatment, 20% of non-metastatic and 22% of metastatic patients received no treatment.

**Conclusion** Most men in this study sought prostate cancer evaluation due to symptoms and were subsequently diagnosed with advanced-stage disease, providing a foundation for future research aimed at understanding the underlying factors behind the observed trends and enabling informed interventions.

Keywords Prostatic neoplasms, Middle East, Disease presentation, Disease management, Diagnostic challenges

Mutlay Sayan

msayan@bwh.harvard.edu

<sup>1</sup>Brigham and Women's Hospital and Dana-Farber Cancer Institute,

Harvard Medical School, Boston, MA, USA

<sup>2</sup>Boston College, Boston, MA, USA

<sup>3</sup>Karadeniz Technical University, Trabzon, Türkiye, Turkey

<sup>4</sup>Kartal Dr. Lütfi Kirdar Education and Research Hospital, Istanbul, Turkey

<sup>5</sup>Marmara University, Istanbul Pendik Education and Research Hospital, Istanbul, Türkiye, Turkey



© The Author(s) 2024. **Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <a href="http://creativecommons.org/licenses/by/4.0/">http://creativecommons.org/licenses/by/4.0/</a>. The Creative Commons Public Domain Dedication waiver (http://creativecommons.org/publicdomain/zero/1.0/) applies to the data made available in this article, unless otherwise stated in a credit line to the data.

<sup>\*</sup>Correspondence:

<sup>&</sup>lt;sup>6</sup>King Hamad University Hospital, Al Sayh, Bahrain

<sup>&</sup>lt;sup>7</sup>Alamal National Hospital for Cancer Management, Baghdad, Iraq

<sup>&</sup>lt;sup>8</sup>Basrah Medical College, Basra, Iraq

<sup>&</sup>lt;sup>9</sup>King Hussein Cancer Center, Amman, Jordan

<sup>&</sup>lt;sup>10</sup>American University of Beirut Medical Center, Beirut, Lebanon

<sup>&</sup>lt;sup>11</sup>Faculty of Medicine, Dalhousie University, Halifax, NS, Canada

<sup>&</sup>lt;sup>12</sup>College of Medicine, Ninevah University, Mosul, Ninevah, Iraq

<sup>&</sup>lt;sup>13</sup>Department of Radiation Oncology, Dana-Farber Cancer Institute, Brigham and Women's Hospital, Harvard Medical School, 75 Francis Street, Boston, MA 02115, USA

Sayan *et al. BMC Urology* (2024) 24:35 Page 2 of 5

# **Background**

Prostate cancer is one of the most common types of cancer affecting men worldwide [1]. Its complex nature presents a significant health burden that varies across geographic regions, age groups, and racial/ethnic populations [2]. Genetic predisposition, lifestyle, and health-care access are important to consider in the diagnosis and prognosis of this disease [3, 4]. While there have been substantial advancements in understanding etiology and treatment strategies, prostate cancer still remains a leading cause of cancer-related morbidity and mortality among men globally.

In contrast to regions like Europe and North America, where extensive research on prostate cancer has been conducted, the Middle East presents a different scenario. The status of prostate cancer in this region remains notably underexplored, resulting in a fragmented understanding of its initial presentation and management [5–7]. One significant reason for this disparity is the absence of wellestablished cancer registries. However, limited available data suggests a consistent rise in the incidence of prostate cancer over the past decade [8]. This increasing incidence highlights the pressing need for comprehensive research efforts in the Middle East. Grasping the disease stage at the initial presentation is a pivotal first step in this direction. Such insights not only provide a clearer picture of the current state of prostate cancer care in the region but also provide the essential data to craft and implement effective policies.

Despite the global prevalence of prostate cancer, there remains a significant knowledge gap concerning its manifestation and management in the Middle East. This study aims to comprehensively assess prostate cancer's clinical presentation and management in the region, providing a foundation for future research and informed policy-making.

## Materials and methods

A retrospective review was conducted on institutional databases from six Middle Eastern countries, Türkiye, Lebanon, Iraq, Syria, Bahrain, and Jordan, to identify patients diagnosed with prostate cancer in 2021. A comprehensive review of seven databases from various institutions was conducted, encompassing six public and one private health care system, all of which are affiliated with academic centers. Prostate cancer diagnosis was confirmed by the treating physician at each participating institution following pathological confirmation. Tissue samples for histopathological analysis were obtained through various methods, including prostate biopsy, biopsy of metastatic sites, or from tissue acquired during radical prostatectomy. Data were collected on demographic details, clinical presentations, and treatment modalities. The staging of prostate cancer was performed by combining clinical assessment, radiological imaging, and pathological findings, following the guidelines outlined in the American Joint Commission on Cancer staging manual, 8th edition. Descriptive analysis was performed on the collected data to provide an overview of the demographic, clinical, and treatment variables.

# Results

A total of 1,136 patients were identified with a median age of 70 (range, 50–84). The baseline patient characteristics are shown in Table 1. Most patients (78%) were diagnosed after developing symptoms and not on routine PSA screening. Diagnostic workup was completed in 87% of the patients. At the time of diagnosis, 35% of men presented with clinical T3 or T4 disease, 54% with Stage IV disease and 50% with Gleason score≥8. The mean PSA at the time of presentation was 84 ng/ml.

Treatment details are shown in Table 2. Among the non-metastatic patients, 24% underwent a radical prostatectomy, 48% received definitive radiotherapy with or without androgen deprivation therapy (ADT), 8% received ADT alone, and 20% received no treatment. No patients received brachytherapy. Hypofractionated radiotherapy was used in 49% of patients. Among the metastatic patients, 56% received ADT with or without additional systemic therapy, 22% had palliative radiotherapy, and 22% received no treatment.

In this study cohort, the distribution of patients with locally advanced disease was as follows: 66 patients (5%) had regional and local lymph node involvement alone (N1 disease), with the majority undergoing definitive radiation therapy in combination with ADT (67%). Additionally, a subset of 20 patients (2%) presented with clinical T3-T4 disease alone, without evidence of lymph node involvement or distant metastasis, with the majority of these patients undergoing radical prostatectomy, either with or without ADT (80%).

# Discussion

In this study, we conducted a comprehensive retrospective review of 1,136 patients across seven institutional databases in six Middle Eastern countries to understand prostate cancer's clinical presentation and management strategies in the region. Our findings indicate most patients were diagnosed after developing symptoms rather than through routine PSA screenings, with a notable number presenting with advanced-stage disease (54% with Stage IV disease) and not receiving any form of treatment (22%). The clinical significance of this study lies in its potential to serve as a foundation for designing future studies aimed at better understanding the underlying reasons behind these findings, ultimately enabling the development of informed interventions.

Sayan *et al. BMC Urology* (2024) 24:35 Page 3 of 5

**Table 1** Demographic and clinical characteristics of the study cohort

| Age, median, range                             | 70<br>(50–84) |
|--|---------------|
| Reason for prostate cancer evaluation, No. (%) | (20 0.1)      |
| Routine surveillance                           | 254 (22)      |
| Patient had symptoms                           | 882 (78)      |
| AJCC tumor stage, No. (%)                      |               |
| T1c  | 90 (10)       |
| T2a  | 110 (12)      |
| T2b  | 166 (18)      |
| T2c  | 235 (25)      |
| T3a  | 148 (16)      |
| T3b  | 90 (10)       |
| T4   | 86 (9)        |
| AJCC nodal stage, No. (%)                      |               |
| N0   | 556 (64)      |
| N1   | 311 (36)      |
| AJCC metastatic stage, No. (%)                 |               |
| MO   | 587 (52)      |
| M1a  | 30 (3)        |
| M1b  | 268 (24)      |
| M1c  | 251 (22)      |
| AJCC stage                                     |               |
| Stage I  | 86 (7)        |
| Stage II                                       | 218 (19)      |
| Stage III                                      | 223 (20)      |
| Stage IV                                       | 609 (54)      |
| Gleason score, No. (%)                         |               |
| 6 (3 + 3)                                      | 106 (11)      |
| 7 (3 + 4)                                      | 169 (18)      |
| 7 (4+3)  | 191 (20)      |
| 8 (4+4, 3+5, or 5+3)                           | 225 (24)      |
| 9 or 10 (4+5, 5+4, or 5+5)                     | 246 (26)      |
| Baseline PSA, mean                             | 83.4          |
| Diagnostic Imaging, No. (%)                    |               |
| Bone scan*                                     | 4 (0)         |
| CT scan*                                       | 42 (4)        |
| MRI*   | 148 (13)      |
| PSMA-PET, with or without other imaging        | 372 (33)      |
| US alone*                                      | 54 (5)        |
| Bone scan + CT scan                            | 93 (8)        |
| Bone Scan + CT scan + MRI                      | 272 (24)      |
| No imaging                                     | 151 (13)      |

Abbreviations AJCC, American Joint Committee on Cancer; PSA, prostate-specific antigen; CT, computed tomography; MRI, magnetic resonance imaging; PSMA-PET, prostate-specific membrane antigen positron emission tomography; US, ultrasound

Recent studies have highlighted the importance of age and serum PSA levels as major risk factors for prostate cancer. A comprehensive multicenter case study revealed that the estimated odds ratios for prostate cancer increase significantly in different age groups corresponding to PSA levels. Specifically, for individuals in their

**Table 2** Treatment characteristics of the study cohort

| Treatment for non-metastatic patients, No. (%) |          |
|--|----------|
| No treatment                                   | 106 (20) |
| Radical prostatectomy alone                    | 84 (16)  |
| Radiotherapy alone                             | 28 (5)   |
| ADT alone                                      | 45 (8)   |
| Radical prostatectomy + radiotherapy + ADT     | 30 (6)   |
| Radical prostatectomy + ADT                    | 10 (2)   |
| Radiotherapy + ADT                             | 228 (43) |
| Treatment for metastatic patients, No. (%)     |          |
| No treatment                                   | 132 (22) |
| ADT +/- additional systemic therapy            | 343 (56) |
| Palliative radiotherapy to metastases          | 140 (22) |

Abbreviations ADT, androgen deprivation therapy

forties with PSA levels between 2.6 and 4 ng/ml, the risk is approximately 12.5 times higher [9]. Moreover, recent findings from a randomized control trial demonstrate the efficacy of PSA screening in reducing metastasis and mortality in men aged 55–74 years. After a median follow-up of 21 years, the study reports rate ratios of prostate cancer-specific mortality at 0.73 (95% CI: 0.61–0.88) and metastasis at 0.67 (95% CI: 0.58–0.78), highlighting the benefits of screening [10].

Several points require further discussion. First, the retrospective design inherently introduces confounding factors that cannot be entirely accounted for. Therefore, these results are hypothesis-generating and should be evaluated in a new cohort study. Despite this limitation, our findings align with the high rates of advancedstage disease presentation observed in small institutional databases [11, 12]. One major contributing factor to this observation could be the lack of prostate cancer awareness, as a significant proportion of patients (78%) in this study sought prostate cancer evaluation due to symptoms, indicating that many may not have been aware of the need for routine screening. Another contributing factor could be the limited practice of routine prostate cancer screening in the region by physicians. Multiple barriers may contribute to this, including a lack of healthcare professional training and knowledge, limited resources or access to screening equipment, time constraints during medical consultations, or the fact that prostate cancer screening may be considered a lower priority compared to other pressing health concerns. To the best of our knowledge, there is currently no comprehensive study assessing the level of prostate cancer awareness or the status of prostate cancer screening practices in the Middle East. Investigating this area would provide valuable insights into the barriers and challenges faced by healthcare systems and individuals in accessing timely prostate cancer diagnosis, thereby contributing to a more comprehensive understanding of the issue. Furthermore, the limited availability of advanced imaging modalities,

<sup>\*</sup>Only the respective imaging modality was used without combining with others

Sayan *et al. BMC Urology* (2024) 24:35 Page 4 of 5

such as PSMA PET scans [13] and multiparametric-MRI [14], in this region may have contributed to the presentation of prostate cancer at more advanced stages.

Second, while 20% of patients with non-metastatic disease did not receive any treatment, it's worth noting that active surveillance, a management strategy often used for low-risk prostate cancer, might have been chosen for these patients. In contrast, a similarly high rate of no treatment (22%) was observed among patients with metastatic disease, in which cases active surveillance is not typically a preferred option. ADT stands as the cornerstone of treatment for metastatic prostate cancer. Furthermore, numerous randomized controlled trials have demonstrated that combination therapy, which incorporates ADT alongside androgen receptor-signaling inhibitors or docetaxel, significantly improves overall survival compared to ADT alone [15-19]. Additionally, the efficacy of radiotherapy in the context of metastatic prostate cancer has been well-established through multiple prospective studies [20-23]. Given the compelling evidence supporting the treatment of patients with metastatic prostate cancer, it remains unclear why 22% of patients with metastasis in this cohort did not receive any form of treatment. This discrepancy raises important questions about the factors contributing to the omission of treatment, which warrants further investigation.

Third, the emergence of the COVID-19 pandemic brought forth unique challenges in healthcare delivery. Notably, our study did not consider the specific impact of COVID-19 on cancer diagnosis and treatment rates. Consequently, the question remains whether the proportion of patients presenting with advanced-stage disease or not receiving treatment would have been similar in the absence of the pandemic [24].

In North America and Europe, prostate cancer is typically detected through PSA testing for early diagnosis, resulting in a significant rise in disease incidence. Consequently, prostate cancer is the most commonly diagnosed cancer among men in these regions [25]. The majority of cases are identified while the cancer remains localized within the prostate, leading to a 5-year survival rate of approximately 98% [25]. However, the Middle East presents a distinct scenario, as evidenced by our study, where the majority of patients (78%) receive their prostate cancer diagnosis after developing symptoms, and 54% of men have Stage IV disease at diagnosis. This indicates a later stage of detection compared to North America and Europe. In Africa, prostate cancer is characterized by higher PSA values, a more frequent presentation of locally advanced cancer, and high-grade disease [26]. This suggests that the disease may be more advanced at the time of diagnosis in this region, similar to the situation in the Middle East.

## Conclusion

In this comprehensive retrospective review of prostate cancer cases across six Middle Eastern countries revealed a concerning pattern where most men sought prostate cancer evaluation due to symptoms and were subsequently diagnosed with advanced-stage disease, while a substantial portion received no treatment. These data should guide future studies to understand the underlying reasons behind these trends, ultimately enabling well-informed interventions to improve prostate cancer care and outcomes in the region.

## Acknowledgements

We thank our research assistants, Noura Wahoud and Aya Matar, for their valuable contribution to data collection.

#### **Author contributions**

Conceptualization: M.S., A.E.H., P.F.O., and L.M.H. Methodology: M.S., S.M., E.A.C., A.E.H., P.F.O., and L.M.H. Data Curation: O.A., A.A.E., M.F.E., I.O.K., Z.I., O.T.A., L.A., R.A.H., and E.A.C. Writing – Original Draft Preparation: M.S. and A.L. Writing – Review & Editing: M.S., A.L., O.A., A.A.E., M.F.E., I.O.K., Z.I., O.T.A., L.A., R.A.H., S.M., E.A.C., A.E.H., P.F.O., and L.M.H. Supervision, M.S. and L.M.H.

#### Funding

This research did not receive any funding.

#### Data availability

No datasets were generated or analysed during the current study.

## **Declarations**

# Ethics approval and consent to participate

The studies involving human participants were reviewed and approved by the Institutional Review Board of Karadeniz Technical University. Written informed consent for participation was waived by the Institutional Review Board of Karadeniz Technical University.

## Consent for publication

Not applicable.

## **Competing interests**

The authors declare no competing interests.

Received: 23 December 2023 / Accepted: 5 February 2024 Published online: 09 February 2024

## References

- Pernar CH, Ebot EM, Wilson KM, Mucci LA. The epidemiology of prostate Cancer. Cold Spring Harbor Perspect Med. 2018;8(12).
- Park SY, Haiman CA, Cheng I, Park SL, Wilkens LR, Kolonel LN, et al. Racial/ Ethnic differences in lifestyle-related factors and prostate Cancer risk: the multiethnic cohort study. Cancer Causes & Control; 2015.
- Layne TM, Graubard BI, Ma X, Mayne ST, Albanes D. Prostate Cancer risk factors in Black and White men in the NIH-AARP Diet and Health Study. Prostate Cancer and Prostatic Diseases; 2018.
- Kazmi N, Haycock PC, Tsilidis KK, Lynch BM, Truong T, Martin RM et al. Appraising Causal relationships of Dietary, Nutritional and Physical-Activity exposures with overall and aggressive prostate Cancer: two-sample mendelianrandomization study based on 79 148 prostate-Cancer cases and 61 106 controls. Int J Epidemiol. 2019.
- Ali AH, Awada H, Nassereldine H, Zeineddine M, Sater ZA, El-Hajj A, et al. Prostate cancer in the arab world: bibliometric review and research priority recommendations. Arab J Urol. 2022;20(2):81–7.

Sayan *et al. BMC Urology* (2024) 24:35 Page 5 of 5

- Mula-Hussain L, Mahdi H, Ramzi ZS, Tolba M, Zaghloul MS, Benbrahim Z, et al. Cancer Burden among Arab World males in 2020: the need for a Better Approach to Improve Outcome. JCO Glob Oncol. 2022;8:e2100407.
- Kearney G, Chen MH, Mula-Hussain L, Skelton M, Eren MF, Orio PF et al. Burden of prostate cancer in the Middle East: a comparative analysis based on global cancer observatory data. Cancer Med. 2023.
- Abbasi-Kangevari M, Saeedi Moghaddam S, Ghamari SH, Azangou-Khyavy M, Malekpour MR, Rezaei N, et al. The burden of prostate cancer in North Africa and Middle East, 1990–2019: findings from the global burden of disease study. Front Oncol. 2022;12:961086.
- Aragona F, Pepe P, Motta M, Saita A, Raciti G, La Rosa P, et al. Incidence of prostate cancer in Sicily: results of a multicenter case-findings protocol. Eur Urol. 2005;47(5):569–74.
- de Meertens VII, Hogenhout A, Remmers R, Roobol S. A detailed evaluation of the effect of prostate-specific Antigen-based screening on morbidity and mortality of prostate Cancer: 21-year follow-up results of the Rotterdam section of the European Randomised study of screening for prostate Cancer. Eur Urol. 2023;84(4):426–34.
- 11. Daher M, Telvizian T, Dagher C, Abdul-Sater Z, Massih SA, Chediak AEL et al. High rates of advanced prostate cancer in the Middle East: analysis from a tertiary care center. Urol Annals. 2021;13(4).
- Eren MF, Kilic SS, Eren AA, Kaplan SO, Teke F, Kutuk T, et al. Radiation therapy for prostate cancer in Syrian refugees: facing the need for change. Front Public Health. 2023;11:1172864.
- Pepe P, Pennisi M. Targeted biopsy in men high risk for prostate Cancer: (68) Ga-PSMA PET/CT Versus mpMRI. Clin Genitourin Cancer. 2023;21(6):639–42.
- Pepe P, Pepe G, Pepe L, Garufi A, Priolo GD, Pennisi M. Cost-effectiveness of Multiparametric MRI in 800 men submitted to repeat prostate biopsy: results of a Public Health Model. Anticancer Res. 2018;38(4):2395–8.
- Fizazi K, Tran N, Fein L, Matsubara N, Rodriguez-Antolin A, Alekseev BY, et al. Abiraterone plus Prednisone in Metastatic, castration-sensitive prostate Cancer. N Engl J Med. 2017;377(4):352–60.
- James ND, de Bono JS, Spears MR, Clarke NW, Mason MD, Dearnaley DP, et al. Abiraterone for prostate Cancer not previously treated with hormone therapy. N Engl J Med. 2017;377(4):338–51.
- Chi KN, Agarwal N, Bjartell A, Chung BH, Pereira de Santana Gomes AJ, Given R, et al. Apalutamide for metastatic, castration-sensitive prostate Cancer. N Engl J Med. 2019;381(1):13–24.

- Davis ID, Martin AJ, Stockler MR, Begbie S, Chi KN, Chowdhury S, et al. Enzalutamide with Standard First-Line therapy in metastatic prostate Cancer. N Engl J Med. 2019;381(2):121–31.
- Kyriakopoulos CE, Chen YH, Carducci MA, Liu G, Jarrard DF, Hahn NM, et al. Chemohormonal therapy in metastatic hormone-sensitive prostate Cancer: long-term survival analysis of the Randomized Phase III E3805 CHAARTED trial. J Clin Oncol. 2018;36(11):1080–7.
- Parker CC, James ND, Brawley CD, Clarke NW, Hoyle AP, Ali A, et al. Radiotherapy to the primary tumour for newly diagnosed, metastatic prostate cancer (STAMPEDE): a randomised controlled phase 3 trial. Lancet. 2018;392(10162):2353–66.
- Tang C, Sherry AD, Haymaker C, Bathala T, Liu S, Fellman B, et al. Addition of Metastasis-Directed therapy to intermittent hormone therapy for oligometastatic prostate Cancer: the EXTEND phase 2 Randomized Clinical Trial. JAMA Oncol. 2023;9(6):825–34.
- Ost P, Reynders D, Decaestecker K, Fonteyne V, Lumen N, De Bruycker A, et al. Surveillance or Metastasis-Directed therapy for oligometastatic prostate Cancer recurrence: a prospective, randomized, Multicenter Phase II Trial. J Clin Oncol. 2018;36(5):446–53.
- Phillips R, Shi WY, Deek M, Radwan N, Lim SJ, Antonarakis ES, et al. Outcomes of Observation vs Stereotactic Ablative Radiation for oligometastatic prostate Cancer: the ORIOLE phase 2 Randomized Clinical Trial. JAMA Oncol. 2020;6(5):650–9.
- Jazieh AR, Akbulut H, Curigliano G, Rogado A, Alsharm AA, Razis ED, et al. Impact of the COVID-19 pandemic on Cancer Care: A Global Collaborative Study. JCO Glob Oncol. 2020;6:1428–38.
- 25. Rawla P. Epidemiology of prostate Cancer. World J Oncol. 2019;10(2):63–89.
- Tindall EA, Monare LR, Petersen DC, van Zyl S, Hardie R-A, Segone AM, et al. Clinical presentation of prostate cancer in Black South africans. Prostate. 2014;74(8):880–91.

## **Publisher's Note**

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.