



Epidemiological study of penile cancer in Pernambuco: experience of two reference centers

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ABSTRACT

Objectives: To investigate and analyze the epidemiological profile of penile cancer in the state of Pernambuco and compare this information with other studies related to the issue.

Material and Methods: We conducted a retrospective, observational and descriptive study of all patients with penile cancer in two reference centers in Pernambuco - Brazil, from 2007 to 2012. The variables studied were: age, region from the state, socio-economic situation, previous postectomy, smoking, time from the beginning of injury to diagnosis, staging of the primary lesion, tumor differentiation, treatment performed and death due to cancer.

Results: The total number of patients was 88. The highest prevalence was seen in those aged between 66 and 75 years. About the socio-economic situation, 67% worked informally and 64.8% received up to two minimum wages. Of all patients, 57% were married and 50% illiterate. The Metropolitan Region of Recife was the one with the highest number of cases, 41%. Tobacco smoking was reported in 48.9% of cases and prior postectomy in 3.4%. Most often it was observed an average period of six months from the onset of symptoms to diagnosis. And when the lesion was diagnosed, it usually had 2 to 5 cm (64.7%), stage T2 in 50% and well differentiated in 79.6%. Partial penectomy was performed in 76.1% and total in 17%. Death was observed in 27.3%.

Conclusion: The clinical profile and epidemiological characteristics found in this study are similar to other national and international studies related to the issue, i.e., typical of underdeveloped or developing countries.

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INTRODUCTION

Penile cancer (PC) is a rare observed tumor in developed countries in North America and Europe. In the USA, the incidence is 0.2/100,000 inhabitants (1); in Spain, the incidence is between 0.7 and 1.5/100,000 (2).

However, in many countries of Africa, South America and Asia, the disease represents an important health issue. Most cases in the world

occur in India, Brazil and Uganda, with an incidence four (3) to six (1) times higher than the above developed countries.

In Brazil, the highest incidences occur in North and Northeast regions, where most penile amputations are performed (4). However, there are very few epidemiological studies in the country in order to categorize that affected population.

The main objective of the present work is to evaluate the epidemiological and clinical

characteristics of penile cancer in the state of Pernambuco (Brazil) in order to gather information about the disease in this region and to compare these data with other published in literature.

MATERIALS AND METHODS

This is a retrospective, observational, descriptive study, performed in the first semester of 2013. The data of the medical records of PC patients from Hospital do Cancer de Pernambuco (HCP) and Hospital Getulio Vargas (HGV) were reviewed. These are reference centers for this disease in the state. The reviewed data were from patients attended from January 2007 to December 2012. These hospitals are located in the city of Recife, capital of the Pernambuco State, situated in the Northeastern region of Brazil. Four patients were excluded: two from the state of Paraíba and two from the state of Alagoas.

The studied variables included: age, region of the state, marital status, work status, degree of education, socio-economic status, previous postectomy, smoking, period from the beginning of lesion un-

til diagnosis, staging of primary lesion (TNM 2010), tumor differentiation, treatment performed, presence and localization of tumor recurrence, treatment of tumor recurrence and death due to PC.

The research was approved by the Ethical Committee of Federal University of Pernambuco.

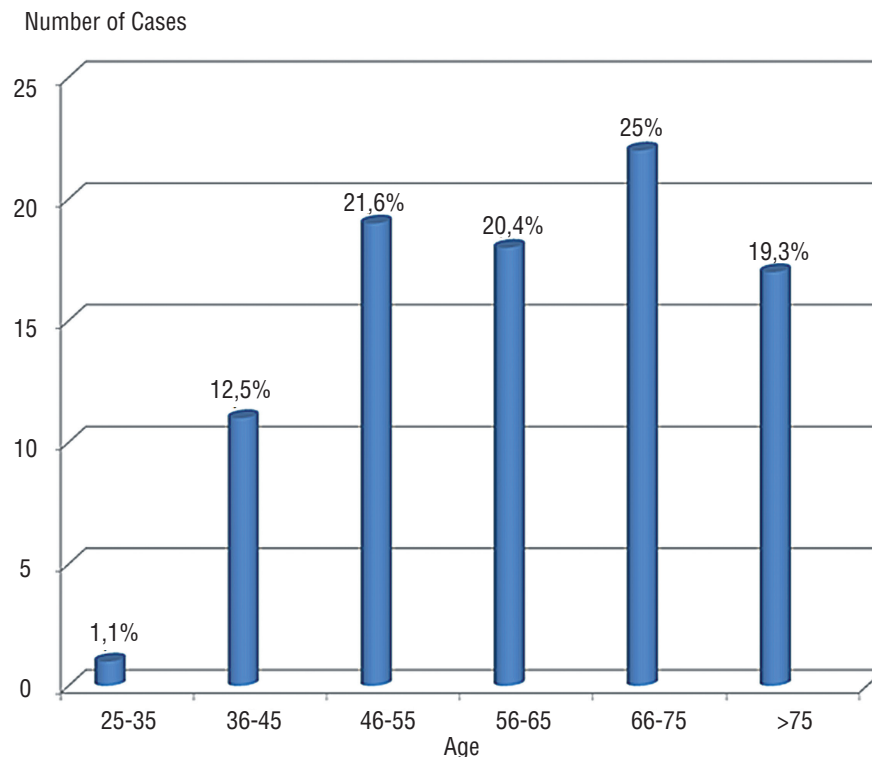
RESULTS

Eighty-eight charts were reviewed, 76 from HCP and 12 from HGC. In 2010, according to the Brazilian Institute of Geography and Statistics, male population of Pernambuco state was 4,229,897, and penile cancer incidence was 2.08/100,000. Median age of patients was 61.2 years (± 12.57) and the highest prevalence was observed in those with 66 to 75 years (25% of total) (Figure-1).

In relation to marital status, 57% were married, 33% single and 10% Widower.

Most had an informal job (67%), 25% had a formal work and 8% were unemployed. 23.8% had an income of less than a minimum wage (MW), 64.8% one to two MW and 11.4% three to four.

Figure 1 - Geographic distribution of penile cancer in Pernambuco.



Fifty percent of patients were illiterate, 43.2% studied only until first grade and 6.8% attended high school.

Figure-2 shows that the metropolitan region of Recife was the region of the state that presented most cases. 48.9% of patients smoked and 3.7% were submitted to a previous postectomy.

In 68.1% of charts there was no information about the period between the initial symptoms and diagnosis. Among those with these data, 39.2% were diagnosed by biopsy of penile lesion that was performed up to six months from the beginning of symptoms, 25% after 7 to 11 months and 35.7% after one or more years.

Tumor size at diagnosis was less than 2 cm in 11 patients (12.5%), 2-5 cm in 57 patients (64.8%) and more than 2 cm in 20 patients (22.7%). Most patients presented T1 or T2 stages (36.4% and 50%, respectively – Table-1); 68.1% were N0 and 31.9% had positive lymph nodes. No distant metastasis was observed. 79.6% of lesions were well differentiated, 13.6% moderately differentiated, 5.7% undifferentiated and 1.1% sarcomatoid.

Surgical treatment is presented in Table-2. Adjuvant chemotherapy (AC) was performed in three cases. Four patients received palliative radiotherapy (RT). CT and RT were associated in two patients.

Six patients received only clinical treatment (terminal patients).

PC relapsed in 28 patients (31.8%), 56% locally and 46.4% inguinal. Recurred lesions were treated according to Table-3.

Death occurred in 24 patients (27.3%) but it was not possible to establish cancer-related death by other causes.

DISCUSSION

PC is the fourth most common tumor in men, after prostate, bladder and kidney cancers; it represents 2% of all malignant tumors of men, and caused 363 deaths in 2010 in Brazil (5).

Frequency is variable, according to the analyzed region. In Brazil, the most frequently mentioned paper about PC epidemiology is the Brumini's et al. work (4), that states that the higher

Figure 2 - Number of cases of penile cancer according to age.

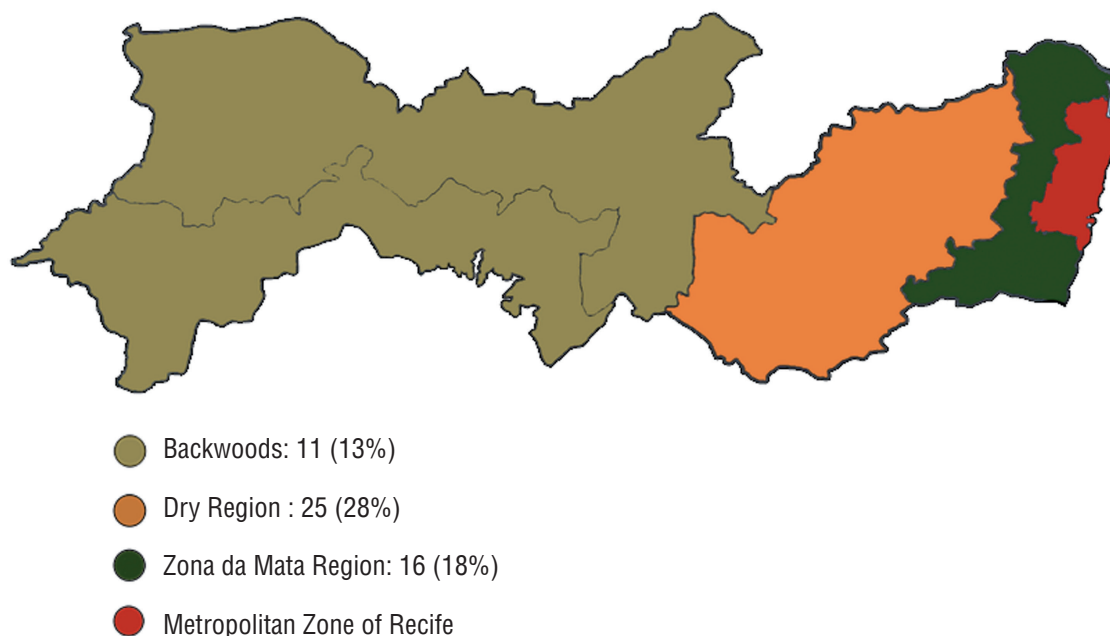


Table 1 - Staging of penile cancer patients.

Staging*	Number of Cases (%)
Tis	Zero
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T1	32 (36.4 %)
T2	44 (50 %)
T3	7 (7.9 %)
T4	5 (5.7 %)
Total	88 (100 %)

* Classification TNM da American Joint Committee on Cancer, 2009.

Table 2 - Treatment.

	No. Patients Treated (%)
Partial penectomy	67 (76.1%)
Total penectomy	15 (17%)
Unilateral lymph node dissection	3 (3.4%)
Bilateral lymph node dissection	14 (15.1%)
No lymph node dissection	65 (73.9%)

Table 3 - Treatment after tumoral recurrence.

Surgery	No. Patients Treated (%)
Surgery + Chemotherapy (CT)	6 (21.4%)
Surgery + Radiotherapy (RT)	7 (25%)
Surgery + CT + RT	3 (10.7%)
CT + RT	3 (10.7%)
CT	1 (3.5%)
RT	1 (3.5%)
No treatment	1 (3.5%)

incidence is observed in the northeast (5.7%) and north regions (5.3%). But this is a study performed in 1982 with data from 1976 to 1980. Favoreto et al. (6) related a higher description of cases in the Southeast region (45.54%), in particular in the state of São Paulo. This fact can be explained due to the higher economic power of that state, to where most cases migrate in order to search for treatment, in particular from the north and northeast regions.

This same dynamics is observed in the state of Pernambuco, where it was observed the highest incidence of PC in the metropolitan area of Recife. The higher economic status of the capital attracts several people from other regions, in search for work and better living conditions with better medical care, allowing for more precise diagnosis and treatments. The same aspects are observed in studies performed in the metropolitan regions of Salvador, capital of Bahia state (7), and Belem, capital of Pará state (8).

The incidence of PC in the Pará study was 5.7/100,000 inhabitants (8), higher than the present series, 2.08/100.000 inhabitants. But this figure is underestimated, since there are others hospitals than these two reference centers in the region with more cases. Even so, the incidence is higher than that of Jews (9), North Americans (9) and Europeans (2).

The higher prevalence of the disease was observed in the sixth and seventh decades of life, similar to other national studies (6,8) and the world (2,10,11). It was also observed a significant amount of PC cases in young adults, with less than 45 years old (13.6%), what was worrying, since mutilation was performed in fully sexual active men.

Frisch et al. (12) described three risk factors for the development of PC: phimosis/long foreskin, low social economic status and bad local hygiene. These factors are coincident with our results: most patients had an informal job (67%), with income lower than two minimum wages and many were illiterates (50%). Most studied patients had a bad cultural status, with compromised personal hygiene, with high risk sexual behavior (unprotected sexual relations, promiscuity) and exposition to sexually transmitted diseases (HPV) that

could be related to PC (13). It is also important to stress the habitus of zoophilia, common in interior regions of the country, increasing the chance of PC occurrence, as related by Zequi et al. (14). This aspect was not analyzed in our series since it was not possible to obtain this information in the reviewed charts.

Phimosis/long foreskin, mentioned by Frisch (12), could be present in 96.6% of patients, since only 3.4% had been previously submitted to postectomy. These features could lead to smegma accumulation and chronic inflammation, precursor to PC (15). Circumcision, as observed in Jews, has a preventive role, when performed after birth (16); Maden et al. (17) stated the incidence of PC is also lower when circumcision is performed in older children or adolescents, and in a recent study by Larke et al. (18) it was proved that when circumcision is performed until 18 years of age it also protects against invasive PC.

Dodge et al. (19) compared Uganda and Kenya, neighbor countries located in Eastern Africa, with similar geopolitical and socio-cultural aspects. But the Kenyans usually submit (due to cultural and religious causes) their adolescents to circumcision, in a ritual of passage from childhood to adult life; only the minority muslim Ugandans are routinely circumcised. The procedure affects directly the incidence of PC in these countries; in Kenya, the incidence is 1.9% of all neoplasms and 7.15% in Uganda, being in this country the most common cancer in men.

On the other hand, in Scandinavia it is not culturally usual to perform circumcision and even so, the incidence of PC is very low, probably to good cultural status and personal hygiene, including the low income population (12). According to this, it is possible to wonder which would be the most efficient method of prevention for our population: better hygiene awareness or routine circumcision for high risk groups. It is important to stress the presence of surgical complication after circumcision and the benefits and risks, and these measures should be studied by health care providers.

Among all studied patients, 58% were married and 51% of these had PC at T1 phase, in accordance to Rippentrop et al. (20), that stated

that married men presented with more precocious disease, probably due to spouse stimulus to seek for health care.

60.7% of patients waited more than 7 months to be diagnosed with PC, in accordance to the Kenyan study (21), where more than 80% of patients were diagnosed after 6 months of symptoms, and to the Belem study (8), where the patients waited for up to 11 months until diagnosis. This fact can be explained by ignorance, taboos, bad health care system, inappropriate treatments by uninformed physicians, delay to referral to urologists; these aspects are associated with late diagnosis and more advanced disease.

There was no significant relation between PC and smoking, as related by Harish et al (22); in our studied populations, smokers and non-smokers were equally present.

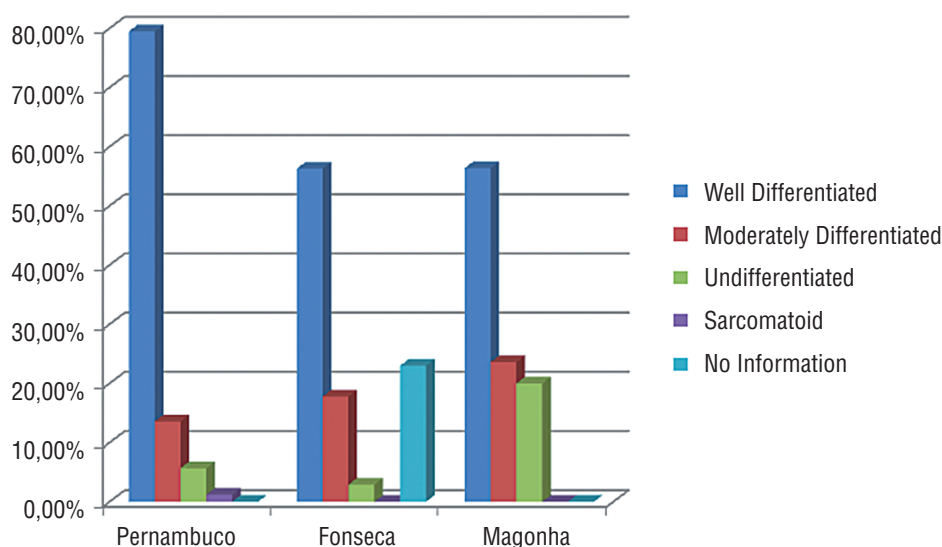
It was also observed that 63.6% of patients presented with more advanced disease ($\geq T2$) and 87.5% with lesion > 2 cm. These results are similar to a Brazilian epidemiological study of PC (6), in a study performed in the state of Pará (8) and in the Kenyan study (21). And different from the North American study (10), where 62.4% of patients were diagnosed in the initial and localized phases. The bigger the lesion and the more invasive, the higher is the possibility of lymph node involvement and worse prognosis (23).

Tumor differentiation had the same characteristics of other papers (8,21), being well differentiated carcinoma the most common observed tumor (Figure-3).

Most patients were submitted to penile amputation in some degree, reflecting the advanced characteristic of the disease.

Adjuvant chemotherapy and palliative radiotherapy, isolated or combined, were used in nine patients. Different treatments were performed in similar clinical settings. These facts reflect the lack of standardization of the treatment of penile cancer nowadays, particularly in relation to lymph node involvement (24-27).

Another aspect is that, even in the presence of relatively easy diagnosis, many patients seek treatment in a stage beyond any possibility of treatment, representing 7% of our series. This fact is in accordance to the Kenyan study (20) (9%) in

Figure 3 - Tumor differentiation.

2000 and to the Salvador-Bahia study (7) (7.3%) in 1984, probably due to the same previously described factors: ignorance, low cultural status, taboos, bad hygiene, etc.

Death occurred in 24 studied patients, but it was not possible to determine the cause of death, if due to PC. Probably this figure is underestimated since many patients lost follow-up and do not report death due to this neoplasm. Mutilation and death related to penile cancer are frequent, affecting self-esteem, causing psychological damage to the patients and to their families.

It is important that health care providers and politicians be aware of this disease, performing campaigns for orientation about this tumor, since it is not a very well-known disease by general population. It is important to stress the need of good hygiene practices, circumcision counseling and to provide good health care access. HPV vaccine can be an alternative for PC prevention but more studies are necessary in order to determine its role. With these measures, there will be a reduction of public health expenses, mutilations and related deaths.

CONCLUSIONS

Epidemiological and clinical aspects of PC in this series are similar to those of other Brazilian (6,8)

and international series (19,21), typical of underdeveloped or developing countries. Better prevention strategies and standardization of treatment are needed in order to reduce the incidence of PC.

ABBREVIATIONS

PC = Penile cancer
 TNM = Tumor – lymph node – metastasis – American Joint Committee on Cancer, 2010.
 HCP = Hospital do Câncer de Pernambuco
 HGV = Hospital Getúlio Vargas
 MW = minimum wage
 CT = chemotherapy
 RT = Radiotherapy
 HPV = Human papillomavirus

CONFLICT OF INTEREST

None declared.

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