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Overactive Bladder Syndrome is Associated With Detrusor Overactivity and Abnormal Voiding Pattern in Nulliparous Women

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Research Article

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Abstract

Pregnancy and childbirth are frequently associated with overactive bladder syndrome (OAB). However, the role of parous effects in OAB among nulliparous (NP) women remains controversial. This study investigated abnormal voiding patterns and DO among NP woman with OAB in comparison with parous women. From August 2011 to December 2018, 906 patients met the inclusion criteria for participation and were divided into three groups: 221 patients in the NP group, 571 patients in the normal spontaneous delivery (NSD) group, and 114 patients in the cesarean section (CS) group. Urodynamic study (UDS) examinations were performed, and the presence of DO, abnormal voiding patterns, and maximum urethral closure pressure (MUCP) were recorded. Data were analyzed using analysis of variance, $\chi 2$ tests, and independent t tests. Compared with parous women in the NSD and CS groups, patients in the NP group had a significantly higher prevalence of abnormal voiding patterns, DO and MUCP. Furthermore, abnormal voiding patterns were significantly associated with DO and MUCP respectively, especially in the NP group. We hypothesized that hypertonicity or poor relaxation of the pelvic muscle in NP women may cause functional BOO, which is related to their OAB.

Introduction

Pregnancy and childbirth are frequently associated with lower urinary tract symptoms (LUTS), for example, increased urinary frequency and urgency, stress urinary incontinence, urgency urinary incontinence (UUI), and voiding difficulty[1,2]. However, numerous nulliparous (NP) women may also present with overactive bladder syndrome (OAB). OAB is a common and chronic syndrome that is defined as urinary urgency or UUI and is usually accompanied by increased frequency and nocturia in the absence of urinary tract infection or some other obvious pathology[3]. The relationship among OAB, childbirth, and the delivery mode remains controversial[1,4].

Despite numerous studies, the mechanism of OAB is not yet fully understood. It is generally considered that detrusor overactivity (DO) plays a role in OAB, but not all OAB patients are diagnosed with DO after urodynamic study (UDS)[5,6]. In addition to DO, bladder outlet obstruction (BOO) may play a role in the development of OAB, because OAB and voiding dysfunction (VD) can coexist[7,8]. VD, which is defined as abnormally slow and/or incomplete micturition, can be classified as BOO (mechanical and functional) and detrusor underactivity (DU)[9,10]. In a comprehensive review, Fusco et al. reported that DO during the filling phase is the compensation phase of BOO-induced bladder remodeling[11]. During the voiding phase, BOO can increase detrusor contractility, which manifests as DO in UDS[11]. Although micturition disorders are frequently classified as storage phase (due to bladder overactivity or sphincteric weakness) and voiding phase (because of failure of the bladder to empty adequately)[12], the symptoms of these two phases may co-exist[13], and the symptoms may not reflect the underlying etiology.

This study examined whether BOO (clinically presented as an abnormal voiding pattern) and DO may play roles in OAB among NP women in comparison with parous women that have undergone

spontaneous delivery (NSD group) or cesarean section (CS group). We retrospectively analyzed LUTS and UDS parameters to identify abnormal voiding patterns and DO among NP women with OAB, and we compared these findings to those observed in parous women.

Methods

The data collection was approved by the Taipei Medical University–Joint Institutional Review Board and the Ethics Committee at Taipei Medical University Hospital in Taiwan (No: N202004096). Data were retrospectively collected from paper or electronic charts from August 2011 to December 2018. A total of 906 patients met the inclusion criteria for the study. All methods were carried out in accordance with relevant guidelines and regulations. We obtained informed consent from all patients by themselves before they were enrolled.

Inclusion and exclusion criteria

All eligible participants opted to undergo UDS examinations. All examinations were performed in the semi-seated position using water media on a urodynamic system (UD-2000, Medical Measurement Systems B.V. (MMS), Dover, NH, USA). A triple-lumen urethral catheter (8 Fr) was inserted into the urethra and then retracted at 2 mm/s. During data collection, UDS examinations were performed by the same physician using the same equipment at the same hospital.

Patients with the following pathological conditions were excluded from the study: urinary tract infection, urogenital tract malignancy, pelvic mass or malignancy, pelvic organ prolapse, active urinary tract stones, intravesical lesion, enlarged uterine size, and pelvic mass. In addition, patients who had a history of medications known to affect voiding dysfunction and who had prior urogenital surgery, diabetes mellitus, and neurogenic lower urinary tract dysfunction were also excluded. Furthermore, patients who refused to receive UDS and women younger than 20 years were also excluded from the study.

Participants were divided into three groups: NP (NP group); only normal spontaneous delivery (NSD) for term pregnancy, regardless of parity (NSD group); and only CS group. In the NP group, gestational-age patients with OAB without a history of pregnancy for more than 12 weeks were included. Patients with OAB who had undergone both NSD and CS were excluded. The flowchart in Fig. 1 shows the classification of women with OAB.

DO was defined as the UDS observation of involuntary detrusor contractions during the filling phase that may be spontaneous or provoked by urgency[14]. The two types of DO are (1) phasic, which may or may not lead to urinary incontinence, and (2) terminal, which is a single involuntary detrusor contraction that frequently results in complete bladder emptying. Abnormal voiding patterns during uroflowmetry were defined as an nonsmooth curve, the presence of multiple interrupted peaks, or an abnormally low flow rate without the use of a catheter (typical uroflowmetry results show a single smooth curve with a maximum flow rate exceeding 15 mL/s and a voided volume above 200 mL)[15,16]. Patients who displayed

these results were considered to have abnormal voiding patterns, regardless of whether they presented with clinical symptoms. The procedures and interpretation of results were performed by one of the authors (H.Y.C.).

Statistical analysis

The central tendency and dispersion of continuous variables are presented as means and standard deviations. Categorical variables are presented as counts and percentages. The continuous variables of the groups were compared using analysis of variance, and categorical variables were compared using the χ^2 test. We further examined the relationship between the status of abnormal voiding patterns and DO among the NP, NSD, and CS groups by performing the χ^2 test. The relationship between the maximum urethral closure pressure (MUCP) level and abnormal voiding pattern status among the different groups was examined using an independent *t* test. A significance level of 0.05 was used, and statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA).

Results

Patients were divided into three groups: 221 patients in the NP group, 571 patients in the NSD group, and 114 patients in the CS group. The severity of symptoms was not quantified using a questionnaire, but all participants reported that these symptoms affected their quality of life.

The demographic information of all patients in the three groups is shown in Table 1. Patients in the NP group were significantly younger than those in the other two groups (mean age: 38.14, 60.44, and 52.09 years for the NP, NSD, and CS groups, respectively, $P < 0.001$). The demographic data (body mass index, age) and symptoms (frequency, nocturia, and urinary incontinence) are shown in Table 1. The NP group had fewer patients with symptomatic stress urinary incontinence (SUI) and urinary urgency incontinence (UUI), which was statistically significant in the symptom of SUI (6.79%, 17.54%, and 28.72% in the NP, CS, and NSD groups, respectively, $P < 0.001$).

Table 1
Lower urinary tract symptoms among nulliparous (NP), normal spontaneous delivery (NSD), and cesarean section (CS) women

Variable	NP		NSD		CS		*P* value*
	N = 221		N = 571		N = 114		
BMI, mean (± SD)	21.85	(± 3.67)	23.23	(± 3.59)	22.34	(± 3.32)	< 0.001
Age, mean (± SD)	38.14	(± 9.59)	60.44	(± 13.08)	52.09	(± 9.83)	< 0.001
Frequency, n (%)	219	(99.10%)	554	(97.02%)	111	(97.37%)	0.23
Nocturia, n (%)	133	(60.18%)	432	(75.66%)	82	(71.93%)	< 0.001
SUI, n (%)	15	(6.79%)	164	(28.72%)	20	(17.54%)	< 0.001
UUI, n (%)	16	(7.24%)	51	(8.93%)	11	(9.65%)	0.68

NP: Nulliparous patients

NSD: Normal spontaneous delivery

CS: Cesarean section

BMI: Body mass index

SUI: Stress urinary incontinence

UUI: Urge urinary incontinence

* Mean (± SD): ANOVA; n (%): χ^2 test

UDS parameters from the NP, NSD, and CS groups are shown in Table 2. The NP group presented with the highest MUCP level, followed by the CS and NSD groups (104.92, 86.42, and 77.91 cmH_2O, respectively, $P < 0.001$). Moreover, the NP group exhibited the highest urethral functional length, followed by the CS and NSD groups (3.10, 2.71, and 2.45 cm, respectively, $P < 0.001$). DO was observed in 69.68% of patients in the NP group; this proportion was significantly higher than that observed in the CS group (48.25%) and the NSD group (46.41%) (Table 2). Furthermore, 65.16% of patients in the NP group presented with abnormal voiding patterns during UDS; this proportion was also significantly higher than that observed in the CS group (42.11%) and the NSD group (38.0%). Notably, the relationship between DO and the presence of an abnormal voiding pattern was significant in the NP group ($P < 0.001$), but not in the NSD and CS groups ($P = 0.05$ and 0.15, respectively) (Table 3). Thus, DO and abnormal voiding patterns were significantly more related in the NP group than in the parous groups.

Table 2
Urodynamic parameters among nulliparous (NP), normal spontaneous delivery (NSD) and cesarean section (CS) women

Variable	NP N = 221		NSD N = 571		CS N = 114		*P* value*
Peak flow, ml/sec, mean (± SD)	18.93	(± 5.66)	21.42	(± 5.81)	20.73	(± 5.95)	< 0.001
Mean flow, ml/sec, mean (± SD)	7.50	(± 4.45)	9.40	(± 4.16)	8.95	(± 4.17)	< 0.001
MUCP, cmH_2O, mean (± SD)	104.92	(± 22.96)	77.91	(± 28.58)	86.42	(± 28.25)	< 0.001
FUL mm, mean (± SD)	3.10	(± 0.58)	2.45	(± 0.59)	2.71	(± 0.58)	< 0.001
FS ml, mean (± SD)	121.51	(± 39.45)	125.96	(± 44.30)	122.02	(± 43.90)	0.35
NS ml, mean (± SD)	201.22	(± 51.69)	208.78	(± 52.10)	194.92	(± 53.08)	0.015
MCC ml, mean (± SD)	339.33	(± 62.61)	345.60	(± 66.36)	325.32	(± 69.64)	0.001
DO, n (%)	154	(69.68%)	265	(46.41%)	55	(48.25%)	< 0.001
Abnormal voiding pattern, n (%)	144	(65.16%)	217	(38.00%)	48	(42.11%)	< 0.001

NP: Nulliparous patients; NSD: Normal spontaneous delivery; CS: Cesarean section DO: detrusor overactivity; FS: first sensation; FUL: functional urethral length; MCC: maximum cystometric capacity; MUCP: maximum urethral closure pressure; NS: normal desire; SD: standard deviation.

* Mean (± SD): ANOVA; n (%): χ^2 test

Table 3
Relationship between detrusor overactivity (DO) and abnormal voiding pattern among nulliparous (NP), normal spontaneous delivery (NSD), and cesarean section (CS) women

	Abnormal void pattern				
Variable	**No**		**Yes**		P **value***
NP, n (%)					
DO (-)	39	(50.65%)	28	(19.44%)	< 0.001
DO (+)	38	(49.35%)	116	(80.56%)	
NSD, n (%)					
DO (-)	201	(56.78%)	105	(48.39%)	0.05
DO (+)	153	(43.22%)	112	(51.61%)	
CS, n (%)					
DO (-)	38	(57.58%)	21	(43.75%)	0.15
DO (+)	28	(42.42%)	27	(56.25%)	

NP: Nulliparous patients; NSD: Normal spontaneous delivery; CS: Cesarean section

DO: detrusor overactivity

* χ^2 test

We further compared the relationship between MUCP and abnormal voiding patterns. In the NP group, 144 patients with abnormal voiding patterns presented with significantly higher MUCP than the 77 patients without abnormal voiding patterns (MUCP: 111.30 vs 92.99 mmH_2O, $P < 0.001$), as shown in Table 4. In the NSD group, 217 patients with abnormal voiding patterns also presented with significantly higher MUCP than was observed in 354 patients without abnormal voiding patterns (MUCP = 82.47 vs 75.11 mmH_2O, $P = 0.003$), as shown in Table 4. In the CS group, 48 patients with abnormal voiding patterns also presented with significantly higher MUCP than was observed in 66 patients without abnormal voiding patterns (MUCP = 95.00 vs 80.18 mmH2O, $P = 0.005$), as shown in Table 4. Thus, patients with abnormal voiding patterns presented with significantly higher MUCP than was observed in patients without abnormal voiding patterns in all of the groups (NP, CS, and NSD with $P < 0.001$, $P < 0.005$, and $P < 0.003$, respectively).

Table 4
Comparison of the maximum urethral closure pressure (MUCP) level between the different status of abnormal voiding patterns in nulliparous (NP), normal spontaneous delivery (NSD), and cesarean section (CS) women

	Abnormal void pattern				
Variable	No		Yes		P value*
NP					
Pt, n	77		144		
MUCP cmH_2O, mean (± SD)	92.99	(± 19.35)	111.30	(± 22.24)	< 0.001
NSD					
Pt, n	354		217		
MUCP cmH2O, mean (± SD)	75.11	(± 27.21)	82.47	(± 30.18)	0.003
CS					
Pt, n	66		48		
MUCP cmH_2O, mean (± SD)	80.18	(± 25.93)	95.00	(± 29.31)	0.005

NP: Nulliparous patients; NSD: Normal spontaneous delivery; CS: Cesarean section

DO: detrusor overactivity; MUCP: maximum urethral closure pressure

*independent *t* test

Discussion

Our findings showed a high prevalence of DO (69.68%) and abnormal voiding patterns (65.16%) among NP women with OAB as compared with parous women. Our finding of VD with an abnormal voiding pattern corroborates the findings of Cho et al., who reported that more than half the women in their study presented with OAB symptoms in conjunction with VD, as revealed by UDS[8]. In addition, Nitti et al. reported the existence of very high overlapping storage (79%) and obstructive symptoms (76%) in 331 non-neurogenic VD women who underwent multichannel video-UDS for non-neurogenic VD[17]. Our previous study showed that an add-on muscle relaxant (baclofen) to antimuscarinics can improve treatment efficacy among women with OAB who present with abnormal voiding patterns[18]. These findings imply that voiding dysfunction might be masked by OAB symptoms. The findings also indicate that the co-existence of OAB and VD is an important clinical problem. Our findings imply that an abnormal voiding pattern, which is indicative of voiding dysfunction, might play a role in the etiology of OAB, especially in NP patients as compared with parous women.

A significant relationship was detected between elevated MUCP and the existence of abnormal void patterns, which may provide evidence of a relationship between pelvic floor hypertonicity and VD. MUCP was used to infer the contraction strength of the levator ani muscle because of the increase in MUCP during pelvic floor muscle contraction (Kegel exercise) in UDS examination[19]. In our study, OAB women with an abnormal voiding pattern presented with significantly higher MUCP compared with those without an abnormal voiding pattern in all groups (Table 4). Thus, women with an abnormal voiding pattern show higher contraction strength of the levator ani muscle or pelvic floor hypertonicity. Our results corroborate those of Zhu et al.[4], who found that poor relaxation of the pelvic floor may be involved in the etiology of OAB in NP women. Peng et al. also reported a high prevalence of the co-existence of poor relaxation in pelvic floor muscles and VD[20]. In addition, abnormal voiding patterns were higher in the NP group (65.16%) than in the CS group (42.11%) and NSD group (38.00%). These findings highlight the importance of the hypertonicity and poor relaxation of the pelvic floor muscles in the etiology of OAB in NP patients.

BOO in women is controversial because of the wide spectrum of symptoms associated with LUTS. Unlike anatomical BOO caused by symptomatic cystocele and uterine prolapse, previous incontinence surgery, or urethral stricture[13], functional BOO can occur at different anatomic levels, for example, pelvic floor (dysfunctional voiding) or external urinary sphincter (Fowler's syndrome), and patients with BOO can present with storage OAB symptoms[21]. Some studies, such as that by Cho et al., reported that over 90% of women with VD exhibited OAB symptoms associated with obstruction in video-UDS findings[8,22,23]. Furthermore, Deindl et al. reported that poor relaxation of the levator muscle or urethral sphincter during micturition is a probable cause of functional BOO in women[24]. Fusco et al. proposed a three-stage model to characterize the changes in hypertrophy, compensation, and decompensation during bladder remodeling induced by BOO[11]. They showed that increased detrusor contractility during the voiding phase combined with DO during the filling phase characterized the compensation phase of bladder remodeling[11]. In this study, as shown in Table 3, the relationship between DO and the presence of an abnormal voiding pattern was statistically significant in the NP group (80.56%) compared with the CS (56.25%) and NSD (51.61%) groups. Thus, an abnormal voiding pattern associated with DO may play a role in OAB among NP patients, but not among NSD or CS patients. Functional BOO may be caused by pelvic floor hypertonicity, leading to the compensative phenomenon of DO in NP women.

The feasibility of using MUCP to assess voiding function has not yet been confirmed. High MUCP is detected in in patients with overactive pelvic floor muscles and LUTS. Therefore, MUCP is used as a proxy for assessing the pelvic floor condition[25]. In our study, MUCP decreased in the order of NP, CS, and NSD, likely indicating the extent of pelvic floor injury caused by pregnancy and birth trauma. Lower MUCP is in concordance with the finding of abnormal voiding patterns. Whether decreasing MUCP could reduce the possibility of abnormal voiding patterns is debatable, and further research is required to clarify the relationship between MUCP and void function.

Uroflowmetry is a potentially useful tool in clinical practice. Pressure flow study (PFS) can be used to differentially diagnose VD as being either due to BOO or detrusor underactivity (DU) based on detrusor pressure measurements[9,13]. Although PFS can provide more sophisticated measurements, it could induce possible functional urethral obstruction due to the presence of the urethral catheter[26]. Therefore, VD due to a presumed “obstruction” can be overdiagnosed based solely on PFS[13]. Because many NP women cannot void with a urethral catheter in place[9,13,26], we did not perform PFS in this study. Nonetheless, uroflowmetry, as compared with multi-channel PFS, can be used as a simple, noninvasive, and relatively inexpensive method for assessing VD in patients. Clothier et al. also reported that using noninvasive urodynamics with a staccato-flow pattern could be used to establish a diagnosis of functional obstructed voiding[15]. Although differentially diagnosing four recognized uroflow patterns (i.e., tower-, staccato-, interrutped-, and pateau-shaped patterns) may be not easy, urofometry is well suited for screening patients, particularly in cases of repeated abnormal flow[15,27].

The limitations of our study are as follows. First, because we did not perform PFS on a daily basis, we were unable to obtain detrusor pressure measurements at maximal flow. Second, the effect of age as a confounding factor cannot be excluded as most of the NP patients were relatively young. Excluding the factors of aging and childbirth, our study highlights the relationship between DO and abnormal voiding patterns among NP women with OAB. In conjunction with the correlation between MUCP and abnormal voiding pattern, we concluded that the abnormal voiding pattern due to hypertonicity of pelvic floor muscle is a possible etiology of OAB among NP women. However, further studies with more patients are required to confirm the pathophysiology of OAB in NP patients.

Our data showed a high prevalence of abnormal voiding patterns among NP women with OAB. Based on the significant relationship among high MUCP, DO, and abnormal void patterns, we hypothesized that hypertonicity or poor relaxation of the pelvic muscles in NP women may cause functional BOO, which is related to their OAB.

Declarations

Data availability: The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

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Author contributions

JJ.F. and HY.C.— contributed to conduct the study, collect data, analyzed and interpret the data, as well as draft the manuscript. JC.W. and YC.Y.—participated in statistical analysis, data interpretation and revised

the manuscript. MP.W.,JC.W.—contributed in consultation of manuscript. HY.C. and MP.W.—contributed substantially to study design and supervision, data interpretation and manuscript editing. All authors critically revised and approved the final manuscript.

Competing Interests Statement

The authors declare no competing interests.

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Figures

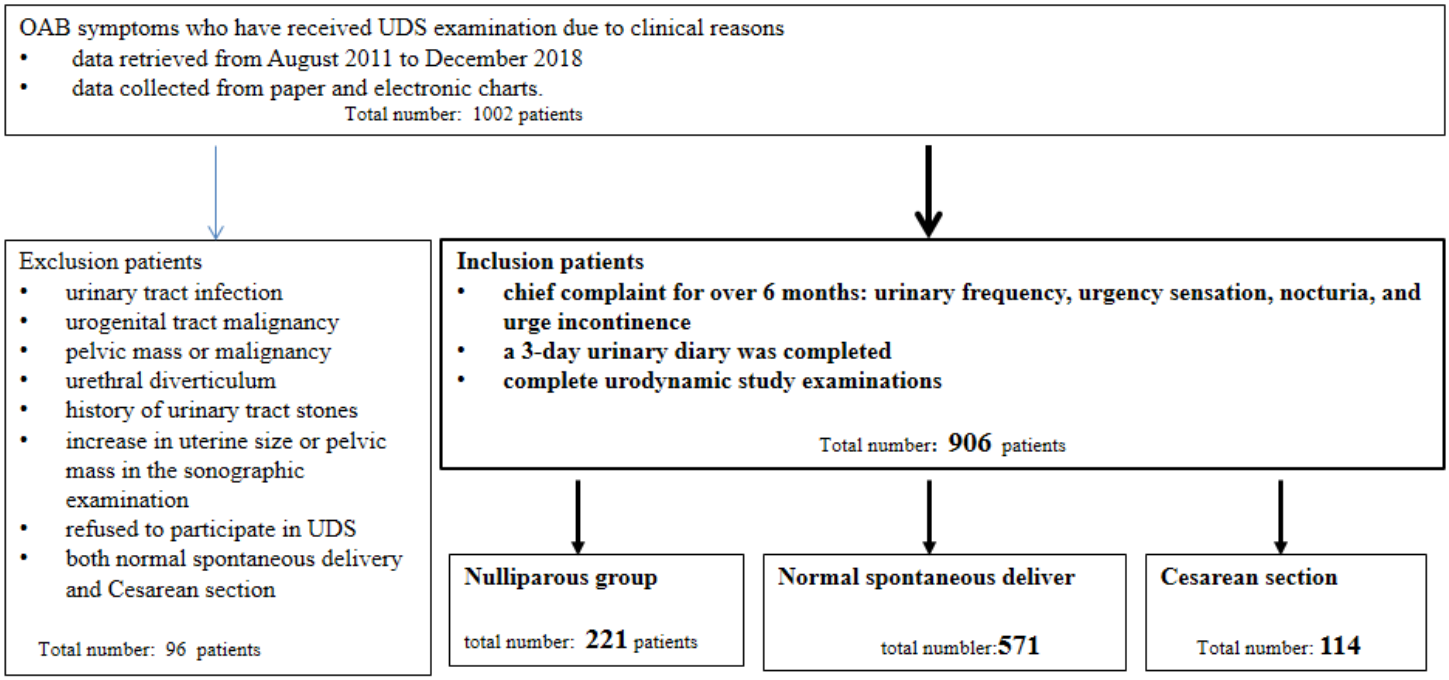

Figure 1

Flow chart showing inclusion and exclusion criteria used in this study.