EPIDEMIOLOGICAL AND GENETICAL PROFILE OF PROSTATE CANCER CASES IN TLEMCEN, WEST ALGERIA

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ABSTRACT
Background: According to WHO, prostate cancer is the second most frequent cancer in men. Prostate cancer is a complex, multifactorial disease with genetic and environmental factors involved in its etiology. The age, family history and the ethno-racial background are the strongest risk factors for prostate cancer.

Objective: To study the epidemiological, genetical and clinical aspects of prostate cancer in Tlemcen’s population.

Methods: We made a cross-sectional study on 184 patients with prostate cancer received at the Urology Division of Tlemcen’s teaching hospital, from 2011 to 2016, resident in Tlemcen’s city. The collected information included the age at diagnosis, the geographical location, family history of cancer, Prostate-specific antigen (PSA) level and Gleason score on biopsy.

Results: The median age of our patients was 73 years with extremes between 53 and 7 years. The most frequent age group was 70-80 years with 50% of the total sample of 184 cases. Seventy-four percent of patients have a very high PSA level (higher than 20 ng/ml). Thirty-two percent of the cases have a highly aggressive cancer, and 66% with moderately aggressive cancer. The examination of family history shows that 37% of patients had family history of cancer, 45% of whom are prostate cancer. The inherited form of prostate cancer is noticed in 4.9% of cases.

Conclusion: This study raises a number of questions, considering the high number of family history noticed in this study, and suggests the existence of genetic determinants, and the interactions gene-environment influencing the genesis of this cancer. An earlier diagnosis is essential, according to these data, especially for men at a “high risk” of this cancer, which will constitute an essential tool for more effective anti-cancer strategy.

KEYWORDS: Epidemiology, Genetics, Predisposition, Family history, Cancer, Prostate, Tlemcen

1. INTRODUCTION
Since many years, the geneticists study the genetic variations between individuals and populations with an aim of understanding their differences and their significances. The West Algerian Zone and particularly the area of Tlemcen, have the particularity of being itself constituted by several subpopulations which have remained very preserved and insulated because of their geographical situation (mountains, cliffs, steppes, etc.) and by their Tribal structures (1). This population has the advantage of being confronted with practices of consanguinities for many generations and the impact of such practices is not always well understood from a practical point of view, even if it is theoretically. Under such conditions, the assessment of morbidity and particularly that of prostate cancer, whose age, ethnic origin and family history are major risk factors (2-4), proves very useful in order to take appropriate actions. According to WHO, prostate cancer is the second most frequent cancer in men, with 1.1 million cases diagnosed in 2012, accounting for 15% of the cancers diagnosed in men, with almost 70% of the cases (759,000) occurring in more developed regions. Prostate cancer incidence varies more than 25-fold worldwide (5). In Algeria, cancer registries place prostate cancer at 4th rank (6), its Standardized incidence rate is estimated at 10.8 per 100,000, with an average age at diagnosis of 71 years (7). The work ame is the study the epidemiological, genetical and clinical aspects of prostate cancer in Tlemcen’s population (West Algeria). This study consists of an analysis of...
the distribution of the various demographic and clinical data related to this morbidity, as well as that of genealogical data; and on the other hand, comparisons with various Mediterranean populations.

2. MATERIALS AND METHODS

2.1. Study design and population

Our study area is part of Tlemcen's city, which is located at the north-western end of Algeria. The population of Tlemcen is estimated in 2010 to 977,206 inhabitants (8). We made a cross-sectional study on 184 patients with prostate cancer received at the Urology Division of Tlemcen’s teaching hospital, from 2011 to 2016, resident in Tlemcen city; by collecting data from a prostate cancer record, established by the Department of Urology. The collected information included: the age at diagnosis, the geographical location, family history of cancer, PSA level and Gleason score on biopsy. This study was approuved by the Tlemcen's University research ethics committee (Conseil d'éthique et de D éontologie de l'Université de Tlemcen. No: CEDUT.TLM.2610.18).

2.2. Data analysis

A descriptive analysis was performed to characterize the subjects. Data were analyzed using Microsoft Excel® 2013 Software and basic statistical measures like mean, median, percentage, etc. were calculated.

3. RESULTS

3.1. Distribution of patients by age groups

Our results show an absence of patients of less than 50 years; the median age of our patients is 73 years with extremes between 53 to 87 years. The age group of 50-60 years is slightly represented with only 6% of the cases, this rate passes to 33% for the age group of 60-70 years. The age group the most affected is that of 70-80 years with 50% of the cases; this rate falls to 13% for the following age group of 80 years and more (Figure 1).

![Figure 1. Distribution of patients by age group.](image)

3.2. Distribution of patients by their geographical location

The results obtained show that more than half of the patients (51%) come from Tlemcen's region, followed by Remchi with 9% of the cases; Then those of Maghnia, Hennaya, and Sabred with respectively 8%, 6% and 5%. Bensekran's region and Ouled Mimoun represent each one 4% of the cases, and those of Ghazaouete, Nedroma, Beni Snouss and Sebdou each one 3% of the cases, and finally Honaine's region and Sidi Djilali with each one 1% of the cases (Figure 2).

3.3. Distribution of patients according to their PSA level

Our results show that the majority of the cases (74%) have a very high PSA level (> 20 ng/ml). We also note that 17% of our cases have a PSA ranging between 10-20 ng/ml, and 7% between 4-10 ng/ml. We noticed also that 2% of cases have a normal PSA (less than 4 ng/ml).

3.4. Distribution of patients according to their Gleason score

In our study, the score of 5 to 7 (Medium differentiated tumor, whose aggressiveness is intermediate) is predominant with 66% of the cases, 32% of cases have a score of 8 to 10 (a slightly differentiated tumor, therefore aggressive), and only 2% of cases have a score of 2 to 4 (Tumor is well differentiated, less aggressive).
3.5. Distribution of patients according to their family history for cancer

The examination of family history shows that 37% of patients had family history of cancer. Among which, 71% are Hormone-driven cancers (45%: prostate cancer, and 26%: other hormone-driven cancers), and 29% are other cancer types. Among the 184 patients, 16.3% had family history of prostate cancer. In addition, 30% of cases with at least one family history of prostate cancer, which constituted 4.9% of the total, met the criteria of hereditary prostate cancer proposed by Carter, namely three cases of prostate cancer in first-degree relatives (father, son or brother) or second degree (nephews, maternal or paternal uncles).

4. DISCUSSION

The results obtained confirm that prostate cancer is a cancer of the elderly, with 75.12% of cases are aged of 65-85 years. Our results agree with work of EUROCARE III (9, 10), which revealed 76.7% of the cases between 65-85 years. The differences between the areas are probably due to their demographic differences (population's size and their structure of age) as prosate cancer is a cancer of elderly men, or due to the differences related to lifestyle and eating habits.

The percentage of patient with PSA level > 20 ng/ml, remains above that found by other authors, in particular those of Saida's city (43.6%) (11) and that of Oran's city (46%) (12). These data may pose the problem of delayed diagnosis of prostate cancer in Tlemcen. It is also found that 2% of cases have a normal PSA (less than 4 ng/ml), which can be explained by the the fact that cancer cells have lost their ability to produce PSA (13). The incidence rate of prostate cancer in the city of Tlemcen is estimated at 4.5 / 100,000. (14), this rate was compared with that of other cities, and it comes out from this comparison that this rate remains higher than that of the town of Oran (1.1%) (15), of Mascara (1.5%) (16), and from Batna (3.6%) (17); on the other hand, it is lower than the national average (7.1) (18), the town of Setif (7.6%) (19) and Algiers (13.57%) (20).

We have also compared the incidence rate of prostate cancer in Tlemcen’s city of Tlemcen with other Maghreb countries. This rate remains lower than that of Libya (9.8) (21), Tunisia (11.8) (22), and Morocco Grand Casablanca (13.5) (23). The comparison of the incidence rate of prostate cancer in Tlemcen’s city with other countries on the
Mediterranean's northern shore shows that this rate is significantly lower than that of Turkey (34.9) (24), Spain (69.5), Italy (81.7) and France (115) (25).

Among the 184 patients, 16.3% had family history of prostate cancer. This rate is 4 times higher than that of Tunisia (26), which had noted a rate of 4%. The rate of patients who met the criteria of hereditary prostate cancer is consistent with that found by Cussenot (27) who estimated it to be 5% in the case of prostate cancer with «Mendelian transmission». The study of family history shows that in the case of prostate cancers in the same sibling, the relative risk can be multiplied by five (28). Earlier diagnosis seems essential, in view of these data, especially for men with "high risk" of this cancer.

5. CONCLUSIONS
This work brings the first epidemiological and genetic data of the prostate cancer in the West Algerian region, and gives an idea on the peculiarities of this region for this type of cancers. On the basis of the findings of this study, it can be hypothesized that the hereditary prostate cancer is relatively high compared to other Mediterranean populations, given the high number of family histories noted in this study. There is now a need to investigate the existence of genetic determinants and gene-environment interactions influencing the genesis of this cancer by case-control studies. An earlier diagnosis is essential, according to these data, especially for men at a "high risk" of this cancer, which will constitute an essential tool for more effective anti-cancer strategy. This study provides hospital-based epidemiological information, but a community-based wider studies are required to arrive at a more precise and accurate understanding of prostate cancer.

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CONFLICT OF INTEREST:
The authors declare that they have no conflict of interests.

AUTHORS' CONTRIBUTIONS:
All authors contributed to this project and article equally. All authors read and approved the final manuscript.

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