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

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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 χ² test based on the Q and I² 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], 0.95 [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

(Original Article)
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 χ² test based on the Q and P tests. When $P \leq 0.05$ 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 potentially eligible studies were further reviewed through full-text 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), or failure to conform to the sensitivity analysis (n = 1). Finally, a total of 28 articles13–40 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

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| Author                | Country       | Sex     | Study Design | Sample Size (Case/Control) | Risk Factors                    | NOS |
|-----------------------|---------------|---------|--------------|----------------------------|---------------------------------|-----|
| Akin et al            | Turkey        | Women   | Case-control | 115/89                     | Age, BMI                        | 6   |
| Alves et al           | Brazil        | Women   | Case-control | 117/49                     | Age, BMI, parity, NP, VD, NVD    | 8   |
| Bunyavejchevin        | Thailand      | Women   | Cohort       | 60/60                      | Age, EL, MS                      | 6   |
| Bunyavejchevin and Veenanarapanich | Thailand | Women | Case-control | 60/120                     | Age, NP, EL, MS                  | 6   |
| Cardozo et al         | USA           | Women   | Case-control | 53/47                      | Age, BMI, race, ES, EL           | 6   |
| Chen et al            | China         | Women   | Case-control | 54/1193                    | VD, menopause                    | 7   |
| Chen et al            | China         | Women   | Case-control | 26/325                     | Age, BMI                        | 6   |
| Cheung et al          | USA           | Both    | Case-control | 160/151                    | Sex                             | 5   |
| Coyne et al           | Canada, Germany, Italy, Switzerland, UK | Both | Case-control | 1434/1434                  | Race, ES, EL, MS                 | 7   |
| Ergenoglu et al       | Turkey        | Women   | Case-control | 51/76                      | Age, BMI, NP, NVD                | 8   |
| Heidler et al         | Austria       | Women   | Case-control | 75/311                     | Age, BMI, parity, smoking, AC    | 6   |
| Ikeda et al           | Japan         | Both    | Case-control | 153/680                    | Age, sex, BMI, smoking, AC       | 7   |
| Jo et al              | Korea         | Both    | Case-control | 130/796                    | Age, sex, EL, MS, smoking, AC    | 5   |
| Liberman et al        | USA           | Both    | Case-control | 483/191                    | Age, sex, BMI, race, ES, EL, MS  | 6   |
| Liu et al             | Taiwan        | Both    | Case-control | 306/1053                   | Age, sex, BMI, smoking, AC       | 6   |
| Ozgur et al           | Turkey        | Women   | Case-control | 94/171                     | Age, smoking                     | 6   |
| Silva-Ramos et al     | Portugal      | Women   | Case-control | 34/36                      | Age                             | 7   |
| Sobhogol and Chanandabee | Iran         | Women   | Case-control | 77/148                     | Age, BMI, parity, NP, VD         | 5   |
| Sut et al             | Turkey        | Women   | Case-control | 109/171                    | Age, BMI, ES, EL, menopause, MS, smoking, AC | 7   |
| Teloken et al         | Brazil        | Both    | Case-control | 160/688                    | Age, sex, BMI, parity, race, EL  | 8   |
| Uzun et al            | Turkey        | Women   | Cohort       | 122/62                     | BMI, menopause                   | 6   |
| Uzun and Zorba        | Turkey        | Women   | Cohort       | 313/208                    | BMI, menopause                   | 5   |
| Yoo et al             | Korea         | Both    | Case-control | 458/1542                   | EL                              | 8   |
| Zahariou et al        | Greece        | Women   | Cohort       | 135/112                    | MS                              | 7   |
| Zhang et al           | China         | Men     | Case-control | 431/1208                   | Age                             | 7   |
| Zhang et al           | China         | Women   | Case-control | 295/775                    | Age, BMI, VD, MS                 | 5   |
| Zhu et al             | China         | Women   | Case-control | 32/272                     | Age, BMI, parity                 | 7   |

AC, alcohol consumption; EL, educational level; ES, employment status; MS, marital status; NP, number of parities; NVD, number of vaginal deliveries; VD, vaginal delivery.
TABLE 2. Main Characteristics of Each Risk Factor

| Risk Factors       | No. Studies | Effect Model | $I^2$, % | $P_h$ | SMDs/ORs | Effect Size (95% CI) | $P$ |
|--------------------|-------------|--------------|----------|-------|----------|----------------------|-----|
| 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  | OR       | 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|

F, fixed-effects model; R, random-effects model; $P_h$, $P$ value of heterogeneity.

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

**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.

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 ($P > 0.05$, $I^2 > 50\%$).

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, 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.
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.42 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.14,29,34,40,43 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.22 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.45 Moreover, Tomaszewski46 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.48 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.51 Joseph et al52 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.53 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 diet.

![FIGURE 3. Forest plot of the association between BMI and OAB.](image1)

![FIGURE 4. Forest plot of the association between employment status and OAB.](image2)
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,20,26 or a negative,28,54,56 association of female sex with OAB, but other studies3,57,58 showed that female sex was an independent risk factor for OAB. Irwin et al26 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 studies27 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 al26 and Cheung et al,20 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 studies3,33 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.26 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.15,17,21,27,36

Many studies59–62 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 al60 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 al61 demonstrated that vaginal delivery increased the risk of pelvic floor disorders. In another study, Rortveit et al62 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.60 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,2,3,8,9,63 and marital status15,16,21,22,26,27,32,37,38 with OAB was addressed in several studies. Consistent with most of the previous experimental results,2,3,8,9,15,16,21,22,26,27,32,37,63 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.64 Salcedo and Sanchez Borrego65 reported that menopause was significantly associated with OAB, with 3.7-fold greater likelihood in menopausal women than in nonmenopausal women. de Boer et al66 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.67 Many previous studies49,50,56,63,66,68,69 have explored the role of smoking in OAB.
Although some studies found no relationship between smoking and OAB, other studies 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; (2) cigarette smoking is correlated with an antitoxicogenic hormonal effect on the bladder and urethra; and (3) nicotine increases the activity of the sympathetic nervous system and exacerbates irritative urinary symptoms. 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. A few studies evaluated the association of alcohol intake with OAB. Some studies showed an inverse association, whereas others reported a positive association. Acute and chronic consumption of alcohol may result in higher serum estrogen levels and reduced androgen levels. These changes in hormone levels can cause urinary symptoms by various mechanisms. In addition, animal studies 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 positive 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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