

## ORIGINAL RESEARCH

# Prevalence and risk factors of urethral, penile, and scrotal cancers in Iranian men during 2004-2015: A national cancer registry-based study

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**Abstract:** **Introduction:** Urethral, penile, and scrotal cancers are rare and represent less than 1% of all malignancies. However, they are associated with a high mortality rate and have a significant effect on patients' quality of life. Penile and urethral cancers comprise 0.6% of all urological cancers. Because of ethnic, geographical, and cultural diversity, risk factors and cancer patterns vary in different communities. We aimed to provide valid information on the prevalence, incidence, and epidemiology of urethral, penile, and scrotal cancers using the National Registry on Cancer of Iran. **Methods:** This retrospective study of 465 patients included all known cases of urethral, penile, and scrotal cancers from the Department of National Registry on Cancer at the Ministry of Health and Medical Education in Iran during 2004-2015. This study examined the demographic characteristics of patients and discussed the risk factors and possible causes of the above-mentioned cancers. **Results:** The mean  $\pm$ SD age at the time of registration was  $58.49 \pm 20.82$  years. The highest and lowest proportions of cases belonged to Tehran/Alborz (14.2%) and Mazandaran (0.65%) provinces, Iran, respectively. Regarding the distribution of records according to a year of registration, these cancers were more prevalent in 2014, and less prevalent in 2004. **Conclusions:** Urethral, penile, and scrotal cancers were more common in Tehran and Alborz. There was a strong possibility that the prevalence of these cancers is linked to the industrial nature of Tehran and Alborz and the prevalence of human papillomavirus.

**Keywords:** Penile Neoplasms; Urethral Neoplasms; Urogenital Neoplasms

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## 1. Introduction

Cancer is one of the leading mortal agents and a major global public health issue. Meanwhile, genitourinary tract cancers are a group of malignancies that, in addition to death, impose a heavy burden on various communities, especially develop-

ing countries(1, 2). Prostate cancer, bladder cancer, and renal cell carcinoma are the most common and much more known malignancies of the genitourinary tract, with an annual incidence of millions of cases and a mortality rate of hundreds of thousands worldwide(3). However, another branch of these cancers in men that are less common and lesser-known are urethral, penile, and scrotal cancers(4). Although these cancers are rare and represent less than 1% of all malignancies, they are associated with a high mortality rate and a significant effect on the patients' quality of life(5-7).

Since most known risk factors for these cancers are catego-

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alized as environmental exposure to infectious and chemical carcinogens, poor hygiene is a significant factor in the higher incidence of the disease in developing countries. On the other hand, religious practices in some cultures, including neonatal circumcision in Islam and Judaism, are among the most known significant protective factors for penile cancer (5, 8, 9). To date, the rarity of these diseases has prevented comprehensive prospective studies, and surveys on this topic are limited to case reports and small case series (10). Iran is a developing Muslim country in the Middle East, where male neonates are routinely circumcised. Due to cultural issues and the improvement of health conditions over the past decades, the general belief is that these cancers might be less common in Iran than in other developing countries. In a report based on the records of Iran Ministry of Health and Medical Education (MOHME) in 2005, the distribution of penile and urethral cancers was 0.6% of all urological cancers (11). However, following the increase of unprotected sexual behavior and the lack of human papillomavirus (HPV) vaccine in the national vaccination program, reports indicate an increase in the prevalence of HPV in Iran (12, 13).

Since HPV is a known risk factor for urinary tract cancers, especially cancers in the genitalia (9), it seems that the previous assumption of a low prevalence of urethral, penile, and scrotal cancers in Iran is debatable. Moreover, the study of epidemiological features is particularly important and helps provide more valid evidence for health policymakers, and in turn, more efficient treatment strategies for clinicians. However, the current knowledge on the prevalence, incidence, and epidemiology of these cancers is limited and incomplete. The Department of National Registry on Cancer located at MOHME in Iran has comprehensive information on cancer patients and their risk factors and outcomes (14). The present study sought to provide valid information on the prevalence, incidence, and epidemiology of urethral, penile, and scrotal cancers using the National Registry on Cancer of Iran.

## 2. Methods

The data of patients in this retrospective study included all known cases of urethral, penile, and scrotal cancers from the Department of National Registry on Cancer located at MOHME in Iran during 2004-2015. One of the limitations of this study is the lack of access to information in recent years. The patients with the pathological diagnosis of urethral, penile, and scrotal cancers available in the database were included in the analysis. Since all the patients' recorded data in the database were retrieved, no exclusion criteria were defined for this survey. Finally, 465 patients with the diagnosis of any urethral, penile, and scrotal cancers were enrolled in the study. Basic patient variables, including age,

marital status, city, and province of residence, were also recorded. As the used database was the National Registry on Cancer, the extracted data provided substantial coverage across nearly the entire geographical regions of Iran. Patients' general characteristics were categorized by year to compare the course of changes in the study interval. Furthermore, the number of patients was reported separately based on marital status and province of residence. The Institutional Board of the Research and Ethics Committee of Shahid Beheshti University of Medical Sciences, Tehran, Iran, approved the design and methodology of this study (ethical no.: IR.SBMU.RETECH.REC.1399.1243).

The patients' data were analyzed using SPSS software (version 21; SPSS, Chicago, IL). Quantitative variables were expressed as mean  $\pm$  standard deviation; however, categorical variables were expressed as frequency and percentage.  $P \leq 0.05$  was considered statistically significant.

## 3. Results

During 2004-2015, the registration information of 465 urethral, penile, and scrotal cancer cases was retrieved from the National Cancer Registry System. Table 1 shows the general characteristics of the patients according to the time of registration. The mean  $\pm$  SD age at the time of registration was  $58.49 \pm 20.82$  years. The highest and lowest proportions of cases belonged to Tehran/Alborz (14.2%) and Mazandaran (0.65%) provinces, respectively (Table 1).

Regarding the distribution of records according to the year of registration (Figure 1), the highest number of these cancers ( $n=67$ ; 14.41%) was reported in 2014; however, the highest incidence proportion (2.98; range: 1.88-4.07) was in 2013. The lowest number of these cancers ( $n=22$ ; 4.73%) was reported in 2004, and the lowest incidence proportion (1.14; range: 1.03-2.27) was also reported in 2004. The number of events has increased annually (Table 2). According to Figure 1, the lowest distribution was in 2004. Table 3 shows the distribution of incidence proportion estimates according to marital status. Most of the patients were married; nevertheless, no accurate judgment can be made because of the insufficient database information in this regard.

## 4. Discussion

Cancer is currently a public concern in the world and is increasing due to increased risk factors (15). In Iran, the prevalence and mortality of various cancers are increasing, including genital cancers (16). There have been numerous studies on the incidence and risk factors for testicular cancer, the rate of which is about 1-2% in men (17); nonetheless, few studies have been conducted on the prevalence and risk factors of penile, scrotum, and urinary tract cancers. Despite the rarity of these cancers, the incidence of these cancers has been in-

creasing in recent years. Akbari and colleagues found that the prevalence rates of penile and urinary tract cancers in Iran were 0.15% and 0.45%, respectively (11).

The present study was conducted on 465 registered cases of urethral, scrotal, and penile cancers through the National Cancer Registry in Iran. The results showed that in recent years the prevalence of these cancers has been increasing, which might be due to increased risk factors, such as unhealthy nutrition, smoking, human immunodeficiency virus, microwaves, and increased prevalence of HPV infection. According to the results of the current study, most of these cancers were diagnosed in the sixth decade of life. Previous studies have shown that the most common age for these cancers is over 50 years (18).

The specific prevalence of these types of cancers cannot be judged due to the incomplete information in the database. These cancers were more common in married individuals, although this is not a correct judgment because most of the patients were married and a small number of patients were single. Most cases were reported in Tehran and Alborz provinces, which could be attributed to environmental pollution in these provinces. The lowest rate is reported in Mazandaran province, which is in contrast to those of Tehran and Alborz provinces. For example, the most common underlying cause of penile cancer is HPV, which according to previous studies, the prevalence of this virus in male cases in Tehran province is higher than in other provinces in Iran.

Due to the lack of a comprehensive HPV vaccination program in Iran, the prevalence of HPV is increasing. In male subjects, HPV-16 has been the most common genotype in urogenital cancers, especially penile cancer. However, genotypes 6 and 11 are commonly observed in genital warts. According to the results of studies, the prevalence rates of genotype 16 among all HPV genotypes were about 5.5% and 16.6% in male and female cases, respectively, which is directly related to urogenital cancers (19). The treatment and prevention of HPV in male cases have been shown to be directly related to penile malignancies and precancerous lesions (20).

One of the limitations of this study is the lack of access to data of recent years as well as the details of patients' medical records. Further studies will be needed in this area.

## 5. Conclusion

Despite the rarity of these cancers, the incidence of these cancers has been increasing in recent years. Urethral, penile, and scrotal cancers are more common in Tehran and Alborz. One possible theory in this regard could be referring patients to Tehran. Due to the industrial nature of these cities and the increase in the amount of pollutants, a connection can be established between these cases and the increase in the rate of urogenital cancers. Considering the increasing prevalence of

urogenital cancers in recent years and the increasing prevalence of HPV, it can be argued that HPV has played a direct role in increasing the incidence of these cancers.

## 6. Appendix

### 6.1. Acknowledgment

We thank the staff at Department of National registry on Cancer located at the Ministry of Health and Medical Education for their cooperation.

### 6.2. Conflict of interest

The authors declare that they have no conflict of interest.

### 6.3. Funding support

None.

### 6.4. Author's contributions

All the authors have the same contribution.

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**Table 1:** General characteristics of the patients according to the time of registration.

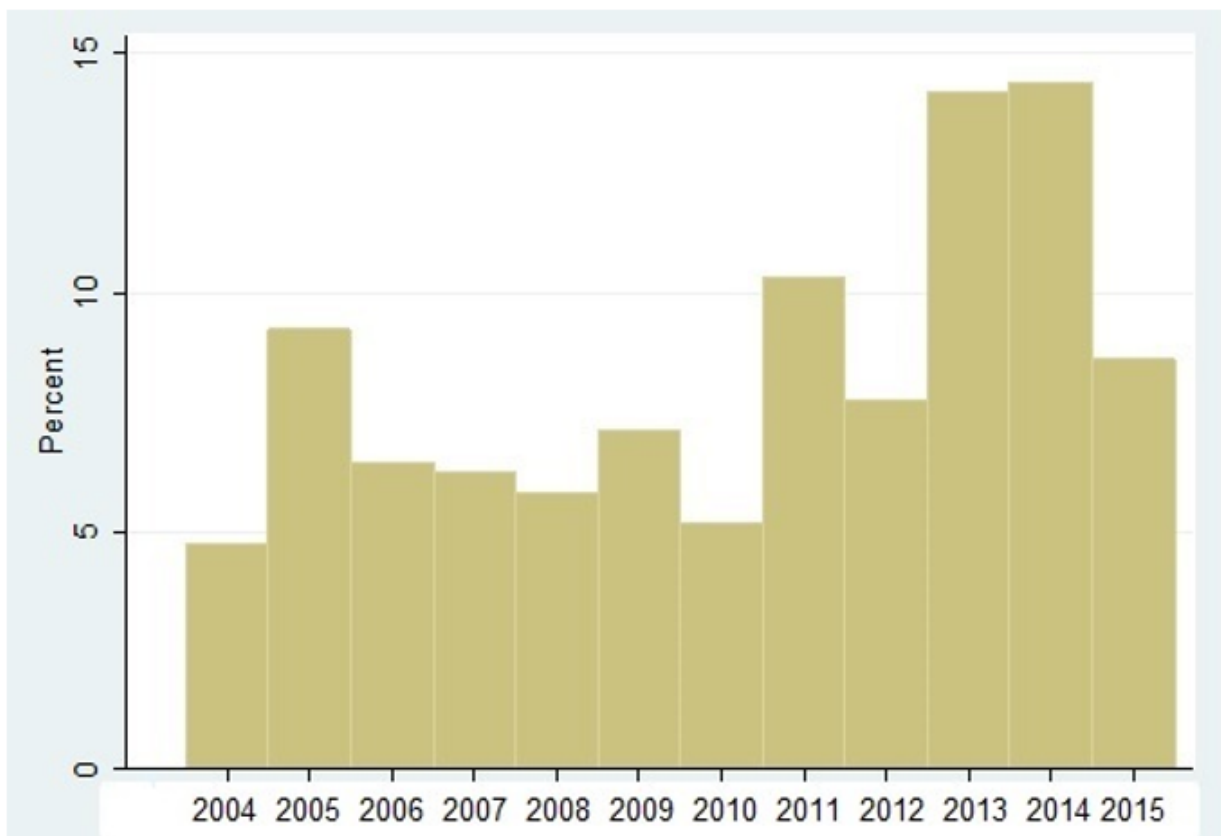
Variable	Total	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Number (%)	465(100%)	22(4.7)	43(9.2)	30(6.4)	29(6.2)	27(5.8)	33(7.1)	24(5.1)	48(10.3)	36(7.7)	66(14.2)	67(14.4)	40(8.6)
Age*	58.49(20.82)	60.0(4.7)	59.4(3.4)	62.4(3.4)	61.3(2.4)	51.4(5.0)	63.3(2.3)	54.7(4.0)	57.4(2.8)	62.6(2.9)	60.7(3.0)	55.9(2.7)	52.9(3.0)
<b>Marital status</b>													
Married	58(89.2)	21(95.4)	37 (86)										
Divorced	3(4.6)	0	3 (6.9)										
Widowed	4(6.1)	1(4.5)	3 (6.9)					NA£					
<b>Diagnosis</b>													
Metastatic	13(2.8%)	NA	NA	NA	NA	8(29.6)	5(15.1)	NA	NA	NA	NA	NA	NA
Transitional cell	6(1.29%)					1(3.7)	2(6)	3(12.5)					
BCC NOS	1(0.22%)					NA	1(3)	NA					
SCC	NA					8(29.6)	11(33.3)	10(41.6)					
Sarcoma	14(3.01%)					3(11.1)	4(12.2)	7(29.1)					
Melanoma	2(0.43%)					1(3.7)	1(3)	NA					
Unknown	400 (86%)	22 (100)	43 (100)	30 (100)	29(100)	6(22.2)	9(27.3)	4(16.6)	48(100)	36(100)	66(100)	67(100)	40(100)
<b>Province of resident</b>													
Tehran/Alborz	66 (14.2)	1(4.5)	2(4.6)	6(20)	2(6.9)	6(22.2)	2(6)	6(25)	0	4(11.1)	15(22.7)	10(14.9)	12(30)
Qom	4 (0.86)	0	1(2.3)	0	0	0	1(3)	0	0	2(5.5)	0	0	0
Qazvin/Markazi	10 (2.1)	2(9)	0	0	1(3.4)	0	3(9)	1(4.1)	0	0	1(1.5)	1(1.5)	1(2.5)
Mazandaran	3 (0.65)	0	0	2(6.6)	0	0	0	0	0	1(2.7)	0	0	0
Isfahan	35 (7.5)	3(13.6)	6(13.9)	2(6.6)	0	5(18.5)	2(6)	1(4.1)	0	3(8.3)	7(10.6)	1(1.5)	5(12.5)
Eastern Azerbaijan	19 (4.1)	0	0	0	1(3.4)	2(7.4)	6(18.1)	1(4.1)	0	3(8.3)	0	4(5.9)	2(5)
Khorasan-Razavi	23 (4.9)	2(9)	2(4.6)	1(3.3)	1(3.4)	3(11.1)	0	3(12.5)	0	2(5.5)	1(1.5)	4(5.9)	4(100)
Fars	40 (8.6)	0	2(4.6)	1(3.3)	5(17.2)	0	5(15.1)	4(16.6)	0	4(11.1)	7(10.6)	7(10.4)	5(12.5)
West Azerbaijan/Ardebil	8 (1.7)	2(9)	2(4.6)	2(6.6)	0	0	0	0	0	1(2.7)	0	0	1(2.5)
Sistan-Baloochestan	5 (1.1)	0	1(2.3)	0	3(10.3)	0	0	0	0	1(2.7)	0	0	0
Kermanshah	17 (3.6)	0	2(4.6)	0	3(10.3)	0	3(9)	1(4.1)	0	2(5.5)	0	5(7.4)	1(2.5)
Kurdistan	7 (1.5)	1(4.5)	2(4.6)	0	1(3.4)	2(7.4)	0	0	0	0	0	0	1(2.5)
Hamadan	17 (3.6)	0	1(2.3)	1(3.3)	2(6.9)	0	2(6)	0	0	1(2.7)	8(12.1)	2(3)	0
Khuzestan/ Kogheloye	40 (8.6)	1(4.5)	5(11.6)	2(6.6)	2(6.9)	4(14.8)	2(6)	4(16.6)	0	4(11.1)	7(10.6)	6(8.9)	3(7.5)
Lorestan	10 (2.1)	1(4.5)	0	2(6.6)	1(3.4)	2(7.4)	1(3)	0	0	1(2.7)	1(1.5)	1(1.5)	0
Ilam	6 (1.3)	1(4.5)	0	0	0	0	1(3)	0	0	0	0	3(4.4)	1(2.5)
Semnan	34 (7.3)	8(36.3)	13(30.2)	6(20)	4(13.8)	0	1(3)	1(4.1)	0	0	0	1(1.5)	0
Yazd	4 (0.86)	0	1(2.3)	0	0	0	1(3)	0	0	1(2.7)	0	1(1.5)	0
Hormozgan/ Bushehr	16 (3.4)	0	1(2.3)	4(13.3)	1(3.4)	(3.7)	0	0	0	1(2.7)	3(4.5)	4(5.9)	1(2.5)
Zanjan	7 (1.5)	0	0	0	0	0	0	0	0	0	2(3)	4(5.9)	1(2.5)
Golestan	33 (7.1)	0	0	1(3.3)	2(6.9)	2(7.4)	3(9)	2(8.3)	0	1(2.7)	8(12.1)	12(17.9)	2(5)

\*mean (SD), £ NA: Not Available.

**Table 2:** Overall incidence proportion (95%CI) of the patients.

Year	Number of events (%)	Incidence proportion* (95%CI)
2004	22 (4.73%)	1.14 (1.03, 2.27)
2005	43 (9.25%)	1.75 (0.372, 3.120)
2006	30 (6.45%)	1.27 (0.569, 1.970)
2007	29 (6.24%)	1.18 (0.551, 1.811)
2008	27 (5.81%)	1.32 (0.920, 1.722)
2009	33 (7.10%)	1.48 (0.61, 2.34)
2010	24 (5.16%)	1.08 (0.760, 1.40)
2011	48 (10.32%)	2.16 (1.52, 2.80)
2012	36 (7.74%)	1.25 (0.77, 1.71)
2013	66 (14.19%)	2.98 (1.88, 4.07)
2014	67 (14.41%)	2.47 (1.32, 3.62)
2015	40 (8.60%)	1.55 (1.29, 1.80)





**Figure 1:** Distribution of records according to year of registration.

**Table 3:** Distribution of incidence proportion estimates according to marital status.

Year	Total		Married		Divorced/ Widowed	
	Number of events (%)	Incidence proportion*(95%CI)	Number of events(%)	Incidence proportion*(95%CI)	Number of events(%)	Incidence proportion*(95%CI)
2004	22(4.73%)	1.14 (1.03, 2.27)	21 (95.4)	0.98 (0.09,1.10)	1 (4.5)	Unavailable Data
2005	43(9.25%)	1.75 (0.372, 3.120)	37 (86)	1.65 (0.99, 2.20)	6 (6.9)	Unavailable Data
2006	30(6.45%)	1.27 (0.569, 1.970)				
2007	29(6.24%)	1.18 (0.551, 1.811)				
2008	27(5.81%)	1.32 (0.920,1.722)				
2009	33(7.10%)	1.48 (0.61, 2.34)				
2010	24(5.16%)	1.08 (0.760, 1.40)			Unavailable Data	
2011	48(10.32%)	2.16 (1.52,2.80)				
2012	36 (7.74%)	1.25 (0.77,1.71)				
2013	66(14.19%)	2.98 (1.88,4.07)				
2014	67(14.41%)	2.47 (1.32,3.62)				
2015	40 (8.60%)	1.55 (1.29,1.80)				