PEYRONIE'S DISEASE

Prevalence, Risk Factors, and Erectile Dysfunction Associated With Peyronie's Disease Among Men Seeking Urological Care

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ABSTRACT

Introduction: Peyronie's disease (PD) is a connective tissue disorder of the penis characterized by an abnormality in collagen structure of penile tunica albuginea.

Aim: We sought to investigate the prevalence, risk factors, and the relationship between erectile dysfunction (ED) and PD in male patients aged 30–80 years seeking urological care.

Methods: This is a cross-sectional study using data collected from October 2016 to October 2017 in an outpatient clinic associated with the Brazilian Public Health System. All men aged 30 to 80 years were invited to participate. Data collected were related to the clinical history and sexual habits of patients using the International Index of Erectile Function, in addition to the physical examination of the penis and laboratory parameters.

Main Outcome Measure: Descriptive statistics and multivariate logistic regression models tested the prevalence, risk factors, and the relationship between ED and PD in male patients.

Results: The study included 656 individuals, who were distributed as per age, marital status, race, educational level, and income. Of these participants, 86 (13.11%) presented with fibrous plaques compatible with PD at the physical examination. Among the risk factors evaluated, PD was associated with diabetes, smoking, and obesity in 43.02, 64.17, and 26.74% of patients, respectively. The presence of penile plaques compatible with PD was more prevalent in men with ED, history of penile trauma, and complaint of penile deformity. There was a higher prevalence of plaques in the distal penis.

Conclusion: The PD among the studied population was associated with risk factors such as diabetes, smoking, and obesity. Other clinical characteristics, such as history of penile trauma, penile deformity, and ED, were reported in patients with PD. There was a higher prevalence of plaques in the distal penis, specifically in the corona of the glans penis. The prevalence of PD was different from that in the published literature, our results show that numbers thus more studies are needed. **Segundo A, Glina S. Prevalence, Risk Factors, and Erectile Dysfunction Associated With Peyronie's Disease Among Men Seeking Urological Care. Sex Med 2020;8:230–236.**

Key Words: Peyronie's Disease; Risk Factors; Erectile Dysfunction; Fibrosis; Penis

INTRODUCTION

Peyronie's disease (PD) is a connective tissue disorder of the penis characterized by an abnormality in the collagen structure of the penile tunica albuginea. This disorder may promote the formation of a fibrous plaque containing a considerable amount of collagen, then modifying elastin framework and fibroblastic proliferation. It can result in alterations in penile anatomy such as penile deformity, a palpable lump in the penis, penile pain during erection, and erectile dysfunction (ED).[1]

According to several authors, PD diagnosis does not necessarily require a complaint as the reason for seeking medical care. A classic study conducted by Smith[2] established a prevalence of PD of 22% when analyzing penile plaques in autopsies, regardless of symptoms. Most patients seek medical care because of penile deformity and/or pain during erection. However, the presence of penile plaques is enough to characterize PD.[3] The minimum requirements for diagnosis of PD include an assessment of clinical history and a comprehensive physical examination of the genitalia.[4]

Table 1. Epidemiological studies on the prevalence of Peyronie's disease

Authors and year	Country	Evaluation	Age range	Prevalence (%)
Lindsay et al, 1991[8]	USA	General population	Not specified	0.38
Schwarzer et al, 2001[9]	Germany	General population	30–80 years	3.2
La Pera et al, 2001[10]	Italy	Smokers	50–60 years	7.2
Rhoden et al, 2001[11]	Brazil	Prostate cancer screening	52–77 years	3.67
Mulhall et al, 2004[12]	USA	Prostate cancer screening	40–80 years	8.9
Kadioglu A. et al, 2004[13]	Turkey	Erectile dysfunction	Not specified	16
El-Sakka 2006[14]	Egypt	Erectile dysfunction	Not specified	7.9
Arafa et al, 2006[15]	Egypt	Diabetic patients and ED	Not specified	20.3
Tefekli et al, 2006[16]	Turkey	Diabetic patients	Not specified	22.5
Akbal et al, 2008[17]	Turkey	Retroperitoneal fibrosis	Not specified	20
Dibenedetti et al, 2011[18]	USA	General population	>18 years	0.5 to 13
Shiraishi 2012[19]	Japan	General population and men undergoing hemodialysis	Not specified	0.6 to 9.2
Romero et al, 2013[20]	Brazil	Prostate cancer screening	>40 years	0.9
Stuntz et al, 2016[21]	USA	General population	>18 years	10.8

ED = erectile dysfunction.

Several risk factors have been associated with PD, including hypertension, smoking, diabetes, and hyperlipidemia, and some of them may aggravate the symptoms in patients. Studies have demonstrated an important association between a more rigid plaque and poor metabolic control of diabetes in PD.[5,6]

Repetitive penile trauma during sexual intercourse would cause lesions in the tunica albuginea with extravasation of blood, which would lead to fibrosis by modifying the mechanism of scar formation. In a recent study, Cohen et al[7] were able to trigger alterations in the extracellular matrix similar to that found in PD after the instillation of blood in the tunica albuginea tissue of rats, which showed increased expression of transforming growth factor-β; matrix metallopeptidase 9, heparanase and biglycan associated with decreased expression of syndecan-1 and aggrecan, suggesting modifications in extracellular matrix remodeling in relation to the physiopathology of PD.[7]

Despite several studies, the incidence and prevalence rates of PD are still unclear. Such rates vary depending on each study, methodology, and population studied. Prevalence rates ranging from 0.39 to 22.5% have been reported in previous studies, which depend on the sampling methodology used. Table 1 shows epidemiological studies on the prevalence of PD based on the methodology and the population studied.[8–21]

There are few studies in the Brazilian literature to characterize the epidemiology of PD. Among these studies, Rhoden et al[11] reported a prevalence of PD of 3.67% in men older than 50 years living in the city of Porto Alegre, Southern Brazil. In another survey conducted by Romero et al[20], the presence of fibrosis suggestive of PD was reported in 0.9% of the studied population, especially in men older than 60 years and diabetic patients living in Curitiba. The objective of this study was to identify the prevalence of PD and presence of penile plaque in male patients aged 30–80 years attending a general urology outpatient clinic in the Northeast region of Brazil, independent of the complaint.

METHODS

The study was carried out following the regulations governing human subject research and was evaluated and approved by the Research Ethics Committee of ABC Medical School. This is a prospective cross-sectional study carried out from October 2016 to October 2017 in an outpatient clinic associated with the Brazilian Public Health System in the city of Patos, in the state of Paraiba, Brazil. In this clinic, patients seeking urological care in several areas of urology are attended regardless of gender and age, characterizing it as a general urology outpatient clinic.

Population

All men aged 30 to 80 years attending the urology outpatient clinic, independent of the complaint, were invited to participate in the study. Exclusion criteria were patients who did not agree or did not undergo some procedure of the study, were not able to answer the questionnaire, or did not accept to be examined.

A total of 2,108 urological consultations were performed during the data collection period, including consultations and
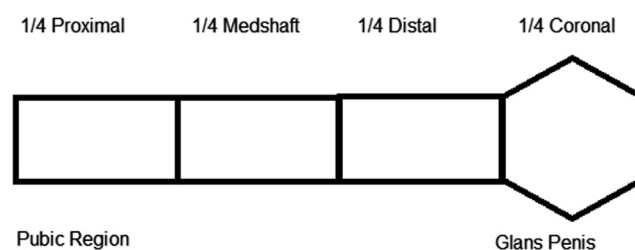

Figure 1. Schematic drawing of the location of the penile plaque.

Table 2. Sociodemographic data of patients

Variable	Without PD (n = 570) n (%)	With PD (n = 86) n (%)	All patients	P value
Patients				
30–80 years	570 (86.89)	86 (13.11)	656 (100)	
Age range				
30–40 years	62 (10.88)	3 (3.49)	65 (9.91)	
41–50 years	101 (17.72)	22 (25.58)	123 (18.75)	
51–60 years	159 (27.89)	26 (30.23)	185 (28.20)	
61–70 years	158 (27.72)	28 (32.56)	186 (28.35)	
71–80 years	90 (15.79)	7 (8.14)	97 (14.79)	
Race				
White	278 (48.77)	37 (43.02)	315 (48.02)	
Black	92 (16.14)	11 (12.79)	103 (15.70)	.252
Brown	200 (35.09)	38 (44.19)	238 (36.28)	
Reason to seek urologic care				
Rectal examination	303 (53.16)	51 (59.30)	354 (53.96)	
Penile curvature	0 (0)	2 (2.33)	2 (0.30)	
Erectile dysfunction	18 (3.16)	6 (6.98)	24 (3.66)	
Hardening of the penis	0 (0)	0 (0)	0 (0)	
Others	249 (43.68)	27 (31.40)	276 (42.07)	
Diabetes				
No	450 (78.95)	47 (54.65)	497 (75.76)	
Yes	95 (16.67)	37 (43.02)	132 (20.12)	<.001*
Do not know	25 (4.39)	2 (2.33)	27 (4.12)	
Hypertension				
No	188 (64.37)	53 (61.63)	428 (65.24)	
Yes	375 (35.63)	32 (37.21)	220 (33.54)	
Do not know	7 (1.23)	1 (1.16)	8 (1.22)	
Dyslipidemia				
No	393 (68.95)	57 (66.28)	450 (68.60)	
Yes	177 (31.05)	29 (33.72)	206 (31.40)	
Obesity				
No	485 (85.09)	63 (73.26)	548 (83.54)	.006*
Yes	85 (14.91)	23 (26.74)	108 (16.46)	
Smoking behavior				
Smoker	66 (11.58)	16 (18.60)	82 (12.50)	
Nonsmoker	294 (51.58)	30 (34.88)	324 (49.39)	
Exsmoker	210 (36.84)	40 (46.51)	250 (38.11)	
Alcohol use				
No	406 (71.23)	69 (80.23)	476 (72.31)	
Yes	164 (28.77)	17 (19.77)	181 (27.59)	
Triglycerides				
<199 mg/dL	466 (81.75)	66 (76.74)	532 (81.10)	
≥200 mg/dL	104 (18.25)	20 (23.26)	124 (18.90)	
Total cholesterol				
<239 mg/dL	480 (84.21)	74 (86.05)	554 (84.45)	
≥240 mg/dL	90 (15.79)	12 (13.95)	102 (15.55)	

PD = Peyronie's disease.
*Chi-squared analysis.

return visits of patients, regardless of age. Inclusion criteria were all men aged 30 to 80 years who attended the urology outpatient clinic during the given period of data collection. Exclusion criteria were subjects who did not agree or did not perform any stage of the investigative processes, did not have the ability to answer the questionnaire, or did not agree to be examined. The
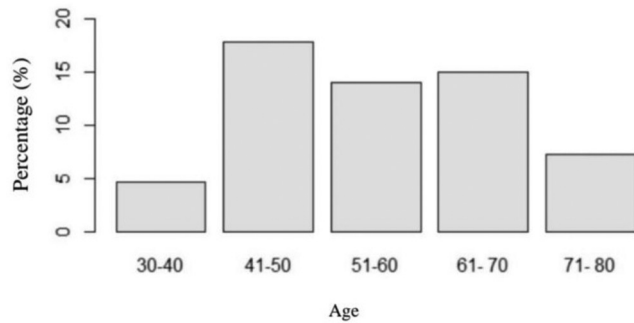
Figure 2. Prevalence of Peyronie's disease by age range.

studied population was selected, with 666 men aged 30 to 80 years by using inclusion criteria, and 10 men did not agree to be examined. A total of 656 men were included to participate.

Initially, patients were assessed for age, marital status, race, education level, family income, and main complaint (grouped in asymptomatic, penile pain, penile curvature, sexual dysfunction, and other complaints). The antecedents (diabetes, obesity, hypertension, dyslipidemia, and Dupuytren's disease), lifestyle (alcohol use, smoking, and drug use), and the regular use of medication were evaluated.

Patients were asked about several aspects of sexual habits, such as numbers of sexual activities, condom use, lubricant use, masturbation frequency, sexual position preferences, most frequent penetration type (vaginal or anal), if the patient have ever had or is having sexual intercourse with animals, age at the beginning of sexual life and sexual preferences, history of penile trauma and complaint of some penile deformity, and, if present, for how many years. The validated International Index of Erectile Function questionnaire was applied for quantifying ED in each age-group and men with and without PD.[22]

For the study, the diagnosis of diabetes was based on self-report and medical diagnosis, use of hypoglycemic drugs, or fasting blood glucose level ≥ 126 mg/dL. Patients with dyslipidemia were diagnosed by self-report and medical diagnosis, use of medication, or when blood cholesterol values were ≥240 mg/dL or blood triglycerides values were ≥200 mg/dL. Body weight and height were evaluated for classification of obesity, and the body mass index (BMI) was calculated by dividing the patient's body weight by the square of the height. Patients with a BMI between 18.5 and < 25 were classified as eutrophic, whereas those with BMI between 25 and 30 were classified as overweight, and men with BMI ≥30 were classified as obese.

Smoking behavior was classified as nonsmokers, ex-smokers, or current smokers. The number of packs of cigarettes smoked per year was calculated for both current smokers and ex-smokers.

All patients underwent a physical examination of the genitalia to identify fibrous plaques, independent of the complaint. After exposure of the genitalia, with the patient in the dorsal decubitus position, the penile shaft was visually inspected and bimanually palpated, extending from the pubic region to the ventral and

Table 3. Multiple Poisson regression model for factors associated with Peyronie's disease

Variables	PR	CI95%	P value
Diabetes			
No	1	-	
Yes	2.99	2.01; 4.44	<.001*
Obesity			
No	1	-	
Yes	1.41	0.90; 2.21	.129
Smoking behavior			
Nonsmoker	1	-	
Exsmoker	1.93	1.09.; 3.42	.022*
Smoker	1.81	1.12; 2.93	.014*
Age range			
30—40 years	1	-	
41—50 years	3.53	1.09; 11.42	.035*
51—60 years	2.42	0.74; 7.88	.140
61—70 years	1.80	0.54; 6.00	.333
>71 years	0.89	0.23; 3.36	.868

PR = Poisson regression.
*Chi-squared analysis.

dorsal glans penis for assessment of hardened areas and sensitivity. Individuals were diagnosed with PD (if fibrous plaques were present) or without PD. In addition, the plaque was classified based on the location, number, and pain in the affected area in patients classified as having PD. The presence and location of penile plaques were evaluated based on their distribution in 4 regions: one-fourth proximal, one-fourth midshaft, one-fourth distal, and one-fourth distal (coronal), in addition to the sensitivity and perception by the patient with plaque (Figure 1).

Statistical Analyses

The data were analyzed descriptively using absolute and relative frequencies. A chi-square test was used for inferential analysis. The dependent variable (group 0, without PD and group 1, with PD) and independent variables (diabetes, obesity, smoking, and age range) were included in the regression model. The prevalence ratio was calculated using multiple Poisson regression (PR) analysis with robust variance and stepwise forward strategy for variable entry.[23,24] The significance level was set at $P < .05$. The program used for analysis was Stata 12.

RESULTS

The study included 656 individuals, who were distributed based on age range, marital status, race, educational level, and income. Because it is a general urology outpatient clinic, the reasons for urologic consultation in most patients (96.07%) were not sexually related (Table 2). Of these participants, 86 (13.11%) had PD, whereas 570 patients (86.89%) did not present any penile fibrous plaque. Of the 86 patients in whom penile plaques were identified, only 2 presented with complaint

Table 4. Clinical characteristics of the patients with or without Peyronie's disease

Variable	Without PD (n = 570) n (%)	With PD (n = 86) n (%)	P value
History of penile trauma			
No	553 (97.01)	77 (89.53)	.002*
Yes	17 (2.99)	9 (10.47)	
Penile deformity			
No	548 (96.14)	70 (81.40)	
Yes	22 (3.86)	16 (18.60)	
Palpable penile plaque			
No	569 (100)	71 (82.56)	
Yes	0 (0.00)	15 (17.44)	

PD = Peyronie's disease.
*Chi-squared analysis.

of penile curvature as the reason for seeking urologic care. The highest prevalence of PD was observed in men older than 50 years; however, the group with plaque had fewer individuals in the 30−40, 41−50, and 71−80 age-groups than the group without fibrous plaques (Table 2). In this study, the prevalence of PD was 13.11% among the 656 patients interviewed. When stratified by age, it was possible to observe a higher prevalence of individuals in the age-group 41−50 (17.89%) years, followed by men in the age-groups of 61−70 and 51−60 years (Figure 2).

The prevalence of diabetes, obesity, and smoking in individuals with PD was 37 (43.02%), 23 (26.74%), and 56 (65.11%), respectively. A significant statistical difference was observed for patients with diabetes and obesity, as well as for lifestyle habits, including smoking (Table 2). Multiple PR analysis is shown in Table 3. The most common risk factors among patients with PD were diabetes (PR = 2.99), smoking for patients who were ex-smokers or smokers (PR = 1.93 and PR = 1.81), and being in the age-group of 41−50 years (PR = 3.53).

More patients with penile plaque reported a history of penile trauma (9; 10.47%) and a complaint of penile deformity (16; 18.60%) than patients without plaque (Table 4). The prevalence of ED by age, as shown in Table 5, higher prevalence and severity of ED were observed in older men. Table 6 shows the prevalence of ED and score in patients with or without PD. Patients with PD had a higher prevalence of moderate (9 patients, 10.47%), mild to moderate (18 patients - 20.93%), and mild (12 patients - 13.95%) ED.

The different locations of fibrous plaque in the penis were evaluated based on their distribution in 4 regions: one-fourth proximal, one-fourth midshaft, one-fourth distal, and one-fourth distal (coronal) (Figure 1). There was a higher prevalence of plaques in the distal penis, specifically in the corona of the glans corresponding to the distal cavernous body (69.7%), followed by the midshaft area (24.7%). The prevalence of plaques was lowest in the proximal region (8.1%), as shown in Table 7.

DISCUSSION

In the literature, the prevalence of PD varies depending on each study and sampling methodology. Moreover, it is also believed that there may be an underreporting of the disease because of patients' reluctance to seek diagnosis or treatment.[25]

In this study, where patients with different urological complaints were attended, the prevalence of PD was 13.11% among the 656 patients interviewed. When stratified by age, it was possible to observe a higher prevalence of individuals in the age-group 41−50 years (17.89%), followed by men in the age-groups of 61−70 and 51−60 years (Figure 2). The fact that the studied population is composed of patients seeking urology care, especially men older than 40 years, can have caused an overestimation of PD prevalence. The prevalence of PD is higher for older men, especially those older than 40 years. Increasing age may decrease the stiffness of the penis, making it more susceptible to microtrauma and the development of fibrous plaques.[11] It is important to highlight that most patients with penile plaque were asymptomatic.

Our data suggest an association between PD and diabetes, obesity, and smoking with prevalence rates of 43.02, 26.74, and 65.11%, respectively, in patients with PD (Tables 2 and 3). Several studies already described the association between PD and

Table 5. Classification of erectile dysfunction by age range

Category (score)	30−40 years (n = 656) n (%)	41−50 years	51−60 years	61−70 years	71−80 years	P value
Severe (6−10)	1 (1.59)	7 (4.88)	10 (5.41)	50 (26.34)	42 (43.30)	
Moderate (11−16)	1 (1.59)	1 (0.81)	9 (4.86)	21 (11.29)	11 (11.34)	
Mild to moderate (17−21)	2 (3.18)	16 (13.01)	20 (10.81)	28 (15.05)	21 (21.65)	<.001*
Mild (22−25)	5 (7.94)	14 (11.38)	28 (15.14)	11 (5.91)	14 (14.43)	
No erectile dysfunction (26−30)	54 (85.7)	86 (69.92)	118 (63.78)	77 (41.40)	9 (9.28)	

*Chi-squared analysis.

Table 6. Prevalence of erectile dysfunction and score in patients with or without Peyronie's disease

Category (score)	Without PD (n = 570) n (%)	With PD (n = 86) n (%)	P value
Severe (6–10)	97 (17.02)	11 (12.79)	
Moderate (11–16)	34 (5.96)	9 (10.47)	
Mild to moderate (17–21)	70 (12.28)	18 (20.93)	<.01*
Mild (22–25)	61 (10.70)	12 (13.95)	
No erectile dysfunction (26–30)	308 (54.04)	36 (41.86)	

PD = Peyronie's disease.
*Chi-squared analysis.

some risk factors. Romero et al[20] reported that the prevalence of diabetes among patients with PD was 10.7% and that diabetes can lead to the development of PD, besides aggravating penile curvature. For men, being in the age-group of 30–59 and above 65 years, being white or brown, as well as being obese were directly associated with a higher prevalence of diabetes.[20]

Smoking is highly associated with PD. La Pera et al[10] observed increased rates of PD with an increasing number of packs of cigarettes smoked per year, especially for individuals who smoked more than 10,000 packs a year. In addition to describing the association between PD and the number of cigarettes/day, El-Sakka and Tayeb[14] also demonstrated an association with smoking time, observing a higher prevalence of PD in individuals who have smoked for more than 5 years.

It is believed that penile traumas during sexual activity cause delamination of the septal fibers with extravasation of blood into the intraluminal spaces, which is associated with perivascular lymphocytic infiltration and plasmocyte inflammatory-cell infiltration in the areolar connective tissue.[26] Our study corroborates these previous results because individuals with PD had a history of penile trauma and penile deformity (Table 4).

This study observed ED in most patients with PD, with the highest frequency for individuals with "mild to moderate ED" (Table 6). When asked the main reason for seeking urological care, 24 (3.66%) men cited ED. In this study, 6.98% of the individuals with penile plaque reported ED as the main reason

Table 7. Distribution of fibrous plaque in the penis

Penile plaque	Without PD (n = 570) n (%)	With PD (n = 86) n (%)
Absent	570 (100)	0 (0.00)
Proximal	0 (0)	3 (3.49)
Midshaft	0 (0)	7 (8.14)
Distal	0 (0)	16 (18.60)
Distal (coronal)	0 (0)	60 (69.77)

PD = Peyronie's disease.

for seeking medical consultation, in contrast to 3.16% in the group without PD (Table 2). The association between PD and ED is a subject of great interest by researchers. Previous studies demonstrate that the prevalence of ED among patients with PD can reach up to 54%.[11]

According to several authors, the most common location of the penile plaques were more commonly found at the base of the penis, followed by the midshaft area and the distal penis.[27] In contrast, our study showed a higher prevalence of plaques in the distal penis, specifically in the corona of glans corresponding to the distal cavernous body (69.7%), followed by the midshaft area (24.7%) and the proximal region (8.1%), as shown in Table 7. We believe that distal plaques would reduce the penile curvature and be less noticeable, thus being less diagnosed. As this study focused on search for hardening in the penile region, we were able to find different results from the literature. Of the 86 men with plaques, only 15 (17.44%) reported having noticed the presence of plaque in their genital organs.

The main limitation is that this study was performed in only one center, which may prevent the generalization of the results. Furthermore, the results differed from the published literature, and the penile plaques were clinically irrelevant because most men were asymptomatic. It would be helpful to follow these men to understand if they will become symptomatic.

The study had no source of external funding. The researchers paid all the expenses and costs related to the research.

CONCLUSION

The PD among the studied population was association with risk factors such as diabetes, smoking, and obesity. Other clinical characteristics, such as history of penile trauma, penile deformity, and ED, were reported in patients with PD. There was a higher prevalence of plaques in the distal penis, specifically in the corona of the glans penis. The prevalence of PD was different from that in the published literature; our results thus show that more studies are needed.

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