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# Associations Between Risk Factors and Overactive Bladder: A Meta-analysis

Jingzhen Zhu, MD, Xiaoyan Hu, MD, Xingyou Dong, MD, and Longkun Li, MD, PhD

**Objective:** The purpose of this study was to investigate the risk factors of overactive bladder (OAB).

**Methods:** The PubMed, Embase, and Cochrane Library databases were retrieved through May 2016. Odds ratios (OR) or standard mean differences (SMDs) with 95% confidence intervals (CIs) were used to evaluate the associations between risk factors and OAB. Heterogeneity among studies was examined using  $\chi^2$  test based on the Q and  $I^2$  tests.

**Results:** A total of 28 articles were analyzed in our study. The results suggested that age and body mass index were significantly higher in OAB patients than in non-OAB controls (SMDs [95% CIs], 0.30 [0.19–0.41] and 0.39 [0.24–0.53]). A significant negative association was found between employment status and OAB (OR [95% CIs], 0.64 [0.46–0.90]). However, sex, educational level, parity, vaginal delivery, race, menopause, marital status, smoking, and alcohol consumption were not significantly different in OAB and non-OAB control patients (ORs [95% CIs], 0.95 [0.59–1.55], 1.04 [0.82, 1.33], 0.98 [0.56–1.70], 1.66 [0.90–3.07], 0.98 [0.75–1.28], 1.84 [0.23–14.70], 0.97 [0.78–1.19], 0.91 [0.77–1.08], and 0.88 [0.71–1.09], respectively). In addition, the number of parities and vaginal deliveries in OAB patients also showed no significant differences compared with non-OAB control patients (SMDs [95% CI], 0.05 [–0.27 to 0.38] and –0.16 [0.40 to 0.09]).

**Conclusions:** This meta-analysis suggests that age and body mass index are associated with increased risks of OAB, whereas employment status is associated with a decreased risk of OAB. Further prospective studies with large sample sizes are needed to confirm this conclusion.

Key Words: meta-analysis, overactive bladder, risk factor

(Female Pelvic Med Reconstr Surg 2019;25: 238-246)

**O** veractive bladder (OAB) is a clinical syndrome defined by the International Continence Society as urinary urgency, with or without urge incontinence, usually with frequency and nocturia, in the absence of infection or other obvious pathological features.<sup>1</sup> The pathogenesis of OAB is poorly understood. Overactive bladder may occur in individuals of all ages and has a high prevalence. In Europe and Canada, a population-based survey estimated the prevalence of OAB to be 12.8% in women and 10.8% in men.<sup>2</sup> In a European SIFO study conducted in 6 countries, the prevalence of OAB in women was estimated to be 17.4%.<sup>3</sup> In the United States, the prevalence reached 16.9%.<sup>4</sup> In the Spanish population, it was reported to be 9.9% in women 25 to 64 years of

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Jingzhen Zhu and Xiaoyan Hu contributed equally to this work. Funding: None.

The authors have declared they have no conflicts of interest.

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DOI: 10.1097/SPV.000000000000531

age.<sup>5</sup> Many epidemiologic surveys conducted in Japan have shown that the prevalence of OAB may be as high as 12.4%.<sup>6</sup> The Korean EPIC study, which was conducted in 2006, revealed the overall prevalence to be 12.2% (10.0% of men, 14.3% of women).<sup>7</sup> In China, the prevalence rate of OAB was estimated to be 6.0% to 8.0% in women 18 years or older.<sup>8,9</sup> Furthermore, some researchers have estimated that the prevalence of OAB will increase to 20.1% by 2018.<sup>10</sup> In addition to its high prevalence, OAB results in both physical and psychological distress to patients and has a negative impact on health-related quality of life.<sup>11</sup> Because OAB is a nonfatal and an embarrassing disease for many patients, its presence may be significantly underreported or underdiagnosed.<sup>12</sup>

Many factors, including age, body mass index (BMI), sex, educational level, parity, vaginal delivery, race, employment status, menopause, marital status, smoking, and alcohol consumption have been considered to be possibly related to OAB. However, the results have been inconsistent. We hypothesized that the differences observed in the associations of specific risk factors with OAB are influenced by methodology and biology. Thus, to clarify these conflicting results, we conducted a meta-analysis to examine the relationships between specific risk factors and OAB.

# MATERIALS AND METHODS

# Search Strategy and Selection Criteria

Two investigators (J.Z.Z. and X.Y.D.) searched the PubMed, Embase, and Cochrane Library databases with no language restriction. Both of the 2 investigators are urologists, and they have been formally trained in evidence-based medicine. The most recent search was performed in May 2016. The keyword-based retrieval was based on combinations of risk factors (including aging, age, body mass index, BMI, sex, gender, education, parity, delivery, vaginal delivery, vaginal birth, race, employment, occupations, work, menopause, marital status, smoking, alcohol and drinking) and OAB. In addition, articles cited in the reference lists of the primary articles were also reviewed. If more than one article had been published using the same data, we selected the most complete or the most recent study.

The criteria for inclusion of studies in our meta-analysis were as follows: (1) the diagnostic criteria of OAB were defined: the experimental group included patients diagnosed as having OAB, and the control group included patients without OAB; (2) the study reported the associations between risk factors and OAB; or (3) the data were available and could be extracted from the article or obtained by calculation. Major reasons for excluding studies included the following: (1) the article was a review, case report, comment, or letter, (2) the article reported research on animals; (3) the article reported the risk factors that had been matched; or (4) based on the sensitivity analysis, the article influenced the overall pooled estimates.

#### **Study Selection**

Titles and abstracts were first screened to confirm potential eligible studies. If the relevance of the article was uncertain, a subsequent full-text evaluation was conducted. All data were independently extracted in duplicate by 2 investigators (J.Z.Z. and X.Y.D.) according to the prespecified selection criteria. Controversial issues were resolved through further discussion. There were no restrictions on the sample size, study type, and language.

# **Data Extraction and Quality Assessment**

The following data were extracted: the first author's name, the year of publication, the country, the sex of the participants, the participant sample size, and the risk factors analyzed (ie, age, BMI, sex, education, parity, vaginal delivery, race, employment status, menopause, marital status, smoking, and alcohol consumption). Education was classified into "high school degree or below" and "bachelor degree or above." The parity was divided into "nulliparous" and "primiparous or multiparous." Vaginal delivery was divided into "no vaginal birth" and "history of vaginal delivery." Race was separated into "Caucasian" and "non-Caucasian." Employment status was classified as "employment" and "unemployment" (retired, homemaker, student, and disabled). Marital status was grouped into "married" and "single" (widowed, divorced or separated, unmarried). In the meta-analysis, we completed the quality assessment according to the primary criteria for nonrandomized and observational studies of the Newcastle-Ottawa Scale (NOS) for assessing quality. This scale evaluates 3 broad perspectives of methodology: subject selection, 0 to 4; comparability of subject, 0 to 2; and clinical outcome, 0 to 3. The scale ranges from 0 to 9 points, with higher points indicating higher study quality. Published series awarded at least 6 points were considered to be of high quality. In this meta-analysis, literature search, study selection, data extraction, and quality assessment were independently performed in duplicate by 2 investigators.

# **Statistical Analysis**

The measured effect sizes were odds ratios (ORs) with 95% confidence intervals (CIs) for binary variables; for continuous variable data, the standard mean differences (SMDs) with 95% CIs were used to determine the relationship between risk factors and OAB. If the 95% CIs of ORs crossed 1 or the 95% CIs of SMDs crossed 0, there was no significant statistical difference between the experimental group and the control group, and the risk factor had a neutral effect on OAB. Heterogeneity among studies was assessed by using the  $\chi^2$  test based on the Q and  $I^2$  tests. When  $I^2 \leq 50\%$  for the Q test, a lack of heterogeneity among studies was indicated, and the summary estimate of each study was calculated using the fixed-effects model. Otherwise, the random-effects model was used. A sensitivity analysis was performed to evaluate the influence of a single study on the overall estimate. In addition, the Begg and Mazumdar adjusted rank correlation and the Egger regression asymmetry tests were conducted to detect publication bias. All P values were for 2-sided tests, and P < 0.05 was considered statistically significant. All statistical analyses were performed by using STATA 12.0 and RevMan 5.2 software, and all methods were conducted according to PRISMA guidelines.

# RESULTS

# Characteristics of 28 Included Studies

A flow diagram showing the details of the study selection process is presented in Figure 1. In all, 2738 potential studies were identified. After screening all titles and abstracts, 2463 articles were excluded. These articles were not associated with our study (n = 1862) or were reviews (n = 454), animal studies (n = 80), case reports (n = 9), or comments or letters (n = 58). A total of 275



FIGURE 1. Flowchart of the study selection process.

potentially eligible studies were further reviewed through fulltext evaluation. In addition, 247 other articles were excluded from our study because of the following reasons: an irrelevant conclusion (n = 159), no control cases (n = 79), no usable data (n = 6), duplicate data (n = 2), or failure to conform to the sensitivity analysis (n = 1). Finally, a total of 28 articles<sup>13–40</sup> that met our inclusion and exclusion criteria were included in this meta-analysis. The mean NOS score was 6.4 (of a possible 9 points), suggesting a high quality of the studies included in this analysis. The general characteristics of all 28 studies are summarized in Table 1.

# **Meta-Analysis**

Fourteen risk factors (ie, age, BMI, sex, education, parity, the number of parities, vaginal delivery, the number of vaginal deliveries, race, employment status, menopause, marital status, smoking, and alcohol consumption) were individually analyzed using a fixed-effects or random-effects model to estimate the association with OAB. The main characteristics of each risk factor are summarized in Table 2. The results suggested that age and BMI were significantly higher in OAB patients than in non-OAB controls; the pooled SMDs (95% CIs) were 0.30 (0.19-0.41) and 0.39 (0.24-0.53), respectively (P < 0.05; Figs. 2, 3). A significant negative association was found between employment status and OAB; the summary OR (95% CI) was 0.64 (0.46–0.90; P < 0.05; Fig. 4). However, sex, education, parity, vaginal delivery, race, menopause, marital status, smoking, and alcohol consumption in OAB patients were not significantly different from those in non-OAB controls (ORs [95% CIs], 0.95 [0.59-1.55], 1.04 [0.82-1.33], 0.98 [0.56-1.70], 1.66 [0.90-3.07], 0.98 [0.75-1.28], 1.84 [0.23-14.70], 0.97 [0.78-1.19], 0.91 [0.77-1.08], and 0.88 [0.71-1.09], respectively; P > 0.05). Furthermore, the number of parities and vaginal deliveries in OAB patients were not significantly different from those in

Akin et al <sup>13</sup> Alves et al <sup>14</sup> Bunyavejchevin <sup>15</sup>		VOC	indiana funda	Sample Size (Case/Control)	Kisk Factors	SON
Alves et al <sup>14</sup> Bunyavejchevin <sup>15</sup>	Turkey	Women	Case-control	115/89	Age, BMI	9
Bunyavejchevin <sup>15</sup>	Brazil	Women	Case-control	117/49	Age, BMI, parity, NP, VD, NVD	8
D 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	Thailand	Women	Cohort	60/60	Age, EL, MS	9
Bunyavejcnevin and veeranarapanicn	Thailand	Women	Case-control	60/120	Age, NP, EL, MS	9
Cardozo et al <sup>17</sup>	USA	Women	Cohort	53/47	Age, BMI, race, ES, EL	9
Chen et al <sup>18</sup>	China	Women	Case-control	54/1193	VD, menopause	7
Chen et al <sup>19</sup>	China	Women	Case-control	26/325	Age, BMI	9
Cheung et al <sup>20</sup>	USA	Both	Case-control	160/151	Sex	5
Coyne et al <sup>21</sup> Coyne et al <sup>21</sup>	Jermany, Italy, Sweden, UK	Both	Case-control	1434/1434	Race, ES, EL, MS	7
Coyne et al <sup>22</sup>	USA	Both	Case-control	7121/5254	ES, EL, MS	8
Ergenoglu et al <sup>23</sup>	Turkey	Women	Case-control	51/76	Age, BMI, NP, NVD	8
Heidler et al <sup>24</sup>	Austria	Women	Case-control	75/311	Age, BMI, parity, smoking, AC	9
Ikeda et al <sup>25</sup>	Japan	Both	Case-control	153/680	Age, sex, BMI, smoking, AC	7
Jo et al <sup>26</sup>	Korea	Both	Case-control	130/796	Age, sex, EL, MS, smoking, AC	5
Liberman et al <sup>27</sup>	USA	Both	Case-control	483/191	Age, sex, BMI, race, ES, EL, MS	9
Liu et al <sup>28</sup>	Taiwan	Both	Case-control	306/1053	Age, sex, BMI, smoking, AC	9
Ozgur et al <sup>29</sup>	Turkey	Women	Case-control	94/171	Age, smoking	9
Silva-Ramos et al <sup>30</sup>	Portugal	Women	Case-control	34/36	Age	7
Sobhgol and Charandabee <sup>31</sup>	Iran	Women	Case-control	77/148	Age, BMI, parity, NP, VD	5
Sut et al <sup>32</sup>	Turkey	Women	Case-control	109/171	Age, BMI, ES, EL, menopause, MS, smoking, AC	7
Teloken et al <sup>33</sup>	Brazil	Both	Case-control	160/688	Age, sex, BMI, parity, race, EL	8
Uzun et al <sup>34</sup>	Turkey	Women	Cohort	122/62	BMI, menopause	9
Uzun and Zorba <sup>35</sup>	Turkey	Women	Cohort	313/208	BMI, menopause	5
Yoo et al <sup>36</sup>	Korea	Both	Case-control	458/1542	EL	8
Zahariou et al <sup>37</sup>	Greece	Women	Cohort	135/112	WS	7
Zhang et al <sup>38</sup>	China	Men	Case-control	431/1208	Age	7
Zhang et al <sup>39</sup>	China	Women	Case-control	295/775	Age, BMI, VD, MS	2
Zhu et al <sup>40</sup>	China	Women	Case-control	32/272	Age, BMI, parity	٢

<b>Risk Factors</b>	No. Studies	Effect Model	$I^2, \%$	P <sub>h</sub>	SMDs/ORs	Effect Size (95% CI)	Р
Age	20	R	79	0.00	SMD	0.30 (0.19 to 0.41)	0.00
BMI	16	R	84	0.00	SMD	0.39 (0.24 to 0.53)	0.00
Sex	6	R	91	0.00	OR	0.95 (0.59 to 1.55)	0.84
Educational level	9	R	69	0.00	OR	1.04 (0.82 to 1.33)	0.74
Parity	5	R	56	0.06	OR	0.98 (0.56 to 1.70)	0.94
No. parities	4	R	77	0.005	SMD	0.05 (-0.27 to 0.38)	0.75
Vaginal delivery	4	R	65	0.03		1.66 (0.90 to 3.07)	0.11
No. vaginal deliveries	2	F	31	0.23	SMD	-0.16 (0.40 to 0.09)	0.20
Race	4	F	0	0.79	OR	0.98 (0.75 to 1.28)	0.87
Employment status	5	R	87	0.00	OR	0.64 (0.46 to 0.90)	0.01
Menopause	4	R	97	0.00	OR	1.84 (0.23 to 14.70)	0.57
Marital status	9	R	78	0.00	OR	0.97 (0.78 to 1.19),	0.76
Smoking	6	F	0	0.60	OR	0.91 (0.77 to 1.08)	0.29
Alcohol consumption	5	F	11	0.34	OR	0.88 (0.71 to 1.09)	0.25

TABLE 2.	Main	Characteristics	of Eacl	n Risk Factor
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non-OAB controls (SMDs [95% CIs], 0.05 [-0.27 to 0.38] and -0.16 [0.40 to 0.09]; P < 0.05). There was no evidence of significant heterogeneity regarding the number of vaginal deliveries, race, smoking, or alcohol consumption (P < 0.05,  $I^2 < 50\%$ ). However, there was evidence of significant heterogeneity in age, BMI, sex, educational level, parity, the number of parities, vaginal delivery, employment status, menopause, and marital status (P > 0.05,  $l^2 > 50\%$ ).

Sensitivity analyses were performed to detect potential sources of heterogeneity in the associations between the considered risk factors and OAB. None of the corresponding pooled SMDs or the summary ORs were materially changed except one study,<sup>41</sup> which was therefore excluded from our meta-analysis. Figure 5 shows the results of the sensitivity analysis of the association between age and OAB; the results of the other sensitivity analyses are not shown because of space limitations. Begg and Egger tests were performed to evaluate the publication bias of the literature; little publication bias was found.

# DISCUSSION

In this meta-analysis, 28 available studies were statistically analyzed to investigate the associations of risk factors with OAB. Our results suggested that age and BMI had a significant positive association with OAB, whereas employment status had a significant negative association with OAB. In addition, no significant association of sex, educational level, parity, vaginal delivery, race, menopause, marital status, smoking, or alcohol consumption with OAB was found.

Overactive bladder is a clinical diagnosis that includes the presence of bothersome urinary symptoms. It is often but not always associated with detrusor overactivity on urodynamic evaluation.

	Exp	eriment	ta	C	ontrol			Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Tota	Mean	SD	Tota	Weight	IV, Random, 95% Cl	IV, Random, 95% Cl
Akin 2015	42.56	9.73	115	39.13	9.55	89	4.9%	0.35 [0.08, 0.63]	— <i>—</i>
Alves 2014	68.4	6.1	117	69.4	6.3	49	4.3%	-0.16 [-0.50, 0.17]	
Bunyavejchev 2005	62.18	13.26	60	54.1	4.7	60	3.9%	0.81 [0.43, 1.18]	
Bunyavejchev 2005	53.6	5.8	60	52	6.1	120	4.5%	0.27 [-0.05, 0.58]	
Cardozo 2014	54.6	11.6	53	40.4	14.3	47	3.5%	1.09 [0.67, 1.51]	<del></del>
Chen 2015	49.62	4.28	26	45.75	4.71	325	3.6%	0.83 [0.42, 1.23]	
Ergenoglu 2013	36.6	7.9	51	38.7	6.9	76	4.1%	-0.29 [-0.64, 0.07]	
Heidler 2011	54.95	11.5	75	53.96	12.8	311	5.2%	0.08 [-0.17, 0.33]	
lkeda 2011	75.54	2.16	153	75.49	2.11	680	6.0%	0.02 [-0.15, 0.20]	
Jo 2012	61.54	9.31	130	57.11	9.44	796	5.9%	0.47 [0.28, 0.66]	
Liberman 2001	58.45	9.13	483	57.47	9.24	191	6.1%	0.11 [-0.06, 0.27]	
Liu 2011	65.1	10.6	306	61.6	10.7	1053	6.5%	0.33 [0.20, 0.46]	
Ozgur 2012	22.07	2.54	94	21.56	1.9	171	5.2%	0.24 [-0.02, 0.49]	— <u> </u>
Silva-Ramos 2013	57.3	12.8	34	51.8	8.7	36	3.0%	0.50 [0.02, 0.98]	
Sobhgol 2008	34.6	8.9	77	31.55	8.1	148	4.9%	0.36 [0.09, 0.64]	
Sut 2012	49.37	6.83	109	47.37	6.42	171	5.3%	0.30 [0.06, 0.54]	
Teloken 2006	30.68	8.41	160	29.39	7.59	688	6.1%	0.17 [-0.01, 0.34]	
Zhang 2010	68	10	431	63	9	1208	6.7%	0.54 [0.43, 0.65]	-
Zhang 2013	31.12	8.35	295	28.95	7.72	775	6.5%	0.27 [0.14, 0.41]	
Zhu 2015	52.06	5.73	32	51.6	6.03	272	4.0%	0.08 [-0.29, 0.44]	
Total (95% CI)			2861			7266	100.0%	0.30 [0.19, 0.41]	•
Heterogeneity: Tau <sup>2</sup> =	0.04; Cł	ni <sup>z</sup> = 88.	47, df=	19 (P <	0.000	001); I <sup>z</sup>	= 79%		
Test for overall effect:	7 = 5.37	(P < 0)	00001)						-1 -0.5 0 0.5 1

FIGURE 2. Forest plot of the association between age and OAB.



	Expe	erimen	ta	C	ontrol		Std. Mean Difference		Std. Mean Difference
Study or Subgroup	Mean	SD	Tota	Mean	SD	Total	Weight	IV, Random, 95% C	I IV, Random, 95% CI
Akin 2015	31.28	4.19	115	26.67	5.03	89	6.0%	1.00 [0.71, 1.30]	
Alves 2014	28	4.5	117	25.3	3.6	49	5.5%	0.63 [0.29, 0.97]	
Cardozo 2014	31.1	6.6	53	26.4	5	47	4.8%	0.79 [0.38, 1.20]	
Chen 2015	23.06	3.19	26	22.49	2.46	325	4.9%	0.23 [-0.17, 0.63]	
Ergenoglu 2013	24.7	3.7	51	24.3	3.4	76	5.3%	0.11 [-0.24, 0.47]	
Heidler 2011	24.75	3.84	75	24.68	3.99	311	6.4%	0.02 [-0.23, 0.27]	
lkeda 2011	24.21	3.31	153	23.78	3.16	680	7.1%	0.13 [-0.04, 0.31]	
Liberman 2001	29.82	2.25	483	29.01	2.27	191	7.2%	0.36 [0.19, 0.53]	-
Liu 2011	26.1	3.8	306	25.9	3.8	1053	7.5%	0.05 [-0.07, 0.18]	
Sobhgol 2008	29	6	77	26.3	5.1	148	6.1%	0.50 [0.22, 0.78]	
Sut 2012	27.91	1.91	109	27.35	1.93	171	6.5%	0.29 [0.05, 0.53]	
Teloken 2006	23.06	3.13	160	22.93	2.99	688	7.2%	0.04 [-0.13, 0.22]	
Uzun 2012	32.4	4.9	122	29.2	3.1	62	5.7%	0.73 [0.41, 1.04]	
Uzun 2012	31.37	5.82	313	27.71	4.81	208	7.1%	0.67 [0.49, 0.85]	
Zhang 2013	21.88	3.25	295	21.09	2.84	775	7.5%	0.27 [0.13, 0.40]	-
Zhu 2015	24.9	2.82	32	23	2.86	272	5.2%	0.66 [0.29, 1.03]	
									-
Total (95% CI)			2487			5145	100.0%	0.39 [0.24, 0.53]	•
Heterogeneity: Tau <sup>2</sup> =	= 0.06; Cł	ni <b>z</b> = 93	1.52, df	= 15 (P	< 0.00	0001); P	²= 84%		
Test for overall effect	Z = 5.37	(P < 0	.00001	)				1	avours (experimental) Eavours (control)

FIGURE 3. Forest plot of the association between BMI and OAB
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Overactive bladder is subclassified as "OAB wet" if associated with urinary incontinence and as "OAB dry" if it is not associated with incontinence. Overactive bladder is a chronic disease, and the severity of OAB symptoms progresses dynamically over long periods, as exemplified by the progression in OAB symptoms from OAB dry to OAB wet. Thus, the treatment paradigm is not only symptom control but also prevention of the worsening of the condition.<sup>42</sup> Although many studies have examined the relationships between risk factors and OAB, conflicting results have been obtained. To prevent OAB as much as possible, we conducted this meta-analysis to determine the risk factors for OAB.

Many studies have indicated a positive association between age and OAB, but other studies have not supported this conclusion.<sup>14,29,34,40,43</sup> In our study, 20 articles reported a relationship between age and OAB, and we found that age had a positive association with OAB. The prevalence of OAB symptoms increased with age in both men and women.<sup>22</sup> Age-related changes in the bladder and pelvic floor tissues and/or in the nervous system contribute to the high prevalence of OAB in elderly women.44 Increased incidence of OAB with age may be linked to cerebrovascular disorders and pelvic tumors.<sup>45</sup> Moreover, Tomaszewski<sup>46</sup> reported that advanced age was associated with decreased bone mineral density and an increased risk of osteoporosis, for which fractures were serious complications. Among elderly people, OAB is associated with an increased risk of falls and fractures, which are often caused by rushing to the toilet. In addition, men 60 years or older have a high prevalence of benign prostatic hyperplasia, which often causes bladder outlet obstruction and contributes to OAB.47 The severity of OAB increases between

40 and 49 years of age, reaches a plateau at 50 to 59 years of age, increases steeply in patients 60 to 69 years of age, continues to rise in patients 70 to 79 years of age, and reaches a plateau in patients older than 80 years.<sup>48</sup> With the gradual aging of the population, OAB is presenting new challenges to the health care system.

With improvement in living standards, unhealthy lifestyles, including high-calorie diets, lack of exercise, and too many hours sitting in front of a computer or television, have contributed to the increased number of individuals with high BMI. The high BMI levels seriously endanger the health of persons of all ages, and many types of diseases are related to obesity. The results of our study showed that BMI was significantly higher in OAB patients than in non-OAB controls. Higher BMI exposes the pelvic floor to increased intra-abdominal and intravesical pressure, which may chronically stretch the pudendal nerve, leading to nerve injury and pelvic floor dysfunction.49 Higher BMI is also more likely to be associated with diabetes and neurological conditions such as diabetic autonomic neuropathy, which may lead to the onset of OAB.50 The pelvic organs and their surrounding muscular and connective supporting tissues are hormone responsive, and increases in BMI are associated with higher levels of estrone and estradiol and lower levels of plasma testosterone.<sup>51</sup> Joseph et al<sup>52</sup> found that increasing levels of BMI were significantly associated with larger prostate volumes. In addition, a previous study has shown that weight loss resulted in improvement of OAB symptoms.<sup>53</sup> Fortunately, as an independent risk factor of OAB, BMI can be intervened. We can control our weight to reduce the risk of OAB and other problems by exercise and a balanced nutritional



FIGURE 4. Forest plot of the association between employment status and OAB.



Meta-analysis random-effects estimates (linear form) Study ommited

FIGURE 5. Sensitivity analysis of the association between age and OAB.

diet. According to our research results, employment status presented a negative association with OAB. The exact mechanism for this is still unclear. Age may certainly confound the relationship between employment and OAB. Older adults are less likely to be employed, and age is significantly higher in OAB cases than in non-OAB controls in our study. Further well-designed cohort studies, which eliminate the influences of age, are necessary to explain the association between employment status and OAB. In addition, we speculate that behavioral changes associated with employment may be beneficial to OAB. However, as is well known, it is impossible to conclude from case–control analysis whether an association is causal. For example, because of their symptoms, individuals with OAB may be less competent in the workplace, which would lead to a lower employment rate.

Some studies found no<sup>20,26</sup> or a negative<sup>28,54–56</sup> association of female sex with OAB, but other studies<sup>33,57,58</sup> showed that female sex was an independent risk factor for OAB. Irwin et al<sup>2</sup> reported a higher prevalence of OAB symptoms in women than in men before 60 years of age, whereas men had a greater prevalence of OAB symptoms after 60 years of age. Other studies<sup>4,7</sup> performed in the United States and Korea reported that although the prevalence of OAB increased linearly in the male population, it decreased in the oldest age group in the female population. In concordance with the results reported by Jo et al<sup>26</sup> and Cheung et al,<sup>20</sup> our analysis also showed that there was no significant difference between men and women in the prevalence of OAB, despite the differences in anatomy and lifestyle habits between men and women.

Precious studies<sup>8,33</sup> have shown a negative relationship between educational level and OAB. The authors of these studies suggested that persons with a higher educational level were more likely to pursue health-promoting behaviors and might have healthier lifestyles, whereas persons with lower educational levels might have a higher prevalence of poor diet, exposure to toxins, and so on.<sup>26</sup> However, in our study, 9 articles comprehensively analyzed the association of educational level (high school degree or below, bachelor degree or above) with OAB, and no significant difference was found. This result is similar to those of a number of other studies.<sup>15–17,21,27,36</sup>

Many studies<sup>59–62</sup> reported the relationship between parturition and OAB, but the results were inconsistent. The EPICC study59 found that multiparous women and women who had undergone vaginal delivery were more likely to have OAB. Palma et al<sup>60</sup> also found that nulliparous women presented fewer OAB symptoms compared with primiparous women and that there were no significant differences between women who had experienced different modes of delivery (vaginal and cesarean). In addition, Lukacz et al<sup>61</sup> demonstrated that vaginal delivery increased the risk of pelvic floor disorders. In another study, Rortveit et al<sup>62</sup> showed that the risk of OAB in women 5 to 10 years after giving birth was not significantly associated with birthing method (vaginal or cesarean). Most studies did not find significant differences in the likelihood of OAB in women who experienced different modes of delivery.<sup>60</sup> In our meta-analysis, parity, the number of parities, vaginal delivery, and the number of vaginal deliveries were analyzed to explore the relationships of these factors to OAB; the results showed that those factors had no significant association with OAB.

The possible association of race<sup>2,3,8,9,63</sup> and marital status <sup>15,16,21,22,26,27,32,37,38</sup> with OAB was addressed in several studies. Consistent with most of the previous experimental results,<sup>2,3,8,9,15,16,21,22,27,32,37,63</sup> our study suggested that race and marital status are not risk factors for OAB.

The World Health Organization defines natural menopause as the permanent cessation of menstruation resulting from the loss of ovarian follicular activity. Natural menopause usually occurs between 45 and 55 years of age. Lack of estrogen is the main cause of menopausal symptoms. The decrease in estrogen, which leads to atrophy of the lower urinary tract and pelvic floor, triggers urinary symptoms, such as frequency, urgency, and nocturia.<sup>64</sup> Salcedo and Sanchez Borrego<sup>65</sup> reported that menopause was significantly associated with OAB, with 3.7-fold greater likelihood in menopausal women than in nonmenopausal women. de Boer et al<sup>66</sup> also demonstrated that menopause was a risk factor for OAB symptoms. Four studies were analyzed in our study; the results showed that there was no significant association between menopause and OAB. Additional studies of this topic with larger sample sizes are needed.

It is well known that cigarette smoking is an intractable and preventable public health problem.<sup>67</sup> Many previous studies<sup>26,50,56,63,66,68,69</sup> have explored the role of smoking in OAB. Although some studies<sup>26,69</sup> found no relationship between smoking and OAB, other studies<sup>50,63</sup> reported that smoking was a risk factor for the onset of OAB. The higher incidence of OAB in smoking populations may be explained by the following: (1) smoking elevates mean serum levels of testosterone and androstenedione<sup>70</sup>; (2) cigarette smoking is correlated with an antiestrogenic hormonal effect on the bladder and urethra<sup>71</sup>; and (3) nicotine increases the activity of the sympathetic nervous system and exacerbates irritative urinary symptoms.<sup>72,73</sup> In the present study, smoking was found to be unrelated to the onset of OAB, although it is an important risk factor for and is involved in the pathogenesis of a variety of disorders.

Chronic alcohol abuse, which can lead to tissue damage and organ dysfunction, is a significant contributor to the global burden of disease.<sup>74</sup> A few studies<sup>8,24–26,28,32,63,69,75</sup> evaluated the association of alcohol intake with OAB. Some studies<sup>69,75</sup> showed an inverse association, whereas others<sup>8,63</sup> reported a positive association. Acute and chronic consumption of alcohol may result in higher serum estrogen levels and reduced androgen levels.<sup>76</sup> These changes in hormone levels can cause urinary symptoms by various mechanism.<sup>40</sup> In addition, animal studies<sup>77,78</sup> have shown that ethanol can reduce the contractility of the detrusor muscle and the urethra. However, in this meta-analysis, no significant association was found between alcohol consumption and OAB. The specific mechanisms need to be elucidated in further studies.

To our knowledge, this is the first systematic review and meta-analysis to explore the risk factors associated with OAB. In our meta-analysis, 28 studies that involved relatively high numbers of cases and controls were included, strengthening the reliability and conclusiveness of our results. However, our study also has some limitations. First, residual confounders and unidentified factors are inevitable in observational studies. Second, the definitions and diagnostic criteria of OAB used in the studies included in our meta-analysis were not completely consistent. Third, the number of cases and controls in some studies was relatively small, and some studies were excluded because of a lack of useful data. Finally, there was strong evidence of heterogeneity among the included studies. Although we detected one major source of heterogeneity by conducting sensitivity analyses, other differences between the studies should be considered.

# CONCLUSIONS

Our research showed that age and BMI had significant positive associations with OAB, whereas employment had a significant negative association with OAB. In addition, we demonstrated that sex, educational level, parity, vaginal delivery, race, menopause, marital status, smoking, and alcohol consumption were not found by these analyses to impact on the risk of OAB. Our results may be helpful in designing effective medical and preventive interventions targeting the susceptible population.

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