

Peyronie's Disease is common in poorly controlled diabetics but is not associated with the Metabolic Syndrome

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Abstract

Purpose: The purpose of the study is to investigate if metabolic syndrome (MS) and other comorbidities are associated with Peyronie's disease (PD).

Methods: A total of 1833 patients retrospectively investigated and divided into two groups: Group A – PD patients ($n = 319$) and Group B – non-PD patients ($n = 1303$). The two groups were fully evaluated for diabetes mellitus (DM) with the glycated hemoglobin (HbA1c), hypertension (HTN), dyslipidemia (DL), obesity by measuring body mass index, total testosterone (T), penile vascular circulation measuring Peak systolic velocity (PSV) as indicator of arterial supply, end-diastolic velocity (EDV) as indicator of venous output, and finally, smoking.

Results: The presence of diabetes was significantly correlated with PD ($P = 0.005$). Patients with diabetes had a 7% higher incidence of PD. However, patients with the highest HbA1c level of >8.5 had an increased odds ratio of 1.6 ($P = 0.025$, confidence interval [CI] = 1.061–2.459) of having PD. Increased age was significantly correlated with PD ($P = 0.025$). For each year of life, the likelihood of having PD increases by an odds ratio of 1.019, or 2% per year ($P = 0.001$, CI = 1.004–1.027). Unexpectedly, DL ($P = 0.006$) and smoking ($P = 0.041$) were associated with lower incidences of PD. Patients with DL or smoking had a 5%–7% lower incidence of PD with an odds ratio of 0.6 ($P = 0.006$, CI = 0.410–0.864). HTN ($P = 0.621$) and the total number of comorbidities ($P = 0.436$) were not correlated with PD. Mean serum T values were statistically ($P = 0.43$) but not clinically significant among patients with Peyronie's versus patients without Peyronie's (4.62 vs. 4.38 ng/ml). Neither low PSV (Fisher's exact test $P = 0.912$) nor abnormal EDV (Fisher's exact test $P = 0.775$) was correlated with the finding of PD.

Conclusions: While MS was not associated with PD, diabetes, particularly poorly controlled diabetes, was associated with an increased rate. Further research into the interaction of PD and metabolic disease is warranted.

Keywords: Diabetes, erectile dysfunction, metabolic syndrome, Peyronie's disease

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INTRODUCTION

Peyronie's disease (PD) was first described in 1742 by Francois Gigot de La Peyronie's.^[1] PD is a well-recognized clinical problem affecting middle-aged and older men. In general, the prevalence of PD ranged from as low as 0.4% and as high as 23%. However, this range reflects the prevalence both in the general population in some studies and specific patient populations presenting to clinics for various reasons, not necessarily complaining of PD.^[2-8]

The exact etiology of PD is unknown, but tunica albuginea injury and subsequent scarring is a suspected cause.^[9] Experimental animal models suggest that trauma alone may not cause PD, suggesting the disease may be caused or worsened by other factors.^[10] A general explanation of this disorder, which has gained acceptance, is that PD is a disorder in which genetically susceptible individuals experience a localized response to endogenous factors such as transforming growth factor- β which is released in response to microtrauma.^[11] Association of PD with increasing age, diabetes mellitus (DM), hypertension (HTN), obesity, dyslipidemia (DL), and smoking were well described.^[3,4,12,13] These associations suggest metabolic derangement may be causative or additive to the formation of PD plaques.

It was reported that 20%–30% of patients with PD have erectile dysfunction (ED) refractory to medical therapy.^[14] However, as men age, the incidence of softer erections increases in general. This is due to hardening of the arteries and other possible concomitant disease processes which may contribute to diminished penile blood flow.^[15] Low testosterone has been suggested as a risk factor for PD that may correlate with disease severity. It was suggested that there might be a common process among men with abnormal erectile physiology and not specifically causative in plaque formation.^[16]

The vascular impairment of erection has been shown in diabetic patients as well as in patients with PD. Age, obesity, smoking, and medical comorbidities were significantly higher in patients with both DM and PD than in patients with any of the conditions alone.^[17] Furthermore, in another case–control study, the authors concluded that in addition to genetic predisposition, trauma of the penis, and systemic vascular diseases are risk factors for PD. Smoking and alcohol consumption also seem to have some role in the development of the disease.^[18] DM was linked to PD and it was also thought that DM probably exaggerates the fibrotic process in PD. Diabetic patients with PD thought to have a higher risk of severe deformity and ED.^[19] DM

was also linked to severe PD and considered as a risk factor for significantly worse vascular status, which was shown by penile duplex Doppler ultrasonography, in men with PD.^[20]

Another important complaint or presentation in PD patients is loss of penile size. Although curvature is the hallmark symptom of disease, shortening can be the most psychologically devastating symptom, occurring in 70% of patients and ranging from 1 to 10 cm. The perceived loss of length and girth is often more disturbing than the deformity itself, all of which can lead to moderate-to-severe depressive symptoms, emotional, and relationship problems.^[11]

We hypothesized that metabolic syndrome (MS) should be highly associated with PD.

METHODS

Approval was obtained from our Institution Research Ethics Committee to perform retrospective chart review at multiple locations at a private andrology/urology center in the Middle East. Charts of 1833 patients who visited our centers from June 2010 to October 2011 were reviewed; almost all those patients visited our clinics for reasons other than PD. The charts of 211 patients did not contain information about the presence or absence of PD, those were excluded from analysis. Careful and detailed medical and sexual history was obtained from all patients. Thorough physical examination including body mass index (BMI) was done to all patients in the study.

Variables collected included: age, presenting complaints (ED, PE, decreased libido, premarital check, decreased penile size, PD, presence or absence of comorbidities (HTN, DM, DL, and smoking), and laboratory workup including testosterone level. The presence of DM, HTN, and DL was confirmed by medical history, medications used, and/or medical records. BMI was manually calculated. MS was determined using the World Health Organization criteria.^[21] PD was diagnosed clinically by identifying the plaques and/or the presence of a deformity. In patients with DM, patients were determined to have well-controlled blood sugars if they had glycated hemoglobin (HbA1c) level $\leq 7\%$. Patients with no history of DM underwent HbA1c level measurement, and patients were given the diagnosis of DM if they had HbA1c value $> 6.5\%$. Penile Doppler ultrasound was done for ED patients and in patients whom plaque and/or deformity was discovered during the physical examination. On penile Doppler studies, normal end-diastolic velocity (EDV) was defined a value being < 5 ml/s. Normal peak systolic velocity (PSV) value was defined as a value ≥ 35 ml/s.

Statistical analysis used included Student's *t*-test, Fisher's exact *t*-test, analysis of the variant, logistic regression analysis, Mann–Whitney U-test, and univariate and multivariate analysis.

RESULTS

A total of 1622 patient charts were analyzed. At the time of initial screening, the overall study population mean age was 41 years (19–82 years). The mean age in patients with PD was 42 years (21–76 years) and the mean age in patients without PD was 41 years ($P = 0.025$). About 81.3% of patients did not have PD ($n = 1303$), while 19.7% did ($n = 319$). The prevalence of PD by age group is shown in Table 1. The mean BMI value was very close in the two groups (29.13 m²/kg and 29.24 m²/kg). Mean HbA1c level in patients with diabetes and PD was 9.3%. Mean HbA1c level in diabetic patients without PD was 8.9% ($P = 0.763$).

Patients' complaints varied by type and count [Table 2]. Most patients presented to the clinic with one or two complaints ($n = 1159$ and 553, respectively).

Existing MS was not associated with an increased prevalence of PD; both groups of patients, with and without MS, had a 20% prevalence of PD ($P = 0.9$) [Table 3].

DM was found in 24% of the population studied ($n = 387$). All of them were type 2. The mean duration of DM was 13.6 years (range from 3 to 21). The presence of DM was significantly associated with PD ($P = 0.005$). Patients with DM had a 7% higher prevalence of PD (OR = 1.5, confidence interval [CI] = 1.14–1.96). When comparing diabetic patients with a HbA1c level $\leq 7\%$ versus diabetic patients with a HbA1c level $> 7\%$, results were insignificant (19% vs. 29% respectively, $P = 0.232$). Additional analysis using logistic regression to comparing diabetic patients with a HbA1c level $\leq 8.5\%$ versus those with HbA1c level $> 8.5\%$ (poor control^[22]) elicited a significant association; a 1.6 increase in odds ratio ($P = 0.025$, CI = 1.061–2.459) for PD in diabetic patients with a HbA1c $> 8.5\%$ [Tables 3 and 4].

Mean serum testosterone values were statistically significant using the Mann–Whitney U-test ($P = 0.043$), but the clinical values were very similar (with PD 4.38 ng/dl and without PD 4.62 ng/dl) [Table 3].

On multivariate analysis controlling for age, increased age was significantly correlated with PD ($P = 0.025$). For each year of life, the likelihood of having PD increases by an odds ratio of 1.019, or 2% per year ($P = 0.001$,

Table 1: Prevalence of Peyronie's disease by age group

Age group	PD present	Total	Percentage
20-39	149	835	17.8
40-49	63	325	19.4
50-59	65	286	22.7
60-69	28	127	22
70-79	14	46	30
80-89	0	3	0

Table 2: Patients' complaints (on presentation)

Presenting complaint	n (%)
ED-like symptoms	185 (58)
Premarital check	124 (39)
Premature ejaculation	101 (32)
LUTS	65 (20)
Decreased libido	31 (10)
Peyronie's	25 (7)
Small size penis	11 (3)

LUTS: Lower urinary tract symptom, ED: Erectile dysfunction

Table 3: Age, body mass index, metabolic syndrome, testosterone and diabetes mellitus, smoking, and dyslipidemia association with Peyronie's disease

	PD absent, mean (range)	PD present, mean (range)	P
BMI (kg/m ²)	29.24 (16-59)	29.13 (16.14-55.62)	0.763
HbA1c, %	8.96 (5.1-14.5)	9.27 (5.6-15.3)	0.763
MS present, %	79.8	20.2	0.9007
MS absent, %	80.4	19.6	
T (ng/dl)	4.629	4.379	0.043
DM present, %	75	25.1	0.005
DM absent, %	82	18	
Smokers, %	84.8	15.2	0.041
Nonsmokers, %	80	20	
DL present, %	84.9	15.1	0.006
DL absent, %	78	22	

PD: Peyronie's disease, BMI: Body mass index, HbA1c: Glycated hemoglobin, T: Testosterone, MS: Metabolic syndrome, DM: Diabetes mellitus, DL: Dyslipidemia

Table 4: Glycated hemoglobin levels association with Peyronie's disease

Fisher's exact <i>t</i> -test		Logistic regression analysis	
Mean value ($P=0.232$)		OR ($P=0.025$)	
≤ 7	> 7	≤ 8.5	> 8.5
19.20%	28.50%	1	1.615

OR: Odds ratio, HbA1c: Glycated hemoglobin

CI = 1.007–1.031). Removing the testosterone variable from multivariate analysis (because it was found to be insignificant on multivariate analysis) changed the likelihood of PD to 1% per year of life ($P = 0.028$).

No correlation was found between low PSV values (Fisher's exact test $P = 0.912$) and abnormal EDV (Fisher's exact test $P = 0.775$) and the diagnosis of PD. Furthermore, comparing patients who had normal PSV and EDV values to patients who had abnormal values of either and/or both showed no significance ($P = 0.659$).

Smoking was inversely associated with PD: 15% in smokers versus 20% in nonsmokers ($P = 0.041$). Smokers comprised 17.8% of our population ($n = 289$). DL was also inversely associated with PD: 15% in patients with DL and 22% in patients without ($P = 0.006$). DL was found in 20.5% ($n = 332$) of patients. HTN ($P = 0.621$) and the total number of comorbidities ($P = 0.436$) were not correlated with PD. HTN was found in 26.6% of patients ($n = 432$) [Table 3].

DISCUSSION

This is the first study to investigate the association between PD and MS. In this series, PD was not associated with MS. The criteria for MS is the presence of DM type 2 and two or more other diseases (HTN, elevated triglycerides or low high-density lipoprotein, a BMI of >30 , and high urinary albumin excretion rate),^[16] but the only metabolic derangement seen to affect PD rates was diabetes, especially uncontrolled diabetes.

Prevalence

We found that the overall prevalence of PD was 20% in a screening population coming to a urology men's health clinic for various complaints, only 7% initially complaining of PD symptoms, and if we add complaining of small size penis to PD symptoms, the percentage would be 10%. Our mean age of 42 years for patients with PD was far less than the mean age reported in other studies.^[2-4,6,7,18,23-28] PD prevalence in our population was evenly distributed by age, only rising to 30% in patients over 70 years. The rate of PD in our patients was much higher than reported elsewhere: 2.8%–8.6% in those 40–69 years old.^[2,26,27] Even in other research describing the prevalence of PD in special groups such as Type 1 and Type 2 DM, preexisting ED, and older patients, the rate of PD ranged from 1 to 9%.^[2,4,18,23,24,27,28] In addition, higher rates of PD prevalence than ours were only reported in research reporting the prevalence of PD in patients older than 80 years.^[2,6,7,9,25,27]

Age

Increasing rates of PD with age has been previously reported.^[2,4] The authors hypothesized that accumulated penile trauma increases over time with accrued sexual activity. Alternatively, the comorbidities thought to cause or worsen PD were generally found in higher rates as patient's age.^[9,28-31] The large size of this population allows for estimation of "by year" increase in PD risk of 2%.

Peyronie's disease and presenting complaint

We found that most patients who were diagnosed with PD did not initially complain of PD symptoms. In most other series, majority of patients (73%–85%) complained of

PD-like symptoms or were aware of the deformities.^[3,7,18,23] The explanation of this is obscure but may represent a lower degree of medical sophistication or sexual health education in this population. Furthermore, the high prevalence of PD in our series could represent efficient screening by sophisticated techniques, but these same techniques were also used in other reports. The most common presenting complaint was ED, and this association has been reported previously.^[2]

Diabetes mellitus

The strong association of DM with PD has been reported elsewhere.^[3,4] However, the significantly higher rate of PD in diabetics with a high HbA1c in our population is the first to be reported as far as we know. Others have shown a lower rate of PD in DM patients with good diabetes control (HbA1c: 4.7%–6.2% vs. 6.2%–7%),^[4] generally supporting our findings of higher prevalence of PD in patients with HbA1c $>8.5\%$. El-Sakka and Tayeb^[3] noted that $>95\%$ of the patients in his cohort with PD had poor diabetes control (HbA1c $>7.0\%$) but did not compare this to patients without PD.

Hypertension

We found that PD was not associated with HTN as reported elsewhere,^[24] but in general, groups that reported an association with HTN studied older patient cohorts.^[2,8] Our cohort, which was as young as 19 (mean: 41 years), may not have been old enough to have a significant baseline rate of HTN.

Smoking

Smoking has been associated with higher prevalence of PD in some studies^[3,4,27] and a lower association in other studies.^[2] Our negative association of smoking with PD does not necessarily indicate a protective effect.

Penile Doppler ultrasonography

Evaluating the penile arterial and venous system showed that PD was not associated with abnormal EDV and/or PSV values. This may be consistent with those authors who reported no association of PD with ED,^[24] as ED is highly associated with abnormal velocities.^[24]

Testosterone

Mean level in both groups (with and without PD) was within normal range; however, patients with PD had a statistically significant lower mean testosterone levels (4.4 ng/ml vs. 4.6 ng/ml), although the absolute difference in values is likely to be practically insignificant.

Total number of comorbidities

We did not show an association with PD and total number of comorbidities. Others have shown that the presence of at least one risk factor predicted severe PD.^[3,7,23]

Limitations and strengths

The limitations in our study include the retrospective nature of our study, the lack of a data regarding the duration of preexisting conditions before the diagnosis of PD, and lack of stratification of PD severity based on plaque size and/or curvature angle. Nonetheless, this dataset is the largest ever reported and represents a valuable cohort of PD patients assessed by an expert group of clinicians. This heterogeneous group allows a highly accurate predictor of the prevalence of PD in this ethnic population. The dataset is further strengthened because the screening population contains many young patients under 40 years of age (51%); moreover, this is the first report to describe PD prevalence in those younger than 40.

CONCLUSIONS

We report a very high prevalence of PD in a population screened by sophisticated techniques in a young population of heterogeneous ethnic males. The high prevalence of PD in this population prompts concern regarding the true prevalence, etiology, and associated factors of this disease. We searched for but did not find an association of PD with MS but did find that very uncontrolled diabetes (HbA1c >8.5%) was associated with higher rates. This high rate of PD in an expertly evaluated population of males may indicate the need for earlier screening of PD in younger patients presenting to men's health clinics with various complaints.

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Conflicts of interest

There are no conflicts of interest.

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