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PREVALENCE OF PROSTATE DISEASES IN A COHORT STUDY CONDUCTED IN RADIOACTIVE CONTAMINATED AREAS IN ARAD COUNTY

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ABSTRACT. The most frequent prostate diseases are: prostatitis in young men, benign prostatic hyperplasia in men over 50 years, and prostate cancer which has long been the disease of elderly, but in recent years has shown increasing frequency in men under 60 years. This study is an observational-prospective study, which aims to appreciate the correlations between the characteristics of Arad County with the occurrence of prostate diseases. We selected 276 patients as follow: 181 patients with benign prostatic hyperplasia, 19 healthy subjects as a control group, 12 patients with prostatic premalignant lesions, and 64 prostate cancer patients. In the last few years Arad County was the leader in cancer incidence with 3.6-3.8 cases per 100 inhabitants. In some areas of Arad County soil and waters are rich in arsenic and uranium and additionally the major concern is in animal farms. The residues from zootechnics can affect the quality of soil and water. These toxic substances can lead to genetic changes, like DNA hypermethylation, that cause cancer illnesses. We observed, that many patients diagnosed with prostate neoplasia come from the high risk areas.
KEYWORDS: benign prostatic hypertrophy, BPH prevalence, prostate cancer, PC prevalence, ASAP, HG-PIN

INTRODUCTION

The most frequent prostate diseases depending on age are: prostatitis in young men, benign prostatic hyperplasia (BPH) is the most common benign tumoral disease in men over 50 years (Herbert L, 2011), and prostate cancer (PC) which has long been the disease of elderly man, but in recent years has shown increasing frequency in men under 60 years.

Despite the high incidence of BPH, the disease is underdiagnosed in our country. In Romania there are about 200,000 men under treatment, but taking into account statistics the number of patients could exceed 900,000. Men tend to go to a doctor only when the symptoms become hard to bear and affect their everyday life (www.medlife.ro).

Complications of the prostate diseases which may occur are: acute urinary retention, impaired bladder emptying, renal failure, recurrent urinary tract infections, bladder stones, or gross hematuria (Seftel AD, 2008; McVary KT, 2011).

It is estimated that 10% of cases of PC are genetically determined and 90% occur sporadically under the influence of environmental factors (Sinescu I, Gluck G, 2008), which cause the appearance of epigenetic changes like DNA methylation. These epigenetic changes can be reversible (Abdul QA, Yu BP, 2017).

In Arad County there are a large number of economic agents whose main activity is livestock breeding. Residues from zoo-technics can affect the quality of soils either by applying them at excessive doses or by directly storing them on unprotected surfaces for infiltration. Excessive livestock manure (estimated at over 45 t / ha) that exceeds plant requirements may adversely affect soil fertility through the influence it can have on physical condition, permeability, water retention capacity, oxygen content etc. (http://apmar.anpm.ro).

In Arad County no wastewater treatment plant works in a manner that ensures adequate drainage of the waste water. Large amounts of domestic water treated inappropriately reach the rivers of the county, being important sources of pollution of surface waters (http://apmar.anpm.ro).

The purpose of our study was to see if there is a correlation between the characteristics of the Arad area and the occurrence of prostate diseases.

MATERIAL AND METHODS

This study is an observational-prospective study, part of the project TE 2854 no. contract 358 / 01.10.2015, project code PN-II-RU-TE-2014-4-2854 funded by UEFISCDI through the Youth Teams Program - PN-II-RU-TE-2014-4, that aims to diagnose prostate malignant and benign diseases in the male population in Arad County, and to evaluate the prevalence of these pathologies.

The study population comprises of male adults over 50 years who provided written consent to participate and fulfill the inclusion criteria.

Our study was performed during a one year period, between October 2015 and September 2016, follow-up every six months. We selected 276 patients as follow: 181 patients with BPH irrespective of age,

social status or ethnicity, 19 healthy subjects as a control group, 12 patients with premalignant lesions of the prostate, and 64 PC patients. For the diagnosis all patients were interviewed for LUTS (low urinary tract symptoms) using the IPSS (international prostate symptom score) questionnaire, heredo-colateral disease, personal medical history, and using transabdominal prostate ultrasonography in conjunction with DRE (digital rectal examination) we evaluated the prostate volume, we collected peripheral venous blood for PSA determination.

We divided Arad County in four quadrants and from each quadrant we took 2 major points for patient evaluation. All statistical analyses were conducted using Microsoft Office Excel 2016.

The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, respects ethical demands that require research with human subjects. Before starting the study, we obtained the agreement of the ethics committee of the Arad County Emergency Hospital and the Western University "Vasile Goldis" in Arad.

RESULTS

We selected 276 patients, and we included them in four cathegories, thus: 181 in BPH group, 64 in PC group, 12 in ASAP (atypical small acinar proliferation)/ HG-PIN (high grade prostatic intraepithelial neoplasia) as the premalignant lesions group and 19 clinically healthy patients, as a control group.

In Figure 1 we can see that 65.58% of patients were included in the BPH group, 23.19% in PC group, 4.35% in premalignant lesions group (ASAP/HG-PIN) and 6.88% of subjects in the control group.

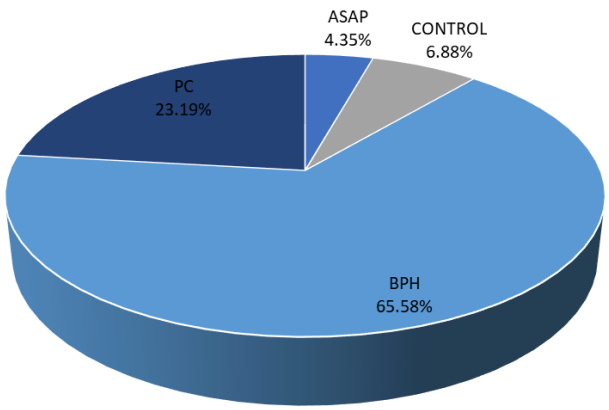

Figure 1. Distribution of the patients in study groups (n=276)

As neither in Arad County nor in Romania there is a database of patients with prostate diseases, we have been pursuing a cohort study covering as many regions as possible for an overall picture of the prevalence of the prostate diseases in Arad County. Most subjects were recruited from rural areas. Because of the study's population's screening nature, we were able to apreciate the compliance of patients in those areas. Figure 2 shows the number of patients enroled for each locality and the percentage of followed up at each consultation. We can observe that only half of the patients included in the study have completed all the controls. The patients, regardless of the origin areas, showed moderate/low compliance with the study, some of which gave up regular controls after the first consultation.

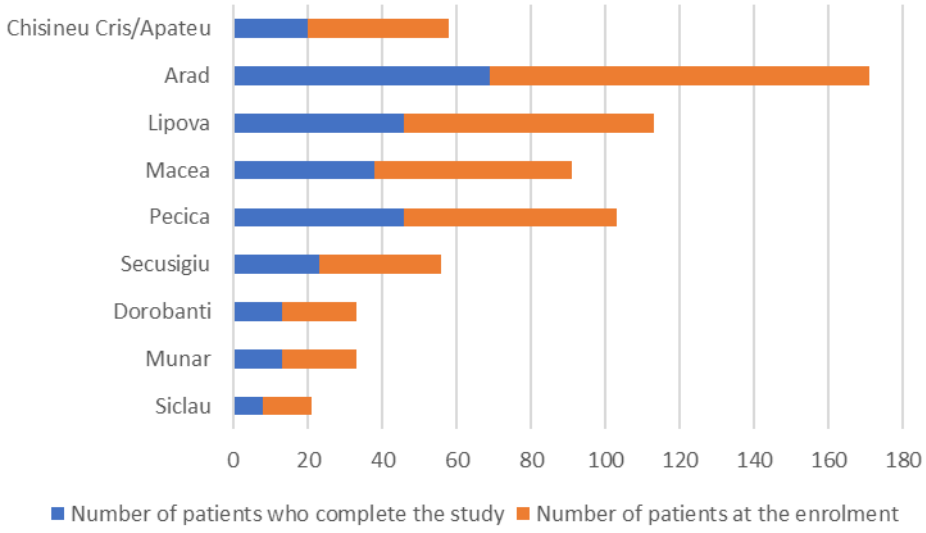

Figure 2 Number of BPH patients by place of origin who have completed the study

As we can see in Figure 3, we divided Arad County in four quadrants and from each quadrant we took several major points for patient evaluation. For the study patients selection we had in view of the diversity in the reliefs of Arad County, so the localities are from the hills, the plain and the meadow of Mureş river and the degree of pollution of that areas. The red circles show the areas where most patients were consulted and enrolled in the study.

Figure 3. Map of Arad County. Areas with most patients enrolled in the study

In the BPH group (n = 181), mean age of patients was 68.31 ± 5.54 years, the youngest subject was 53 years old and the oldest 83. In the 51-60 age group we included 4.97% of patients. Most patients were enrolled between 61-70 years and 60.77%, respectively. Patients over the age of 70 years were 34.35% of whom two were over 80 years of age. In the control group (n = 19) the mean age of the patients was 62.21 ± 3.1 years. In the age group of 51-60 years, 21.05% were enrolled, and between 61-70 years we identified 78.95%. The youngest patient was 58 years of age and the oldest 70 (Figure 4). In the PC group the patients mean age was 68.84±6.32 years, and in the ASAP/HG-PIN group was 67.76±5.74 years. We diagnosed three patients under the age of 60 with PC, the youngest being 54 years old. Patients being enrolled predominantly in the age group of 60-70 years in both groups.

We noticed a slight imbalance between the average age of the patients between the four groups, the control group being younger, which may suggest that the occurrence of prostate malignant and benign diseases is depending on age.

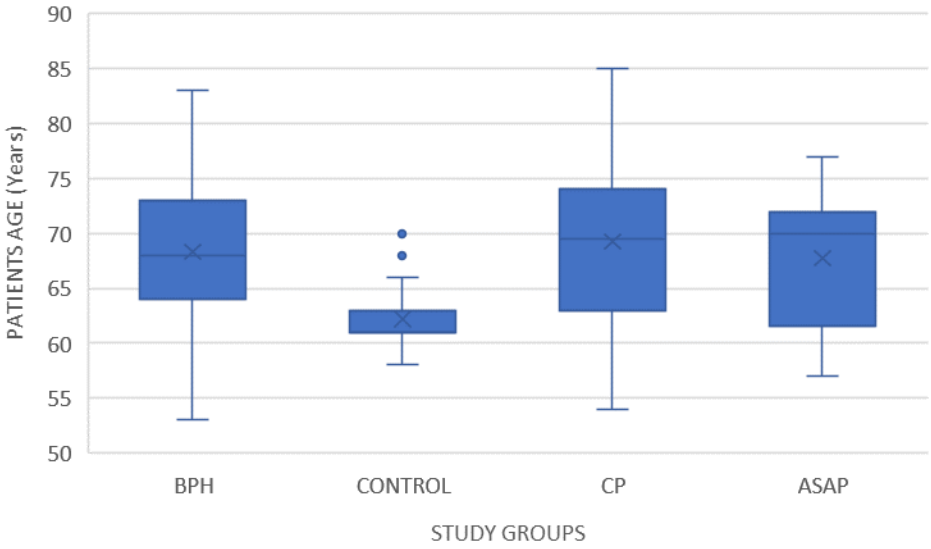

Figure 4 Distribution of patients by age and study groups

In Romania Arad County is the leader in cancer incidence, with 3.6 cases per 100 inhabitants, the national average were 2%. It is well known that in Arad County exists areas with high risk of pollution with different toxic agents (arsenic, uranium, animal farms). In Figure 3 and Tabel 1 we can notice the prevalence of the prostate diseases according to the environment origin of patients. We observed, that many patients diagnosed with PC come from the high risk areas.

Tabel 1. Distribution of patients by pathology and environmental origin

	Arad	Lipova	Macea	Pecica	Secusigiu	Dorobanti	Munar	Siclau	Chisineu Cris/Apateu
ASAP/HG-PIN	7	2	1	1			1		0
CONTROL	2	5	3	7	1	1			0

BPH	36	26	34	35	13	10	10	7	10
PC	24	13	0	3	9	2	2	1	10

Patients in the ASAP group were closely monitored by PSA at 3-month periodic controls. According to urological guidelines, these patients require re-biopsy at 6 months. Two of the patients repeated the biopsy, but we get negative results. Other patients refused re-biopsy, in these patients the PSA values being constant or decreased slightly over time (http://www.uroweb.org).

The most of the patients come from rural areas due to lack of health education, lack of doctors and periodic checks, and the mentality that they go to the doctor only when a severe deterioration of the general condition occurs.

DISCUSSION

Studies have shown that BPH may co-exist with PC, and the higher the pollution the higher the risk of cancer development.

The incidence of cancer cases per 100 people is the best indicator that can reveal a complete picture of this problem. Arad County ranks first in national cancer cases. According to data from the Health Knowledge Bulletin (http://www.dsparad.ro), 3.8 out of a hundred people in Arad County suffer from cancer. The same document reveals that the number of cancerous patients increased in Arad in the first semester of 2013 compared to the same period in 2012. In 2012 in Romania Arad County was the leader in cancer incidence too, with 3.6 cases per 100 inhabitants, when the national average were 2% (http://www.dsparad.ro , http://www.aradon.ro).

In 2016 in Arad County were detected not less than 1,767 new cases of malignant tumors. Most new cases - 258 - are colorectal cancer, followed by: bronchial-pulmonary cancer (236 cases), breast cancer (199 cases), skin cancer (102 cases), PC (101 cases), stomach cancer (76 cases), bladder cancer (73 cases), cervical cancer (71 cases), pancreatic cancer (58 cases) and liver cancer (56 cases). The 1,767 new cases of cancer found in 2016 add to about 13,500 cases of cancer already in the records of Arad's doctors over the past years (http://www.dsparad.ro , http://www.aradon.ro).

Groundwater contamination by arsenic is a serious threat to mankind all over the world. It can also enter food chain causing wide spread distribution throughout the plant and animal kingdoms. However, fish, fruits, and vegetables primarily contain organic arsenic, a few recent studies report 85–95% inorganic arsenic in rice and vegetables, which suggest more studies for standardisation. Humans are exposed to this toxic arsenic primarily from air, food, and water. In many countries all over the world arsenic pollution is due to natural groundwater contamination as well as industrial effluent and drainage problems (B Kumar 2002).

According to a report on health and the environment developed by the National Center for Risk Monitoring in the Community Environment, there are areas in Arad County with high concentration of arsenic in deep waters, of geological etiology. The population supplying with drinking water is made up of deep waters to a significant extent (https://cnmrmc.insp.gov.ro). Out of the 11 samples of water taken from Arad County and analyzed by specialists to determine the concentration of arsenic, six were troubled. The localities where high concentrations of arsenic were found are in descending order: Apateu, Pecica, Pilu, Mişca, Chişineu Criş and Peregu Mic (https://cnmrmc.insp.gov.ro).

Apuseni mountains in western Romania are rich in uranium. The exploitation of uranium started in 1950. The mines reached the territory of three counties: Arad, Alba and Bihor. In the Apuseni Mountains over 400 km of mining galleries were drilled. The mining operations of radioactive metals have been closed without too much environmental protection (https://www.green-report.ro, http://www.ziua.ro/).

This is why population screening and the implementation of prevention methods are very important.

CONCLUSIONS

Complete investigations of the patients are very important in the diagnosis of prostate diseases, because the differential diagnosis between BPH and PC can be difficult sometimes.

Arad County is an area at high risk for cancer illnesses due to the high concentration of arsenic in deep waters.

The age of developing PC decreases, though the patients show low compliance with the study, some of them gave up regular controls after the first consultation.

Sanitary education programs are needed as Arad County is at increased risk for illnesses.

Although we conducted a diagnostic campaign, due to the lack of patient interest and due to a huge number of patients who are oriented for diagnosis and treatment in other hospital centers than Arad our data may be incomplete.

Further studies are needed to demonstrate the link between the characteristics of the Arad County and prostate diseases.

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