
The Epidemiology of Penile Cancer

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Abstract: Penile cancer is an uncommon type of malignancy. In 2020, globally, 36068 new cases were diagnosed according to the International Agency for Research on Cancer. The majority (over 95%) of penile cancers are squamous cell carcinoma. Penile cancer generally affects men from low socio-economic groups with poor hygienic standards. The highest figures have been recorded in countries such as South America, Africa, and India. Human papilloma virus (HPV16-18) infection, phimosis, and smoking have been found to be the strongest risk factors for penile cancer, and they can significantly increase its incidence. Penile cancer usually affects patients late in life, with the highest incidence recorded in the >60-year age group.

Keywords: epidemiology of penile cancer; human papilloma virus and penile cancer; incidence of penile cancer; penile cancer around the globe; risk factors for penile cancer

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INTRODUCTION

Penile cancer is a rare tumor. With 36068 cases, it occupies 30th position on the list of the most common cancers recorded worldwide (1). The vast majority (over 95%) of penile cancer are squamous cell carcinoma. The most common are Grade 1–2 tumors (2). Penile cancer is typical of non-industrialized countries with low hygiene and education standards (3–6). Its incidence varies greatly from country-to-country. The highest rates are reported in South America, South Africa, and India. The incidence increases with age, being the highest in the >60 year age group (7). This chapter provides an overview of the global incidence and risk factors of penile cancer.

RISK FACTORS

Several risk factors, such as Phimosis, human papilloma virus (HPV), smoking, and low social economic status have been found to associated to penile cancer (5).

Phimosis

Phimosis is strongly correlated to penile cancer and should not be considered a mere physiologic after the age of 6 years (8). According to the available literature, Phimosis is among the strongest risk factors for penile cancer (9). In 1986, Hellberg et al. reported a relative risk of 64.6 for penile cancer among men with phimosis (10). A meta-analysis showed an odds ratio of 21.1 (95% CI 5.6–26.2) (11). In a study in Washington state by Daling and co-workers, phimosis was associated with a significant 11.4-fold increase in risk of invasive penile cancer and 3.8-fold increased risk of carcinoma *in situ* (12).

Circumcision and hygiene

A recent consensus meeting in Brazil by The Brazilian Urology, Clinical Oncology, Radiation Oncology, and Pathology Societies (5) found evidence that circumcision of newborns (13) reduces the risk of penile cancer, in particular, the most invasive type (13). The European Urology guidelines support this evidence stating, “Neonatal circumcision reduces the incidence of penile cancer; however, it does not seem to reduce the risk of PeIN (Penile intra-epithelial neoplasia)” (14). This though do not apply to circumcision in adulthood (5). Circumcision does seem, however, to protect against penile HPV infection in adults, especially in HIV-positive patients (15) and helps to maintain adequate genital hygiene, which is also essential in reducing the risk of malignancy (16).

Human papilloma virus

There is a rich documentation available about penile cancer and HPV (17). According to De Martel (18), of the 26000 cases of penile cancer recorded by

GLOBOCAN in 2012, 13000 cases (50%) were attributable to HPV. Of these, 9100 cases (73%) were caused by the HPV 16/18 strains. Chaux et al. found that patients with a sexual history of >10 lifetime female partners were more prone to contract HPV-positive tumors compared to those with <6 lifetime partners (4). HPV vaccination reduces the risk of penile cancer, as it results in a significant decrease in genital, precancerous, and malignant lesions (19).

Smoking

Smoking is a direct, independent, dose-related risk factor for penile cancer; multiple studies have shown an association between tobacco smoking and penile cancer. Tsen et al., in their case-control study, showed a 2.4-fold risk increase in those who have ever smoked and an even higher incidence (OR 3.1) in current smokers (20). A 230-case Brazilian study found that over 50% of penile cancer patients with squamous cell carcinoma were smokers (21). In Chaux's study, those figures were even higher (76%) (4). A study with age-matched controls in India reported a dose response association between penile cancer and various forms of tobacco use (smoking, chewed tobacco, and even snuffed tobacco) (22).

Education and socio-economic status

It has been demonstrated in multiple studies that penile cancer generally affects patients belonging to low socio-economic groups (23). Chaux et al found that most of the patients affected by penile cancer, lived in rural or suburban regions and received only elementary education (<6 years of school). The gross family income was below the minimum wage in most cases. About 50% of patients in Brazil present at an advanced stage at diagnosis (24). Moreover, one of the main causes of delay is the lack of knowledge and embarrassment (25). Educational campaigns for penile-lesion identification might improve the early diagnosis of penile cancer and should be encouraged as penile cancer has an easily recognizable slow-growing pattern.

PENILE CANCER AROUND THE GLOBE

Penile cancer is a rare cancer. With 36,068 cases and 13,211 deaths in 2020, it occupies the 30th position for incidence and the 31st place for number of deaths among all cancer (1). Its age standardized rate per 100,000 inhabitants (ASR) is around 0.8 and vary greatly around the globe (1, 3). Penile cancer generally affects populations from developing countries such as South America, South Africa, and South-Central Asia (Table 1). In North America and Europe, it ranges from 0.51 to 0.94, while certain African and South American countries show a two or three-fold increased incidence (Table 2). In this regard, the ASR of penile carcinoma in Uganda, Botswana, and Paraguay are among the highest worldwide, with a reported values of 4.6, 4.4, and 3.4, respectively, according to latest available data from the International Agency for Research on Cancer (IARC) 2020.

TABLE 1 Cases of penile cancer worldwide in 2020

GLOBOCAN 2020		Penile cancer figures by Continent	
Continent	Crude numbers	ASR (World) (Cases per 100.000 men)	Cum. risk
World	36068	0.80	0.21
Latin America and the Caribbean	4988	1.3	0.41
Europe	6762	0.94	0.25
Asia	20315	0.74	0.18
Oceania	202	0.64	0.17
Africa	2060	0.53	0.13
Northern America	1741	0.51	0.15

Stratified per geographical area and ordered by ASR (11).

TABLE 2 Cases of penile cancer recorded in South America

GLOBOCAN 2020		Top 10 list of Latin America by penile cancer incidence	
Country	Crude numbers	ASR (World) (Cases per 100.000 men)	Cum. risk
Latin America and the Caribbean	4988	1.3	0.41
Saint Lucia	5	3.9	1.24
Paraguay	115	3.4	0.98
Bolivia, Plurinational State of	159	2.0	1.61
Colombia	550	1.9	0.54
Honduras	70	1.9	0.46
Venezuela, Bolivarian Republic of	270	1.8	0.51
Dominican Republic	101	1.8	0.38
Argentina	407	1.6	0.34
Suriname	4	1.5	0.22
Peru	285	1.4	0.56
Nicaragua	34	1.3	0.29

Stratified per geographical area and ordered by ASR (1).

North America

North America has historically a low incidence of penile cancer with an ASR of 0.51 cases per 100,000 men (1). The incidence of penile cancer among all races combined was found to be higher in the South (0.442 per 100,000) and significantly lower in the West (0.328 per 100,000) than in the other regions of the United States. The lowest incidence was found among Asia-Pacific Islander men in the West (0.184 per 100,000), whereas the highest rate was found in White men in the North-East and West (0.381 and 0.342 per 100,000 respectively). In contrast, Black men had the highest rates in the South (0.477 per 100,000) and Midwest (0.417 per 100,000). Overall, the highest rate of penile cancer was found among Black men in the South (0.477 per 100,000) (26). In terms of time trends, Goodman et al. found significant ($P = 0.0002$) decrease of -1.2% in the average annual incidence rate between 1973 and 2003. The drop was more accentuated for Black than White men: the average percent change in incidence was -1.9% for Black men ($P = 0.004$) and -1.1% for Whites ($P = 0.0009$) during the 31-year time period analyzed (26). In terms of age of diagnosis, a comprehensive epidemiological study, showed that median age at diagnosis of penile squamous cell carcinoma was 68 years, although considerable variation by race and ethnicity was found. Afro-Caribbean ethnicities were diagnosed at younger ages (median 62 years) compared with whites (median 68 years) ($P < .00001$) and Asians/Pacific Islanders (median 68 years). Hispanics were diagnosed at substantially younger ages (median 58 years) compared with non-Hispanics (median 69 years) ($P < .00001$) (27).

South America

South America is one of the areas with the highest number of penile cancer cases in the World with a total of 4988 in 2021 and ASR of 1.3 case per 100,000 men (1) (Table 2). In 2021, Brazil accounted for the highest number of cases (1658 cases and ASR of 1.3) but not the highest incidence. Saint Lucia and Paraguay have ASR almost three times higher, 3.9 and 3.4, respectively, followed by Bolivia, Colombia and Venezuela. Unfortunately, large epidemiological studies are currently not available in South America. A prospective study in Paraguay showed that the average patient age was 62 years old and that the majority of them lived in rural or suburban regions with only elementary education (4). In Brazil, a similar work showed similar results with 39.2% of the patients above the age of 66 and only 21.04% under the age of 46 (24). Similarly, to the Paraguayan study, it was found that most of the cases (149 cases - 53.02%) were identified in the North and North-East regions of the country, where the human development index is the lowest.

Europe

According to the IARC, the ASR of penile cancer in Europe is 0.94 cases per 100,000 men (Table 2). It usually affects patients in their 60s or older with only a

few cases before age 50 (28). The highest incidence is recorded in Macedonia, 1.7. Moreover, there are a few countries such as Poland, United Kingdom and Germany that exceed the European average figure with an ASR of 1.3, 1.2, and 1.1 cases per 100,000 males, respectively. A recent review from Arya et al. showed that ASR in England rates have increased from 1.10 in 1979 to 1.33 cases in 100,000 men in 2009. The rise in ASR was more marked from 2000 to 2009. The crude number of cases diagnosed each year has increased from 1979 to 2009 by 70.1% (241 cases compared to 410 cases). By comparison, in the Netherlands, the 3-year moving average incidence rate also showed an increase from 1.4 to 1.5 per 100,000 men-year during 1989–2006 (29), although these figures also included data on the incidence of carcinoma in situ. In Saxony, Germany, a similar trend has been documented with an ASR increase from 1.2 per 100,000 in 1961 to 1.8 per 100,000 in 2012. During the period 2003 to 2012, the incidence rate (ESR) increased statistically significantly from 0.9 per 100,000 in 2003 to 1.8 per 100,000 in 2012 (28). In contrast, studies from Finland and Denmark have demonstrated a decrease in incidence rates (16, 30).

Africa

The African region accounts for a relatively low number of penile cancers; 2060 cases were recorded in 2020 (1). However, it hosts few of the countries with the highest incidence in the world, such as Eswatini and Uganda, which have an ASR of respectively 7 and 4.6 cases per 100,000 men. There is a generalized lack of information about the epidemiology of this disease, as many others in this region of the world, which is highly likely to be due to the lack of funding and the poor quality of the healthcare systems. True figures are likely to be higher, considering the endemicity of HPV infection and sexually transmitted diseases. As noted in other areas of the world, the incidence of penile cancer is higher in low- and middle-income countries (31) which account for about 10% of penile cancers in certain regions of Africa (32).

Middle East, Asia, and Oceania

According to the latest figures provided by the IARC, the Asian area accounts for the highest number of penile cancer cases in the world, whereas Oceania occupy the last position. However, if we look at the age standardized rates, they both sit well below the world average rate (0.8 cases per 100,000) with 0.74 and 0.64 cases per 100,000 respectively. In 2020, 20315 cases were recorded in Asia, which represents 56.3% of the total (1), whilst only 202 cases were reported in Oceania (1.8%). India is the leading country in Asia per incidence rate; with 1.6 cases per 100,000 is second only to Nepal (1.7). In 2020, 10677 cases were recorded, which represented 52.5% of the total Asian cases (20315) and 29.6% globally (36068) (1). Despite the lack of accurate information, the incidence in the area might be reducing. A comprehensive review done by Cardona et al. in 2017 showed an ASR of 1.81 cases per 100,000 men when referring to the 1980–1989 period (3). China, with 4628 cases and an ASR of 0.42 per 100,000 men, is one of the countries with the lowest rate of penile cancer, not only in Asia, but worldwide (1).

CONCLUSION

Penile cancer is a rare malignancy. With 36068 cases recorded in 2020, it occupies the 30th position of the commonest cancers and the 31st per mortality (13211 cases). Over 95% of penile cancer diagnosed are squamous cell carcinoma type, and the majority are Grade 1 and 2. It has been observed that penile cancer is more common in non- or low-industrialized countries, in particular in those where hygienic standards and income are the lowest. South America, Africa, and India are the area where the incident is the highest. The population affected is generally old, with the highest figures recorded in the over 60-year age groups. Multiple risks factors have been identified with HPV infection as strongest factor. It is believed that over 50% of the penile cancer are attributable to HPV, and of these, 73% caused by the HPV 16/18 strains. Phimosis and smoking increase the risk of penile cancer—1.4 and 2.4 times, respectively. Strong emphasis will have to be given to prevention, awareness, and HPV vaccination programs.

Conflict of Interest: The author declares no potential conflicts of interest with respect to research, authorship and/or publication of this article.

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