

Association of Erectile Dysfunction with Atopic Dermatitis: A Population-Based Case-Control Study

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ABSTRACT

Introduction. Some studies have highlighted the high prevalence of erectile dysfunction (ED) in patients with dermatological diseases such as psoriasis, chronic hand eczema, and systemic sclerosis. However, to date, there is still no study that has explored the relationship between ED and atopic dermatitis (AD).

Aim. Using a population-based data set, this case-control study aimed to examine the association of ED with prior AD by comparing the risk of prior AD between patients with ED and matched controls in Taiwan.

Methods. This study used administrative claims data from the Taiwan National Health Insurance program. We identified 3,997 patients with newly diagnosed ED as cases and randomly selected 19,985 subjects without a history of ED as controls. Conditional logistic regression was used to calculate the odds ratio (OR) and corresponding 95% confidence interval (CI) for previously diagnosed AD between cases and controls.

Main Outcome Measure. The prevalence and risk of having been previously diagnosed with AD between cases and controls were calculated.

Results. Of the 23,982 sampled subjects, 1,758 (7.3%) had been previously diagnosed with AD; it was found among 425 (10.6%) cases and among 1,333 (6.7%) controls ($P < 0.001$). Conditional logistic regression analysis demonstrated that cases were more likely to have prior AD than controls (OR = 1.60, 95% CI = 1.42–1.80, $P < 0.001$) after adjusting for monthly income, geographic location, urbanization level, hypertension, diabetes, coronary heart disease, hyperlipidemia, obesity, and alcohol abuse/alcohol dependence syndrome.

Conclusions. There was an association between ED and prior AD. We suggest that clinicians should be more attentive to sexual complaints from patients with AD. **Chung S-D, Keller JJ, and Lin H-C. Association of erectile dysfunction with atopic dermatitis: A population-based case-control study. J Sex Med 2012;9:679–685.**

Key Words. Chronic Inflammatory Disorders; Erectile Dysfunction; Atopic Dermatitis

Introduction

Erectile dysfunction (ED) is defined as the inability to obtain or maintain an erection sufficient for adequate sexual performance and is a common problem among attendees of urological clinics [1,2]. It is estimated that more than 150 million men worldwide are afflicted with ED, and the global prevalence is increasing along with aging population trends [3,4]. ED usually leads to a severe and lasting negative impact on health, quality of life, and partnership [5,6].

The coexistence of ED with different diseases has gained interest in recent years. It has been shown that the development of ED is associated with cardiovascular diseases, diabetes, obesity, chronic obstructive pulmonary disease, and chronic liver disease [6–10]. Currently, although the coexistence of ED with different diseases has become a popular and important health concern, the subject is still very new to the dermatologic arena. Some studies have highlighted the high prevalence of ED in patients with psoriasis [11], chronic hand eczema [12], and systemic sclerosis

[13–15]. However, to date, there has been no large-scale population-based study conducted to explore the relationship between ED and atopic dermatitis (AD). AD is one of the most frequent chronic inflammatory skin disorders characterized by eczema, pruritus, and cutaneous hyperactivity to allergic triggers [16,17]. Although AD is not life-threatening, it is an uncomfortable and highly visible disorder. The symptoms of AD such as itching, pain, burning/stinging, sensation, irritation, and bleeding may lead to psychiatric consequences and sexual dysfunction [18–21].

One recent study by Cheng et al. has indicated that patients with AD have a high prevalence of ED [22]. On the one hand, they reported that the prevalence rates of ED in the normal Asian population were 15.1%, 29.6%, and 40.6% for age groups 20–29, 30–39, and 40–49 years, respectively. On the other hand, the prevalence rates of ED among Japanese patients with AD were found to be 23.7%, 38.4%, and 51.3% for age groups 20–29, 30–39, and 40–49 years, respectively. Another study by Misery et al. suggested that AD substantially affects sexual desire, and that the impact of AD is significant for both the patient and the partner [18]. Similarly, one study by Long et al. observed that 19% of AD subjects reported that their sex lives were affected by the disease [19]. Finlay also indicated that 34% of AD subjects reported that the disease had an effect on their sexual relationships [20]. Niemeier et al. compared the sexual behavior of 53 patients with psoriasis, 24 patients with AD, and 52 controls with healthy skin [21]. They found that patients with skin diseases had significantly impaired sex lives compared with those with healthy skin.

Although a number of studies have attempted to examine the impact of AD on sexual function, no study has attempted to explore the association between AD and ED. To fill this gap in the literature, this case-control study utilized a nationwide population-based data set to examine the association of ED with prior AD by comparing the risk of prior AD between patients with ED and matched controls in Taiwan.

Methods

Database

This population-based case-control study was conducted in Taiwan, which had about 23 million inhabitants as of 2007. We used administrative claims data sourced from the Longitudinal Health Insurance Database 2000 (LHID2000). The

LHID2000 was created by the Taiwan National Health Research Institute and includes all the original claims data as well as registration files of 1,000,000 individuals randomly sampled from the 2000 Registry for Beneficiaries of the National Health Insurance (NHI) program. The LHID2000 allows researchers to trace all the medical services and diagnoses of these selected 1,000,000 individuals since the initiation of the NHI program in 1995. Numerous researchers have used this data set to conduct and publish studies in peer-reviewed journals [23,24].

This study was exempted from full review by an Institutional Review Board (IRB) after consulting with the director of the Taipei Medical University IRB since the LHID2000 consists of de-identified secondary data released to the public for research purposes.

Patients with ED

The cases in this study were selected by first identifying all the subjects who received a principal diagnosis of ED (impotence, organic (International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) code 607.84) during ambulatory care visits between January 2004 and December 2009 ($N = 4,890$). In order to increase the validity of ED diagnosis, this study only included ED patients who had received at least two ED diagnoses during the period between 2004 and 2009, with at least one diagnosis being made by a urologist. We further excluded patients under 18 years of age ($N = 2$) because of the small case number in this age group. In addition, those patients who had received an ED diagnosis prior to 2004 were excluded in order to increase the possibility of only including newly diagnosed ED cases ($N = 891$). As a result, the cases in this study included 3,997 patients with ED. We regarded the date of the first diagnosis of ED as the index date for cases.

Selection of Controls

The controls in this study were likewise extracted from the LHID2000. First, we excluded all the subjects who had received a diagnosis of ED since the inauguration of the NHI in 1995. Those subjects aged <18 years old were also excluded. We then retrieved 19,985 controls matched with the cases (5:1 ratio with cases) in terms of age in intervals of 10 years (18–30, 30–39, 40–49, 50–59, 60–69, and ≥ 70) and index year. We considered

the date of the first use of ambulatory care occurring during the index year as the index date for controls.

Exposure Assessment

We identified AD cases based on a diagnosis of atopic dermatitis (ICD-9-CM codes 691). The diagnosis of AD is mainly based on the findings of a physical examination and a review of the patient's medical history. However, there are no laboratory findings or histological features that specifically define atopic dermatitis. In order to increase diagnostic validity, we only selected patients who had received two or more AD diagnoses prior to the index date, with at least one being made by a dermatologist. In addition, in this study, we only considered AD cases if the atopic dermatitis occurred before the index date.

Statistical Analysis

We used the SAS system (SAS System for Windows, Version 8.2, SAS Institute Inc, Cary, NC, USA) to perform all the statistical analyses conducted in this study. We used the chi-square test to examine differences in monthly income

(NT \$0–15,840, NT \$15,841–25,000, $\geq$ NT \$25,001), geographic location (Northern, Central, Eastern, and Southern Taiwan), and urbanization level of the patient's residence (5 levels, with 1 being the most urbanized and 5 being the least) as well as comorbidities (hypertension, diabetes, coronary heart disease (CHD), hyperlipidemia, obesity, and alcohol abuse/alcohol dependence syndrome) between cases and controls. We only included these comorbidities if they occurred before the index date. Furthermore, we used conditional logistic regression (conditioned on age [10-year intervals] and index year) to calculate odds ratios (OR) and corresponding 95% confidence intervals (CI) for previously diagnosed AD between cases and controls. The conventional $P \leq 0.05$ was used to assess statistical significance.

Results

Table 1 presents the descriptive data for the 3,997 cases and 19,985 controls. Of the 23,982 sampled subjects, the mean age was 50.6 years with a standard deviation of 15.0 years; about 50% were aged between 40 and 59 years old. As for sociodemographic characteristics, there was no significant

Table 1 Demographic characteristics of patients with erectile dysfunction and controls in Taiwan in the years 2004–2009 (N = 23,982)

Variable	Patients with erectile dysfunction (N = 3,997)		Controls (N = 19,985)		P value
	Total no.	%	Total no.	%	
Age (years)					1.000
18–29	352	8.8	1,760	8.8	
30–39	546	13.7	2,730	13.7	
40–49	937	23.4	4,685	23.4	
50–59	1,112	27.8	5,560	27.8	
60–69	638	16.0	3,190	16.0	
≥ 70	412	10.3	2,060	10.3	
Monthly income					0.739
NT \$1–15,840	1,272	31.8	6,235	31.2	
NT \$15,841–25,000	1,268	31.7	6,395	32.0	
$\geq$ NT \$25,001	1,457	36.5	7,355	36.8	
Hyperlipidemia	1,062	26.6	3,083	15.4	<0.001
Diabetes	885	22.1	2,423	12.1	<0.001
Hypertension	1,398	35.0	4,914	24.6	<0.001
Coronary heart disease	592	14.8	1,736	8.7	<0.001
Obesity	18	0.5	50	0.3	0.030
Alcohol abuse/alcohol dependence syndrome	22	0.6	78	0.4	0.152
Geographic region					0.714
Northern	2,050	51.3	10,252	51.3	
Central	892	22.3	4,597	23.0	
Eastern	955	23.9	4,637	23.2	
Southern	100	2.5	499	2.5	
Urbanization level					0.502
1 (most urbanized)	1,400	35.0	6,995	35.0	
2	1,214	30.4	5,976	29.9	
3	628	15.7	3,018	15.1	
4	446	11.2	2,398	12.0	
5 (least urbanized)	309	7.7	1,598	8.0	

Table 2 Prevalence and crude odds ratios for atopic disorders among the sampled patients

Presence of atopic dermatitis	Total (N = 23,982)		Patients with erectile dysfunction (N = 3,997)		Controls (N = 19,985)	
	N, %		N, %		N, %	
Yes	1,758	7.3	425	10.6	1,333	6.7
Crude OR (95% CI)	—		1.67*** (1.48–1.87)		1.00	

***Indicates $P < 0.001$

Notes: Odds ratio (OR) was calculated by conditional logistic regression which was conditioned on age group

difference in the distribution of monthly income, geographic location, or urbanization level of the patient's residence between cases and controls. As for comorbidities, cases were more likely to have hyperlipidemia (26.6% vs. 15.4%, $P < 0.001$), diabetes (22.1% vs. 12.1%, $P < 0.001$), hypertension (35.0% vs. 24.6%, $P < 0.001$), CHD (14.8% vs. 8.7%, $P < 0.001$), and obesity (0.5% vs. 0.3%, $P = 0.030$) than controls. However, no significant difference in the prevalence of alcohol abuse/alcohol dependence syndrome between cases and controls was observed.

The prevalence of prior AD between cases and controls is presented in Table 2. It shows that of the 23,982 sampled subjects, 1,758 (7.3%) had received a diagnosis of AD prior to their index date; atopic dermatitis was found in 425 (10.6%) cases and in 1,333 (6.7%) controls ($P < 0.001$). Conditional logistic regression analysis (conditioned on age [10-year intervals] and index year) further suggested that the OR of prior AD for cases was 1.67 (95% CI = 1.48–1.87; $P < 0.001$) when compared with controls.

Table 3 shows the covariate-adjusted OR of prior AD between cases and controls. Conditional logistic regression analysis revealed that cases were more likely to have prior AD than controls (OR = 1.60, 95% CI = 1.42–1.80, $P < 0.001$) after adjusting for monthly income, geographic location, urbanization level, hypertension, diabetes, CHD, hyperlipidemia, obesity, and alcohol abuse/alcohol dependence syndrome. As expected, a much higher proportion of hypertension (OR = 1.22), diabetes (OR = 1.54), CHD (OR = 1.36), and hyperlipidemia (OR = 1.46) was found among cases when compared with controls after adjusting for potential confounders.

Discussion

There has long been an appreciation that skin diseases may have a negative effect on sufferers' sexual lives [25]. In one study conducted on subjects drawn from a Turkish dermatology outpatient depart-

ment, those suffering from skin diseases were also found to suffer from more impaired "sexual lives" than control subjects [26]. In addition, Goulding found that ED is very common among dermatology outpatients [11]. As far as we know, this is the first study to document the association between ED and AD using a population-based data set. In this case-control study, AD was found in 425 (10.6%) cases and in 1,333 (6.7%) controls. After adjusting for patient sociodemographic characteristics, comorbidities, obesity, and alcohol abuse/alcohol dependence syndrome, we found that ED patients had a 1.60-fold higher risk of having been previously diagnosed with AD than controls.

Although the actual mechanisms contributing to the association between ED and AD remain

Table 3 Covariate-adjusted odds ratios for psoriasis among the sampled patients (N = 23,982)

Variables	Presence of erectile dysfunction		
	Odds ratio	95% CI	P value
Prior atopic dermatitis			
Yes	1.60	1.42–1.80	<0.001
No (reference group)	1.00		
Monthly income			
NT \$1–15,840	1.00		
NT \$15,841–25,000	0.96	0.88–1.05	0.335
≥NT \$25,001	1.15	1.05–1.25	0.002
Hyperlipidemia	1.46	1.34–1.60	<0.001
Diabetes	1.54	1.39–1.69	<0.001
Hypertension	1.22	1.12–1.33	<0.001
Coronary heart disease	1.36	1.22–1.51	<0.001
Obesity	1.36	0.79–2.36	0.267
Alcohol abuse/alcohol dependence syndrome	1.41	0.87–2.28	0.162
Geographic region			
Northern (reference group)	1.00		
Central	1.06	0.96–1.16	0.259
Eastern	0.93	0.85–1.02	0.136
Southern	1.11	0.88–1.41	0.371
Urbanization level			
1 (reference group)	1.00		
2	0.91	0.83–0.99	0.037
3	0.77	0.69–0.86	<0.001
4	0.73	0.64–0.83	<0.001
5	0.68	0.59–0.79	<0.001

CI = confidence interval

unclear, there is evidence of a pathophysiological link between inflammation, altered endothelial function, and ED. Since AD is an inflammatory skin manifestation associated with atopy [27], and chemokines and cytokines in peripheral blood and skin cells orchestrate atopic skin inflammation [28], one possible mechanism of the underlying linkage between AD and ED might be systemic inflammation. One review study by Vlachopoulos demonstrated that the presence and severity of ED are associated with markers and mediators of sub-clinical inflammation and endothelial dysfunction [29]. Systemic inflammation may subsequently contribute to endothelial dysfunction [29], which is central to the pathogenesis of ED [30,31]. Furthermore, the inverse association between erectile performance and oxidative stress has been highlighted recently [32]. Increased production of reactive oxygen species (such as superoxide and peroxynitrite) in subjects with cardiovascular risk factors decrease the bioavailability of nitric oxide and may lead to ED. Therefore, the mechanism behind atopic skin inflammation might also contribute to the development of ED.

Since ED has a serious impact on quality of life [33], it should be looked for and treated in patients with AD. Goulding et al. found that among those patients suffering from a skin disease who admitted dissatisfaction with their erectile ability, the majority wanted to receive more information on the nature of ED and its management [11]. This is in contrast to the tendency of health care professionals to rarely acknowledge the potential for such problems, and reflects a significant unmet clinical need.

Dermatologists should be alert to the association between AD and ED, and are encouraged to advise or arrange sexual consultations for patients with AD. We suggest that an assessment of sexual function should be part of the routine holistic care provided for patients with AD. Moreover, when evaluating a patient complaining of impotence, AD should be considered. Early identification of individuals with ED would allow for the prompt referral and treatment that would improve their quality of life.

The strength of our study lies in its longitudinal and large population-based database. Its use allowed us to avoid many of the problems, such as selection biases, inherent in studies utilizing data taken from voluntary registries or hospital-referred study patients. Furthermore, the large sample size allowed for the adjustment of known and important confounders, while maintaining the

statistical power necessary to detect associations. Moreover, over 98% of Taiwan's residents are of Han Chinese ethnicity, which largely prevents the possibility of confounding by race.

Despite these advantages, our findings need to be interpreted with caution due to the following limitations. First, the ED and AD diagnoses are sourced from an administrative database and therefore may be less accurate than diagnoses undertaken individually through a standardized procedure. To avoid mistaken diagnoses, we only selected patients who had been diagnosed at least twice with both ED and AD. Second, individual information such as patient characteristics and lifestyle related factors (e.g., family history, diet, physical activity level, and sexual activity) were not available through the administrative data set. These factors may have influenced the endothelial function of an individual [33]. Third, although in Taiwan, ED is diagnosed based on the results of a self-administered International Index of Erectile Dysfunction (IIEF-5) questionnaire, in our study, the raw scores of this questionnaire were not available in our administrative data set and we defined ED by ICD-9-CM codes. Therefore, we were not able to differentiate between varying degrees of ED severity. Lastly, since discussing sexuality is relatively culturally taboo in Taiwan, many patients with ED may not wish to see a specialist despite their disability. These factors might have contributed to the seemingly low frequency of ED, when compared with studies conducted in Western countries [9,34]. Therefore, it is possible that some of the controls in this study were also suffering from ED on account of Taiwanese cultural taboos. However, if such a bias exists in the data, the results of our analysis would be biased toward the null.

This study succeeded in making a novel association between ED and prior AD. We suggest that physicians be more attentive to the sexual complaints of patients with AD in order to more promptly propose a therapy and refer them to other specialists for multidisciplinary management. Since the exact mechanisms underlying these associations are not yet known, future studies are recommended, both to replicate the results seen here and to clarify the mechanisms behind them. This will allow for a more specific interpretation of these findings.

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Statement of Authorship

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