



## Incidence of Ambulatory Care Visits and Association with Comorbidities of Overactive Bladder in Taiwan

Hsin-Li Liu<sup>1</sup>, Kai-Yu Tseng<sup>1</sup>, Shu-Ching Chiu<sup>1</sup>, Horng-Mo Lee<sup>2</sup>, Yueh-Chin Chung<sup>1,\*</sup>

<sup>1</sup>Department of Nursing, Central Taiwan University of Science and Technology, Taichung, Taiwan

<sup>2</sup>School of Medical Laboratory Sciences and Biotechnology, Taipei Medical University, Taipei, Taiwan

**\*Corresponding Author:** Yueh-Chin Chung, Ph.D. Department of Nursing, Central Taiwan University of Science and Technology, Taichung, Taiwan, No.666, Buzih Road, Beitun District, Taichung City 40601, Taiwan. **Email:** ycchung@ctust.edu.tw

### Abstract

**Objectives:** The present study is designed to explore the incidence of ambulatory care visits and association with comorbidities of overactive bladder (OAB) in Taiwan.

**Methods:** Data from the National Health Insurance Research Database (NHIRD) 2005 containing all of the original claim data of 1,000,000 beneficiaries enrolled in 2005 were randomly sampled from the 2005 Registry for Beneficiaries (ID) of the NHIRD and then statistically analyzed in terms of percentage, incidence of ambulatory care visits, odds ratio (OR), and 95% confidence intervals.

**Results:** The subjects enrolled in this study included females (62.93%) mostly aged 51 to 60 years (19.97%) and males (19.68%) aged 71 to 80 years. The ratio of females to males was 0.8–2.51:1.0. Overall, the annual incidence of ambulatory care visits increased from 2.1% in 2006 to 2.9% in 2009. The annual incidence of ambulatory care visits of females and males reached the maximum of 3.5% and 2.3% in 2009. In females, comorbidities, such as frequent urination, urinary incontinence (UI), and urinary calculi, and menopause ( $OR > 1$ ;  $P < 0.05$ ). In males, frequent urination, nocturnal enuresis, UI, benign prostatic hypertrophy and anxiety state ( $OR > 1$ ;  $P < 0.05$ ) were associated with OAB.

**Conclusions:** The incidence of ambulatory care visits of patients with OAB in Taiwan was low. OAB may significantly affect the quality of life. Thus, the medical attention and effective treatment for patients with OAB should be enhanced.

**Abbreviations:** OAB: overactive bladder, UI: urinary incontinence, UUI: urge urinary incontinence, SUI: stress urinary incontinence, LUTS: lower urinary tract symptoms, ICD: international classification of diseases, NHIRD: National Health Insurance Research Database, OR: odds ratio.

**Keywords:** overactive bladder; incidence; ambulatory care visits; comorbidities; National Health Insurance Research Database.

### 1. INTRODUCTION

Overactive bladder (OAB), a common but easily neglected condition accompanied with bladder hypersensitivity or contraction abnormalities and often resulting in urgent urination, frequent urination, nocturnal enuresis, or urinary incontinence (UI), causes embarrassment and may interfere with normal life[1]. Wein and Rovner emphasized that OAB covers a very wide range, including urge urinary incontinence (UUI), a portion of mixed UI, a portion of stress urinary incontinence (SUI)[2], and a sense of urgency in urine, which is the main symptom of OAB[3].

The prevalence of OAB also increases with age, that is, 12% to 22% of affected individuals are over 40 years old and 30% to 40% of such individuals are over 75 years old; one-third of these patients present signs of UI[4]. Stewart, Herzog, and We in reported that 21 million people in the United States experience urinary frequency and urinary urgency but not UI, and 3.3 billion patients manifest OAB[5]. The attack rate of OAB may increase with age, and 60% showed symptoms, but only 27% received treatment. The prevalence of OAB may also increase with age and may affect 5.9% to 16% of males and 6.0% to 16.9% of females [6].

Moorthy, Lapitan, Quek, and Lim surveyed 2,369 male patients with a mean age of 18 to 70 years in 11 Asian countries in 1998 and found that 709 patients (29.9%) suffered from OAB, and 43.0% of these patients were at the working age; the incidence of OAB increased with age, and the age group of over 70 years accounted for 53.0%[7]. Abrams et al. indicated that females present a higher risks of OAB than males [8].

About 10% to 18% of the Taiwanese population showed varying degrees of OAB, and the prevalence rate increases with age. Among 23 million Taiwanese, approximately 4.14 million people are at a serious risk of OAB, but only 13% of these individuals have sought medical attention [9]. The prevalence of OAB among females aged over 20 years in Taiwan is 36.0%[10]. Irwin et al. estimated that 0.303 billion females aged more than 20 years will experience UI, 0.255 billion females will suffer from stress incontinence, 53 million females will complain of mixed incontinence, and 33 million of females will manifest UI by 2018; approximately 0.298 billion individuals will suffer from OAB[11]. The prevalence of UI among females is greater than that among males, and their medians correspond to 27.6-58.4% and 10.5%[12,13].

The risk factors of OAB in females include urinary tract infection, SUI, interstitial cystitis, menopause, polyuria, diabetes, heart failure, medication, and aging ( $P<0.05$ )[14,15]. The risk factors of OAB for males are aging, constipation, and prostate enlargement ( $P<0.05$ )[16,17]. Surgical treatments, cystic calculus, obesity, and neurological abnormalities, such as stroke, Parkinson's disease, anxiety, and lower urinary tract symptoms (LUTS), are also factors contributing to OAB[18]. The prevalence of LUTS is 41%, which increases with age; for the age groups of 18 to 49, 50 to 64, and  $\geq 65$  years, the prevalence rates correspond to 14.1%, 41.5%, and 60.8%[19], and SUI accounts for about 50%[20,21].

With regard to the effects of OAB on living quality, the survey results in the 11 Asian countries showed that 53% of Asian women have developed symptoms of OAB, but only 21% of these women have sought medical attention. The 2014 survey in Taiwan also revealed that 35% of Taiwanese women were

aware of their OAB symptoms. OAB symptoms often negatively affect the social life, work, mood, family life, and sex life of patients and thus seriously affect their quality of life [18, 19, 22-30].

With the effects of OAB symptoms on their careers, the daily work of 24.9% of male patients is affected and job decisions for 10% of male patients are underdetermined and thus prompt them to change jobs or become dismissed; early retirement is documented in 7.8% of male patients; female patients also experience similar cases [6,28].

OAB affecting the quality of life in the healthcare system has been extensively investigated. Therefore, this study examined the annual incidence of ambulatory care visits, gender ratio, and comorbidity of OAB by using the relevant data from the National Health Insurance Research Database of Taiwan from 2003 to 2010 and by providing research data regarding the current condition of OAB in Taiwan and other factors to predict its future condition.

## **2. MATERIALS AND METHODS**

### **2.1. Data Collection**

This paper presents a longitudinal study with data sourced from the relevant outpatient and medical insurance files of LHID 2005. The LHID 2005 contains all the original claim data of 1,000,000 beneficiaries enrolled in 2005 and randomly sampled from the 2005 Registry for Beneficiaries (ID) of the National Health Insurance Research Database (NHIRD), which was released once every 40,000 beneficiaries were sampled and then updated once a year. In this study, the column (ACODE\_ICD9\_1) of the international classification of diseases(ICD) in the outpatient files (CD) of the National Health Insurance Research Database is cited, with the first three codes in front of the ICD representing the current diagnosis of a subject investigated, thereby obtaining the primary diagnostic distribution and dividing the diagnosis districts into 18 groups.

The present study included 503 males and 854 females, comprising a total of 1,357 subjects. The patients enrolled were diagnosed of OAB from 2003 to 2010 (ICD-9-CM: 596.51 patients). The diagnostic codes of comorbidities are as follows: diabetes mellitus (250), multiple sclerosis (MS) (340), secondary parkinsonism (332.1), renal calculus (592), ureteral calculus

(592.1), acute cystitis (595), frequent urination (788.41), nocturnal enuresis (788.43), UI (788.31), other urination abnormalities (788.69), benign prostatic hypertrophy (BPH) (600), menopause (627.2, 627.8, 627.9), and anxiety state (300.00, 300.02, 300.09). This study was approved by the NHRI Review Committee and by the Institutional Review Board of the China Medical University Hospital, Taichung, Taiwan (CMUH103-REC1-088).

**2.2. Statistical Analysis**

SPSS17.0 statistical software was used for data reduction and subsequent analysis. The age/sex distribution of 2003 to 2010 OAB patients was analyzed in terms of percentage. The annual consultation rate was calculated on the basis of gender to provide data of the current situation of OAB in Taiwan. The presence of OAB comorbidity in different genders is quantified by odds ratio (OR). Accordingly, 95% confidence interval was used for correlation and significance. The significance level ( $\alpha$ ) was set to 0.05.

**3. RESULTS**

In this study, 503 males and 854 females, comprising a total of 1,357 cases, were enrolled. After the age/ gender grouping, 918 cases were found to present hereditary OAB, and the control group was composed of 1,827 subjects. The subjects enrolled were mostly at the age of 51 to 60 years old (19.97%). Among these subjects, females accounted for 62.93%, and most of them are at the age of 51 to 60 years old (20.96%); majority of males are at the age of 71 to 80 years old (19.68%). The gender ratio of females to males was 0.8–2.51:1.0, and this ratio varies with age. Differences were found between the genders, particularly in the age groups of 21 to 30, 31 to 40, 41 to 50, 51 to 60, and 61 to 70 years old ( $P < 0.0001$ ) (Table 1).

As shown in Table 2, the overall annual incidence of ambulatory care visits increased from 2.1% in 2006 to 2.9% in 2009; the annual incidence of ambulatory care visits of females reached the maximum by up to 3.5% at most in 2009, whereas that of males reached the peak at 2.3% in 2009; differences were found in terms of gender in the annual incidence of ambulatory care visits in 2004, 2005, 2008, 2009 and 2010 ( $P < 0.0001$ ).

**Table1.** Average sex-specific percentage of overactive bladder, 2003–2010

Age	Overactive bladder			Female/male ratio	OR (95% CI)	P value
	Female	Male	Total			
<10	4 (0.47)	5 (0.99)	9 (0.66)	0.8:1	0.79 (0.21 to 3.04)	0.7335
11-20	16 (1.87)	14 (2.78)	30 (2.21)	1.14:1	1.17 (0.54 to 2.55)	0.6922
21-30	96 (11.24)	48 (5.42)	144 (10.61)	2:1	26.00 (8.88 to 76.13)	<0.0001
31-40	90 (10.54)	59 (11.73)	149 (10.98)	1.53:1	6.25 (2.91 to 13.44)	<0.0001
41-50	171 (20.02)	68 (13.52)	239 (17.61)	2.51:1	2.83 (2.10 to 3.80)	<0.0001
51-60	179 (20.96)	92 (18.29)	271 (19.97)	1.95:1	2.151 (1.65 to 2.81)	<0.0001
61-70	141 (16.51)	78 (15.51)	219 (16.14)	1.81:1	1.94 (1.45 to 2.60)	<0.0001
71-80	118 (13.82)	99 (19.68)	217 (15.99)	1.19:1	1.23 (0.92 to 1.62)	0.1724
81-90	41 (4.80)	38 (7.55)	79 (5.82)	1.08:1	1.13 (0.65 to 1.99)	0.6644
Total	854 (62.93)	503 (37.07)	1357 (100.00)	1.70:1	5.78 (4.67 to 7.17)	<0.0001

OR = odds ratio, CI = confidence interval

**Table2.** Annual incidence<sup>1</sup> of overactive bladder, 2003–2010

Year	Female	Male	Total	Female/male ratio	OR (95% CI)	P value
2003	14 (0.3)	3 (0.1)	17 (0.2)	4.67:1	5.27 (1.46 to 18.94)	0.0110
2004	54 (1.2)	16 (0.3)	70 (0.7)	3.37:1	6.16 (3.18 to 11.97)	<0.0001
2005	91 (2.0)	46 (1.0)	137 (1.5)	1.98:1	11.87 (5.39 to 26.15)	<0.0001
2006	99 (2.2)	96 (2.0)	195 (2.1)	1.03:1	4.13 (0.45 to 37.57)	0.2087
2007	131 (2.8)	79 (1.7)	210 (2.2)	1.66:1	1.76 (1.31 to 2.36)	0.0002
2008	146 (3.2)	72 (1.5)	218 (2.3)	2.03:1	2.20 (1.64 to 2.97)	<0.0001
2009	163 (3.5)	107 (2.3)	270 (2.9)	1.52:1	1.81 (1.40 to 2.35)	<0.0001
2010	156 (3.4)	84 (1.8)	240 (2.6)	1.86:1	2.02 (1.52 to 2.67)	<0.0001
Total	854 (2.3)	503 (1.3)	1357 (1.8)	1.70:1	5.78 (4.66 to 7.17)	<0.0001

OR = odds ratio, CI = confidence interval.

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Annual incidence (per 100 people/year) is the number of new cases of overactive bladder in patients divided by the size of the population at risk each year.

**Table 3.** Comparison of overactive-bladder-related comorbidities in males versus females

Disease	ICD-9 code	Female		OR (95% CI)	P value	Male		OR (95% CI)	P value
		Control group	Comparison group			Control group	Comparison group		
		N	N			N	N		
Type 2 diabetes mellitus	250	24	254	0.07(0.05 to 0.11)	<0.0001	15	274	0.04 (0.02 to 0.07)	<0.0001
Multiple sclerosis	340	1	8	0.12(0.01 to 0.95)	0.0443	0	9	0.05 (0.03 to 0.84)	0.0372
Secondary parkinsonism	332.1	2	12	0.15(0.03 to 0.69)	0.0146	0	11	0.04 (0.00 to 0.67)	0.0251
Calculus of kidney	592	33	19	2.10 (1.10 to 4.02)	0.0060	19	203	0.74 (0.59 to 0.93)	0.0108
Calculus of ureter	592.1	11	8	0.65 (0.28 to 1.48)	0.3033	6	55	0.05 (0.03 to 0.13)	<0.0001
Acute cystitis	595	135	95	1.49 (1.13 to 1.96)	0.0053	7	99	0.00 (0.00 to 0.01)	<0.0001
Urinary frequency	788.41	122	92	1.37 (1.03 to 1.83)	0.0305	51	26	2.96 (1.63 to 5.37)	0.0003
Nocturia	788.43	23	13	1.99 (0.95 to 4.22)	0.0688	20	6	3.92 (1.50 to 10.23)	0.0053
Urge incontinence	788.31	50	25	3.00(1.65 to 5.46)	0.0003	41	4	1.53 (1.19 to 1.98)	0.0001
Hesitancy of micturition	788.69	0	2	0.19 (0.01 to 4.14)	0.2949	0	1	0.33 (0.01 to 8.19)	0.4988
Hypertrophy (benign) of prostate	600			-	-	234	1	612.19(38.12 to 9832.32)	<0.0001
Menopausal or female climacteric states	627.2, 627.8, 627.9	48	10	8.31 (3.87 to 17.80)	<0.0001			-	-
Anxiety state, unspecified	30000, 30002, 30009	29	399	0.05 (0.03 to 0.07)	<0.0001	15	1	17.47 (2.26 to 135.02)	0.0061
		501	937			417	890		

OR = odds ratio, CI = confidence interval; Ninth revision of the ICD-9-CM (The International Classification of Diseases, Clinical Modification) was used to code and classify morbidity data from outpatient records.

Overactive bladder of Female Denominator (Number of occurrences):501; Male Denominator (Number of occurrences): 417

Non: Overactive bladder of Female Denominator (Number of occurrences): 937; Male Denominator (Number of occurrences): 890



After the age/sex grouping, 918 hereditary OAB cases and 1,827 non-hereditary OAB cases were included for analysis. In terms of the comorbidity of OAB, the OAB-related comorbidities among females included renal calculus, acute cystitis, frequent urination, UI, and menopause ( $OR > 1$ ;  $P < 0.05$ ), whereas those among males involved frequent urination, nocturnal enuresis, UI, BPH, and anxiety state ( $OR > 1$ ;  $P < 0.006$ ). Up to 48 females with hereditary OAB showed menopausal symptoms, and 10 females with non-hereditary OAB presented menopausal symptoms. The risks for females with hereditary OAB complications and menopausal symptoms were 8.31 times as those of the normal group (95% CI 3.87-17.80); 50 females with hereditary OAB showed UI symptoms, whereas 25 cases with non-hereditary OAB presented such symptoms. The risks for females with hereditary OAB complications and UI were thrice as those of the normal group (95% CI 1.65-5.46); 33 females with hereditary OAB exhibited renal calculus, and 19 females with non-hereditary OAB displayed renal calculus. The risks for females with hereditary OAB complications and renal calculus were 2.10 times as those of the normal control group (95% CI 1.10 -4.02). Up to 234 males with hereditary OAB presented BPH symptoms, whereas only one male with non-hereditary OAB demonstrated such symptoms. The risks for males with hereditary OAB complications and BPH symptoms were 612.19 times as those of the normal control group (95% CI 38.12-9832.32); 15 males with hereditary OAB were in anxiety state, whereas only one male with non-hereditary OAB was in the same state. The risks for males with hereditary OAB complications and remaining in anxiety state were 17.47 times as those of the normal group (95% CI 2.27-135.02). Twenty males with hereditary OAB presented nocturnal enuresis symptoms, and only six males with non-hereditary OAB showed such symptoms. The risks for males with hereditary OAB complications and nocturnal enuresis symptoms were 3.92 times as those of the normal control group (95% CI 1.50-10.23) (Table 3).

#### 4. DISCUSSION

The present study is the first to explore the consultation rate of OAB in Taiwan on the basis of massive nationwide data. This study, which is characterized by large sample size and massive medical data, is relatively objective, and this study covers the deficiencies of previous studies in terms of various factors, including follow-up, response rate, or recall bias.

The subjects investigated were mainly at the age of 51 to 60 years old (19.97%). Females with OAB were mostly at the age of 51 to 60 years old (20.96%), whereas males with such diseases were at the age of 71 to 80 years old (19.68%). These findings indicate that the incidence of OAB may increase with age [13].

The results showed that more females suffer from OAB; in terms of OAB incidence, the ratio of females to males is 0.8–2.51:1.0; at the age of 21 to 70 years old, females are in the majority with greater risks for developing OAB than males[8]. Overall, the annual incidence of ambulatory care visits among all the subjects increased from 2.1% to 2.9% in 2006; the annual incidence of ambulatory care visits of females was 3.5% at most, whereas that of males was 2.3%; differences were found between genders in the annual incidence of ambulatory care visits in 2004, 2005, and 2008 up to 2010 ( $p < 0.0001$ ); the average incidence of ambulatory care visits of females was 2.3%, which was higher than that of males (1.3%). About 10% to 18% of the Taiwanese population suffer from OAB; in particular, the prevalence of OAB among females over 20 years old was up to 36.0%[10], but only 13% of them have ever sought for medical attention[6]. As relevant survey results showed, compared with other countries, 60% of the European population suffer from OAB symptoms, and only 27% of them have received treatment[5]. The incidence of OAB among females in Switzerland was 20%, and the cure rate was 42%[11]. The results showed that the incidence of ambulatory care visits of OAB in Taiwan was low on the basis of the sampling results of the NHIRD because (1) the Orientals are more conservative, and they often think that urinary tract disease is a disease to be ashamed of; thus, they are unwilling to seek medical attention; and (2) many people consider that urinary incontinence is a sign of normal aging, without the need of seeing a

doctor, thus delaying the optimal time for treatment and seriously affecting the quality of life[29]. The prevalence of LUTS was 41%, which may increase with age[19], and SUI approximately accounted for 50% of this prevalence[20,21].

OAB comorbidities among females include frequent urination. Milson et al. (2001) reported that the attack rate of OAB is 16.6%, and 85% of OAB patients develop frequent urination; the attack rate increases with age, in which 60% presented symptoms, but only 27% received treatment. The risks for females with hereditary OAB complications developing UI are 3.00 times as the normal control group, and the prevalence of UI among females varies significantly from 4.8% to 58.4%. The prevalence of UI roughly increases with age, and the most common symptom of UI is SUI, approximately accounting for 50% [2, 13]. The study on Swedish females from 1991 to 2007, the incidence of UI was 21%, and the cure rate was 34%; although the cure rate was not low, 66% of the females have suffered from UI in the 16 years. The risks for females with hereditary OAB developing menopause and those for females with OAB complications suffering from menopausal symptoms were generally 8.31 times as those of the normal control group because post-menopausal females easily leak urine as a result of reduced secretion of female hormones and urethral mucosal atrophy [15].

The risks for males with OAB hereditary complications developing nocturnal enuresis symptoms were generally 3.92 times as those of the normal control group. In epidemiological studies on LUTS, such as those on UI, about 41% to 62% of males suffered from LUTS, the incidence among adults over 60 years old increased up to 60.8% to 81%[19,29], and SUI approximately accounted for 50%[20]. LUTS such as frequent urination, nocturnal enuresis, urgent urination, UI, difficulty in urination, intermittent urination, and acute urinary retention are all typical benign BPH symptoms. The risks for males with hereditary OAB complications and BPH symptoms are generally 612.18 times as those of the normal control group. LUTS and BPH symptoms are also important contributory factors to OAB, negatively affecting sleep quality and mental health[18,19,27,30]. The risks for males with hereditary OAB complications and remaining in an anxiety state were generally 17.47 times as those of the normal control group. Milsom[6,18]

found in his studies on the effects of OAB on patients' personal development in marketplace that 2% or 3% of OAB patients are in anxiety state, and they often worry about accidents sometimes happening in the rush.

However, certain limitations affect this study. For example, additional physiological data are impossible to access as evidence from NHIRD. As such, only ICD9-CM can be used to distinguish diseases. If patients are unaware that such symptoms are curable or they fail to seek medical treatment, they are slipping through the present study. In addition, the coverage of NHIRD is very limited in terms of education, lifestyle, or social support. Therefore, data collection in the form of questionnaire or qualitative survey is recommended in the future to completely control the effects of other factors.

In Conclusion, a systemic review on the relevant literature worldwide indicated that OAB may significantly affect work and life quality and increase healthcare spending, and the healthcare spending on OAB patients may increase with age. The statistics of the consultation rate in the present study are relatively low. The literature verified that the prevalence of OAB is far above the actual consultation rate. Thus, the consultation and effective curative rates should be improved.

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