



Clinicopathological Characteristics of Prostate Cancer in Tlemcen (Northwestern Algeria)

MOQADDEM Zakarya^{1,2}, AOUAR Amaria^{2,3}, KAZI TANI Nassim⁴, HAMDAOUI Houari^{1,2}, KHATER Sara^{1,2}, MOUSSOUNI Abdellatif³, SIDI-YAKHLEF Adel³, BELKHATIR Djamel², CHABNI Nafissa¹

¹ CancerLab Laboratory, University of Tlemcen, Algeria

² Laboratory of Human Actions' Valorisation for Protection of Environment and Application in Public Health, University of Tlemcen, Algeria.

³ Anthropology Laboratory, University of Tlemcen, Algeria

⁴ Division of Urology, The University Hospital of Tlemcen, Algeria

Type of article: Original

Abstract

Background: Prostate cancer is the main cause of cancer death in men in about 48 countries, including several sub-Saharan African, Caribbean, Central and South American countries. Despite the prevalence of prostate cancer, little is known about its etiology. Limited data exist for North Africa, and Algeria in particular, at the crossroads of Sub-Saharan Africa, the Middle East, southern Europe, and the Mediterranean region.

Objective: This study aimed to determine the relationship between a family history of cancer and age at diagnosis, and to assess the effect of a family history of cancer and prostate-specific antigen (PSA) levels on tumor prognosis.

Methods: This cross-sectional study was conducted on the records of 184 patients with prostate cancer confirmed by biopsy, diagnosed between 2011 and 2016 at the Urology Division of Tlemcen's teaching hospital. The collected data included the age at diagnosis, PSA level on presentation, Gleason score on biopsy, and a family history of cancer. Univariate statistical analyses were performed using ANOVA, independent-samples t-test, and Fisher's exact test in Minitab® 17.

Results: Men who had first-degree female relatives with breast cancer had a younger mean age at diagnosis (67.31 y) than those who did not have the same family history (72.3 y) ($p=0.02$). Positive first-degree family history for prostate cancer was associated with favorable tumor prognosis (Gleason ≤ 6) at the time of diagnosis ($p<0.001$). There was also a significant moderate positive correlation (Pearson correlation = 0.35) between PSA level and Gleason score ($p<0.001$).

Conclusion: Our data suggest an association between positive first-degree family history for breast/prostate cancer and the age of onset. Positive first-degree family history for prostate cancer appears to predict a favorable tumor prognosis. The Gleason score seems to rise with the PSA level. Men with a family history of prostate/breast cancer might start prostate cancer screening earlier than those without the same family history.

This study raises several questions that need to be addressed in future research. Prospective cohort studies would help identify and assess ethnic, genetic, hormonal, and environmental risk factors, and investigate the interactions influencing the genesis of this cancer, thereby guiding public health plans for cancer control and intervention strategies (screening, treatment, and survivor care).

Keywords: Prostate Cancer, Epidemiology, Public health, Family history, Screening, Algeria

1. Introduction

According to the recent data, prostate cancer is the second most commonly diagnosed cancer in men with more than 4 million newly diagnosed cases in 2020, and the fifth leading cause of cancer death with around 375,000 deaths

Corresponding author:

MOQADDEM Zakarya. 22, Rue Abi Ayad Abdelkrim Fg Pasteur B.P 119 13000, Tlemcen, Algérie.

Tel: 043.41.11.89, Fax: 043.41.11.91, E-mail: moqaddem.zakarya@gmail.com

Received: July 27, 2021, Accepted: November 08, 2021, Published: December 2021

Ethics approval: Tlemcen Research Ethics Committee (ref: CEDUT/DZ/021/127)

© 2021 The Authors. This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

worldwide in 2020 (1). In terms of incidence, the rates of prostate cancer are three times higher in developed countries than countries in transition (37.5 and 11.3 per 100,000, respectively), while the difference in mortality rates is less evident (respectively 8.1 and 5.9 per 100,000) (2). One in 25 men worldwide is likely to receive a prostate cancer diagnosis within his lifetime (3). According to cancer registries, prostate cancer is the fifth most commonly diagnosed cancer and the sixth leading cause of cancer death in men in Algeria, with a standardized incidence rate estimated at 10.8 per 100,000 and an average age at diagnosis of 71 years (4). There is a significant geographic variation in prostate cancer incidence worldwide. Genetic and environmental components are among the key risk factors (5). Ethnicity, age, diet, and family history also appear to be important aspects influencing the genesis and progression of this cancer (6). The current study aimed to determine the relationship between a family history of cancer and the age at diagnosis, and to assess the effect of the family history of cancer and prostate-specific antigen (PSA) levels on tumor prognosis.

2. Material and Methods

The study setting was the Tlemcen region, Northwestern Algeria, with an estimated population of 977,206 in 2010 (7). This cross-sectional study was conducted using the records of 184 patients with prostate cancer confirmed by biopsy, diagnosed between 2011 and 2016 at the Urology Division of Tlemcen's teaching hospital. The collected data included the age at diagnosis, PSA level on presentation, Gleason score on biopsy, and the family history of cancer. This study has been approved by the University of Tlemcen Research Ethics Committee (ref: CEDUT/DZ/021/127). Univariate statistical analyses were conducted using ANOVA, independent-samples t-test, and Fisher's exact test in Minitab® 17.

3. Results

Men with a first-degree female relative who had breast cancer had a younger mean age at diagnosis (67.31 years; 95% CI: 63.23, 71.38) than those who did not have a similar family history (72.3 years; 95% CI: 71.14, 73.47) ($p=0.02$) (Table 1). The positive first-degree family history for prostate cancer was associated with a favorable tumor prognosis (Gleason ≤ 6) at the time of diagnosis (Fisher's exact test $p<0.001$) (Table 2). An association was observed between low PSA levels and favorable tumor prognosis (Gleason ≤ 6) at the time of diagnosis (Fisher's exact test $p<0.001$) (Figure 1). We also found a significant positive correlation (Pearson correlation = 0.35) between the PSA level and Gleason score ($p<0.001$).

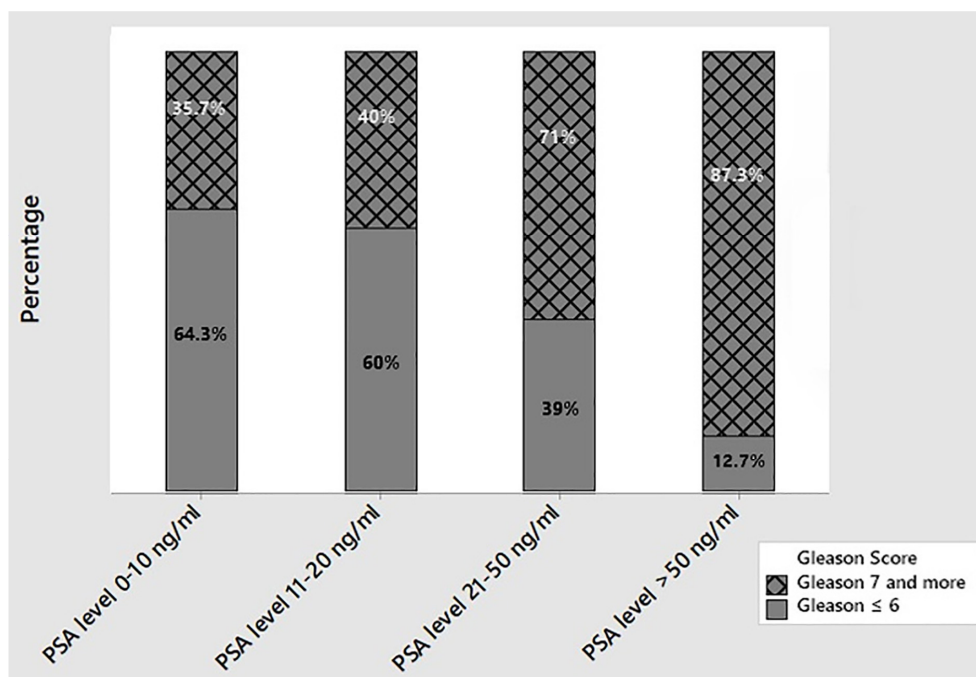


Figure 1. Relation PSA level and Gleason Score

Table 1. Relation between family history and mean age at diagnosis

Family history	Mean age at diagnosis (year)		p-value*
	Positive family history	Negative family history	
CaP among 1 st degree relatives	70.16	72.14	0.2
Father with CaP	66.86	72.13	0.06
Breast cancer among 1 st degree relatives	67.31	72.3	0.02*
Breast/CaP among 1 st degree relatives	69.31	72.46	0.04*
CaP among 1 st or 2 nd degree relatives	71.68	71.96	0.8
Breast/CaP among 1 st or 2 nd degree relatives	71.18	72.14	0.48

* One-way ANOVA

Table 2. Relation between family history and Gleason score

Family history	Gleason \leq 6	Gleason 7 and more
Positive 1 st degree family history of prostate cancer	61.5%	38.5%
Negative 1 st degree family history of prostate cancer	27.9%	72.1%

4. Discussion

Our study showed that men who had a first-degree female relative with breast cancer had a younger mean age at diagnosis. Many studies have concluded that these men run a higher risk of prostate cancer (8-10), while others have been unable to demonstrate such a relationship (11, 12). The age of onset of prostate cancer in the affected first-degree relatives seems to be important, too, as a younger age of onset was correlated with an increased risk (11, 13-15). Considering the known relationship between breast cancer and BRCA1/2 mutations and the obvious risk of prostate cancer for BRCA-carrying men, heritable BRCA gene mutation could explain one of the biological mechanisms involved in the hereditary form of the disease (16-18).

First-degree family history for prostate cancer in our study appears to predict a favorable tumor prognosis. The role played by the family history in prostate cancer prediction is largely recognized, but the role of the family history on prostate cancer prognosis remains controversial. Two large studies, both in the pre-prostate-specific antigen (PSA) era, considered family history as a predictor of fatal prostate cancer (19, 20); nevertheless, studies of the PSA era have failed to confirm such a negative impact of family history on prostate cancer prognosis (21-24). More recent studies demonstrated that men with a positive family history of prostate cancer appear to have better overall survival outcomes (25-27). This could be explained by the fact that men with a positive family history for prostate cancer are increasingly unlikely to manifest aggressive tumors; alternatively, because they are more aware of their own potential risk, they may seek an earlier detection, be diagnosed with earlier-stage cancer and, thus, have favorable tumor prognosis.

In our study, there was a positive correlation between serum PSA values and Gleason scores, which was consistent with other research findings in Asia, Africa, and Europe (28-31). However, other studies have shown no statistically significant correlation between PSA level and tumor grading by Gleason score in prostatic cancer patients with bone metastasis (32).

This study provides the first clinicopathological data on prostate cancer in western Algeria, and provides an overview of the peculiarities of this region for prostate cancer. Still, there were some limitations: 1) A retrospective study design may lead to some inaccuracies; 2) there were insufficient or unavailable data, especially on the age at diagnosis of cancer, among relatives; and 3) the number of cases was relatively smaller as this was a hospital-based study. Larger and more complete studies should be conducted to overcome these weaknesses.

5. Conclusions

Our data suggest a link between positive first-degree family history for breast/prostate cancer and the age of onset. A positive history of prostate cancer in first-degree relatives appears to predict a favorable tumor prognosis. The Gleason score seems to rise with the PSA level. Men with a family history of prostate/breast cancer might start prostate cancer screening earlier than those without the same family history. This study raises questions that need to be addressed in future research. Prospective cohort studies would help identify and assess ethnic, genetic, hormonal, and environmental risk factors, and investigate the interactions influencing the genesis of this cancer, thereby guiding public health plans for cancer control and intervention strategies (screening, treatment, and survivor care).

Acknowledgments:

The authors would like to thank all staff of Urology department of Tlemcen's University Hospital and all those who gave generous help and advice in the elaboration of this work.

Conflict of Interest:

There is no conflict of interest to be declared.

Authors' contributions:

All authors contributed to this project and article equally. All authors read and approved the final manuscript.

References:

- 1) Global Cancer Observatory (GLOBOCAN) 2020: Cancer Today. Lyon, France: International Agency for Research on Cancer. Available from: <https://gco.iarc.fr/today/home>
- 2) Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA Cancer J Clin.* 2021 May;71(3):209-249. doi: 10.3322/caac.21660, PMID: 33538338
- 3) Bray F, Ferlay J, Soerjomataram I, Siegel R.L, Torre L.A, 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. doi: 10.3322/caac.21492, PMID: 30207593
- 4) Hamdi Cherif M, Bidoli E, Birri S, et al. Cancer estimation of incidence and survival in Algeria 2014. *J Cancer Res Ther.* 2015; 3: 100-104. doi: 10.14312/2052-4994.2015-14
- 5) Bostwick, David G, Burke H-B, et al. Human prostate cancer risk factors. *Cancer: Interdisciplinary International Journal of the American Cancer Society.* 2004; 101: 2371-2490. doi: 10.1002/cncr.20408, PMID: 15495199
- 6) GANN, Peter H. Risk factors for prostate cancer. *Reviews in urology.* 2002; 4: S3-S10.
- 7) ONS: Office National des Statistiques. Available from: <http://www.ons.dz/> (accessed 28/01/18)
- 8) Gronberg H, Damber L, Damber JE. Familial prostate cancer in Sweden. A nationwide register cohort study. *Cancer.* 1996; 77: 138-43. doi: 10.1002/(SICI)1097-0142(19960101)77:1<138::AID-CNCR23>3.0.CO;2-5
- 9) Cerhan JR, Parker AS, Putnam SD, et al. Family history and prostate cancer risk in a population - based cohort of Iowa men. *Cancer Epidemiol Biomarkers Prev.* 1999; 8: 53-60.
- 10) Thiessen EU. Concerning a familial association between breast cancer and both prostatic and uterine malignancies. *Cancer.* 1974; 34: 1102-1107. doi: 10.1002/1097-0142(197410)34:4<1102::AID-CNCR2820340421>3.0.CO;2-5
- 11) Whittemore AS, Wu AH, Kolonel LN, et al. Family history and prostate cancer risk in black, white, and Asian men in the United States and Canada. *Am J Epidemiol.* 1995; 141: 732-40. doi: 10.1093/oxfordjournals.aje.a117495, PMID: 7535977
- 12) Rodriguez C, Calle EE, Tatham LM, et al. Family history of breast cancer as a predictor for fatal prostate cancer. *Epidemiology.* 1998; 9: 525-9. doi: 10.1097/00001648-199809000-00009, PMID: 9730031
- 13) Bratt O, Kristoffersson U, Lundgren R, Olsson H. Familial and hereditary prostate cancer in southern Sweden. A population - based case - control study. *Eur J Cancer.* 1999; 35: 272-7. doi: 10.1016/S0959-8049(98)00358-X
- 14) Zeegers MP, Jellema A, Ostrer H. Empiric risk of prostate carcinoma for relatives of patients with prostate carcinoma: a meta-analysis. *Cancer.* 2003; 97: 1894-1903. doi: 10.1002/cncr.11262, PMID: 12673715
- 15) Johns LE, Houlston RS. A systematic review and meta-analysis of familial prostate cancer risk. *BJU Int.* 2003; 91: 789-94. doi: 10.1046/j.1464-410X.2003.04232.x, PMID: 12780833
- 16) Liede A, Karlan BY, Narod SA. Cancer risks for male carriers of germline mutations in BRCA1 or BRCA2: a review of the literature. *J Clin Oncol* 2004; 22: 735-42. doi: 10.1200/JCO.2004.05.055, PMID: 14966099
- 17) Gallagher DJ, Gaudet MM, Pal P et al. Germline BRCA mutations denote a clinicopathologic subset of prostate cancer. *Clin Cancer Res* 2010; 16: 2115-21. doi: 10.1158/1078-0432.CCR-09-2871, PMID: 20215531, PMCID: PMC3713614
- 18) Andrieu N, Clavel F, Auquier A, et al. Association between breast cancer and family malignancies. *Eur J Cancer.* 1991; 27: 244-8. doi: 10.1016/0277-5379(91)90506-9

- 19) Rodriguez C, Calle EE, Miracle-McMahill HL, Tatham LM, Wingo PA, Thun MJ. Family history and risk of fatal prostate cancer. *Epidemiology* 1997; 8: 653-7. doi: 10.1097/00001648-199711000-00011, PMID: 9345665
- 20) Kupelian PA, Kupelian VA, Witte JS, Macklis R, Klein EA. Family history of prostate cancer in patients with localized prostate cancer: an independent predictor of treatment outcome. *J Clin Oncol* 1997; 15: 1478-80. doi: 10.1200/JCO.1997.15.4.1478, PMID: 9193343
- 21) Azzouzi AR, Valeri A, Cormier L, Fournier G, Mangin P, Cussenot O. Familial prostate cancer cases before and after radical prostatectomy do not show any aggressiveness compared with sporadic cases. *Urology* 2003; 61: 1193-7. doi: 10.1016/S0090-4295(03)00033-5
- 22) Gronberg H, Damber L, Tavelin B, Damber JE. No difference in survival between sporadic, familial and hereditary prostate cancer. *Br J Urol* 1998; 82: 564-7. doi: 10.1046/j.1464-410X.1998.00801.x, PMID: 9806189
- 23) Hanlon AL, Hanks GE. Patterns of inheritance and outcome in patients treated with external beam radiation for prostate cancer. *Urology* 1998; 52: 735-8. doi: 10.1016/S0090-4295(98)00398-7
- 24) Valeri A, Azzouzi R, Drelon E, Delannoy A, Mangin P, Fournier G. Early-onset hereditary prostate cancer is not associated with specific clinical and biological features. *Prostate* 2000; 45: 66-71. doi: 10.1002/1097-0045(20000915)45:1<66::AID-PROS8>3.0.CO;2-W
- 25) Kotsis SV, Spencer SL, Peyser PA, Montie JE, Cooney KA. Early onset prostate cancer: predictors of clinical grade. *J Urol*. 2002; 167: 1659-63. doi: 10.1016/S0022-5347(05)65173-7
- 26) Rohrmann S, Roberts WW, Walsh PC, Platz EA. Family history of prostate cancer and obesity in relation to high - grade disease and extraprostatic extension in young men with prostate cancer. *Prostate*. 2003; 55: 140-146. doi: 10.1002/pros.10211, PMID: 12661039
- 27) Ang, M., Borg, M., O'Callaghan, M.E. et al. Survival outcomes in men with a positive family history of prostate cancer: a registry based study. *BMC Cancer* 2020; 20: 894. doi: 10.1186/s12885-020-07174-9, PMID: 32948129, PMCID: PMC7499864
- 28) Whiteland H, Spencer-Harty S, Hywel T, et al. Putative prognostic epithelial-to-mesenchymal transition biomarkers for aggressive prostate cancer. *Experimental and molecular pathology*. 2013; 95: 220-6. doi: 10.1016/j.yexmp.2013.07.010, PMID: 23933194
- 29) Sanjaya, I, Putu Gde, et al. Correlation between Low Gleason Score and Prostate Specific Antigen Levels with Incidence of Bone Metastases in Prostate Cancer Patients: When to Omit Bone Scans?. *Asian Pacific Journal of Cancer Prevention* 2013; 14: 4973-6. doi: 10.7314/APJCP.2013.14.9.4973, PMID: 24175761
- 30) Okolo, C.A., Akinosun, O.M., Shittu, O.B. et al. Correlation of serum PSA and Gleason score in Nigerian men with prostate cancer. *Afr J Urol* 2008; 14: 15-22. doi: 10.1007/BF02994508
- 31) Helpap B, Egevad L. Correlation of modified Gleason grading of prostate carcinoma with age, serum prostate specific antigen and tumor extent in needle biopsy specimens. *Analytical and Quantitative Cytology and Histology*. 2008 Jun;30(3):133-8.
- 32) Kanthilatha P, Gauri S.A, Ranjini K, Padmaraj H. Diagnostic correlation between serum PSA, gleason score and bone scan results in prostatic cancer patients with bone metastasis. *British Biomedical Bulletin* 2015; 3: 1-7.