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RESEARCH ARTICLE

Incidence Trend of Prostate Cancer in Markazi Province (Center of Iran), Results of Population-based Cancer Registry, and Application of Joinpoint Regression Model, 2012-2017

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Abstract:

Background:

Cancer control, prevention, and treatment, as one of the most common diseases in the world, are a priority of healthcare and treatment around the world. Prostate cancer is one of the most common cancers in the elderly. This study was conducted to determine prostate cancer incidence and its trends in Markazi province, Iran, from 2012 to 2017.

Methods:

In this epidemiological study, all confirmed prostate cancer cases registered in the population-based regional cancer registry of Markazi province, Iran, were included. Crude, age-specific, and age-standardized incidence rates (ASR) of prostate cancer were calculated per 100000 population. ASR was calculated by direct method and using the world standard population. Time trends were assessed using Joinpoint regression analysis, and the average annual percentage change (AAPC) was calculated.

Results:

674 new prostate cancer patients were registered in Markazi province from 2012 to 2017. 89.3% of prostate cancer patients were 60 years old and older, and the highest age-specific incidence rate was in the ≥80 years age group (379.78 per 100000). The ASR of prostate cancer during the study period was 15, 12.9, 9.4, 16.6, 16.2, and 15.4 per 100,000 people, respectively. AAPC was calculated as 3.6% (95%CI: -8.6 to 17.5), but it was not statistically significant (p=0.474).

Conclusion:

ASR for prostate cancer in Markazi province during 2012-2017 did not exhibit significant increasing trends. Also, AAPC changes were not significant. Investigating the impact of early diagnosis using screening and also risk factors, such as working in the metal and chemical industries, is recommended for future studies. Also, it is suggested to check the long-term ASR trend.

Keywords: Prostatic neoplasms, Incidence, Epidemiology, Annual percent changes, Cardiovascular diseases, Prostate cancer.

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1. INTRODUCTION

Following cardiovascular diseases, cancer is the most common cause of years of life lost (YLL), disability-adjusted life years (DALY), and death in the world [1]. It is predicted that new cases of global cancer will increase by 47% and will reach from 19.3 million in 2020 to 28.4 million in 2040. This rise will probably occur more in developing countries [2], and approximately 60% of cancers will be diagnosed in people over 65 years old [3]. A possible increase in cancer mortality is also expected in future years due to diagnosis and treatment delays that have occurred during the COVID-19 pandemic [4].

Prostate cancer (PC) is ranked the second most common cancer and the fifth cause of cancer mortality in men worldwide with more than 1.4 million new cases and 375 thousand deaths in 2020 [2].

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PC incidence and mortality have stabilized or declined recently in the majority of countries across the world [5]. However, there has been observed an increasing trend in Iran [6]. The incidence of PC varies widely in different parts of the world, with the highest rate seen in Northern Europe (age-standardized incidence rate (ASR): 83 per 100000) and the lowest in South Central Asia (ASR: 6.3 per 100000) [2]. It is also higher in developed countries compared to developing countries (37.5 and 11.3 per 100,000) [2].

Unlike previous studies that have shown a decreasing or stable trend in most countries, in a study that was conducted in 89 countries, the results showed that the ASR of PC increased in 65 countries, decreased in 9 countries, and remained stable in 15 countries, and the average annual percentage changes (AAPC) fluctuated from 0.23% in Argentina to 4.54% in the Republic of Moldova [7]. Furthermore, in Turkey, the ASIR of PC has increased significantly between 2004 to 2015 [8], while in Spain [9] and Canada, there has been found no significant increase in ASIR [10].

To the best of our knowledge, there is no comprehensive similar study to assess the incidence rate of PC in Markazi province and, since this province is considered an air-polluted province, and a significant proportion of men are employed in the metal and chemical industries or the agricultural sector, their exposure to chemicals is higher, so the hypothesis is raised that the incidence of PC in this province is high. On the other hand, control, management, and prevention of diseases always require information obtained from continuous and updated studies, so the current epidemiological study has been conducted to determine PC incidence and trends in the Markazi province of Iran from 2012 to 2017.

2. METHODS

This was an epidemiological study in which we have analyzed the data collected from a population-based cancer registry in Markazi province from 2012 to 2017 to calculate the incidence rate and AAPC of PC.

Markazi province is the fourteenth largest province of Iran, which is known as the industrial capital of Iran. The cancer registration program in Markazi province has been upgraded from pathology-based to population-based since 2006. In a population-based cancer registry, data are collected from various sources, such as hospitals, the death registry, as well as pathology reports, and in general, any center where there is a possibility of referral of a patient with cancer.

After obtaining approval from the research ethics committee, data were obtained by the researchers from the Arak University of Medical Sciences Cancer Registry Secretariat in an Excel file, including patients' first and last names, father's name, national ID, date of birth, age at diagnosis, address, city of residence, date and method of cancer diagnosis, and morphologic codes for PC cases (coding C61.9 based on ICD-O-3).

The data were then sorted alphabetically and checked several times manually using demographic information and morphology codes to identify duplicate registrations and remove them. Patients whose residential addresses were outside of the Markazi province were also deleted. There were two groups of duplications. The first group had similar cases in the same year reported from different sources, and the second group had similar cases between different years, and in this, only an earlier report was considered as a new case. In this process, 72 cases were excluded from the analysis. Most of them were related to the data obtained for the years 2012 and 2013. Finally, 674 cases were included in the analysis.

Crude incidence rates were calculated by dividing the total number of new cases of PC in each year by the number of at-risk population and age-specific incidence rates, and further dividing the number of PC by the number of at-risk population in each age group per 100,000 people (<50, 50-59, 60-69, 70-79, >80). Age-standardized incidence rates (ASR) were also calculated by direct standardization method using the world standard population. All incidence rates have been reported per 100,000 people.

The population of Markazi province in the 2016 Iran census (1,413,959 people, including 717,026 men and 696,933 women) was used to estimate other year's populations by employing a geometric growth formula.

2.1. Statistical Analysis

AAPC and Joinpoint Regression analysis were used to determine PC trends in the Markazi province of Iran during 2012-2017. Joinpoints are points when trends change and divide the considered period into shorter ones with different AAPCs. APCs are considered statically significant when $p<0.05$. The average annual percent change (AAPC) shows the whole period trend. If there is no joinpoint, APC and AAPC will be equal. Microsoft Excel 2016 was used to calculate age-specific incidence rates, STATA version 14 (Stata Corp, College Station, TX, USA) was used to calculate crude incidence rates (CIR), and ASR and Joinpoint Regression Program V.4.9.1.5, one of the software related to the Surveillance, Epidemiology and End Results (SEER) program, was used to calculate AAPC and trends.

3. RESULTS

There were 674 new PC cases in Markazi during 2012-2017. Most of them were reported from Arak, the capital of Markazi province. 89.3% of patients were above 60 years old and the mean age (±standard deviation) at diagnosis of PC was 73.90±11.73 years old.

Table **1** shows the percentage of microscopic verified percent (MV%) of PC in Markazi province. MV% increased from 44.2% in 2012 to 62.8% in 2017, and its average was 55.2%. Adenocarcinoma has been found to be the most frequent morphology.

Table 1. Microscopic verified percentage of prostate cancer in Markazi province from 2012 to 2017.

Years	2012	2013	2014	2015	2016	2017
MV%	44.2	43.9	51.4	63.1	61.2	62.8

Note: MV%: Microscopic verified percent.

Table 2. Prostate cancer frequency and age-specific incidence rates in Markazi province, Iran, during 2012-2017.

Years	2012		2013		2014		2015		2016		2017	
Age groups	**N**	**IR**	**N**	**IR**	**N**	**IR**	**N**	**IR**	**N**	**IR**	**N**	**IR**
50>	2	0.33	3	0.50	2	0.33	2	0.33	3	0.51	3	0.51
50-59	9	15.41	8	13.67	5	8.52	11	18.71	11	15.45	13	18.12
60-69	22	74.44	14	47.27	13	43.80	27	90.78	24	64.37	34	90.46
70-79	43	166.84	38	147.12	23	88.86	44	169.64	46	203.44	34	149.17
80≤	37	316.05	42	357.99	31	263.67	38	322.55	55	379.78	37	253.44

Table 3. Crude and age-standardized incidence rates of prostate cancer in Markazi province per 100000 population from 2012 to 2017.

-	2012	2013	2014	2015	2016	2017
Count	113	105	74	122	139	121
CIR	15.8	14.6	10.3	16.9	19.2	16.5
ASR (95%CI)	15 (12-18)	12.9 (10.3-15.6)	9.4 (7.1-11.7)	16.6 (13.4-19.8)	16.2 (13.3-19)	15.4 (12.5-18.3)

Table **2** shows age-specific PC incidence rates (IR) and the frequency of new cases in the male population of Markazi province during 2012-2017. The age-specific incidence rate of PC increased with age in all the studied years. The highest age-specific incidence rates were observed in the ≥80 age group.

Table **3** shows crude and age-standardized incidence rates of PC. PC CIR ranged from 10.3 (in 2014) to 19.2 (in 2016) per 100,000, while ASR ranged from 9.4 (in 2014) to 16.6 (in 2015) per 100,000. The average ASRs and CIRs were 14.25 and 15.55 per 100000 population, respectively.

Table **3** presents the PC ASR trend in the Markazi province. Joinpoint regression analysis did not show any joinpoint during 2012-2017. An increase in PC ASR with AAPC of 3.6% (95% CI: -8.6 to 17.5) was seen in Markazi, but it was non-significant (P=0.474). Due to the lack of joinpoint in this period, APC and AAPC were equal.

4. DISCUSSION

In the current study, the main results revealed that the PC ASIRs in Markazi province during 2012-2017 were 15, 12.9, 9.4, 16.6, 16.2, and 15.4 per 100,000 people, respectively, with AAPC of 3.6% (95% CI: -8.6 to 17.5). In GLOBACAN 2020, this rate has been reported as 30.7 per 100,000 people globally and 21.2 per 100,000 people in Iran [2, 11].

Based on GBD 2019, the APC for PC incidence rate at the global level was reported as 0.26 (95% CI: 0.15–0.37), and it was 2.01 for Iran, and 2.45 for Turkey, which shows a significant increase in the incidence rate. On the other hand, APC for developed countries, such as the United States of America (−0.84), Canada (−1.14), and Switzerland (−0.45), has significantly decreased between 1990 and 2019 [6]. In our study, the AAPC was reported as 3.6%, and this finding is in line with the results reported by GBD for Iran.

In another study, the average ASIR of PC in Iran was reported as 18.3 per 100,000 people during 2014-2016, which is higher compared to the Markazi province during the mentioned years [12]. However, the ASIR of PC in Iran in Hassanipour *et al.*'s meta-analysis [13] was reported at 9.11 per 100,000 people (1988-2012), and in Moradi *et al.*'s meta-analysis [14], it was reported as 8.7 per 100,000 people (1996-2012), which is lower than that in Markazi province.

According to the GBD data, the PC incidence rate has almost stabilized trend in the world from 1990 to 2019, but it has increased by approximately 2.01% annually in Iran [6]. Many of Iran's neighboring countries have also shown an increasing trend [6]. In Turkey, between 2004 and 2015, the ASIR for PC has increased significantly, from 24.9 to 33.1 per 100,000 people [8].

In Spain, after more than 20 years of increasing trends, the incidence of PC has stabilized recently [9]. In Canada, during 1992-2010, despite the increasing trend of PC crude incidence rates, there was no significant increase in ASIRs, which can be a sign of the aging population in this country [10]. In the current study conducted in Markazi province, despite the annual changes of 3.6% in PC ASIRs, this cancer has not exhibited a statically significant upward trend in those 6 years; however, compared to a previous study conducted in Markazi province during 2006-2011, PC ASIR has almost tripled [15]. This sudden increase can be due to an improvement in the population-based cancer registry program and its implementation, increased diagnoses in medical care units, as well as a possible increase in the prevalence of PC risk factors, such as obesity, inactivity, and change in diet patterns [16].

The average age of PC incidence in the Markazi province has been found to be 73.90 years. The age-specific incidence rate of PC has been found to increase with age, and the highest frequency and the highest age-specific incidence rate can be assigned to ≥80 years. In Canada, the average age of patients was 68.5 years and the highest frequency of patients was in the age range of 60-79 years [10]. These findings confirm the effect of advancing age on PC incidence [16].

The average microscopic verified percentage for PC was only 55.2%, but it increased by 62.8% in 2017. This rate was 68.28% for all cancers in 2014 in Iran [17].

Arak, the capital of Markazi province, had the most PC records. The reason could be the fact that Arak has the largest population and concentration of diagnostic and therapeutic centers.

The current study has investigated the trend of PC over a 6-year period. We suggest that longer trends of the incidence and mortality of cancer should be investigated in future studies. Conducting epidemiological studies to determine the risk factors of cancers and their prevalence and changes over time in Markazi province seems necessary. It is recommended to conduct studies to determine the contribution of each demographic change (such as population aging and population growth) and the prevalence of risk factors to the alternating cancer incidence trends.

CONCLUSION

ASR for prostate cancer in Markazi province during the years 2012-2017 has not been found to have significant increasing trends. Also, AAPC changes have not been observed to be significant. Investigation of the impact of early diagnosis using screening and also risk factors, such as working in the metal and chemical industries, is recommended in future studies. It is also suggested to check long-term ASR trends.

AUTHORS' CONTRIBUTION

Kosar EyvaziNasab, Ali Alimohammadi, and Amir Almasi-Hashiani contributed to the conceptualization of the study, methodology, original draft preparation, and review and editing. Kosar EyvaziNasab and Amir Almasi-Hashiani performed formal analysis, data curation, and statistical analysis. Ali Alimohammadi and Amir Almasi-Hashiani supervised the study. All authors have read and agreed to the published version of the manuscript.

LIST OF ABBREVIATIONS

AAPC	=	Average Annual Percentage Change
ASR	=	Age-standardized Incidence Rates
YLL	=	Years of Life Lost
DALY	=	Disability-adjusted Life Years
PC	=	Prostate Cance
CIR	=	Crude Incidence Rates

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study was approved by the Ethics Committee of Arak University of Medical Sciences (Ethical code: IR.ARAKMU.REC.1401.089).

HUMAN AND ANIMAL RIGHTS

No animals were used in this research. All procedures performed in studies involving human participants were in accordance with the ethical standards of institutional and/or research committee, and with the 1975 Declaration of Helsinki, as revised in 2013.

CONSENT FOR PUBLICATION

Not applicable.

AVAILABILITY OF DATA AND MATERIALS

The datasets used and analyzed during the current study are available from the corresponding author [A.A.H] upon reasonable request.

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CONFLICT OF INTEREST

All authors declare no conflict of interest.

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