Cluster Analysis in Women with Overactive Bladder Syndrome: Identification of Clinical Subgroups Based on Symptom Severity

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ABSTRACT

OBJECTIVE: The aim of this study was to classify women with overactive bladder (OAB) syndrome using cluster analysis based on symptom severity, quality of life related to urinary functions, and bladder diary data.

STUDY DESIGN: This cross-sectional study included 62 women diagnosed with overactive bladder (OAB) syndrome and an Overactive Bladder Symptom Score (OABSS)≥10.5. Participants completed the OABSS, Incontinence Impact Questionnaire-7 (IIQ-7), Urogenital Distress Inventory-6 (UDI-6), and a three-day bladder diary. Cluster analysis was performed using the k-means algorithm based on symptom severity, quality of life, and bladder diary data. Differences between clusters were tested using the Kruskal-Wallis and Mann-Whitney U tests.

RESULTS: The cluster analysis identified three distinct groups: the severe symptom cluster (n=17), the moderate symptom cluster (n=25), and the mild symptom cluster (n=20). The severe symptom cluster had the highest OABSS scores, the most frequent voiding episodes, and the lowest maximum voided volume ($p<0.05$). The mild symptom cluster exhibited the lowest OABSS scores, the best bladder function, and the highest IIQ-7 and UDI-6 scores ($p<0.05$). The moderate symptom cluster fell between the severe and mild clusters in terms of symptom severity.

CONCLUSION: In this study, cluster analysis was used to classify OAB patients into subgroups based on symptom severity, quality of life-related to urinary function, and bladder function. As a result of the analysis, participants were categorized into three groups: severe - moderate - mild symptom clusters. It was determined that as symptom severity increased, bladder function deteriorated, and the impact on quality of life became more significant.

Keywords: Bladder diary; Cluster analysis; Overactive bladder; Quality of life; Symptom severity

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Introduction

Overactive bladder (OAB) syndrome, characterized by symptoms such as urgency, frequency, nocturia, and urge urinary incontinence, is a common lower urinary tract disorder. OAB syndrome is more prevalent in women than in men and significantly impacts physical, psychosocial, and emotional health, leading to a marked decrease in quality of life (1,2). The severity of OAB symptoms varies significantly among patients, necessitating the identification of symptom-based subgroups and the development of personalized treatment approaches (3-5). Various scales and assessment tools, such as urinary diaries, are used for the diagnosis and severity evaluation of OAB. However, existing studies typically assess OAB evaluation methods independently and do not integrate different symptom aspects into a comprehensive classification (6-10).

There are several studies in the literature that use clustering analysis to classify OAB patients based on symptom profiles. Firouzmand et al. (11), focused on examining the diagnostic power of biomarkers (e.g., ATP, IL-5) for OAB syndrome in their clustering analysis studies based on biomarkers

and OAB symptom scores. As a result of their analysis, they classified patients into two groups: low symptom score group and high symptom score group. Gross et al. (12) classified OAB patients into two subgroups based on their analysis: the urinary cluster, characterized predominantly by urinary symptoms, and the systemic cluster, in which anxiety, depression, psychological stress, and traumatic factors were the primary determinants. In both studies, important clinical data such as bladder diaries, which objectively assess bladder functions, were not included in the analyses.

The bladder diary is an objective assessment tool that allows us to observe patients' daily urinary habits. In addition to providing insight into patients' urination patterns, the bladder diary enables the evaluation of urinary and bladder functions. It offers a more objective perspective in the clinical assessment of OAB by complementing the subjective data obtained through symptom questionnaires (6). A review of the literature reveals that subjective findings derived solely from questionnaire data are insufficient for classifying the severity of OAB symptoms, highlighting the necessity of integrating objective bladder function data. Therefore, this study aimed to classify OAB patients into subgroups using cluster analysis based on OAB symptom assessment tools and bladder diary data.

Material and Method

This study had a descriptive and cross-sectional research design. The study was approved by the Non-Interventional Research Ethics Committee of the Hacettepe University (decision no: GO19/11-40, meeting date: April 24, 2019), and all participants provided written informed consent for the use of their data in accordance with the Declaration of Helsinki. The study was conducted at Hacettepe University, Pelvic Health and Women's Health Physiotherapy and Rehabilitation Unit between April 2019 – 2020.

Participants: This study included women who exhibited symptoms of overactive bladder (OAB), met the diagnostic criteria defined by the International Continence Society (ICS) (13), and had an Overactive Bladder Symptom Score (OABSS) of 10.5 or higher (14). The diagnosis of OAB was made by a specialist physician based on these criteria. Inclusion criteria required participants to be at least 18 years old and to agree to complete a three-day bladder diary.

Participants were excluded if they had a current urinary tract infection, interstitial cystitis, bladder stones, anatomical pathologies such as urethral stricture, ongoing pregnancy, postpartum period of less than six months, pelvic organ prolapse of stage 3 or higher, neurological or oncological diseases, or a history of major pelvic surgery.

Assessments: Before administering the questionnaires, a detailed medical history related to OAB syndrome was obtained from all participants, and their age, body mass index (BMI), parity, mode of delivery, and postmenopausal status were recorded.

Overactive Bladder Symptom Score (OABSS): The OABSS was used to assess OAB symptoms. The OABSS is a 7-item scale that evaluates parameters such as daytime and nighttime urinary frequency, urgency frequency, urge incontinence, and bladder control. Each item is scored between "0 – 4," with a total score ranging from "0-28." Higher scores indicate more severe OAB symptoms (7). The OABSS was administered to all participants before inclusion in the study to determine the severity of their OAB symptoms. The Turkish version of the OABSS has demonstrated strong internal consistency (Cronbach's α=0.95) and test-retest reliability (ICC=0.93-0.95, p=0.001) in validation and reliability studies, with an optimal cutoff score of 10.5 for diagnosing OAB (14). In this study, participants with an OABSS score above 10.5 were included.

Incontinence Impact Questionnaire-7 (IIQ-7) and Urogenital Distress Inventory-6 (UDI-6): The IIQ-7 and UDI-6 were used to assess the impact of OAB symptoms on women's quality of life and the level of distress associated with these symptoms (15). The IIQ-7 is a 7-item questionnaire that evaluates the effects of urinary incontinence on physical activity, travel, social life, and emotional health. Each item is scored between 0-3, with a total score ranging from 0-100. Higher scores indicate a greater negative impact of urinary incontinence on daily quality of life. The UDI-6 is a 6-item questionnaire that assesses the distress levels associated with lower urinary tract symptoms. It evaluates symptoms such as frequency, urgency, urge incontinence, and stress incontinence, focusing on how these symptoms are perceived by patients and their impact on daily life. Both scales were administered to all participants to assess the effect of OAB symptoms on daily life. The Turkish versions of the IIQ-7 and UDI-6 have demonstrated high internal consistency (Cronbach's α=0.87 for IIQ-7 and 0.89 for UDI-6) and strong test-retest reliability (Spearman's rho=0.99, $p<0.001$) in validation and reliability studies (16).

Bladder Diary: A 3-day bladder diary was used to assess participants' bladder and urinary functions. Participants were instructed to complete a 24-hour bladder diary on alternate days within one week after the initial evaluation, for a total of three days. The diary required participants to record daytime and nighttime (24-hour) voiding frequency, voided volume, and episodes of urge incontinence. After data collection, the average values from the three bladder diaries were calculated and used in the analyses (17).

Cluster Analysis: Cluster analysis was performed to classify OAB patients into subgroups. The cluster analysis included the variables OABSS, IIQ-7, UDI-6, total voiding frequency (daytime and nighttime), maximum voided volume, and number of urge incontinence episodes. Cluster analysis

was used to categorize OAB patients into subgroups based on symptom severity, quality of life-related to urinary function, and objective measurements related to bladder function to define distinct clinical patient profiles.

The K-means algorithm was used as the clustering method (18). The K-means algorithm assigned observations to clusters using Euclidean distance and grouped each participant by minimizing their distance to cluster centers. The Elbow method and Silhouette score were used to determine the optimal number of clusters and different cluster numbers were compared for model validation. The separation of the clusters obtained through clustering was examined using Principal Component Analysis (PCA). As a result of the clustering analysis, three subgroups were identified: Cluster 0 (severe symptom cluster; highest symptom severity, frequent urination, low voided volume, high urge incontinence), Cluster 1 (moderate symptom cluster; moderate symptom severity, high voided volume, low urge incontinence), and Cluster 2 (mild symptom cluster; mild symptom burden, lowest urge incontinence).

The Kruskal-Wallis test was applied to determine statistical differences between the groups obtained from the clustering analysis. For variables with significant differences, pairwise comparisons were performed using the Mann-Whitney U test. The chi-square (χ^2) test was used to assess differences between categorical variables. The analyses were conducted using IBM SPSS Statistics v26. The Elbow method, Silhouette score, and PCA, which were used to determine the optimal number of clusters, were performed using the Python programming language. The power of the study was calculated using G*Power 3.1. In the analysis based on OABSS scores ($p < 0.001$) among the groups classified by symptom severity (severe symptom cluster: n=17, moderate symptom cluster: n=25, mild symptom cluster: n=20), the effect size was determined as 0.8, and the power of the study was calculated as 0.98.

Results

The mean age of the 62 participants included in the study (Figure 1) was 50.55 ± 9.52 years, and the mean BMI was 26.77 ± 4.33 kg/m². In this study, clustering analysis was conducted based on symptom severity (OABSS), bladder function (voiding frequency, volume), and quality of life (IIQ-7, UDI-6) data. As a result of the clustering analysis, the 62 women with OAB syndrome included in the study were divided into three groups based on symptom severity: cluster 0 (severe symptom cluster), cluster 1 (moderate symptom cluster), and cluster 2 (mild symptom cluster). The PCA results demonstrated a clear distinction between the clusters (Figure 2). In the PCA graph, the severe symptom cluster was distinctly separated from the other two clusters, while the moderate and mild symptom clusters showed partial overlap. Examination of the PCA results revealed that OABSS, total voiding frequency, number of urge incontinence episodes, and maximum voided volume were the most influential variables in distinguishing the clusters. Cluster 0 (n=17) had the highest OABSS scores, the most frequent voiding episodes, and the lowest maximum voided volume, with the highest number of urge incontinence episodes. Cluster 1 (n=25) was positioned between cluster 0 and cluster 2 in terms of symptom severity; it was more similar to cluster 0 in terms of voiding frequency and quality of life but showed voiding volume characteristics closer to cluster 2. Cluster 2 (n=20) had the lowest symptom severity, the best bladder function, and the most favorable quality of life scores. The differences between the groups in terms of OABSS, IIQ-7, UDI-6 scores, and bladder diary parameters were statistically significant ($p < 0.05$).

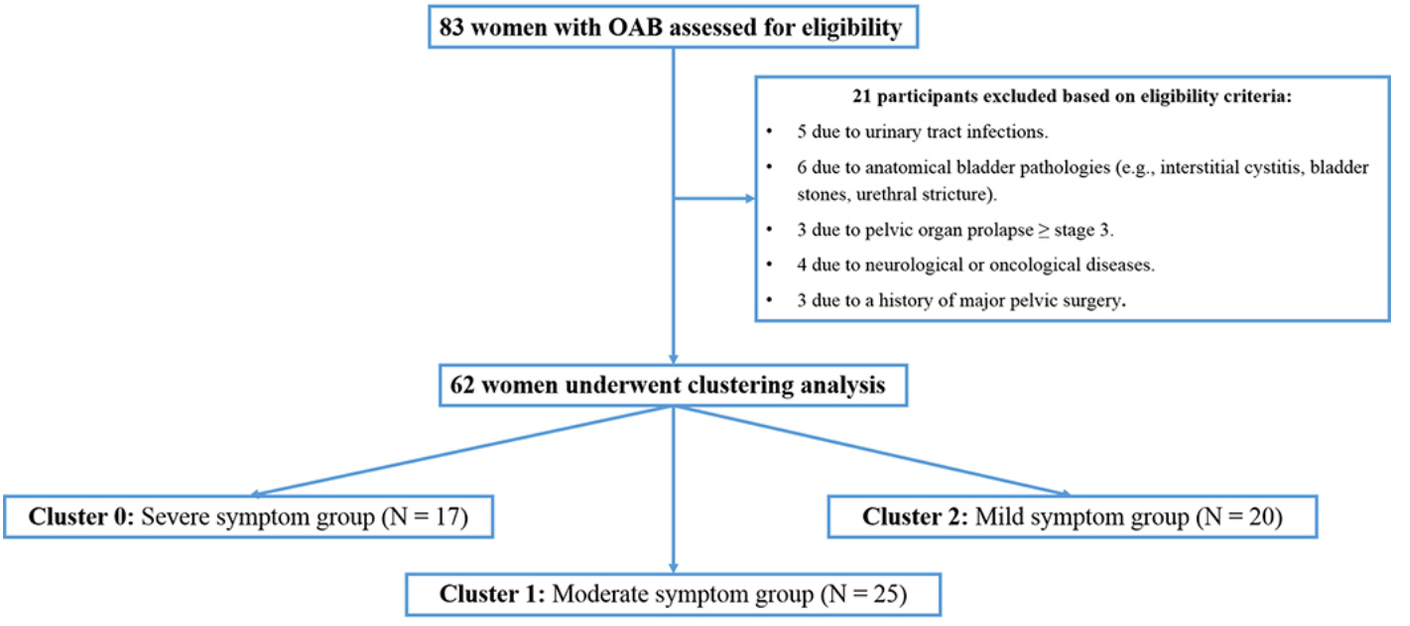

Figure 1: *Flow chart of the participants*

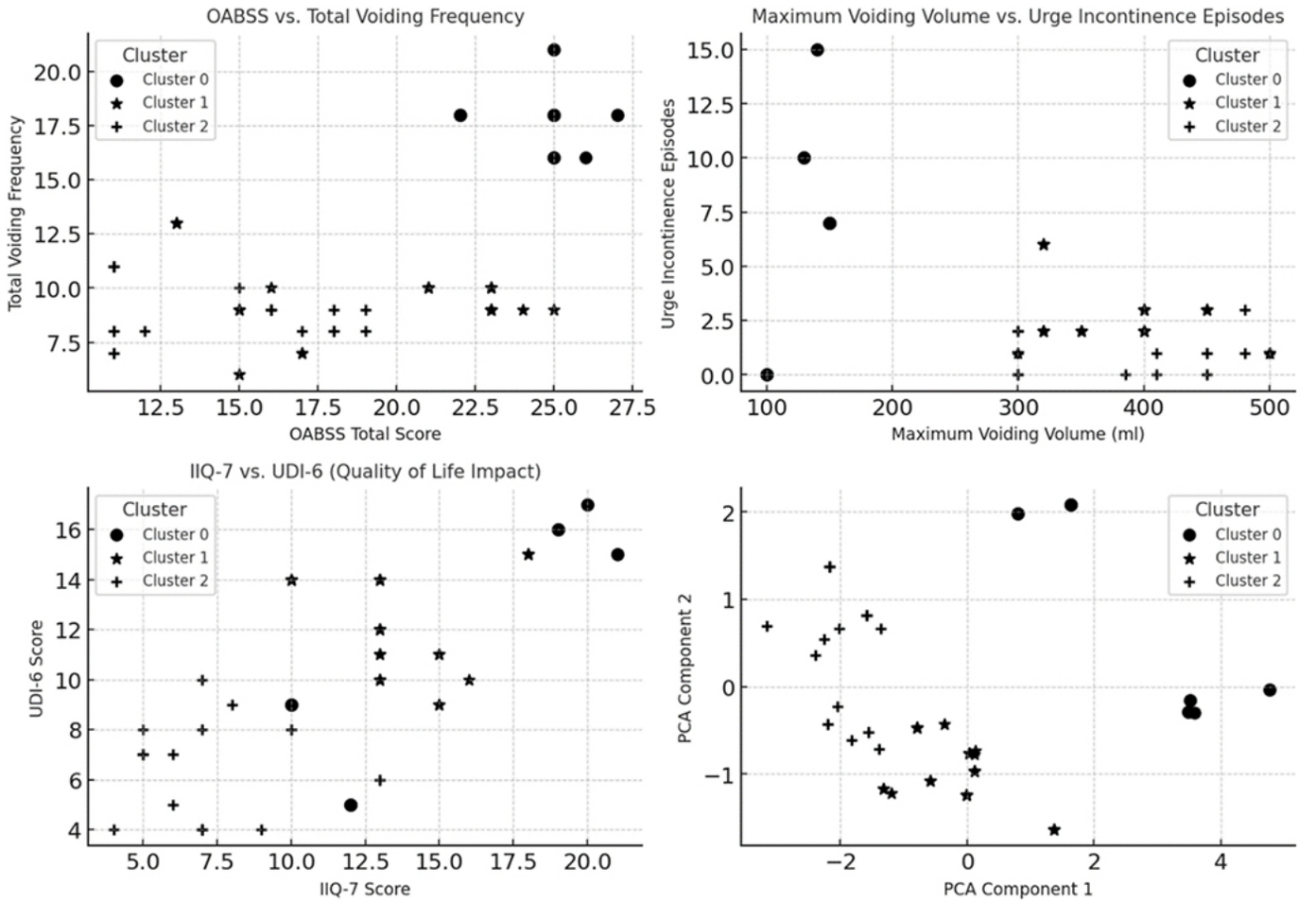

Figure 2. *Scatter plots illustrate the distribution of participants across three clusters based on urinary and quality-of-life measures. ● = Severe Symptom Cluster, * = Moderate Symptom Cluster, + = Mild Symptom Cluster.*

There was no statistically significant difference between the clusters in terms of age, BMI, parity, mode of delivery, or postmenopausal status (p>0.05) (Table I). However, significant differences were observed among the clusters regarding OABSS, IIQ-7, and UDI-6 scores (p<0.05). The OABSS score was found to be significantly higher as symptom severity increased across the clusters (p<0.001). Regarding IIQ-7 scores, a significant difference was found between the mild symptom cluster and both the moderate and severe symptom clusters (p=0.001, p=0.027, respectively), while no significant difference was observed between the moderate and severe clusters (p=0.167). In terms of UDI-6 scores, the mild symptom cluster had the lowest values compared to the moderate and severe symptom clusters (p=0.013, p<0.001, respectively), whereas there was no significant difference between the moderate and severe symptom clusters (p=0.989) (Table II).

Table I: *Comparison of descriptive data among mild, moderate, and severe overactive bladder symptom severity groups determined by cluster cnalysis*

	Severe OAB cluster (n=17)	**Moderate OAB custer (n=25)**	**Mild OAB Cluster (n=20)**	**p**
Age (year)	56.00 (43.00-61.00)	51.00 (42.00-56.00)	43.00 (40.00-54.00)	0.112
BMI (kg/m²)	26.35 (21.22-26.35)	25.91 (24.84-28.23)	26.64 (23.44-30.49)	0.640
Parity	2.00 (2.00-3.00)	3.00 (2.00-4.00)	2.00 (2.00-3.00)	0.429
Mode of delivery				0.764
Nulliparous	-	-	-	
Vaginal delivery	11 (64.71%)	17 (70.83%)	14 (66.67%)	
Cesarean delivery	2 (11.76%)	5 (20.83%)	7 (33.33%)	
Mixed delivery	4 (23.53%)	2 (8.33%)	-	
Postmenopausal status (yes)	12 (70.59%)	15 (62.5%)	10 (47.62%)	0.340

BMI: Body mass index, kg/m²: kilograms per square meter. OAB: Overactive bladder. Numerical data were presented as median and interquartile range, while categorical data were presented as numbers and percentages. p: Comparisons among the three groups.

Table II: *Comparison of mild, moderate, and severe overactive bladder symptom severity groups determined by cluster analysis based on symptom questionnaire scores*

	Severe OAB cluster (n=17)	Moderate OAB cluster (n=25)	Mild OAB cluster (n=20)	p[1]
OABSS	25.00 (25.00-25.00)	22.00 (16.75-23.00)	13.00 (11.00-17.00)	<0.001*
p[2]	<0.001* mild-severe	<0.001* moderate-severe	<0.001* mild-moderate	
IIQ-7	12.00 (12.00-19.00)	13.00 (10.00-13.50)	8.00 (7.00-13.00)	0.003*
p[2]	0.027 mild-severe	0.167 moderate-severe	0.001* mild-moderate	
UDI-6	9.00 (5.00-16.00)	12.00 (11.00-14.00)	8.00 (4.00-9.00)	<0.001*
p[2]	<0.001* mild-severe	0.989 moderate-severe	0.013* mild-moderate	

OAB: Overactive bladder, OABSS: Overactive bladder symptom score. IIQ-7: Incontinence impact questionnaire-7. UDI-6: Urogenital distress Inventory-6. Numerical data were presented as median and interquartile range. (*): Statistically significant difference. p1: Comparisons among the three groups. p2: Subgroup comparisons.

There was a significant difference among the clusters in terms of bladder diary parameters ($p<0.05$). The 24-hour total voiding frequency was the lowest in the mild symptom cluster compared to the moderate and severe symptom clusters ($p<0.001$). No significant difference was observed between the moderate and severe symptom clusters ($p=0.943$). The maximum voided volume was significantly higher in the mild symptom cluster compared to the moderate and severe symptom clusters and in the moderate symptom cluster compared to the severe symptom cluster ($p<0.001$, $p=0.008$, respectively). The number of urge incontinence episodes was significantly lower in the mild symptom cluster compared to the moderate and severe symptom clusters and in the moderate symptom cluster compared to the severe symptom cluster ($p<0.001$, $p=0.003$, $p<0.001$, respectively) (Table III).

Discussion

This study aimed to classify patients with OAB syndrome using cluster analysis based on OABSS, IIQ-7, UDI-6, and bladder diary data. As a result of the cluster analysis, patients were categorized into severe, moderate, and mild symptom clusters. This study makes a significant contribution to the literature by enabling the evaluation of OAB patients not only through symptom questionnaires but also with objective bladder function parameters.

In our study, the groups identified through cluster analysis showed significant differences in symptom severity, quality of life, bladder, and urinary functions. The severe symptom group had the highest OABSS scores and included individuals with the most frequent voiding and the lowest voided volume. In terms of quality of life scores related to urinary function, a significant difference was found between the mild and moderate symptom groups. However, the absence of a significant difference between the moderate and severe groups suggests that the impact of urinary dysfunction on quality of life may plateau at a certain severity level. The severe symptom cluster was identified as the group with the lowest maximum voided volume and the highest number of urge incontinence episodes.

Table III*: Comparison of mild, moderate, and severe overactive bladder symptom severity groups determined by cluster analysis in terms of bladder diary data*

	Severe OAB cluster (n=17)	Moderate OAB custer (n=25)	Mild OAB cluster (n=20)	p[1]
24-h voiding frequency (n)	18.00 (18.00-18.00)	9.00 (8.00-11.00)	9.00 (9.00-10.00)	<0.001*
p2	<0.001* mild-severe	<0.001* mild-moderate	0.943 moderate-severe	
Daytime voiding frequency (n)	14.00 (14.00-14.00)	7.00 (6.00-9.00)	7.00 (6.00-9.00)	<0.001*
p2	<0.001* mild-severe	<0.001* mild-moderate	0.212 moderate-severe	
Nocturnal voiding frequency (n)	4.00 (3.00-4.00)	2.00 (1.00-2.00)	1.50 (1.00-2.00)	<0.001*
p2	<0.001* mild-severe	<0.001* mild-moderate	0.269 moderate-severe	
Maximum voided volume (mL)	140.00 (130.00-150.00)	450.00 (300.00-450.00)	335.00 (320.00-400.00)	<0.001*
p2	<0.001* mild-severe	<0.001* mild-moderate	0.008* moderate-severe	
Mean voided volume (mL)	105.00 (102.60-130.50)	238.40 (200.00-287.00)	177.00 (162.20-196.62)	<0.001*
p2	<0.001* mild-severe	<0.001* mild-moderate	0.001* moderate-severe	
Mean daytime voided volume (mL)	110.00 (100.80-120.00)	245.00 (212.00-300.00)	175.80 (155.00-189.00)	<0.001*
p2	<0.001* mild-severe	<0.001* mild-moderate	<0.001* moderate-severe	
Mean nocturnal voided volume (mL)	113.30 (111.00-115.00)	220.00 (200.00-270.00)	240.00 (212.50-310.00)	<0.001*
p2	<0.0* mild-severe	<0.001* mild-moderate	0.629 moderate-severe	
Number of urge incontinence episodes	7.00 (7.00-10.00)	1.00 (0.00-1.00)	2.00 (2.00-3.00)	<0.001*
p2	0.003* mild-severe	<0.001* mild-moderate	<0.001* moderate-severe	

OAB: Overactive bladder. mL: Milliliters. Numerical data were presented as median and interquartile range. (*): Statistically significant difference. (*): Statistically significant difference. p1: Comparisons among the three groups. p2: Subgroup comparisons

This indicates that the reduction in bladder capacity and impairment of bladder function contribute to the worsening of OAB symptoms. These findings highlight the necessity of developing personalized treatment approaches instead of standard therapies in the management of OAB patients (19-21).

In this study, cluster analysis was performed to classify OAB patients into subgroups based on symptom severity, providing significant contributions to clinical practice. In the literature, various criteria such as symptom scores, biomarkers, or voiding behaviors have been used to classify OAB patients. Firouzmand et al. (11), classified OAB patients into low and high symptom score groups using biomarkers such as ATP and IL-5 but did not evaluate clinical factors such as bladder functions or quality of life parameters. Similarly, Gross et al. (12) clustered OAB patients based on their psychosocial burden, dividing them into subgroups characterized by urinary symptoms and systemic factors such as anxiety, depression, psychological stress, and traumatic experiences. However, these studies did not comprehensively assess bladder functions. In the present study, a more comprehensive analysis was conducted by integrating both subjective symptom scores and objective measurements of bladder functions in the classification of OAB patients. This approach allows for the classification of OAB patients based not only on their symptom profiles but also on their functional characteristics.

In most studies conducting cluster analysis in OAB patients, both male and female individuals have been evaluated, focusing on the overall distribution of OAB in the general population. Since OAB is more prevalent in women and its etiology is influenced by gender-specific factors, studies focusing specifically on the female population are of particular importance. Blaivas et al. (22) classified OAB patients into phenotypes using variables such as uroflowmetry and voided volume but did not consider symptom severity and bladder functions together. In contrast, Miller et al. (23) evaluated only female individuals and focused on voiding habits and fluid intake in their cluster analysis. In the present study, a more comprehensive classification was performed by integrating subjective symptom questionnaires with objective measurements such as bladder diaries. This approach may contribute to identifying specific clinical profiles of OAB in women and developing personalized treatment strategies.

In our study, the classification of participants with OAB into severe, moderate, and mild symptom clusters based on OAB symptom severity, quality of life-related to urinary parameters, and bladder diary findings provides significant clinical implications for the personalized management of OAB patients. The groups identified through cluster analysis differed in terms of symptom severity, bladder functions, and their impact on quality of life. These findings support the implementation of personalized treatment strategies based on symptom severity rather than a one-size-fits-all approach. Patients with mild symptoms may benefit more from conservative approaches such as lifestyle modifications and bladder training, whereas those in the moderate and severe symptom clusters may require more advanced treatment approaches, including pharmacological and/or invasive treatment options (24-26). Future studies testing the effectiveness of such patient classifications based on cluster analysis could contribute to making treatment plans more targeted and individualized.

Limitations and Strengths: Evaluating OAB symptoms using both subjective and objective methods is one of the strengths of this study. This approach has enabled a more comprehensive identification of clinical subgroups of OAB. The use of advanced statistical methods has facilitated a better understanding of the heterogeneous patient population, providing a more detailed characterization of different clinical profiles and allowing for the development of more targeted treatment strategies for OAB management. The integration of the findings into clinical practice is a significant advantage of this study. Besides, this study has several major limitations. First, since the study was designed cross-sectionally, changes in symptoms over time among the clusters could not be examined. However, the current cross-sectional design may serve as an important starting point for understanding how cluster analysis results can be applied in clinical practice. Second, only female patients were included in the study, and the symptom burden and effects of OAB on bladder function in males were not assessed. Given that OAB is more prevalent in women and that its etiology is influenced by sex-specific factors, focusing on the female population has allowed for more specific data on the clinical management of OAB in women. Third, we did not evaluate psychosocial factors in women in this study, and we acknowledge that psychosocial factors may influence the perception and severity of OAB symptoms. However, in this study, we primarily focused on a clustering analysis based on objective and subjective OAB severity, bladder functions, and quality of life assessments. Including psychosocial factors in future studies will help us better understand the interaction between these aspects. Lastly, the absence of urodynamic tests and neurological evaluations in our study limited our ability to comprehensively distinguish anatomical and physiological differences in OAB phenotypes. Since our study aimed to provide a classification model applicable to clinical practice, symptom and quality-of-life questionnaires along with bladder diary data were preferred. Although urodynamic tests and neurological assessments provide valuable data on urinary parameters, their routine application in all patients is not practical. However, future studies incorporating these assessments may offer valuable insights into the underlying pathophysiological mechanisms in the classification of OAB patients based on symptom severity.

Conclusion

In this study, cluster analysis was used to classify OAB pa-

tients into subgroups based on symptom severity, quality of life-related to urinary function, and bladder function. As a result of the analysis, participants were categorized into three groups: severe symptom cluster, moderate symptom cluster, and mild symptom cluster. It was determined that as symptom severity increased, bladder function deteriorated, and the impact on quality of life was more pronounced. These findings suggest that patients with mild symptoms may primarily benefit from conservative approaches such as lifestyle modifications and bladder training, while those in the moderate and severe symptom clusters may require more advanced treatment approaches, including pharmacological and/or invasive treatment options. Future studies should focus on integrating cluster analysis into clinical decision-making processes to evaluate the effectiveness of patient-centered treatment strategies.

Declarations

Ethics approval and consent to participate: The study was approved by the Non-Interventional Research Ethics Committee of Hacettepe University (decision no: GO19/11-40, meeting date: April 24, 2019), and all participants provided written informed consent for the use of their data in accordance with the Declaration of Helsinki.

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Availability of data and materials: The data supporting this study is available through the corresponding author upon reasonable request.

Authors' Contributions: Concept: EB, MSB, NO, TA; Design: EB, MSB, NO, TA; Data Collection or Processing: EB; Analysis or Interpretation: EB, TA; Literature Review: EB; Writing: EB; Critical Review: TA, MSB, NO.

Competing interests: The authors declare that they have no competing interests.

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