Compatibility of the urodynamic findings and mixed urinary incontinence symptoms

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Abstract

Introduction: Mixed urinary incontinence (MUI) is one of the most common problems of middle-aged women besides pelvic organ prolapses (POPs), and associated urinary symptoms are common disorders among older women whose treatment is necessary for the improvement of quality of life. This study aimed to evaluate the agreement between the symptoms of patients with MUI and urodynamic findings.

Methods: This analytic cross-sectional study was conducted on 170 MUI patients who underwent urodynamic evaluation for confirmation of the presumptive diagnosis. Findings comprise patients with “voiding phase symptoms”, “detrusor overactivity” (DO), “bladder hypersensitivity”, and “stress urinary incontinence” (SUI). The Kappa coefficient was used to evaluate the agreement between the symptoms and urodynamic findings. Sensitivity, specificity, and agreement of symptoms with corresponding urodynamic findings were determined. Univariate logistic regression was used to estimate the predictive value of clinical history compared to urodynamic findings.

Results: According to the results, the mean (SD) age of women was 51.87 (11.20). The mean bladder capacity was 339.6 (134.24), and post-void residual was 35.46 (43.89) ml. We determined a sensitivity of 75%, a specificity of 78.3%, a positive predictive value (PPV) of 86.3%, and a 63.2% negative predictive value (NPV) for SUI symptoms. According to the chi-square test results and Cohen Kappa values, there was no agreement between the symptoms of patients with MUI and bladder hypersensitivity, DO, and SUI. The only agreement was observed between the urinary frequency and voiding phase symptoms (Cohen kappa: 0.124; P value = 0.003).

Conclusion: There was no agreement between urodynamic findings and MUI symptoms except for urinary frequency and voiding phase symptoms. Since no comprehensive study has been conducted on the correlation between the symptoms of patients with MUI and urodynamic findings in our setting, the necessity to conduct large clinical studies is recommended.

Keywords: Urinary incontinence, Urodynamics, Bladder outlet obstruction, Detrusor overactivity, Bladder hypersensitivity
lack of access of a number of patients to this functional test, the cost and time of this test in some areas, and the unwillingness of patients to perform this modality, despite the mandatory performing of it for pre-operative evaluation of patients with POP, determining the priority of performing urodynamics in patients with incontinence is essential. So far, no comprehensive study has been conducted on the compatibility of symptoms of MUI patients with urodynamic findings in our setting, the goal of this study was to assess the degree of agreement between urodynamic findings and the symptoms of MUI patients as well as the predictive power of clinical history in comparison to urodynamic data.

Methods
This study is an observational analytic cross-sectional study conducted after approval by the regional ethics committee of Tabriz University of Medical Sciences (IR. TBZMED.REC.1400.1085) and consent of Taleghani and Alzahra hospitals. All patients referred to the outpatient clinic with MUI, who were candidates for urodynamic studies between October 2020 and September 2021, were included. Necessary information was collected from the patients’ medical records.

Urodynamic study
In the current study, the patients were categorized based on their clinical symptoms and underwent urodynamic evaluation for confirmation of presumptive clinical diagnosis. Findings comprise patients with “Bladder outlet obstruction”, “detrusor overactivity” (DO), “bladder hypersensitivity”, and “stress urinary incontinence” (SUI) groups.

DO is defined by ICS as “lower urinary tract/pelvic floor symptoms when detrusor muscle contractions occur during filling cystometry”.

Hypersensitivity is defined by ICS as increased nerve activity from a standardized stimulus with an expected tissue клинического отклика.

SUI is defined by ICS as a “Complaint of involuntary loss of urine on effort or physical exertion including sporting activities, or on sneezing or coughing”.

Voiding symptoms are defined by ICS as lower urinary tract symptoms (LUTS) experienced during the voiding phase (experienced during micturition).

The urodynamic testing (Andromeda Medical Systems, vesical catheter size 6 Fr, with filling rate of 30 drops/minute) in all cases was performed by a urogynecologist with ten years of experience in a urodynamic center. The person reviewing the urodynamic results of the patients participating in the study is the same for all patients and was a urogynecology fellow.

Urodynamic studies consist of uroflowmetry (to evaluate the urination pattern of possible obstruction of the bladder outlet and strength of the bladder muscles), and cystometry during the filling and voiding phase. ICS standard term for urodynamics is all the measurements that assess LUT function or dysfunction by the measurement of relevant physiological parameters.

Sample size calculation
According to the results of Haddad et al, which reported a positive predictive value (PPV) of 40% to the diagnosis of UI symptoms and 80% power and 95% confidence and P0 equal to 50%, the required sample size of 170 cases was obtained.

Eligibility criteria
Criteria for inclusion of patients in the study included patients with prolapse that do not protrude from the hymen ring (by the POP quantification system) and these patients are candidates for urodynamic testing for additional evaluation before surgery due to concomitant urinary problems; incontinent patients without any cure with medical treatment who were candidates for urodynamic testing; and patients with enterocoele (bowel protrusion) and urinary problems at the same time who were candidates for surgery.

Patients with advanced prolapse (i.e. more than 1 cm below the hymen ring), with a history of previous prolapse or UI surgery, neurogenic lower urinary tract dysfunction, or patients with intestinal dysfunction, including diarrhea and chronic constipation, and patients with a history of radical (extensive) pelvic surgery or radiation (pelvic radiation) were excluded from the study.

Statistical analysis
The degree of agreement between urodynamic data and the symptoms of MUI patients was assessed using the kappa coefficient. Similar to correlation coefficients, kappa can be in the range of -1 to 1, where 0 represents the amount of agreement expected from random chance, and 1 represents perfect agreement between the raters. Cohen recommended that the Kappa result be interpreted as follows: values 0 indicate no agreement, 0.01-0.20 indicate no to little agreement, 0.21-0.40 indicate reasonable agreement, 0.41-0.60 indicate moderate agreement, 0.61-0.80 indicate substantial agreement and 0.81-1.00 denote practically perfect agreement. Sensitivity, also known as the “true positive rate,” specificity, PPV, which is the percentage of test-takers who actually have the disease, and negative predictive value (NPV), which is the percentage of test-takers without the disease, were calculated based on the MUI symptoms or urodynamic findings in relation to the correspondent urodynamic findings. Moreover, univariate logistic regression was utilized to assess the clinical history’s predictive power in comparison to urodynamic data. The statistical analysis was performed using SPSS version 26.0.

Results
According to data from 170 eligible women, the mean
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The mean age of women was 51.87 (11.20). The youngest woman was 27, and the oldest was 79 years old. The mean body mass index (BMI) was 28.91(4.53) kg/m², and the participants had a mean of 4.14 (2.02) gravidity and 3.42 (1.49) parity with a live child. The mean bladder capacity was 339.6 mL (134.24) (minimum: 2; maximum: 578 ml), and post-void residual (PVR) was 35.46 (43.89) (minimum: 0; maximum: 345 mL). Of a total of 170 women, more than half of the women were in menopause (57%), and premenopausal women were in the next rank (25.9%) (Table 1). The prevalence of LUTS is summarized in Table 2. The chief complaint of women with MUI with or without POPs based on the predominance of urge or stress incontinence is summarized in Table 3. Twenty-eight percent of cases had urgency-predominant MUI, while 26% of MUI patients had a predominance of SUI. The common LUTS that were reported in eligible women were urgency (92%), frequency (82%), and nocturia (35%). Other symptoms were reported in less than 10% of women. Only 7% of women had sexual dysfunction, and 5% complained of coital incontinence. According to the POPs-Q, half of the women had stage II POPs, and 32% had stage I POPs. Enterocele in 54% and the perineal defect was detected in 57% of women. Sixty-eight women had good levator ani muscle strength, while in only 6% of women, its function was poor. Another finding in the examination was hypermobility of the urethra in 58%, positive cough test in 57%, and positive empty bladder supine stress test (ESST) in 16% of individuals. According to the results of the chi-square test, and Cohen kappa values there was no agreement between the symptoms of patients with MUI and bladder hypersensitivity, DO.

Table 1. Demographic and midwifery characteristics of study populations

<table>
<thead>
<tr>
<th>Variables</th>
<th>Age, mean (SD; minimum-maximum)</th>
<th>BMI, mean (SD; minimum-maximum)</th>
<th>Gravid, mean (SD; minimum-maximum)</th>
<th>Parity, mean (SD; minimum-maximum)</th>
<th>Alive, mean (SD; minimum-maximum)</th>
<th>NVD, mean (SD; minimum-maximum)</th>
<th>CS, Median (minimum-maximum)</th>
<th>Marital status, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>51.87 (11.20; 27-79)</td>
<td>28.96 (4.47; 19.25-45.33)</td>
<td>4.14 (2.06; 0-11)</td>
<td>4.19 (2.02; 1-9)</td>
<td>3.42 (1.49; 0-5)</td>
<td>3.18 (1.92; 0-10)</td>
<td>0 (0-3)</td>
<td>Married 153 (90.0)</td>
</tr>
<tr>
<td>BMI</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Single 17 (10.0)</td>
</tr>
<tr>
<td>POP stage, No. (%)</td>
<td>0</td>
<td>11 (6.5)</td>
<td>55 (32.4)</td>
<td>104 (61.2)</td>
<td>91 (51.5)</td>
<td>99 (58.2)</td>
<td></td>
<td>POP stage, No. (%)</td>
</tr>
<tr>
<td>Surgical history, No. (%)</td>
<td>91 (53.5)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Surgical history, No. (%)</td>
</tr>
<tr>
<td>Reproductive age, No. (%)</td>
<td>29 (17.1)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Reproductive age, No. (%)</td>
</tr>
<tr>
<td>Pre-menopause, No. (%)</td>
<td>44 (25.9)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Pre-menopause, No. (%)</td>
</tr>
<tr>
<td>Menopause, No. (%)</td>
<td>97 (57.1)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Menopause, No. (%)</td>
</tr>
<tr>
<td>Cigarette smoking, No. (%)</td>
<td>5 (2.9)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Cigarette smoking, No. (%)</td>
</tr>
<tr>
<td>Levator ani muscle strength, No. (%)</td>
<td>114 (67.1)</td>
<td>45 (26.5)</td>
<td>10 (5.9)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Levator ani muscle strength, No. (%)</td>
</tr>
</tbody>
</table>
| BMI: Body mass index; NVD: normal vaginal delivery; CS: Cesarean section; POP: Pelvic organ prolapse.

Table 2. Frequency of LUTS in study populations

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency</td>
<td>139 (81.8)</td>
<td>31 (18.2)</td>
</tr>
<tr>
<td>Nocturia</td>
<td>59 (34.7)</td>
<td>111 (85.3)</td>
</tr>
<tr>
<td>2-times</td>
<td>8 (19.0)</td>
<td></td>
</tr>
<tr>
<td>3-times</td>
<td>7 (16.7)</td>
<td></td>
</tr>
<tr>
<td>4-times</td>
<td>21 (50.0)</td>
<td></td>
</tr>
<tr>
<td>8-times</td>
<td>6 (14.3)</td>
<td></td>
</tr>
<tr>
<td>Recurrent UTI</td>
<td>4 (2.4)</td>
<td>166 (97.6)</td>
</tr>
<tr>
<td>Lower urinary tract infection</td>
<td>15 (8.8)</td>
<td>155 (91.2)</td>
</tr>
<tr>
<td>Weak stream</td>
<td>0 (0.0)</td>
<td>170 (100.0)</td>
</tr>
<tr>
<td>Hematuria</td>
<td>0 (0.0)</td>
<td>170 (100.0)</td>
</tr>
<tr>
<td>Coital incontinence</td>
<td>8 (4.7)</td>
<td>162 (95.3)</td>
</tr>
<tr>
<td>Urgency</td>
<td>39 (22.9)</td>
<td></td>
</tr>
<tr>
<td>Often</td>
<td>44 (25.9)</td>
<td></td>
</tr>
<tr>
<td>Most of the time</td>
<td>85 (50.0)</td>
<td></td>
</tr>
<tr>
<td>UII</td>
<td>3 (1.8)</td>
<td></td>
</tr>
<tr>
<td>Once in a while</td>
<td>38 (22.4)</td>
<td></td>
</tr>
<tr>
<td>Most of the time</td>
<td>123 (72.4)</td>
<td></td>
</tr>
<tr>
<td>UI during lifting</td>
<td>8 (4.7)</td>
<td></td>
</tr>
<tr>
<td>(UU)I</td>
<td>100 (58.8)</td>
<td></td>
</tr>
<tr>
<td>Most of the time</td>
<td>55 (32.4)</td>
<td></td>
</tr>
<tr>
<td>UI during exercise</td>
<td>10 (5.9)</td>
<td></td>
</tr>
<tr>
<td>Most of the time</td>
<td>58 (34.1)</td>
<td></td>
</tr>
<tr>
<td>UTI: urinary tract infection</td>
<td>90 (52.9)</td>
<td></td>
</tr>
</tbody>
</table>

UTI: urinary tract infection.
and SUI. The only agreement was observed between the urinary frequency, and voiding phase symptoms (Cohen kappa: 0.124; P value = 0.003) (Tables 4-6).

**Detrusor overactivity**

According to the results, 86 women had DO, with 315.1 (127.7) mL of bladder capacity, and 35.81 (45.80) mL of PVR. The result showed that the odds of DO in women with a VLPP < 60 cmH2O is 75% lower than in the non-leak group (OR [95% CI]: 0.25 [0.06-0.99]; P = 0.049). In the cases with VLPP between 60 and 90 cmH2O, this odd was 78% lower than in the group without leak (OR [95% CI]: 0.22 [0.07-0.74]; P = 0.015).

In terms of filling cystometry, the results showed that for every 10-cc increase in bladder capacity, the odds of DO decrease by 3% (OR [95% CI]: 0.997 [0.995-0.999]; P = 0.017).

The chance of DO in patients with hypermotility of the urethra is 74% lower than in women without hypermotility (OR [95% CI]: 0.26 [0.13-0.49]; P < 0.001).

In addition, the odds of DO in individuals with a positive cough test were 70% lower than in cases with a negative cough test (OR [95% CI]: 0.30 [0.16-0.58]; P = 0.001).

**Bladder hypersensitivity**

Bladder hypersensitivity was detected in 13 women. These findings had higher odds to occur in women with a history of 2 or more cesarean sections than women without a history of cesarean section (OR [95% CI]: 3.94 [1.10-14.07]; P = 0.035).

Women who often had urine leak during sneezing and coughing are 76% less likely to have hypersensitivity than individuals with urine incontinence once in a while (OR [95% CI]: 0.24 [0.06-0.93]; P = 0.039).

In addition, the odds of hypersensitivity in cases with wet clothes while bending over or lifting something
heavy was often 98% lower than in women without this symptom (OR [95% CI]: 0.02 (0.001-0.74); \(P=0.033\)).

Women with a positive cough test have a 79% lower chance of hypersensitivity than women with a negative cough test (OR [95% CI]: 0.21 [0.06-0.78]; \(P=0.020\)).

Voiding phase symptoms
Nine women out of 170 had voiding phase symptoms according to the results of urodynamics. However, the results of the regression model didn’t find any association between urodynamic parameters as well as demographic or midwifery parameters such as Gravida/Parity, abortion, live birth, and the history of normal vaginal delivery (NVD) or cesarean section (CS) with the obstructive disorder.

Sensitivity, specificity, PPV, and NPV
We calculated a sensitivity of 75%, specificity of 78.3%, PPV of 86.3%, and 63.2% NPV for SUI symptoms in relation to corresponding urodynamic SUI findings based on the patient’s symptoms and urodynamic data.

Discussion
The urodynamic test, although intrusive and expensive, is the "gold standard" for UI diagnosis, even if clinical history is the initial diagnostic technique. Urodynamics, however, is not available to many patients, and some women, particularly in low-income countries, are reluctant to undergo this method due to its expense. Consequently, the current study’s objectives were to assess the consistency between urodynamic findings and the symptoms of MUI patients as well as the predictive power of clinical history in comparison to urodynamic data. Our results demonstrated a sensitivity of 75%, specificity of 78.3%, PPV of 86.3%, and NPV of 63.2% for SUI symptoms when compared to equivalent urodynamic data.
SUI findings. The only association between LUTS was found between urine frequency and symptoms during the voiding phase. Also, among the 170 included women with MUI, the probabilities of DO were 75% and 78% lower in instances with a Valsalva leak point pressure (VLPP) between 60 and 90 cmH2O as compared to the group without a leak, respectively. In terms of filling cystometry, the results showed that for every 10-cc increase in bladder capacity, the odds of DO decrease by 3%. The chance of DO in patients with hypermotility of the urethra was lower in than in cases without hypermotility. In the cases with a positive cough test, the odds of DO, and hypersensitivity were lower than in the women with a negative cough test.

Women with a history of two or more cesarean sections had a higher likelihood of developing bladder hypersensitivity than women without a history of cesarean sections. Women who frequently leaked urine when coughing and sneezing were 76% less likely to have hypersensitivity than those who just occasionally did so. Also, the likelihood of hypersensitivity was frequently lower in women with damp garments than in women who weren’t experiencing this symptom when bending over and lifting anything heavy.

Urodynamics offers factual data on the occurrence of LUTS, which can be used to evaluate a person’s lower urinary tract function (LUT) in connection to what is known about the normal or pathological physiology of the urinary tract. The primary goal of treatment for lower urinary tract dysfunction (LUTD) is symptom relief. LUTS may be associated with a number of pathophysiological processes, although symptom-based diagnosis is frequently incorrect, particularly in patients with neurogenic LUTD. Hence, gathering objective data is crucial for a precise diagnosis.

Although LUTS do not correlate well with the diagnosis provided by urodynamic study (UDS), previous studies have demonstrated a weak link between leak point pressure (LPP) and the severity of measurable or symptomatic UI as well as a weak correlation between symptoms and the results of UDS (particularly cystometry) in individuals with UI. Regular, non-invasive testing such as uroflowmetry and residual urine measurement are available for LUTS patients. Other UDSs are invasive tests and should only be used in specific situations, such as when conservative treatment is ineffective or when considering invasive treatment, to control the UI and protect the upper urinary tract by creating a low-pressure reservoir, to evaluate the therapeutic effects, and to engage in biofeedback training.

DO is found in 10%–20% of healthy participants with normal UDS. When the patient is sitting up during cystometry, it has been seen to happen more frequently than when they are supine. The patient’s position during the filling cystometry should be considered as a result, since it may affect the possibility of DO. Results from provocative cystometry should be interpreted in the context of the patient’s symptoms and the plausibility of the findings. Women with a VLPP of 60 cmH2O had 75% lower odds of developing DO than those in the non-leak group. In comparison to the group without leak, this odd was 78% lower in the cases with VLPP between 60 and 90 cmH2O. In the absence of detrusor contraction, VLPP is defined by the ICS as intra-bladder pressure that is larger than the mechanism of restraint and results in urine leakage. It is established that LPP is a helpful technique for determining the severity of SUI, the effectiveness of treatment, and the presence of an internal sphincter deficiency that is clinically significant, especially before deciding on surgical correction for SUI. Given that 76% of women with SUI type III had VLPP values < 60 cm H2O, it has been suggested that VLPP be used to diagnose SUI type III. Women in the prior study who had a VLPP of more than 90 cm H2O had type II SUI.

In terms of filling cystometry, the results showed that for every 10-cc increase in bladder capacity, the odds of DO decrease by 3%. In addition, the chance of DO in patients with hypermotility of the urethra is 74% lower than in women without hypermotility. From a highly dynamic urethra with good internal function to a sedentary urethra with poor internal function, patients with SUI exhibit a variety of urethral traits. Although the term “a poor intrinsic function of the urethra” is misleading, this ailment is nevertheless referred to as an internal sphincter deficiency.

In the present investigation, cases with a positive cough test had odds of DO that were 70% lower than cases with a negative cough test. The other finding concerned the fact that women with a history of two or more cesarean sections had a higher rate of bladder hypersensitivity than women without such a history. It is undeniable fact that urinary symptoms worsen in late pregnancy and after delivery, but the exact reason why this can be the case isn’t always clear because it may be caused by a number of different factors. The etiology of LUTS during pregnancy and postpartum, as well as whether a baby’s delivery method can affect the likelihood that urinary symptoms will manifest, are additional topics of discussion. For all UI types, prevalence estimates from studies done during pregnancy range from 32% to 64%, and for UI stress, including mixed incontinence, which affects 6% to 29% of postpartum patients, they range from 40% to 59%. Estimating the prevalence of postpartum UI is challenging since it may vary depending on the number of prior deliveries, the delivery type, and the history of past incontinence.

Research suggests that it may become more common with age and reproduction, although the exact mechanisms are yet unknown. Our results showed that women who had often urine leaks during sneezing and coughing are 76% less likely to have hypersensitivity than individuals with one in a while. In addition, the odds of hypersensitivity in cases
with wet clothes while bending over and lifting something heavy was often 98% lower than in women without this symptom. Women with a positive cough test have a 79% lower chance of hypersensitivity than women with a negative cough test, which was in accordance with the published evidence.

A systematic review evaluated the association between urodynamic findings and LUTS in cerebral palsy patients and reported that excluding hesitancy, there were no clear differences in LUTS, and urodynamic findings between children and adults. In the present study, we didn’t find any agreement between various LUTS and urodynamic findings, except for a slight agreement for frequency and voiding phase symptoms ($P = 0.003$).

Since POPs and associated urinary symptoms are common disorders among older women that need to be treated to increase life expectancy and improve QoL, it is important for the patient to complain and discover the hidden cases of incontinence, especially in the elderly, as well as with POPs cases. Due to the lack of access of a number of patients with incontinence to this functional test, as well as the cost and time of UDS and also the unwillingness of a group of patients to perform this test, determining the priority of performing urodynamics in patients with MUI is essential, and either performing this test may be helpful in completing the diagnostic process along with the patient’s history. For example, in the cases where they have urge incontinence symptoms and no DO on UDS, we do not change the patients’ diagnosis if UDS findings did not describe the patient’s symptoms. In the current study, we just looked for any agreement between the clinical symptoms and urodynamic findings, however, except for the urinary frequency and voiding phase symptoms, we couldn’t find any strong agreement between the symptoms and UDS findings that may be due to the small size of our eligible patients. In light of our findings, additional LUTS performed poorly as urodynamic findings predictions. This demonstrates how important urodynamic evaluation is in determining bladder function and providing helpful data to patient counseling in order to develop the best possible treatment recommendations. Since no comprehensive study has been conducted on the correlation between the symptoms of patients with MUI and urodynamic findings in our setting, the necessity to conduct large clinical studies is recommended. However, we should consider that repeating urodynamics after prolapse correction may lead to different results.

**Conclusion**

The most frequent LUTS among MUI patients were urgency, frequency, and nocturia. In relation to corresponding urodynamic SUI data, we calculated a sensitivity of 75%, a specificity of 78.3%, a PPV of 86.3%, and an NPV of 63.2% for SUI symptoms. According to the results, there was no agreement between the symptoms of patients with MUI and bladder hypersensitivity, DO, and SUI. The only slight agreement was observed between the urinary frequency and voiding phase symptoms. Since no comprehensive study has been conducted on the correlation between the symptoms of patients with MUI and urodynamic findings in our setting, the necessity to conduct large clinical studies is recommended.

**Study Highlights**

**What is current knowledge?**
- Mixed urinary incontinence (MUI) is one of the most common problems of middle-aged women.
- Treatment is necessary for the improvement of quality of life.
- Agreement between the symptoms of patients with MUI and urodynamic findings is unclear.

**What is new here?**
- There was no agreement between the symptoms of patients with MUI and bladder hypersensitivity and detrusor overactivity.
- There was no agreement between the symptoms of patients with MUI and Stress urinary incontinence (SUI).
- The only agreement was observed between the urinary frequency and voiding phase symptoms.

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- **Data curation**: Fatemeh Mallah, Parvin Bastani.
- **Formal analysis**: Hanieh Salehi-Pourmehr.
- **Investigation**: Fatemeh Mallah, Parvin Bastani.
- **Methodology**: Fatemeh Mallah, Parvin Bastani, Aila Kari.
- **Project administration**: Fatemeh Mallah, Aila Kari.
- **Resources**: Hanieh Salehi-Pourmehr, Ehsan Sepehran.
- **Software**: Hanieh Salehi-Pourmehr, Ehsan Sepehran.
- **Supervision**: Fatemeh Mallah, Parvin Bastani.
- **Validation**: Fatemeh Mallah, Parvin Bastani.
- **Visualization**: Fatemeh Mallah, Parvin Bastani.
- **Writing–original draft**: Aila Kari, Hanieh Salehi-Pourmehr, Ehsan Sepehran.
- **Writing–review & editing**: All authors.

**Competing Interests**

The authors declare no conflict of interest.

**Ethical Approval**

The regional ethics committee of Tabriz University of Medical Sciences approved this study. (IR.TBZMED.REC.1400.1085).

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