Risk of psychiatric disorders in overactive bladder syndrome: a nationwide cohort study in Taiwan

Nian-Sheng Tzeng,[1,2] Hsin-An Chang,[1,2] Chi-Hsiang Chung,[3,4,5] Yu-Chen Kao,[1,6] Hui-Wen Yeh,[1,7,8,9] Chin-Bin Yeh,[1] Wei-Shan Chiang,[1] San-Yuan Huang,[1] Ru-Band Lu,[1,10] Wu-Chien Chien[3,4,11]

► Additional material is published online only. To view please visit the journal online (http://dx.doi.org/10.1136/jim-2018-000835).

For numbered affiliations see end of article.

Correspondence to
Professor Wu-Chien Chien, Department of Medical Research, Tri-Service General Hospital, National Defense Medical Center, Taipei 11490, Republic of China; chienwu@ndmctsgh.edu.tw

Accepted 6 September 2018
Published Online First 1 October 2018

To cite: Tzeng N-S, Chang H-A, Chung C-H, *et al*. *J Investig Med* 2019;**67**:312–318.

ABSTRACT

Population-based cohort study investigating the risk of depression and other psychiatric disorders for patients with overactive bladder (OAB) syndrome is unavailable. This study investigated the subsequent risk of psychiatric disorders among patients with OAB in an Asian population. Using data from the National Health Insurance Research Database of Taiwan, we established a cohort with 811 patients in an exposed group with OAB between January 1, 2000 and December 31, 2000, and a non-exposed group, without OAB, of 2433 patients without OAB matched by age and year of diagnosis. The occurrence of psychiatric disorders and Cox regression model measured adjusted HRs (aHR) were monitored until the end of 2013. The overall incidence of psychiatric disorders was 41.7% higher in the exposed group with OAB than in the non-exposed group without OAB (14.2% vs 10.1%, p<0.001), with an aHR of 1.34 (95% CI 1.12 to 1.80, p<0.001) for the OAB cohort. OAB was associated with the increased risk of dementia, anxiety, depressive, sleep, and psychotic disorders, with aHRs as 1.53 (p=0.040), 1.61 (p<0.001), 2.10 (p<0.001), 1.43 (p<0.001), and 2.49 (p=0.002), respectively. The risk of psychiatric disorders, including depression and anxiety, is significantly higher in patients with OAB than in those without OAB. Evaluation of psychiatric status in patients with OAB is strongly recommended.

Significance of this study

What is already known about this subject?

- Previous studies have found that patients with overactive bladder (OAB) syndrome are at increased risk of anxiety disorder, depressive disorder, obstructive sleep apnea, and post-traumatic stress disorder.
- The association between OAB and a range psychiatric disorders has not yet been studied.

What are the new findings?

- Compared with previous research about the association between OAB and affective, sleep and other mental health problems, this population-based study focused on investigating whether OAB was associated with the risk of psychiatric disorders.
- OAB was associated with the risk of psychiatric disorders (adjusted HR (aHR): 1.34, 95% CI 1.12 to 1.80, p<0.001), when adjusting for sex, age, monthly income, urbanization level, geographic region, and comorbidities.
- OAB was associated with an increased risk of developing dementia, anxiety, depressive, sleep, and psychotic disorders, with aHRs as 1.53 (p=0.040), 1.61 (p<0.001), 2.10 (p<0.001), 1.43 (p<0.001), and 2.49 (p=0.002), respectively.

How might these results change the focus of research or clinical practice?

- If the risk of psychiatric disorders in OAB is a causal association, then the results would remind the clinicians who care patients with OAB to provide careful monitoring of these patients' mental conditions in the clinical practice.

INTRODUCTION

Overactive bladder (OAB) syndrome is defined as 'urgency, with or without urge incontinence, usually with frequency and nocturia, in the absence of infection or other proven pathology.[1 2] Community studies had showed that the prevalence of OAB was estimated to be around 16%–17% in different countries.[3 4] Several researchers found that patients with OAB had suffered from this disabling condition associated with the considerable negative impact on their quality of life, quality of sleep, and mental health, such as guilty feelings, depression, loss of feeling of esteem, and fears.[5 6]

Some studies have revealed that OAB was associated with postpartum depression,[7] obstructive sleep apnea,[8] and one study about the female veterans also found that OAB was associated with post-traumatic stress disorder (PTSD), anxiety, and depression.[9] However, whether OAB was associated with the risk of psychiatric disorders has not been studied. We hypothesized that we could examine whether OAB was associated with a range of psychiatric disorders by using the National Health Insurance Research Database (NHIRD), a nationwide,

population-based registry. The present study is also to investigate the impact of medications for OAB on the association with the psychiatric disorders.

MATERIALS AND METHODS

Data sources

The National Health Insurance (NHI) Program was launched in Taiwan in 1995, and as of June 2009, it included contracts with 97% of the medical providers, with approximately 23 million beneficiaries, or more than 99% of the entire population of Taiwan.[10] Several studies have demonstrated the accuracy and validity of the diagnoses in the NHIRD.[11–13] The NHIRD uses the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) codes to record diagnoses.[14] The NHI Administration randomly reviews the records of ambulatory care visits and inpatient claims periodically to verify the accuracy of the diagnoses.[15]

Sampled study population

The present study used a retrospective, matched-cohort design. Patients with OAB were selected from 1 year between January 1, 2000 and December 31, 2000, according to the ICD-9-CM codes: 596.51. In Taiwan, OAB is defined as a 'symptom syndrome', marked by urgency, with or without urge incontinence, usually with frequency and nocturia, in the absence of an underlying metabolic or pathologic condition,[1] and this definition was then formalized in the 'Standardization of Terminology in Lower Urinary Tract Function: Report from the Standardization Sub-committee of the International Continence Society'.[2 16] And the reason why we just enrolled patients with OAB and controls within 1 year, between January 1, 2000 and December 31, 2000 is to make sure all the subjects were followed up in the same period, similar to several previous studies.[17–19] All diagnoses of OAB were made by board-certified urologists, and gynecologists (in female patients). Those diagnoses of psychiatric disorders in this study were made by board-certified psychiatrists. In addition, while we reviewed previous literatures about OAB research, using the NHIRD, the definitions of OAB in their studies were the records of OAB combined with antimuscarinic medications,[20–22] ≦2 visits for OAB in 1 year,[23–25] or ≧3 visits for OAB in 1 year.[26] For obtaining relative confirmatory diagnosis of OAB, each enrolled patient was required to have made at least 3 outpatient visits within the 1 consecutive year study according to the OAB ICD-9-CM code.[26] The patients diagnosed with psychiatric disorders before 2000, or before the first visit for OAB, and all patients aged <20 years were also excluded. In this study, we used data from the NHIRD to investigate the association between patients with OAB and psychiatric disorders over a 13-year period, from the 1 million Longitudinal Health Insurance Database in Taiwan (2000–2013). A total of 3244 enrolled patients, with 811 OAB subjects, and 2433 controls, with 1:3 age, sex, and index date-matched control group without OAB in this study (online supplementary figure S1).

Covariates

The covariates were sex, age groups (20–29, 30–39, 40–49, 50–59, 60–69, ≧70 years), comorbidity, areas of residence (north, center, south, and east of Taiwan), urbanization levels of residence (levels 1–4), seasons, and monthly insurance premiums (in New Taiwan dollars (NT$); <18,000; 18,000–34,999; ≥35,000). Charlson Comorbidity Index (CCI) defined the comorbidity.[27 28] The population and various indicators defined the urbanization levels. Level 1 was defined as a population >1,250,000; level 2 was defined as a population between 500,000 and 1,249,999; and urbanization levels 3 and 4 were defined as a population between 149,999 and 499,999, and <149,999, respectively.[29] Since 1 study found that there are seasonal symptom changes in OAB,[30] we included the seasons that the patients searched for medical help as covariates.

Antimuscarinic medications reimbursed by the NHI for OAB, such as trospium, imipramine, flavoxate, propiverine, oxybutynin, tolterodine, and solifenacin, were also collected from the database. The data of the defined daily dose (DDD) were obtained from the WHO Collaborating Centre for Drug Statistics Methodology (https://www.whocc.no/), and the duration of the usage of antimuscarinic medications was calculated by dividing the cumulative doses by the DDD of the antimuscarinic medications.

Outcome measurements

The data on all of the study subjects were collected for the time period between January 1, 2000 and December 31, 2000, until the onset of those psychiatric disorders, including dementia (ICD-9-CM 290.0, 290.10–290.13, 292.20–292.21, 290.3, 290.41–290.43, 290.8–290.9, and 331.0), anxiety disorders (ICD-9-CM 300), depressive disorders (ICD-9-CM 296.2–296.3, 300.4, and 311), bipolar disorders (ICD-9-CM 296.0, and 296.4–296.8), sleep disorders (ICD-9-CM 307.4 and 780.5), psychotic disorders (ICD-9-CM 295, and 297–298), adjustment disorders (ICD-9-CM 309, excluding 309.81), PTSD, and acute stress disorder (ICD-9-CM 308 and 309.81). Each patient with psychiatric disorders was required to have made at least 3 outpatient visits within the 1-year study period.

Statistical analysis

All statistical analyses were performed using the IBM Statistical Product and Service Solutions (SPSS) for Windows, V.22.0 (IBM). χ^2 test and t-test were used to evaluate the distributions of the categorical and continuous variables, respectively. The Fisher's exact test for the categorical variables was used to statistically examine the differences between the two cohorts. Cox regression model was used to determine the risk of psychiatric disorders, and the results were present as HR with a 95% CI. The difference in the risk of psychiatric disorders between the study and control groups was estimated using the Kaplan-Meier method with the log-rank test. A two-tailed p value <0.05 was considered to indicate the statistical significance.

RESULTS

Sample characteristics

Table 1 shows that there was a marginal difference of CCI scores between the OAB cohort and the control group (0.19±0.68 and 0.15±0.49; p=0.032). The difference between the two groups was not statistically significant in the distribution of sex, age, and monthly income between

Table 1 Characteristics of study at the baseline

OAB	With		Without		
Variables	**n**	**%**	**n**	**%**	**p Values**
Total	811	25.0	2433	75.0	
Gender					0.999
Male	371	45.7	1113	45.8	
Female	440	54.3	1320	54.3	
Age (y)	53.8±16.7		53.4±16.8		0.556
Age group (y)					0.999
20–29	82	10.1	246	10.1	
30–39	122	15.0	366	15.0	
40–49	157	19.4	471	19.4	
50–59	122	15.0	366	15.0	
60–69	167	20.6	501	20.6	
≧70	161	19.9	483	19.9	
Charlson Comorbidity Index (CCI)	0.2±0.7		0.2±0.5		0.032
Medication (d)					0.182
Without	291	35.9	796	32.7	
1–29	448	55.2	1386	57.0	
≧30	72	8.9	251	10.3	
Season					<0.001
Spring (March to May)	236	29.1	627	25.8	
Summer (June to August)	179	22.1	425	17.5	
Autumn (September to November)	192	23.7	617	25.4	
Winter (December to February)	204	25.1	764	31.4	
Location					<0.001
Northern Taiwan	437	53.9	1016	41.8	
Middle Taiwan	177	21.8	592	24.3	
Southern Taiwan	165	20.4	488	20.1	
Eastern Taiwan	29	3.6	324	13.3	
Outlet islands	3	0.4	13	0.5	
Urbanization level					<0.001
1 (highest)	444	54.8	725	29.8	
2	222	27.4	866	35.6	
3	55	6.8	294	12.1	
4 (lowest)	90	11.1	548	22.5	
Insured premium (NT$)					0.484
<18,000	794	97.9	2364	97.2	
18,000–34,999	13	1.6	56	2.3	
≧35,000	4	0.5	13	0.5	

p Value (category variable: X^2/Fisher's exact test; continuous variable: t-test).
OAB, overactive bladder.

these two groups. The OAB cohort inclined to search for medical help in the springs, live in the Northern Taiwan, and reside more in the places of urbanization level 1.

Kaplan-Meier model for the cumulative risk of psychiatric disorders

Of the total 3244 enrollees, 115 from the 811 (14.2%) in the OAB cohort, in comparison to 245 from the 2433 (10.1%). Kaplan-Meier survival analysis revealed the difference was statistically significant in the development of psychiatric disorders (log-rank, p<0.001, figure 1).

The risk of psychiatric disorders in OAB cohort

Table 2 shows that in the Cox regression model, the HR of the OAB cohort in the development of psychiatric disorders was 1.34 (adjusted HR, 95%CI 1.12 to 1.80, p<0.001), compared with the non- OAB cohort, after adjustment for sex, age, comorbidity (CCI scores), anticholinergic medications for OAB, seasons, residence/regions, and monthly incomes. Men were associated with a lower risk than women of developing psychiatric disorders. The groups with ages of 30 and older were associated with a lower risk than the younger group aged 20–29. Usage of medications for OAB was not associated with an increased risk of psychiatric disorders.

Subgroup analysis in the HR of psychiatric disorders in OAB cohort

Table 3 depicts that the OAB cohort was associated with an increased risk of psychiatric disorders, in comparison to the non-OAB cohort, regardless of sex, age, CCI scores, duration of OAB medications usage (1–29 days, ≧30

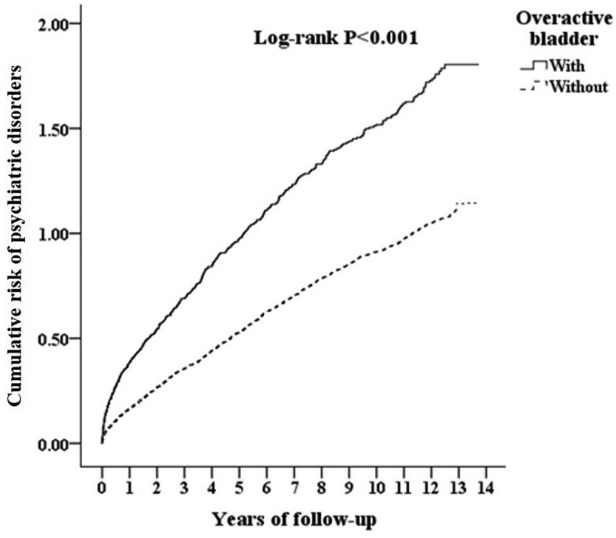

Figure 1 Cumulative risk of psychiatric disorders among aged 20 and over stratified by overactive bladder (OAB) with log-rank test.

days), and residence/regions, in the subgroup analysis. The patients with OAB with monthly insurance premiums of NT$<18,000 and NT$18,000–34,999 were in association with an increased risk of psychiatric disorders.

Risk of different psychiatric disorders in OAB cohort

Table 4 reveals that OAB was associated with an increased risk of dementia, anxiety disorder, depressive disorders, sleep disorders, and psychotic disorders, with the adjusted HRs as 1.53 (p=0.040), 1.61 (p<0.001), 2.10 (p<0.001), 1.43 (p<0.001), and 2.49 (p=0.002), respectively.

The comparison of psychiatric outpatient visits between the OAB and OAB cohorts

The average psychiatric outpatient visits in the OAB cohort and non-OAB cohort were 6.20 (SD ±6.91) and 5.63 (SD ±7.84) times in the period before the psychiatric diagnoses were made or the end of the study (table 5). The difference between the two groups was not statistically significant (p=0.065).

The sensitivity test for the risk of psychiatric disorders in Cox regression model

Table 6 shows that even after excluding the psychiatric diagnoses in the first 2 years after OAB diagnosis, an adjusted HR was 1.29 (95% CI 1.10 to 1.77, p=0.001).

DISCUSSION

Association between OAB and the risk of psychiatric disorders

The study showed that the adult patients with OAB had an increased risk of psychiatric disorders. Even after adjusting for covariates, the overall adjusted HR was 1.34 (adjusted HR, 95% CI 1.12 to 1.80, p<0.001). In other words, the adult patients with OAB had a 1.34-fold increased risk of developing psychiatric disorders. The Kaplan-Meier analysis revealed that the OAB cohort had a significantly higher cumulative risk of psychiatric disorders in comparison to the controls. The younger OAB subjects were at a higher risk of developing psychiatric disorders.

Comparison of this study to previous literatures

Several hospital or office-based studies have found that OAB was correlated with psychiatric disorders in female patients, including postpartum depression,[7] and obsessive-compulsive disorder.[31] One study showed that in 172 recently deployed female veterans, 375 (22%) have had

Table 2 Factors of psychiatric disorders by using Cox regression

	Crude HR	95% CI	95% CI	p Values	Adjusted HR	95% CI	95% CI	p Values
OAB								
Without	Reference				Reference			
With	1.48	1.14	1.85	<0.001	1.34	1.12	1.80	<0.001
Gender								
Male	0.88	0.77	0.94	0.001	0.83	0.77	0.90	<0.001
Female	Reference				Reference			
Age group (y)								
20–29	Reference				Reference			
30–39	0.47	0.39	0.59	<0.001	0.44	0.37	0.56	<0.001
40–49	0.58	0.44	0.79	<0.001	0.55	0.44	0.79	<0.001
50–59	0.58	0.46	0.67	<0.001	0.54	0.42	0.67	<0.001
60–69	0.73	0.59	0.90	<0.001	0.75	0.60	0.91	0.003
≧70	0.60	0.43	0.68	<0.001	0.58	0.44	0.68	<0.001
CCI	0.94	0.3	1.03	0.064	0.87	0.81	0.93	<0.001
Medication (d)								
Without	Reference				Reference			
1–29	0.93	0.71	1.04	0.093	0.96	0.87	1.05	0.211
≧30	0.99	0.83	1.11	0.277	1.08	0.93	1.25	0.344

Adjusted HR: adjusted variables listed in table 1.
CCI, Charlson Comorbidity Index; OAB, overactive bladder.

Table 3 Factors of psychiatric disorders stratified by variables listed in the table by using Cox regression

	With OAB versus without OAB (reference)							
Variables	**Crude HR**	**95% CI**	**95% CI**	**p Values**	**Adjusted HR**	**95% CI**	**95% CI**	**p Values**
Total	1.48	1.14	1.85	<0.001	1.34	1.12	1.80	<0.001
Gender								
Male	1.67	1.54	1.99	<0.001	1.65	1.52	1.99	<0.001
Female	1.53	1.35	1.79	<0.001	1.53	1.34	1.76	<0.001
Age group (y)								
20–29	2.48	1.66	3.19	<0.001	2.53	1.70	3.23	<0.001
30–39	1.76	1.24	2.31	<0.001	1.79	1.28	2.31	<0.001
40–49	1.72	1.46	2.13	<0.001	1.73	1.48	2.15	<0.001
50–59	1.71	1.31	2.20	<0.001	1.72	1.35	2.21	<0.001
60–69	1.39	1.13	1.79	<0.001	1.36	1.10	1.77	<0.001
≧70	1.23	1.10	1.67	0.001	1.21	1.02	1.57	<0.001
Medication (d)								
Without	1.43	1.32	1.68	<0.001	1.58	1.34	1.71	<0.001
1–29	1.50	1.43	1.70	<0.001	1.61	1.46	1.72	<0.001
≧30	1.50	1.10	2.10	0.001	1.60	1.13	2.15	<0.001
Season								
Spring	1.30	1.06	1.52	0.012	1.25	1.03	1.50	0.017
Summer	1.67	1.41	2.00	<0.001	1.78	1.43	2.09	<0.001
Autumn	1.86	1.68	2.30	<0.001	1.99	1.70	2.44	<0.001
Winter	1.59	1.38	2.01	<0.001	1.53	1.33	2.00	<0.001
Urbanization level								
1 (highest)	1.64	1.29	1.79	<0.001	1.65	1.32	1.84	<0.001
2	1.68	1.36	1.94	<0.001	1.70	1.45	2.04	<0.001
3	1.31	0.99	1.84	0.058	1.32	1.01	1.98	0.043
4 (lowest)	1.43	1.11	1.99	0.001	1.55	1.22	2.01	0.001
Insured premium (NT$)								
<18,000	2.47	1.54	3.40	<0.001	1.63	1.41	2.01	<0.001
18,000–34,999	3.12	1.00	10.47	0.049	4.41	1.73	13.45	0.007
≧35,000	6.55	0.72	19.64	0.277	7.30	0.89	21.99	0.189

Adjusted HR: adjusted variables listed in table 1.
OAB, overactive bladder.

OAB, and the incidence and adjusted OR of mental health outcomes included PTSD (19%; OR: 2.7), anxiety (21%; OR: 2.7), depression (10%; OR: 2.5) and prior sexual assault (27%; OR: 1.4).[9] For the studies about urine incontinence, one of the symptoms of OAB, 1 study found that there is a bidirectional influence between urine incontinence and depression or anxiety symptoms,[32] and another study found that women with depressive symptoms or a history of depression were more likely to report subsequent urine incontinence symptoms.[33] One previous study using the NHIRD found that the adjusted HR for depressive disorder in OAB women who received antimuscarinics was 1.38,

Table 4 Factors of subgroup of psychiatric disorders by using Cox regression

	With OAB	Without OAB	With OAB versus without OAB (reference)			
Psychiatric disorders	**Event**	**Event**	**Adjusted HR**	**95% CI**	**95% CI**	**p Values**
Total	115	245	1.34	1.12	1.80	<0.001
Dementia	7	15	1.53	1.01	1.96	0.040
Anxiety disorders	40	81	1.61	1.40	1.88	<0.001
Depressive disorders	11	14	2.10	1.50	3.06	<0.001
Bipolar disorders	1	1	0.68	0.17	3.00	0.574
Sleep disorders	59	123	1.43	1.20	1.75	<0.001
Psychotic disorders	2	3	2.49	1.10	4.89	0.002
Adjustment disorders	0	2	0	–	–	0.959
PTSD and acute stress disorder	1	4	0.94	0.40	2.45	0.930

Adjusted HR: adjusted for all variables listed in table 1.
OAB, overactive bladder; PTSD, post-traumatic stress disorder.

Table 5 Comparing psychiatric outpatient visits between with and without OAB

OAB	With	Without	p Values
Psychiatric outpatient visits	6.2±6.9	5.6±7.8	0.065

p: t-test.
OAB, overactive bladder.

when compared with those OAB women who did not receive antimuscarinics.[34] This is the first study on the topic whether OAB was associated with overall risk of psychiatric disorders, by using a nationwide, population-based data set, regardless of usage of antimuscarinics or not.

The prevalence of OAB in this study

In this claims data set, the prevalence within 2000 was only 0.048% (811 in 1,685,500 individuals), which was much lower than other studies.[3 4] There are several possible explanations. First, this indicates the difference between questionnaire-collected information in the community and the diagnosis by specialists, such as urologist or gynecologists, as aforementioned, in the claims data set. Second, help-seeking behaviors might play a role: one previous study found that only 6% and 7% of female patients with urinary incontinence, or OAB-wet, in 1991 and 2007, respectively, had sought help from the healthcare system, even in the USA.[35] Therefore, this claims data set treatment prevalence might represent patients who showed more need in seeking medical help in the population. We have compared the number of psychiatric outpatient visits between the OAB cohort and non-exposed group without OAB, to clarify whether the OAB cohort was being more likely to be evaluated and diagnosed with psychiatric services. Also there was no difference in psychiatric outpatient visits between these groups. Furthermore, even after excluding the psychiatric diagnoses in the first 2 years after OAB diagnosis, the OAB was associated with an increased risk of psychiatric disorders. However, we need more studies for the reason why the prevalence rate of OAB in the study is so low.

The impact of sex differences in the prevalence of OAB

In the OAB subjects, female subjects (54.3%) were slightly higher than male subjects (45.7%). This finding was compatible with the results of other studies, in that OAB was found to be a more frequent condition in women than in men. The subgroup analysis revealed that both female (adjusted HR=1.53, 95% CI 1.34 to 1.76, p<0.001) and male (adjusted HR=1.65, 95% CI 1.52 to 1.99, p<0.001) patients were associated with an increased risk of developing psychiatric disorders. This finding should, therefore, remind clinicians that both women and men could suffer from OAB, as well as the risk of subsequent psychiatric disorders.

Table 6 Sensitivity test and factors of psychiatric disorders by using Cox regression

	With OAB versus without OAB (reference)		
Sensitivity analysis	Adjusted HR	95% CI	p Values
Overall	1.34	1.12 to 1.80	<0.001
First 2 y psychiatric diagnoses excluded	1.29	1.10 to 1.77	0.001

Adjusted HR: adjusted variables listed in table 1.
OAB, overactive bladder.

Possible mechanisms for the increased risk of psychiatric disorders in patients with OAB

The underlying mechanisms of the association between OAB and psychiatric disorders remain unclear. One hypothesis mentioned that the central sensitization was an induced state of spinal hypersensitivity that was associated with a variety of chronic pain disorders that share many attributes with OAB.[36] Several animal studies have revealed that stress might contribute to symptom exacerbation in many disease states, including functional disorders, including OAB.[37–40] These facts hint that OAB and psychiatric disorder might share a common pathophysiology. For dementia, muscarinic receptors could play a role in both OAB and the cognitive function.[41] This might also provide an explanations that antimuscarinics for OAB were not associated with the decreased risk of psychiatric disorders, since these medications only act on the bladder, and not on the central nervous systems.

Limitations

This study has several limitations. First, we used the insurance claims to identify the data patients with OAB or psychiatric disorders; however, no data on the severity, functional impairment, and impact on their partners or family were available. Second, no records of body mass index, genetic, and environmental factors were included in the data set. Third, the claims data set was not able to include the descriptions of the predominance in urine urgency, urge incontinence, and nocturia. Fourth, the numbers were low in some subgroups of psychiatric disorders, such as bipolar disorder, adjustment disorder, acute stress disorder and PTSD, therefore this fact limits the possibility in generalization of the association between OAB in these disorders.

CONCLUSION

This study has shown evidence to support that the OAB cohort has an increased risk of developing psychiatric disorders. Other large or national data sets should be completed to confirm this finding and to explore the underlying mechanisms. This finding should, indeed, remind clinicians that both women and men could suffer from OAB, as well as the risk of subsequent psychiatric disorders.

Author affiliations
[1]Department of Psychiatry, School of Medicine, Tri-Service General Hospital, National Defense Medical Center, Taipei, Republic of China
[2]Student Counseling Center, National Defense Medical Center, Taipei, Republic of China
[3]Department of Medical Research, Tri-Service General Hospital, National Defense Medical Center, Taipei, Republic of China
[4]School of Public Health, National Defense Medical Center, Taipei, Republic of China
[5]Taiwanese Injury Prevention and Safety Promotion Association, Taipei, Republic of China
[6]Department of Psychiatry, Tri-Service General Hospital, Song-Shan Branch, National Defense Medical Center, Taipei, Republic of China
[7]Institute of Bioinformatics and System Biology, National Chiao Tung University, Hsinchu, Republic of China
[8]Department of Nursing, School of Nursing, Tri-Service General Hospital, National Defense Medical Center, Taipei, Republic of China

[9]Department of Nursing, Kang-Ning University (Taipei Campus), Taipei, Republic of China
[10]Department of Psychiatry, College of Medicine and Hospital, National Cheng-Kung University, Tainan, Republic of China
[11]Institute of Life Sciences, National Defense Medical Center, Taipei, Republic of China

Acknowledgements The authors thank Professors Chang-Huei Tsao, Yung-Fu Wu and Fu-Huang Lin for their help in the administrative work and academic guidance in supporting the completion in this study.

Contributors NST and WCC conceived the study, participated in its design and coordination, data interpretation, performed the statistical analysis and drafted the manuscript. WCC, CHC, HWY, HAC, RBL and YCK participated in the design of the study and data interpretation. CBY, SYH and WSC participated in the statistical analysis and data interpretation. NST wrote the paper. All authors have read and approved the final manuscript as submitted.

Funding This work was supported by Tri-Service General Hospital Research Foundation (grant numbers TSGH-C105-130, TSGH-C106-106, TSGH-C107-106, TSGH-C107-004).

Competing interests None declared.

Patient consent Not required.

Ethics approval This study was conducted in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki). The Institutional Review Board of the Tri-Service General Hospital approved this study and waived the need of individual consents since all the identification data were encrypted in the NHIRD (IRB number 1-104-05-145 and 1-106-05-055).

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

1 Abrams P, Wein AJ. The overactive bladder and incontinence: definitions and a plea for discussion. *Neurourol Urodyn* 1999;18:413–6.
2 Abrams P, Cardozo L, Fall M, *et al*. The standardisation of terminology in lower urinary tract function: report from the standardisation sub-committee of the International Continence Society. *Urology* 2003;61:37–49.
3 Stewart WF, Van Rooyen JB, Cundiff GW, *et al*. Prevalence and burden of overactive bladder in the United States. *World J Urol* 2003;20:327–36.
4 Yu HJ, Liu CY, Lee KL, *et al*. Overactive bladder syndrome among community-dwelling adults in Taiwan: prevalence, correlates, perception, and treatment seeking. *Urol Int* 2006;77:327–33.
5 Abrams P, Kelleher CJ, Kerr LA, *et al*. Overactive bladder significantly affects quality of life. *Am J Manag Care* 2000;6:S580–90.
6 Tubaro A. Defining overactive bladder: epidemiology and burden of disease. *Urology* 2004;64:2–6.
7 Hullfish KL, Fenner DE, Sorser SA, *et al*. Postpartum depression, urge urinary incontinence, and overactive bladder syndrome: is there an association? *Int Urogynecol J Pelvic Floor Dysfunct* 2007;18:1121–6.
8 Lowenstein L, Kenton K, Brubaker L, *et al*. The relationship between obstructive sleep apnea, nocturia, and daytime overactive bladder syndrome in women. *Am J Obstet Gynecol* 2008;198:598.e1–e5.
9 Bradley CS, Nygaard IE, Torner JC, *et al*. Overactive bladder and mental health symptoms in recently deployed female veterans. *J Urol* 2014;191:1327–32.
10 Ho Chan WS. Taiwan's healthcare report 2010. *Epma J* 2010;1:563–85.
11 Cheng CL, Kao YH, Lin SJ, *et al*. Validation of the National health insurance research database with ischemic stroke cases in Taiwan. *Pharmacoepidemiol Drug Saf* 2011;20:236–42.
12 Liang JA, Sun LM, Muo CH, *et al*. The analysis of depression and subsequent cancer risk in Taiwan. *Cancer Epidemiol Biomarkers Prev* 2011;20:473–5.
13 Chou IC, Lin HC, Lin CC, *et al*. Tourette syndrome and risk of depression: a population-based cohort study in Taiwan. *J Dev Behav Pediatr* 2013;34:181–5.
14 Chinese Hospital Association. *ICD-9-CM English-Chinese Dictionary*. Taipei, Taiwan: Chinese Hospital Association Press, 2000.
15 Ministry of Justice, 2014. National health Insurance reimbursement regulations [web site] http://law.moj.gov.tw/LawClass/LawAllIf.aspx?PCode=L0060006 (accessed 12 Apr 2018).
16 Wein A. Symptom-based diagnosis of overactive bladder: an overview. *Can Urol Assoc J* 2011;5:S135–6.
17 Tzeng NS, Chung CH, Lin FH, *et al*. Anti-herpetic medications and reduced risk of dementia in patients with herpes simplex virus infections-a nationwide, population-based cohort study in Taiwan. *Neurotherapeutics* 2018;15:417–29.
18 Tzeng NS, Chung CH, Lin FH, *et al*. Risk of dementia in adults with ADHD: a nationwide, population-based cohort Study in Taiwan. *J Atten Disord* 2017:108705471771405.
19 Tzeng NS, Chung CH, Liu FC, *et al*. Fibromyalgia and risk of dementia-a nationwide, population-based, cohort study. *Am J Med Sci* 2018;355:153–61.
20 Cheng CL, Li JR, Lin CH, *et al*. Positive association of female overactive bladder symptoms and estrogen deprivation: a nationwide population-based cohort study in Taiwan. *Medicine* 2016;95:e4107.
21 Kao LT, Huang CY, Lin HC, *et al*. No increased risk of fracture in patients receiving antimuscarinics for overactive bladder syndrome: a retrospective cohort study. *J Clin Pharmacol* 2018;58:727–32.
22 Chung SD, Weng SS, Huang CY, *et al*. Antimuscarinic use in females with overactive bladder syndrome increases the risk of depressive disorder: a 3-year follow-up study. *J Clin Pharmacol* 2017;57:1064–70.
23 Wu MP, Hsu YW, Weng SF, *et al*. Healthcare-seeking prevalence of lower urinary tract symptoms among national health insurance enrollees in Taiwan, 2000-2009. *Urology* 2013;81:61–5.
24 Lin FY, Yang YC, Lin CL, *et al*. Increased risk of overactive bladder in patients with idiopathic Parkinson's disease: Insight from a nationwide population-based cohort study. *PLoS One* 2018;13:e0193783.
25 Chen HM, Lin CC, Kang CS, *et al*. Bladder pain syndrome/interstitial cystitis increase the risk of coronary heart disease. *Neurourol Urodyn* 2014;33:511–5.
26 Wu MP, Weng SF, Hsu YW, *et al*. Medical attendance for lower urinary tract symptoms is associated with subsequent increased risk of outpatient visits and hospitalizations based on a nationwide population-based database. *PLoS One* 2013;8:e57825.
27 Charlson ME, Pompei P, Ales KL, *et al*. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987;40:373–83.
28 Charlson ME, Charlson RE, Peterson JC, *et al*. The Charlson comorbidity index is adapted to predict costs of chronic disease in primary care patients. *J Clin Epidemiol* 2008;61:1234–40.
29 Chang CY, Chen WL, Liou YF, *et al*. Increased risk of major depression in the three years following a femoral neck fracture--a national population-based follow-up study. *PLoS One* 2014;9:e89867.
30 Yoo S, Oh S, Kim HS, *et al*. Impact of serum 25-OH vitamin D level on lower urinary tract symptoms in men: a step towards reducing overactive bladder. *BJU Int* 2018.
31 Ahn KS, Hong HP, Kweon HJ, *et al*. Correlation between overactive bladder syndrome and obsessive compulsive disorder in women. *Korean J Fam Med* 2016;37:25–30.
32 Felde G, Ebbesen MH, Hunskaar S. Anxiety and depression associated with urinary incontinence. A 10-year follow-up study from the Norwegian HUNT study (EPINCONT). *Neurourol Urodyn* 2017;36:322–8.
33 Mishra GD, Barker MS, Herber-Gast GC, *et al*. Depression and the incidence of urinary incontinence symptoms among young women: Results from a prospective cohort study. *Maturitas* 2015;81:456–61.
34 Chao PC, Chien WC, Chung CH, *et al*. Cognitive enhancers associated with decreased risk of injury in patients with dementia: a nationwide cohort study in Taiwan. *J Investig Med* 2018;66:684–92.
35 Wennberg AL, Molander U, Fall M, *et al*. Lower urinary tract symptoms: lack of change in prevalence and help-seeking behaviour in two population-based surveys of women in 1991 and 2007. *BJU Int* 2009;104:954–9.
36 Reynolds WS, Dmochowski R, Wein A, *et al*. Does central sensitization help explain idiopathic overactive bladder? *Nat Rev Urol* 2016;13:481–91.
37 Andersson KE. Mechanisms of Disease: central nervous system involvement in overactive bladder syndrome. *Nat Clin Pract Urol* 2004;1:103–8.
38 Klausner AP, Steers WD. Corticotropin releasing factor: a mediator of emotional influences on bladder function. *J Urol* 2004;172:2570–3.
39 Bazi T, Hajj-Hussein IA, Awwad J, *et al*. A modulating effect of epigallocatechin gallate (EGCG), a tea catechin, on the bladder of rats exposed to water avoidance stress. *Neurourol Urodyn* 2013;32:287–92.
40 Merrill L, Malley S, Vizzard MA. Repeated variate stress in male rats induces increased voiding frequency, somatic sensitivity, and urinary bladder nerve growth factor expression. *Am J Physiol Regul Integr Comp Physiol* 2013;305:R147–56.
41 Yokoyama O, Komatsu K, Ishiura Y, *et al*. Overactive bladder--experimental aspects. *Scand J Urol Nephrol Suppl* 2002:59–64.