ORIGINAL ARTICLE

Vol. 39 (1): 55-62, January - February, 2013
doi: 10.1590/S1677-5538.IBJU.2013.01.08

Prevalence and risk factors for penile lesions/anomalies in a cohort of Brazilian men ≥ 40 years of age

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ABSTRACT

Purpose: To report the prevalence and risk factors of penile lesions/anomalies in a Metropolitan Brazilian city.

Materials and Methods: All participants undergoing prostate cancer screening in the city of Curitiba were systematically examined to identify penile lesions including cutaneous mycosis, sexually transmitted diseases, penile cancer, meatal stenosis, hypospadias, and Peyronie's disease. Outcomes of interest included the prevalence and the relative risk and 95% confidence intervals of the lesions/anomalies according to age, school level, race, personal history of diabetes, arterial hypertension, nonspecific urethritis, and vasectomy.

Results: Balanoposthitis occurred in 11.8% of all participants, with an increased risk in those with diabetes (RR = 1.73), or past history of nonspecific urethritis (RR = 1.58); tinea of the penis was present in 0.2%; condyloma acuminata in 0.5%; herpes virus infection in 0.4%; urethral discharge in 0.2%; genital vitiligo in 0.7%, with an increased prevalence in non-white men (RR = 4.43), and in subjects with lower school level (RR = 7.24); phimosis in 0.5%, with a nearly 7-fold increased risk in diabetics; lichen sclerosus in 0.3%; stenosis of the external urethral meatus in 0.7%, with a higher prevalence in subjects with lichen sclerosus (RR = 214.9), and in those older than 60 years of age (RR = 3.57); hypospadia in 0.6%; fibrosis suggestive of Peyronie's disease in 0.9%, especially in men older than 60 years (RR = 4.59) and with diabetes (RR = 3.91); and penile cancer in 0.06%.

Conclusion: We estimated the prevalence and risk factors of commonly seen penile diseases in an adult cohort of Brazilian men.

ARTICLE INFO

Key words:
Epidemiology; etiology; Prevalence; Penile diseases

Int Braz J Urol. 2013; 39: 55-62

Submitted for publication:
January 16, 2012

Accepted after revision:
July 19, 2012

INTRODUCTION

Genital lesions/anomalies are commonly seen in the office practice. Although these lesions are frequently referred to urologists, they are often discovered incidentally during physical examination by various other specialists including general physicians and surgeons.

The prevalence of genital lesion/anomalies is difficult to estimate. Results differ according to age, gender, racial/ethnic influences, geographic location, comorbidities, and socioeconomic status of the patient. The setting in which the study is conducted (based in the population/community or hospital/clinic setting), the type of study (retrospective or prospective), and the type of diagnostic

assessment (clinical, laboratorial, or by imaging studies) also influence prevalence levels.

Epidemiological studies are important because they contribute to the appropriate approach of the conditions, improving awareness, promoting educational practices and preventive measures, and expediting treatment. They may also allow for intra- and inter-country comparisons, temporal variations between different ages and time periods, and to guide future research evaluating pathogenesis, etiology and risk factors of these diseases.

Prospective epidemiological studies about common genital diseases are limited worldwide, with only scant reports from Brazil. The objective of this manuscript is to report the prevalence and risk factors of penile lesions/anomalies collected prospectively in a cohort of participants in the Metropolitan Brazilian City of Curitiba.

MATERIALS AND METHODS

Between December 2006 and April 2011, 1731 subjects were included in this research. Participants were men aged 40 years or older undergoing outpatient urologic evaluation in the City of Curitiba (PR) as part of a free prostate cancer screening program conducted by the City employees' Health Care System. The study protocol was reviewed and approved by the Institutional Ethics Committee on Human Research (registry number 2253.147/2010-06).

During evaluation, participants were classified by a single examiner as white, or non-white (including brown or black) race; they answered a general questionnaire including age, school level, personal history of diabetes or arterial hypertension, and past history of nonspecific urethritis or vasectomy (Table-1); and were offered a complete genital-pelvic examination.

Urological examination was standardized as follows, and it was performed in all participants in the supine position by a single examiner. Penile inspection with prepuce retraction was performed to identify cutaneous lesions including balanoposthitis, sexually transmitted diseases (STDs), penile cancer, and other infectious/inflammatory, hypochromic or hyperchromic lesions. Lesions/anomalies of the urethral meatus such as meatal stenosis and hypospadia were also registered, and the penile shaft was palpated for areas of thickening or fibrosis suggestive of Peyronie's disease.

Outcomes of interest included the prevalence of penile lesions/anomalies, and the relative risk (RR) and 95% confidence intervals (95% CI) of the lesions/anomalies according to age ($\geq$ 60 vs. < 60 years), school level (elementary school or lower vs. high-school or higher), race (non-white vs. white), personal history of diabetes, arterial hypertension, nonspecific urethritis, and vasectomy (yes vs. no, to all). Statistics were calculated using the Fisher´s Exact Test or Pearson´s Chi-square Test, whichever appropriate, and statistical significance was set when $p < 0.05$ or when the 95% CI did not include the null hypothesis (RR = 1.00).

RESULTS

Cutaneous lesions of the penis were identified in 15.2% (263/1731) of participants. Balanoposthitis was responsible for most of these lesions (77.6%, 204/263), corresponding to 11.8% (204/1731) of all participants, and it was associated with tinea cruris in 28.9% (59/204) of them. Balanoposthitis occurred more commonly in participants with diabetes (RR = 1.73, $p < 0.05$), and past history of nonspecific urethritis (RR = 1.58, $p < 0.05$) (Table-2). Tinea of the penis was present in 1.5% (4/263) of skin lesions and 0.2% (4/1731) overall, 75% (3/4) of which had associated balanoposthitis or tinea cruris. The risk-adjusted prevalence of balanoposthitis and tinea of the penis are summarized in Table-2.

Sexually transmitted diseases (STDs) corresponded to 1.3% (22/1731) of all participants. Condyloma acuminata were responsible for 40.9% (9/22) of STDs and 0.5% (9/1731) of all participants. Herpes virus infections were responsible for 31.8% (7/22) of STDs and 0.4% (7/1731) of all individuals. Urethral discharge, and other nonspecific ulcerous lesions (negative syphilis serology), corresponded each to 13.6% (3/22) of STDs and 0.2% (3/1731) overall. The age-adjusted risk for all STDs was decreased for men > 60 years in comparison with those < 60 years (0.5% vs. 1.8%, $p < 0.05$). Participants with high-school or higher education

presented an increased prevalence of herpes virus infection than those individuals with lower school level (0.7% vs. 0.0%, p < 0.05) (Table-2).

Other infectious/inflammatory lesions encountered included phimosis, responsible for 3.0% (8/263) of penile skin lesions and 0.5% (8/1731) overall; lichen sclerosus in five men (1.9% [5/263] and 0.3% [5/1731]); and psoriasis in one (0.4% [1/263] and 0.06% [1/1731]). Risk-adjusted prevalence of these lesions demonstrated that phimosis was more common in subjects with history of diabetes (RR = 6.88, p < 0.05). The prevalence of lichen sclerosus was non-significantly increased in men with lower education level, and in those with a history of diabetes (Table-2).

Table 1 - Demographic and clinical characteristics of study population.

Characteristic	Number	Percent (%)
Age		
< 60 years	1352	78.1
≥ 60 years	379	21.9
Total	**1731**	**100.0**
School level		
Elementary school or lower	647	37.4
High school or higher	937	54.1
Missing data	147	8.5
Race		
White	643	37.1
Non-white (black or brown)	588	34.0
Missing data	500	28.9
Arterial hypertension		
Yes	595	34.4
No	1133	65.4
Missing data	3	0.2
Diabetes mellitus		
Yes	180	10.4
No	1548	89.4
Missing data	3	0.2
Past history of nonspecific urethritis		
Yes	497	28.7
No	1012	58.5
Missing data	222	12.8
Past history of vasectomy		
Yes	210	12.1
No	1518	87.7
Missing data	3	0.2

Hypochromic or hyperchromic lesions were identified in 10.3% (27/263) of all skin lesions on the penis. Genital vitiligo was responsible for 4.6% (12/263) and 0.7% (12/1731) of the cutaneous lesions and the complete sample, respectively. Vitiligo was more prevalent in non-white men than in white men (RR = 4.43, p < 0.05), as well as in subjects with lower school level (RR = 7.24, p < 0.05) (Table-2).

Traumatic lesions including post-coital excoriation, superficial hemorrhagic effusion, and keloid were identified in one participant each (0.4% [1/263] and 0.06% [1/1731]). A median raphe cyst of the penis was found in one subject (0.4% [1/263] and 0.06% [1/1731]), and biopsy--confirmed penile cancer was also diagnosed in one man (0.4% [1/263] and 0.06% [1/1731]).

Twenty-two (1.3%, 22/1731) participants presented with lesions at the urethral meatus. Stenosis of the external urethral meatus was identified in 0.7% (12/1731) of all participants. Meatal stenosis was more frequent in men with lichen sclerosus compared to those without it (25.0% vs. 0.1%, RR = 214.9, 95% CI 39.38-1172.40, p < 0.05), and in men aged 60 years or more in comparison with those < 60 years (RR = 3.57, p < 0.05). Subjects with a past history of nonspecific urethritis had a nonsignificant increased risk of meatal stenosis (Table-2). Hypospadia was detected in 0.6% (10/1731) of the participants, eight of which (80%, 8/10) were situated on the glans penis, and two (20%, 2/10) on the coronal sulcus. Meatal stenosis was not detected in any of these subjects. The risk-adjusted prevalence of hypospadias is summarized in Table-2.

Palpation of the penile shaft revealed a circumscribed area of fibrosis suggestive of Peyronie's disease in 0.9% (15/1731) of the participants. A higher risk was identified in men > 60 years (RR = 4.59, p < 0.05), and in diabetics (RR = 3.91, p < 0.05) (Table-2).

Table 2 - Prevalence of penile diseases, and relative risks (RR) and 95% confidence intervals (CI) of the lesions/anomalies according to age, school level, race, and history of diabetes mellitus, arterial hypertension, nonspecific urethritis, and vasectomy.

	Age ≥ 60 vs. <60 RR 95% CI	School-level Elementary School vs. High-School or higher RR 95% CI	Race Non-white vs. White RR 95% CI	Diabetes Yes vs. No RR 95% CI	Arterial hypertension Yes vs. No RR 95% CI	Past history of nonspecific urethritis Yes vs. No RR 95% CI	Past history of vasectomy Yes vs. No RR 95% CI
Balanoposthitis	12.1 vs. 11.7 1.04 0.76-1.41	11.4 vs. 11.6 0.98 0.74-1.30	11.1 vs. 10.4 1.06 0.77-1.46	18.9 vs. 10.9 (*) 1.73 1.24-2.42	13.4 vs. 10.9 1.24 0.95-1.61	14.7 vs. 9.3 (*) 1.58 1.19-2.11	12.4 vs. 11.7 1.06 0.72-1.56
Tinea of the Penis	0.5 vs. 0.1 3.57 0.50-25.24	0.0 vs. 0.4 0.00 0.00-NaN	0.0 vs. 0.3 0.00 0.00-NaN	0.0 vs. 0.3 0.00 0.00-NaN	0.2 vs. 0.3 0.63 0.07-6.09	0.6 vs. 0.1 6.11 0.64-58.58	0.5 vs. 0.2 2.41 0.25-23.06
Sexually Transmitted Diseases	0.5 vs. 1.8 (*) 0.30 0.07-1.24	1.1 vs. 2.0 0.53 0.23-1.26	1.2 vs. 1.6 0.77 0.29-2.00	0.6 vs. 1.0 0.53 0.07-4.00	1.0 vs. 1.9 0.54 0.22-1.34	1.8 vs. 1.3 1.41 0.61-3.28	1.0 vs. 1.6 0.58 0.14-2.42
Condyloma Acuminata	0.0 vs. 0.7 0.00 0.00-NaN	0.6 vs. 0.4 1.45 0.36-5.77	0.7 vs. 0.3 2.19 0.40-11.90	0.0 vs. 0.6 0.00 0.00-NaN	0.7 vs. 0.4 1.52 0.41-5.65	0.6 vs. 0.5 1.22 0.29-5.09	0.0 vs. 0.6 0.00 0.00-NaN
Herpesvirus Infection	0.0 vs. 0.5 0.00 0.00-NaN	0.0 vs. 0.7 (*) 0.00 0.00-NaN	0.2 vs. 0.5 0.36 0.04-3.49	0.0 vs. 0.5 0.00 0.00-NaN	0.2 vs. 0.5 0.31 0.04-2.63	0.6 vs. 0.3 2.04 0.41-10.05	0.5 vs. 0.4 1.20 0.15-9.96
Phimosis	1.1 vs. 0.4 2.85 0.77-10.58	0.6 vs. 0.3 1.93 0.43-8.60	0.3 vs. 0.3 1.09 0.20-23.80	2.2 vs. 0.3 (*) 6.88 1.86-25.39	0.8 vs. 0.4 2.38 0.64-8.83	0.0 vs. 0.7 0.00 0.00-NaN	0.0 vs. 0.6 0.00 0.00-NaN
Lichen Sclerosus	0.3 vs. 0.3 0.89 0.10-7.96	0.5 vs. 0.1 4.34 0.45-41.68	0.3 vs. 0.2 2.19 0.20-24.06	0.6 vs. 0.3 2.15 0.24-19.13	0.0 vs. 0.4 0.00 0.00-NaN	0.2 vs. 0.3 0.68 0.07-6.51	0.0 vs. 0.3 0.00 0.00-NaN
Genital Vitiligo	0.8 vs. 0.7 1.19 0.32-4.37	1.5 vs. 0.2 (*) 7.24 1.59-32.94	1.4 vs. 0.3 (*) 4.43 0.94-20.76	0.0 vs. 0.8 0.00 0.00-NaN	0.5 vs. 0.8 0.63 0.17-2.34	0.8 vs. 0.6 1.36 0.38-4.79	1.4 vs. 0.6 2.41 0.66-8.83
Meatal Stenosis	1.6 vs. 0.4 (*) 3.57 1.16-11.00	0.6 vs. 0.4 1.45 0.36-5.77	0.3 vs. 0.6 0.55 0.10-2.97	1.1 vs. 0.6 1.72 0.38-7.79	0.3 vs. 0.9 0.39 0.09-1.76	0.8 vs. 0.3 2.71 0.61-12.08	0.5 vs. 0.7 0.66 0.09-5.06
Hypospadia	1.6 vs. 1.0 1.53 0.59-3.95	1.2 vs. 1.1 1.16 0.46-2.92	0.9 vs. 0.8 1.09 0.32-3.76	1.1 vs. 1.2 0.96 0.22-4.08	0.7 vs. 1.4 0.48 0.16-142	1.6 vs. 0.9 1.82 0.70-4.68	1.0 vs. 1.2 0.80 0.19-3.44
Fibrosis (Peyronie)	2.4 vs. 0.5 (*) 4.59 1.72-12.23	0.9 vs. 0.6 1.45 0.47-4.47	0.5 vs. 0.5 1.09 0.22-5.40	2.8 vs. 0.7 (*) 3.91 1.37-11.12	1.3 vs. 0.7 1.90 0.72-5.05	0.6 vs. 0.7 0.87 0.23-3.36	1.4 vs. 0.9 1.67 0.48-5.81

(*) Statistically significant difference (Fisher's exact test of Pearson's Chi-square test)

DISCUSSION

Penile mycosis

In the present study, penile mycosis was identified in 11.9% of all participants: balanoposthitis in 99.0%, and tinea of the penis in 1.9%.

Balanoposthitis is the inflammation of the foreskin/glans penis caused by multiple infectious and noninfectious agents. It occurs at any age, especially in uncircumcised men, accounting for 11%-13% of them (1,2). It is more common in diabetics (3), in whom it is frequently chronic or recurrent, with an increased risk of 73% compared to non-diabetics in the present research. We also found a higher prevalence of balanoposthitis in men with past history of nonspecific urethritis.

Tinea of the penis is a relatively uncommon mycotic infection of the penile shaft (4,5), with an incidence of 1.2% of men with dermatophytosis (4). It is frequently associated to balanoposthitis or other dermatophytosis (4-6). In our study, the prevalence of penile tinea was increased by 257% in men > 60 years, and by more than 6-fold in participants with a past history of nonspecific urethritis. However, the small number of participants with penile tinea prevented a significant correlation when controlling the analysis for potential risk factors.

Sexually Transmitted Diseases

The prevalence of STDs varies according to the etiologic agent, and the age, gender, socioeconomic factors, and sexual behavior of the patient. In Brazil, the prevalence of STDs in men > 20 years-old is 7.1%, diminishing progressively with the increasing of age, with a RR = 6.5 in the group of 20-30 years-old, compared to those > 70 years-old (7). In our study, STDs were identified in 1.8% of men between 40-60 years of age, and 0.5% of those > 60 years-old.

Condiloma acuminata (genital warts) are caused by human papillomavirus (HPV), the most common viral STD in the world (8,9). The prevalence of genital warts is 1.1% in Brazilian men between 20-49 years-old (7) and it was 0.5% in the participants aged > 40 years-old evaluated in our study. However, visible genital warts are detectable in only a small percentage of HPV carriers (9). In a study evaluating men with clinical suspicion of HPV infection through DNA testing, the prevalence of HPV was 0.4% at the ages of 61-70 years, 3.1% at 51-60 years, 8.3% at 41-50 years, 19.8% at 31-40 years, and 50.3% at 21-30 years (9).

In our study, the risk-adjusted prevalence of all STDs was similar between non-white and white participants, similarly to several studies (10,11), although others show an increased risk of some STDs among blacks, compared to white individuals (12).

Genital herpes virus (HSV) is a frequently under-recognized and underestimated STD because infection is often subclinical (13). In the US, although the estimated seroprevalence of HSV is about 25%-28% of the population (14,15), 88.4% of people with laboratory evidence of HSV are unaware of their diagnosis (15). In our cohort, the overall prevalence of HSV identified through a group of blisters and/or ulcers was 0.4% of all participants.

The annual prevalence of Chlamydia and Gonorrhea (nonspecific urethritis) in the sexually active population in Brazil is estimated collectively as 60.8% of all STDs, followed by syphilis in 16.2%, HPV in 11.9%, and HSV in 11.1% (16). In the present study, the prevalence of urethral discharge was only 13.6% of all STDs, and there were no laboratory-confirmed cases of syphilis. The prevalence of HPV and HSV, on the other hand, reached respectively 40.9% and 31.8% of all STDs.

The low rates of nonspecific urethritis in this series may be explained by the frequently asymptomatic or oligosymptomatic clinical manifestations of urethritis caused by Chlamydia. However, although nonspecific urethritis and syphilis are estimated as the most prevalent STDs in all age-groups in Brazil (16), HPV and HSV may be more prevalent in older age groups because they are chronic, frequently recurrent, and up to this day noncurable diseases.

Phimosis

Phimosis is a congenital or acquired narrowing of the prepuce that hinders or prevents the retraction of the foreskin over the glans penis. At birth, a physiologic phimosis caused by natural adhesions between the prepuce and the glans is

gradually separated by intermittent penile erections and accumulation of epithelial debris under the prepuce (17). The prevalence of phimosis is 58% at 1 year of life, 10%-35% at 3 years, 8% at 6 years, and less than 1% by 17 years of age (18). In the present study, phimosis was observed in 0.5% of men > 40 years, more commonly in diabetics, that had an increased risk of nearly 7-fold compared to non-diabetics.

Lichen sclerosus

Lichen sclerosus (balanitis xerotica obliterans), which commonly appears as white plaques on the glans, often with involvement of the prepuce that becomes thickened and non-retractile, occurs at any age. The underlying cause is unknown (19), but it has been frequently associated with phimosis, either as a cause or as a consequence (17,20).

The prevalence of lichen sclerosus in the general population is estimated to be 0.1%-0.3% (21). In our study, although it reached a 334% higher prevalence in men with low school level, and it was 115% increased among men with a history of diabetes; statistical analysis was non-significant, probably due to the low prevalence of lichen sclerosus.

Genital vitiligo

Vitiligo is an acquired disorder of skin depigmentation that affects 0.5%-2% of the population, and it is limited to the genitalia in less than 0.3% of men (22,23). It is particularly more noticeable in darker-skinned individuals (23), with a prevalence 4.4-fold higher in non-whites than in whites in our cohort, as well as a 7.2-fold increased risk in men with lower school level than in those with higher education.

Meatal stenosis

Urethral meatal stenosis is a narrowing of the urethra at the external meatus. One of the most common causes of meatal stenosis is lichen sclerosus, but it also occurs in adults after inflammation, specific or nonspecific urethral infections, and urethral instrumentation or surgery (21). The prevalence of meatal stenosis in our study was 0.7%, with an increased risk in men with lichen sclerosus, and in those > 60 years. The risk of meatal stenosis in participants with past history of nonspecific urethritis was increased by 171%, but it did not reach statistical significance.

Hypospadia

Hypospadia is an abnormal ventral opening of the urethral meatus anywhere from the ventral aspect of the glans penis to the perineum. In the US, the prevalence of hypospadias is up to 0.8% of live male births, 87% of which are glandular or coronal (24). In Brazil, the prevalence of hypospadias is approximately 1.8%-4.1% of live male births (25,26).

Hypospadia in the adult is uncommon and frequently overlooked because most severe cases are treated during childhood, and the remaining cases are clinically insignificant or merely unaesthetic. In our cohort of men > 40 years-old, hypospadias were present in 0.6%, all of which were located on the glans penis or the coronal sulcus, and none were associated with meatal stenosis.

Penile cancer

Cancer of the penis is a rare neoplasm, with a prevalence that varies according to different geographic regions between countries, and within a single country. In Brazil, penile cancer accounts for 2.1% of male malignancies, with the highest incidence in the Northeast region (5.3%), and the lowest in the Southern region (1.2%), where the present study was conducted (27).

Penile cancer occurs more frequently in the sixth decade of life. Risk-factors for the development of penile cancer include phimosis, STDs, lichen sclerosus, low socioeconomic level, and poor personal hygiene (27-29).

Peyronie's disease

This disorder is characterized by fibrotic plaques of the tunica albuginea penis, and its etiology remains obscure (30). The reported prevalence of Peyronie's disease is around 0.4%-3.2% (30,31), reaching values of up to 6.5% > 70 years of age. Our results showed an overall 0.9% prevalence of palpable penile fibrosis suggestive of Peyronie's disease, with a 4.6-fold increased risk in men > 60 years. In agreement with the results reported in our study, diabetes seems to be a po-

tential risk factor for Peyronie's disease, with a 3 to 4-fold increased risk of the disease (30).

Strengths and limitations of the study

Although this survey is strengthened by a prospective and systematic collection of data performed by a single examiner in a medium-sized cohort of subjects, it has several limitations. First, it involves exclusively men > 40 years of age from an established private Health Care System, and therefore should be extrapolated with caution. However, it approaches two specific age-range of adults (40-60 years, and > 60 years of age), allowing important insights about the prevalence and risk factors of several diseases more or less common to these age groups. Second, with the exception of cancer, we did not routinely use biopsy or laboratory tests to confirm the clinical diagnosis of the lesions encountered. This practice is commonly used and clinically recommended for most lesions/anomalies because complementary examination will not modify treatment, but it is not adequate for research purposes because it may result in false positive/negative bias. Additionally, the prevalence of lesions/anomalies in our cohort did not include conditions previously treated (e.g. history of circumcision) or in clinical remission (e.g. history of herpes virus infection). One of the most interesting aspects of our cohort, however, is the establishment of several epidemiological risk factors poorly evaluated in the literature for penile lesions/anomalies. Future studies should validate the consistency of these associations.

CONCLUSIONS

Penile lesions/anomalies are frequently found in the adult population. They may have multiple causes, including infectious, inflammatory, traumatic, congenital, or idiopathic. We estimated the prevalence and risk factors of penile diseases commonly seen in the office in an adult cohort of Brazilian men.

ACKNOWLEDGEMENTS

This article is part of a doctoral dissertation in development by the main author at the Federal University of Paraná, Brazil.

CONFLICT OF INTEREST

None declared.

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