Linguistic and Clinical Validation of The Persian Acute Cystitis Symptom Score in Farsi-Speaking Women

Kamaleddin Hassanzadeh[1], Nasim Sharifzadeh[2], Mohsen Mohammadrahimi[3]*, Kurt G. Naber[4], Jakhongir Alidjanov[5], Adrian Pilatz[6], Florian M. Wagenlehner[7], Kavous Shahsavarinia[8], Hanieh Salehi-Pourmehr[9]*, Sakineh Hajebrahimi[10]

Purpose: Uncomplicated acute cystitis (uAC) is a prevalent condition among women that imposes both physical and psychological burdens. The Acute Cystitis Symptom Score (ACSS) was developed to improve the clinical diagnosis and assessment of patient-reported treatment outcomes in women with uAC. Given the lack of a validated instrument in Farsi, this study aimed to develop and validate a Persian version of the ACSS to support diagnostic accuracy and research in Farsi-speaking populations.

Materials and Methods: The Persian ACSS underwent linguistic validation strictly following international manuals and recommendations approved by the relevant authorities, and its reliability and validity were assessed.

Results: The study involved 100 Farsi-speaking women with varying levels of education, including 50 patients diagnosed with uAC and 50 control participants (controls). The mean (standard deviation) age of the patients was 41.0 (8.0) years and did not differ statistically from that of the controls (39.9 [9.8] years). Using a predefined cutoff score of $\geq$ 6 in the "Typical" domain, receiver operating characteristic curve analysis demonstrated a sensitivity of 96% and a specificity of 96% for diagnosing uAC. Among the 40 patients who attended the follow-up visit, symptom severity and quality of life improved significantly, although the scores of some items did not reach the levels observed in controls at baseline.

Conclusion: The Persian ACSS is a valid and reliable tool with high diagnostic accuracy and utility for monitoring treatment outcomes in women with uAC. It fills a critical gap and may serve as a valuable instrument for epidemiological and clinical studies among Farsi-speaking women.

Keywords: cystitis; female; urinary tract infections; surveys and questionnaires; Acute Cystitis Symptom Score; ACSS

INTRODUCTION

Uncomplicated acute cystitis (uAC), one of the most widespread infectious conditions in women, has a significant impact on daily activities and mental well-being owing to its distressing symptoms.[1–3] According to the European Association of Urology (EAU) guidelines, uAC is defined as acute, sporadic, or recurrent cystitis limited to nonpregnant women with no known relevant anatomical or functional abnormalities of the urinary tract and no comorbidities. The diagnosis can be made with high probability based on a focused history of lower urinary tract symptoms (dysuria, frequency, and urgency) and the absence of vaginal discharge.[4] Therefore, general practitioners often prescribe treatment based solely on telephone consulta-

[1]Department of Urology, Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran. E-mail: drhassanzadehka@yahoo.com.
[2]Student Research Committee, Tabriz University of Medical Sciences, Tabriz, Iran. E-mail: nasimsharifzade99@gmail.com.
[3]Department of Urology, Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran. E-mail: Mohammadrahimi@tbzmed.ac.ir.
[4]Department of Urology, Technical University of Munich, 80333 Munich, Germany. E-mail: kurt@nbers.de.
[5]Clinic of Urology, Pediatric Urology and Andrology, Justus Liebig University Giessen, 35390 Giessen, Germany. E-mail: jakhongir.alidjanov@gmail.com.
[6]Clinic of Urology, Pediatric Urology and Andrology, Justus Liebig University Giessen, 35390 Giessen, Germany. E-mail: adrian.pilatz@chiru.med.uni-giessen.de.
[7]Clinic of Urology, Pediatric Urology and Andrology, Justus Liebig University Giessen, 35390 Giessen, Germany. E-mail: Florian.Wagenlehner@chiru.med.uni-giessen.de.
[8]Research Center for Evidence-Based Medicine, Iranian EBM Centre: A JBI Centre of Excellence, Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran. E-mail: kavous.shahsavari@yahoo.com.
[9]Research Center for Evidence-Based Medicine, Iranian EBM Centre: A JBI Centre of Excellence, Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran. E-mail: poormehrh@yahoo.com.
[10]Research Center for Evidence-Based Medicine, Iranian EBM Centre: A JBI Centre of Excellence, Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran. E-mail: hajebrahimis@gmail.com.
*Correspondence: Research Center for Evidence-Based Medicine, Faculty of Medicine, Tabriz University of Medical Sciences, Azadi Street, Golgasht Avenue, Tabriz, East Azerbaijan, Iran. Postal code: 51666/15731
Tel: +98 914 310 9053; Fax: +98 41 3334 2219. E-mail: poormehrh@yahoo.com; salehiha@tbzmed.ac.ir.
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Table 1A. Persian ACSS© questionnaire (Part A, diagnostic form).

پرسشنامه نمره‌دهی علایم سیستیت حاد نسخه فارسی

اولین معاینه– قسمت الف

فرم تشخیصی

ساعت و تاریخ ارزیابی

لطفا تعیین کنید که آیا علایم زیر را طی ۲۴ ساعت گذشته داشته اید و شدت آن علایم چقدر بوده است ؟ لطفا فقط یکی از جواب ها را برای هر شکایت علامت بزنید

		۰	۱	۲	۳
علایم تیپیک (معمول)	۱ تکرر ادراری با حجم ادراری کم (مراجعه به توالت به دفعات زیاد)	خیر	بلی (خفیف) تا ٤ بار در روز	بلی (متوسط) ٥تا٦ بار در روز	بلی (شدید) ۷تا۸ بار در روز
	۲ ادرار کردن فوریتی (میل فوری به ادرار کردن بطور ناگهانی و غیر قابل کنترل)	خیر	بلی (خفیف)	بلی (متوسط)	بلی (شدید) ۹تا۱۰ بار در روز
	۳ احساس درد سوزشی موقع ادرار کردن	خیر	بلی (خفیف)	بلی (متوسط)	بلی (شدید)
	٤ احساس عدم تخلیه کامل مثانه (بعد از ادرار کردن احساس ادرار کردن مجدد دارید)	خیر	بلی (خفیف)	بلی (متوسط)	بلی (شدید)
	٥ احساس درد در قسمت تحتانی شکم که ربطی به ادرار کردن ندارد	خیر	بلی (خفیف)	بلی (متوسط)	بلی (شدید)
	٦ وجود خون در ادرار (بدون قاعدگی)	خیر	بلی (خفیف)	بلی (متوسط)	بلی (شدید)
	جمع نتایج "علایم تیپیک"=	امتیاز			
افتراق دهنده ها	۷ درد پهلو (درد یکطرفه یا دوطرفه در قسمت تحتانی پشت)	خیر	بلی (خفیف)	بلی (متوسط)	بلی (شدید)
	۸ ترشح غیرطبیعی واژینال	خیر	بلی (خفیف)	بلی (متوسط)	بلی (شدید)
	۹ ترشح از پیشابراه (سوراخ خروجی پیشابراه)که ربطی به ادرار کردن ندارد	خیر	بلی (خفیف)	بلی (متوسط)	بلی (شدید)
	۱۰ تب/درجه حرارت بالای بدن (لطفا اگر اندازه گیری شده علامت بزنید)	خیر (≤37,5 °C)	بلی (خفیف) (37,6–37,9 °C)	بلی (متوسط) (38,0–38,9 °C)	بلی (شدید) (≥39,0 °C)
	جمع نتایج "افتراق دهنده ها"=	امتیاز			

لطفا تعیین کنید که بخاطر شکایاتتان در ۲۴ ساعت گذشته چقدر ناراحتی تحمل کرده اید ؟ لطفا فقط یکی از گزینه ها را که با شرایط شما مناسب تر است علامت بزنید

کیفیت زندگی

۱۱
۰ - هیچ ناراحتی احساس نشده است (هیچ علامت و شکایتی وجود ندارد .من طبق معمول خوب هستم.)
۱-احساس ناراحتی خفیف دارم.(من نسبت به روزهای معمول تا حدی بدتر هستم)
۲- احساس ناراحتی متوسط دارم (من خودم را کاملا بد حس میکنم)
۳- احساس ناراحتی شدید دارم (احساس من وحشتناک است)

۱۲ لطفا تعیین کنید که شکایات و علایم شما در ۲۴ ساعت گذشته چقدر در فعالیت ها و کار روزمره شما تداخل کرده است ؟ لطفا فقط یکی از گزینه ها را که با شرایط شما مناسب تر است علامت بزنید.

۰-اصلا تداخل نکرده است (طبق معمول روزانه کار می کنم)
۱-تداخل کم داشته است (کارکردن توام با مختصر ناراحتی بوده است)
۲- تداخل متوسط (انجام کار روزانه نیاز به تلاش بیشتری داشت)
۳-تداخل شدید (کار روزانه یا انجام فعالیت ها غیر ممکن شده است)

۱۳ لطفا تعیین کنید که شکایات و علایم شما در ۲۴ ساعت گذشته چقدر در عفالیت های اجتماعی شما اثر گذاشته است (مثل دیدار مردم و ملاقات با دوستان) لطفا فقط یکی از گزینه ها را علامت بزنید
۰- اصلا تداخل نداشته است (قادر به لذت بردن از فعالیت های اجتماعی نرمال هستم)
۱- تداخل کم(فعالیت های اجتماعی کمتر از معمول)
۲- تداخل متوسط(مجبورم بیشتر در خانه بمانم)
۳- تداخل شدید(علایم نمی گذارند از خانه بیرون برم)

جمع نتایج "کیفیت زندگی"= امتیاز

لطفا تعیین کنید که آیا علایم زیر را موقع کامل کردن پرسشنامه داشته اید ؟

سایر	۱٤ قاعدگی	خیر	بلی
	علایم قبل از قاعدگی (سندرم PMS)	خیر	بلی
	علایم سندردم منوپوز (مثل گر گرفتگی)	خیر	بلی
	حاملگی	خیر	بلی
	دیابت شیریت تشخیص داده شده (قند خون بالا)	خیر	بلی

tions, addressing the patient's concerns and symptoms.[5]

Despite the central role of symptom assessment in diagnosing uAC, no validated Farsi-language instrument has previously existed to standardize the evaluation of acute cystitis symptoms, assess disease severity, or monitor treatment outcomes. The absence of a validated tool creates important clinical and research gaps, including inconsistency in diagnostic decision-making, limited ability to stratify symptom severity, and difficulty in comparing treatment outcomes across studies or clinical settings in Farsi-speaking populations.

The Acute Cystitis Symptom Score (ACSS) is a self-administered questionnaire developed to assist and improve the clinical diagnosis and management of uAC in women and to monitor their patient-reported treatment outcomes.[6] Originally created in the Uzbek and Russian languages,[6,7] the ACSS has shown high reliability, validity, and discriminatory ability and has since been translated into 15 other languages (https://acss.world/). The primary aim of the current study was to produce a linguistically and clinically validated Persian (Farsi) version of the ACSS and to evaluate its psychometric performance, including reliability, validity, and diag-

Table 1B. Persian ACSS© questionnaire (Part B, follow-up form).

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معاینه کنترل– قسمت ب (پیامدهای گزارش شده توسط بیمار) ساعت و تاریخ ارزیابی
فرم پیگیری
لطفاً مشخص کنید که آیا از اولین باری که این پرسشنامه را تکمیل کرده اید، تغییراتی در علائم خود داشته اید:
۰- بله احساس می کنم طبیعی هستم (همه علائم از بین رفته اند)
۱- بله، احساس خیلی بهتری دارم (بیشتر علائم از بین رفته اند)
۲-بله، تا حدودی احساس بهتری دارم (فقط برخی علائم از بین رفته اند)
۳- خیر، به سختی هیچ تغییری وجود دارد (من هنوز هم تقریباً همان علائم را دارم)
٤- بله، احساس بدتری دارم (وضعیت من بدتر است).
تمامی سوالات قسمت الف تکرار خواهند شد.

Abbreviation: ACSS, Acute Cystitis Symptom Score.

nostic accuracy, among Farsi-speaking women.

MATERIALS AND METHODS

Study Design

This prospective observational study, with cross-sectional diagnostic validation and longitudinal follow-up assessment, was conducted at Imam Reza General Hospital, Tabriz, Iran. The study was approved by the regional ethics committee of Tabriz University of Medical Sciences (approval number: IR.TBZMED.REC.1403.065).

Study Tool

The ACSS comprises 18 items categorized into 4 domains: typical symptoms ("Typical"), differential symptoms ("Differential"), quality of life ("QoL"), and additional conditions ("Additional"). The follow-up Part B of the ACSS also includes the "Dynamics" domain for patient self-report of the overall posttreatment outcome. Items in the "Typical," "Differential," and "QoL" domains are rated on a Likert-type scale to assess symptom severity, whereas items in the "Additional" domain require binary "Yes/No" responses. On the Likert-type scale, symptoms are rated from 0 to 3 as "no symptom," "mild," "moderate," and "severe." The "Dynamics" domain consists of 5 responses (rated from 0 to 4) on the current state of well-being: "feeling back to normal," "much better," "somewhat better," "barely any changes," and "feeling worse."[8] In this study, the "Dynamics" domain was used to define a successful clinical outcome, which was classified as patients reporting that they felt "back to normal" or "much better." This definition aligns with international ACSS validation protocols.

Translation and Linguistic Validation of the ACSS

The process of translation and linguistic validation of the Persian ACSS was carried out in accordance with the "Linguistic Validation Manual for Patient-Reported Outcomes Instruments" and was similar to that applied in our previous studies.[9]

To translate the American English master version of the ACSS[8] into the Persian target language, 2 native Farsi-speaking translators, both specialized in English and with expertise in cystitis, worked independently. On completion of their forward translations, the translators were unblinded and merged their versions into a single unified document. The unified version was back-translated into American English by another independent translator fluent in English. The master and back-translated English versions were then compared. All identified discrepancies were resolved through group discussions, and all resulting corrections led to revisions of the Persian version. The final version of the Persian ACSS was reviewed by the research authorities for feedback on its content, clarity, and simplicity (**Tables 1A and 1B**).

Content Validity Assessment

The content validity of the Persian ACSS was evaluated using both the content validity ratio (CVR) and the content validity index (CVI). A panel of 10 experts (including urologists, evidence-based medicine [EBM] specialists, and linguists) rated each item for necessity, relevance, clarity, and simplicity using a 4-point Likert scale.

The CVR was calculated using the Lawshe method, based on the following formula:

$$CVR = (ne - N/2) / (N/2)$$

Table 3. Internal consistency of the ACSS domains.

Domain	Number of items	Cronbach alpha (95% CI)
Typical	6	0.93 (0.91-0.95)
Differential	4	0.73 (0.65-0.79)
QoL	3	0.97 (0.96-0.98)
All domains of the ACSS except "Additional"	13	0.93 (0.92-0.94)

Abbreviations: ACSS, Acute Cystitis Symptom Score; CI, confidence interval; QoL, quality of life.

Table 4. Areas under the receiver operating characteristic (ROC) curve of the items and domains of the Persian ACSS.

Item/Domain	AUC (95% CI)
Frequent urination	0.99 (0.98-1.00)
Urgent urination	0.99 (0.97-1.00)
Dysuria (painful urination)	0.95 (0.90-0.99)
Sense of incomplete bladder emptying	0.97 (0.94-1.00)
Suprapubic pain	0.86 (0.79-0.93)
Visible blood in urine	0.59 (0.52-0.66)
Flank pain	0.68 (0.60-0.76)
Vaginal discharge	0.64 (0.57-0.72)
Urethral discharge	0.58 (0.52-0.64)
Sense of fever or chills	0.57 (0.50-0.64)
General discomfort	0.93 (0.88-0.98)
Impact on everyday activities	0.94 (0.89-0.98)
Impact on social life	0.92 (0.86-0.97)
Summary score of the "Typical" domain	0.99 (0.98-1.00)
Summary score of the "Differential" domain	0.68 (0.59-0.77)
Summary score of the "QoL" domain	0.95 (0.91-0.99)

Abbreviations: ACSS, Acute Cystitis Symptom Score; AUC, area under the curve; CI, confidence interval; QoL, quality of life.

where ne represents the number of experts rating an item as "essential" and N is the total number of experts. According to the Lawshe table, a CVR $\geq$ 0.62 was considered acceptable for 10 experts.

The CVI was computed at both the item level (I-CVI) and the scale level (S-CVI/Ave, average method). Items with an I-CVI $\geq$ 0.78 and an overall S-CVI/Ave $\geq$ 0.90 were deemed to have excellent content validity. Discrepancies were discussed, and items with lower ratings were revised before finalization.

Sample Size Justification

Although a formal sample size calculation was not conducted before recruitment, the selected sample (n = 100; 50 patients and 50 controls) is consistent with widely accepted recommendations for questionnaire validation studies, which typically require 5 to 10 participants per item and a minimum of 100 respondents for stable factor analysis. The chosen sample size also aligns with several previous ACSS validation studies. A post hoc power analysis confirmed that the achieved sample provided excellent statistical power (>97%) across domains.

Study Definitions, Study Population, and Group Allocation

In this study, uAC was defined based on patient-reported symptoms, interviews, physical examination findings, urinalysis, and urine culture. Urine samples were tested for common uropathogenic bacteria and yeasts, and a colony count of $\geq$ 105 colony-forming units (CFU)/mL was considered significant for microbiological diagnosis.

Farsi-speaking women aged 18 years or older were recruited for the study. Patients presenting with typical uAC symptoms at the time of admission to Imam Reza General Hospital, whose diagnosis was subsequently confirmed microbiologically, were included in the patient group. Urinalysis and urine culture were performed before and after treatment, which was administered according to the EAU guidelines on urological infections.[4]

The control group comprised women attending various departments of Imam Reza General Hospital who had no suspicion of urinary tract infection (UTI) and were managed according to the relevant guidelines and standards. Exclusion criteria included diabetes mellitus and the use of pharmacological or herbal treatments. All respondents were asked to complete the linguistically validated Persian version of the ACSS.

Two urologists were involved in the double-blinded group allocation process: one was blinded to the ACSS results, whereas the other was blinded to all investigations except the ACSS results.

Statistical Analysis

The internal consistency of the Persian ACSS was assessed using the Cronbach alpha and split-half reliability with the Spearman rank correlation coefficient.

In addition to the Cronbach alpha, the intraclass correlation coefficient (ICC) was calculated to evaluate test-retest reliability. The ICC was computed using a 2-way random-effects model (average measures). ICC values above 0.75 were considered indicative of good reliability, whereas values above 0.90 represented excellent reliability.

The construct validity of the Persian ACSS was assessed through exploratory factor analysis (EFA) using principal component analysis (PCA) with varimax rotation. Sampling adequacy was verified using the Kaiser-Meyer-Olkin (KMO) statistic, and the Bartlett test of sphericity confirmed the appropriateness of the data for factor analysis. Factors with eigenvalues >1 were retained, and items with factor loadings $\geq$ 0.40 were considered significant.

The number of extracted factors was determined using the Kaiser criterion (eigenvalues >1) and by visual inspection of the scree plot to identify the point at which

Table 5. Diagnostic metrics at different cutoff points for the "Typical" summary score of the Persian ACSS.

Parameter	Cutoff point of the summary score of the "Typical" domain	
	5 and higher	6 and higher
True-negative count	47	48
True-positive count	49	48
False-negative count	1	2
False-positive count	3	2
Diagnostic odds ratio divided by 100	7.68	5.76
Sensitivity (95% CI)	0.98 (0.94-1.00)	0.96 (0.90-1.00)
Specificity (95% CI)	0.94 (0.86-1.00)	0.96 (0.90-1.00)
Accuracy (95% CI)	0.96 (0.92-0.99)	0.96 (0.92-0.99)
Negative predictive value (95% CI)	0.98 (0.94-1.00)	0.96 (0.90-1.00)
Positive predictive value (95% CI)	0.94 (0.88-1.00)	0.96 (0.91-1.00)
Precision (95% CI)	0.94 (0.88-1.00)	0.96 (0.91-1.00)
False discovery rate (95% CI)	0.06 (0.00-0.12)	0.04 (0.00-0.10)
Youden index (95% CI)	0.92 (0.84-0.98)	0.92 (0.84-0.98)
Distance to the top left corner of the ROC space (95% CI)	0.00 (0.00-0.02)	0.00 (0.00-0.02)

Abbreviations: ACSS, Acute Cystitis Symptom Score; CI, confidence interval; ROC, receiver operating characteristic.

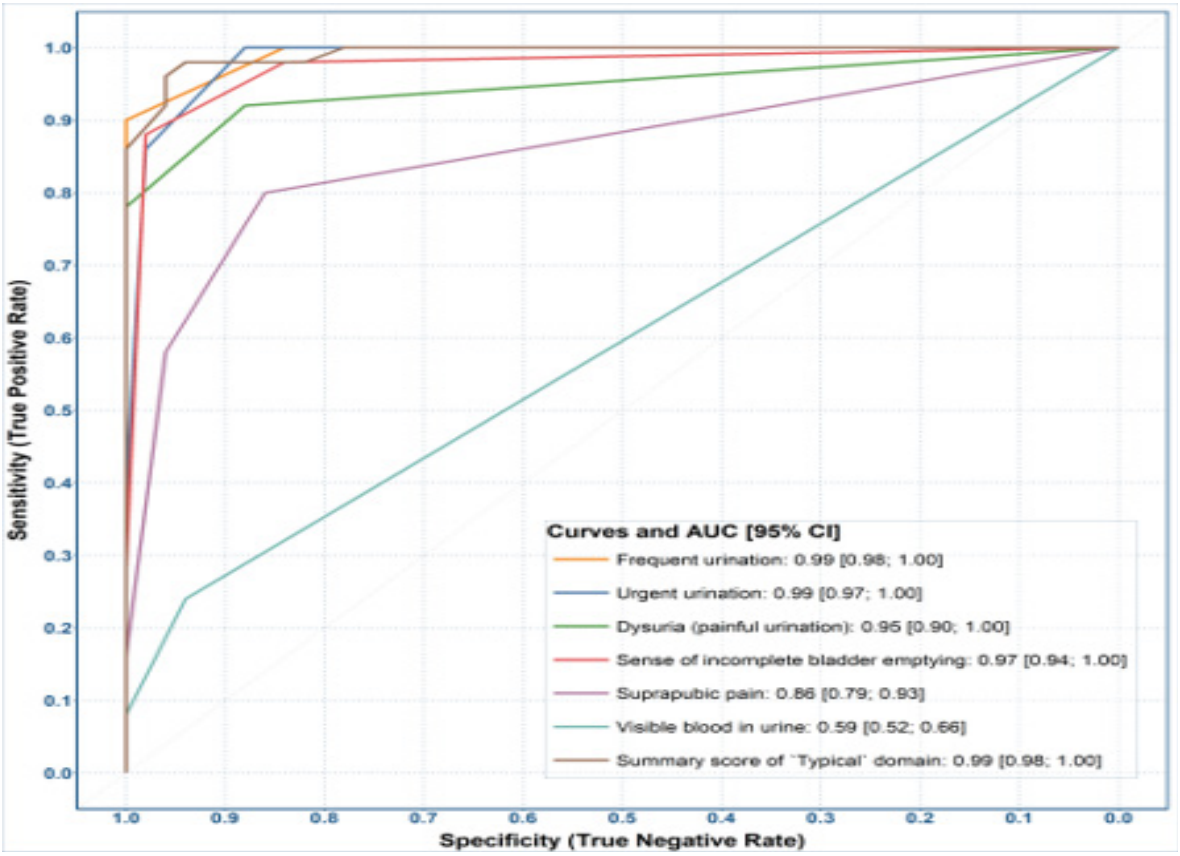


Figure 1. Receiver operating characteristic (ROC) analysis of the "Typical" domain score at baseline (BL) (controls, n = 50; patients at BL, n = 50).

the curve flattened (the "elbow" criterion).

The diagnostic performance of the Persian ACSS was assessed using specificity, sensitivity, the Youden index, accuracy, receiver operating characteristic (ROC) curve analysis, and other relevant diagnostic metrics.

Continuous variables were reported as arithmetic means and medians, whereas categorical and discrete variables, including prevalence data, were presented as frequencies (percentages). Dispersion around central tendency was presented using the standard deviation (SD), interquartile range (IQR), and 95% confidence interval (CI), where appropriate.

The normality of data distribution was evaluated using the Kolmogorov-Smirnov test, complemented by visual inspection of quantile-quantile (Q-Q) plots (**Supplementary File 2; Figures S1 and S2**). For comparative analysis, we used parametric tests, including the Student t test with the Welch correction for unequal variances. For nonparametric comparisons between independent groups (controls vs patients), the χ^2 test was used for categorical and nominal variables (the underlying assumptions of no expected cell count <1 and no more than 20% of expected cell counts <5 were checked before analysis for every comparison; these assumptions were met for all variables except menopausal flushing symptoms, for which the Fisher exact test was used instead), whereas the Wilcoxon-Mann-Whitney *U* test was used for continuous and ordinal variables. Comparisons of matched groups (patients at baseline [BL] vs patients at follow-up [FU]) were conducted using the McNemar test for categorical and nominal variables and the Wilcoxon signed-rank test for continuous variables (**Supplementary File 2; Figure S3**), after visual confirmation of a reasonably symmetrical distribution of the paired differences for the Typical Symptoms, QoL, and total ACSS scores, as recommended for small samples; the differences in the Differential domain were asymmetric (zero-inflated), so the results for this domain should be interpreted with additional caution.[24]

As the sample size was not calculated before the study, we conducted a post hoc power analysis to assess the statistical power of the study.[10] The effect size for each domain was calculated using Cohen's d based on the observed means and SDs of the summary scores for the 3 domains of the Persian ACSS: "Typical," "Differential," and "QoL."[11] A sample size of 50 participants per group was assumed for the analysis.

P values were adjusted using the Benjamini-Hochberg and Bonferroni corrections, where appropriate. Statistical significance was set at a *P* value of .05.

All statistical analyses and graphical representations of the results were performed using RStudio v.2024.12.1+563 (RStudio Team) with the corresponding R packages.[12–15]

RESULTS

Post Hoc Power Analysis of the Study

Post hoc power analysis revealed that the study had adequate statistical power to detect significant differences between the patient and control groups across all 3 domains of the Persian ACSS. The calculated power



Figure 2. Box plots of the ACSS item scores obtained by controls (n = 50) and patients (n = 40) at the baseline (BL) and follow-up (FU) visits.

ranged from 0.977 to 1.00, demonstrating that the study had sufficient power (97.7% to 100%) to detect differences in symptom severity between the groups, with the largest effect size observed in the Typical Symptoms domain.

Demographics

A total of 100 women with a mean (SD) age of 40.5 (9.0) years and different levels of education participated in the study. The patient group consisted of 50 women diagnosed with uAC, with a mean (SD) age of 41.0 (8.0) years. The control group included 50 women who were not suspected of having UTI, with a mean (SD) age of 39.9 (9.8) years ($P = .556$). Age was normally distributed in both groups according to the Kolmogorov-Smirnov and Shapiro-Wilk tests (all $P > .10$), supporting the mean (SD) as the appropriate summary statistic, which was used consistently throughout this manuscript.

None of the participants in the control group had pyuria or positive nitrite results on urine dipstick testing. However, some reported urinary symptoms related to other urological conditions, such as overactive bladder, urinary stones, or interstitial cystitis. There were no cases of bladder cancer or other neoplasms in either group. More detailed demographic characteristics of the respondents are shown in **Table 2**.

All 100 participants were included in the analyses of diagnostic metrics and internal consistency of the Persian ACSS. However, 10 of the 50 patients (20%) were lost to FU and were excluded from the comparative analyses of therapeutic outcomes.

Comparative Analysis and Diagnostics

Figures 2 and 3 present box plots illustrating the individual item scores and the summary scores of the "Typical," "Differential," and "QoL" domains of the Persian ACSS, respectively. A total of 40 patients (80%) completed both the BL and FU assessments; therefore, all longitudinal analyses (BL vs FU comparisons) were based on this subgroup of 40 patients. These figures reflect that the paired data represent only those patients who attended both visits (n = 40).

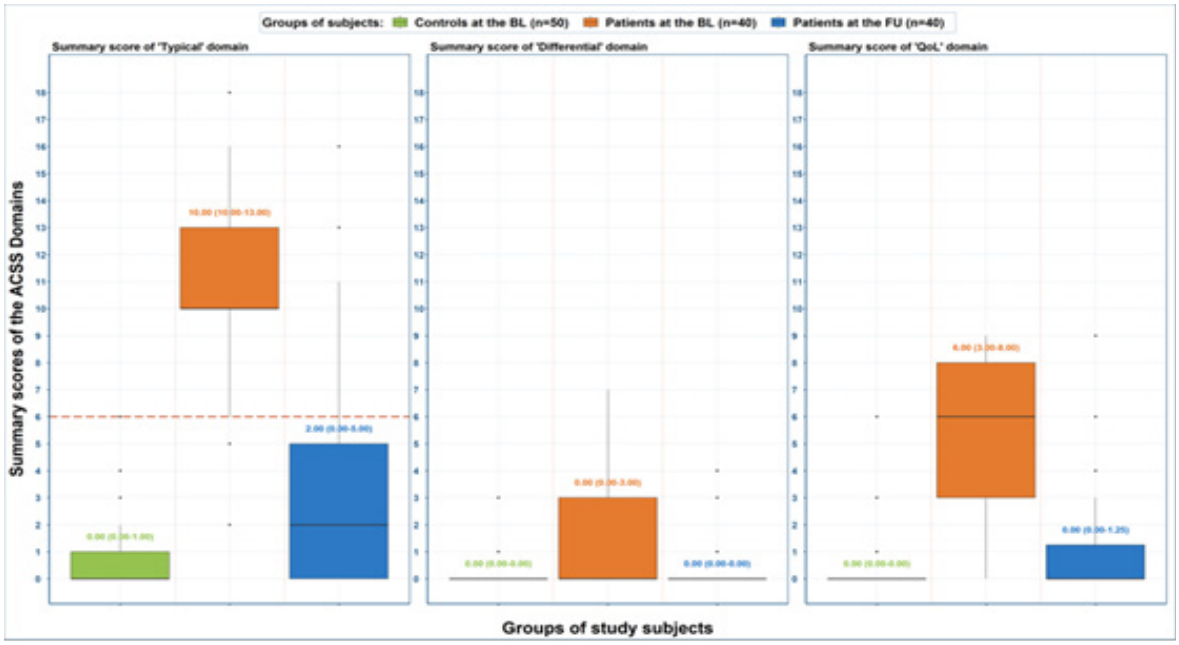
Supplementary Table 1 and Supplementary Figure 1 detail the distribution of respondents according to their responses to the Persian ACSS items across the different study visits.

Internal Consistency and Diagnostic Performance of the Persian ACSS

The internal consistency values for the 3 domains of the Persian ACSS are presented in **Table 3**.

Test-Retest Reliability and Construct Validity

The test-retest reliability of the Persian ACSS showed an ICC of 0.746 (95% CI, 0.617–0.846). Although this value meets the conventional threshold for "good" reliability according to Koo and Li (2016), it lies at the



lower boundary of this category. Nevertheless, the ICC is highly consistent with the values reported for other language versions of the ACSS, and strategies such as larger retest samples and longer test-retest intervals may help clarify and improve the stability of this estimate in future validation studies.

Exploratory factor analysis extracted 4 main components with eigenvalues greater than 1, collectively explaining 70.7% of the total variance. The first factor, corresponding to the Typical Symptoms domain, ac-

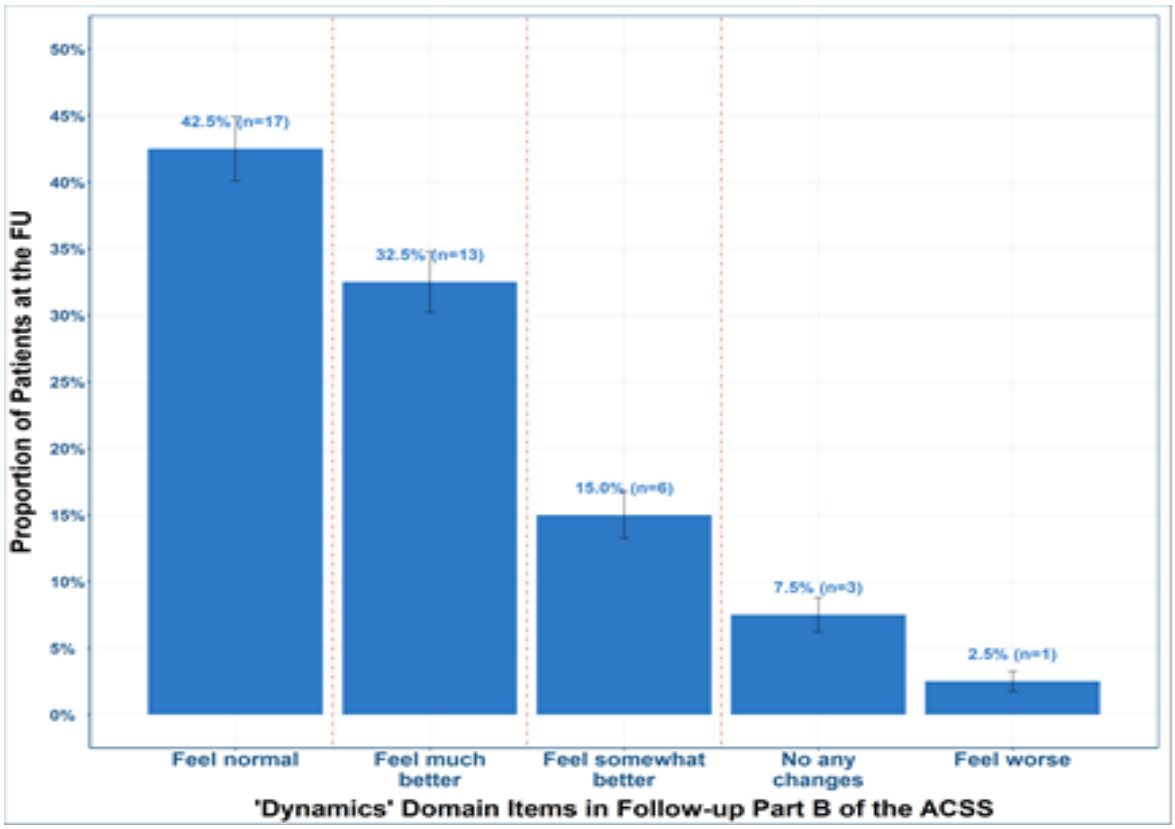


Figure 4. Overall clinical outcome in patients (n = 40) at the follow-up (FU) visit according to the "Dynamics" domain.

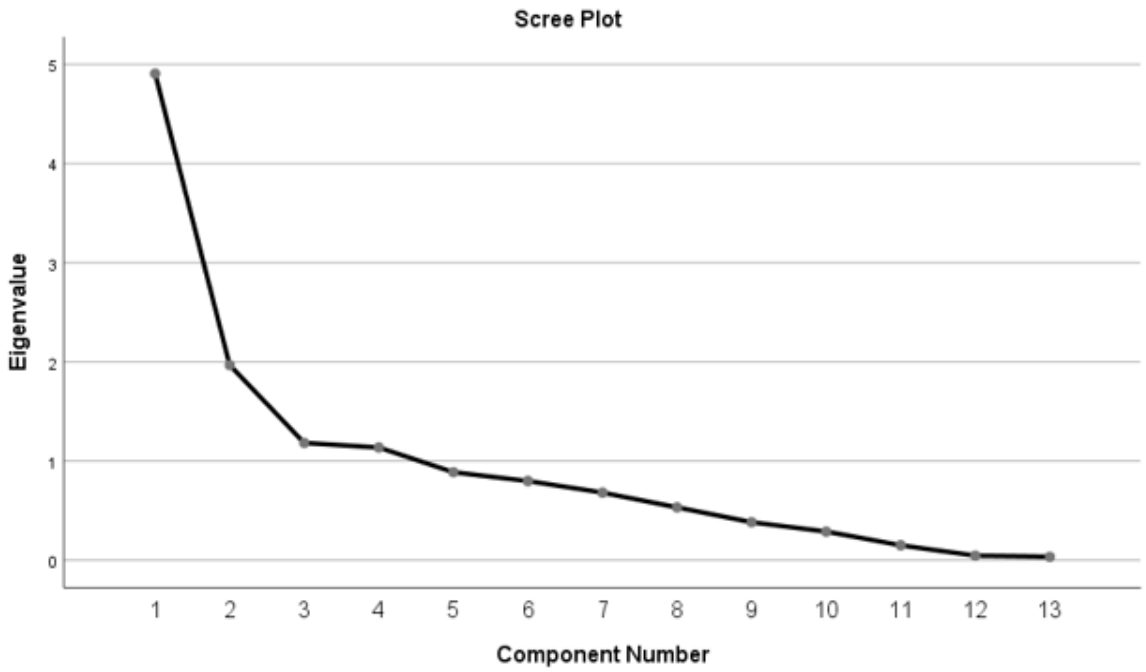


Figure 5. Scree plot of eigenvalues obtained from exploratory factor analysis (principal component analysis with varimax rotation). The clear inflection after the fourth component indicates a 4-factor solution consistent with the theoretical structure of the ACSS.

counted for 37.8% of the variance, followed by Differential Symptoms (15.1%), Quality of Life (9.1%), and Additional Conditions (8.7%).

High communalities (>0.60) were observed for most items, including frequency, urgency, dysuria, and incomplete bladder emptying, confirming their strong contributions to the underlying construct. Rotated factor loadings showed clear clustering of items consistent with the original ACSS domains, supporting the structural validity of the Persian version.

The scree plot (**Figure 5**) confirmed the presence of 4 dominant factors, showing a clear inflection point after the fourth component. This pattern supported the retention of 4 factors corresponding to the conceptual domains of the ACSS (Typical Symptoms, Differential Symptoms, Quality of Life, and Additional Conditions). The steep decline in eigenvalues before the elbow point and the gradual leveling afterward indicated that these 4 components captured the major proportion of the total variance (70.7%), whereas additional components contributed minimally.

Content Validity

The expert panel confirmed the excellent content validity of the Persian ACSS. The CVR values for individual items ranged from 0.70 to 1.00, exceeding the minimum acceptable threshold of 0.62 for 10 experts.

The I-CVI ranged from 0.83 to 1.00, and the S-CVI/Ave was 0.94, indicating high agreement among experts regarding item relevance and clarity.

Specifically, items within the Typical and QoL domains achieved a perfect CVI (1.00), whereas minor linguistic adjustments were made in the Differential and Additional domains to improve clarity. No item was eliminated, and all 18 items were retained in the final Persian version of the ACSS.

The results of the ROC curve analysis for the 6 individual items of the "Typical" domain and their summary score are shown in **Figure 1**. Among these, the items "frequent urination" and "urgent urination" and the summary score of the "Typical" domain of the Persian ACSS demonstrated the highest area under the curve (AUC) for diagnosing uAC. These values, along with the AUCs for the other items and domains of the Persian ACSS, are detailed in **Table 4**.

Pairwise comparison of the domain-level AUCs using the DeLong test confirmed that the Typical Symptoms domain (AUC = 0.992) discriminated uAC significantly better than the Differential domain (AUC = 0.681; difference = 0.311; $P < .001$) and the QoL domain (AUC = 0.954; difference = 0.038; $P = .039$) but did not differ significantly from the total ACSS score (AUC = 0.991; difference = 0.002; $P = .59$). This supports the use of the Typical Symptoms domain alone as the primary diagnostic score, since its discriminatory performance was statistically indistinguishable from that of the total ACSS score (Supplementary File 2; Figure S4).

Table 5 presents the diagnostic metrics for 2 candidate cutoff points (≥ 5 and ≥ 6) of the summary score of the "Typical" domain for the clinical diagnosis of uAC in patients at BL (n = 50) compared with controls (n = 50). Using a cutoff score of ≥ 6 in the "Typical" domain, the Persian ACSS demonstrated excellent diagnostic accuracy, with a sensitivity of 96% and a specificity of 96%, confirming its strong discriminatory performance in identifying women with uAC. Diagnostic performance was comparable at both cutoff points, with equivalent accuracy (96%) and Youden index (0.92) for ≥ 5 and ≥ 6. The cutoff of ≥ 6 was adopted as the predefined threshold for the Persian ACSS, as it achieved this performance with a more balanced sensitivity (96%) and specificity (96%).

Supplementary **Table 2** provides the median (IQR)

scores for the items and domains of the Persian ACSS. Most individual item scores and summary domain scores of the Persian ACSS differed significantly between patients and controls ($P < .05$) (**Figures 2 and 3; Supplementary Table 2**). Symptom severity distributions also showed significant differences (Supplementary Figures 1–3, bar and scatter plots). Among patients assessed at both BL and FU (n = 40), all ACSS item and domain scores changed significantly, except for "visible blood in urine," which was rare at BL and absent at FU. Compared with controls, the 40 patients at FU had statistically significant differences in the item scores of the "Typical" and "QoL" domains, except for "visible blood in urine," whereas no significant difference was found in the items of the "Differential" domain.

The overall clinical outcome of patients at FU, as assessed by the "Dynamics" domain, is presented in Figure 4. A successful clinical outcome was defined as patients reporting that they felt "back to normal" or at least "much better," which applied to 75.0% of patients. The remaining 25.0% reported feeling only "somewhat better" (15.0%), experiencing "no changes" (7.5%), or "feeling worse" (2.5%).

DISCUSSION

This study demonstrates that the Persian version of the ACSS is a valid, reliable, and diagnostically accurate instrument for the assessment of uAC in Farsi-speaking women. The tool showed an excellent ability to distinguish between patients with uAC and controls. It also demonstrated robust internal consistency, a stable factorial structure, and strong test-retest reliability. These findings confirm that the Persian ACSS maintains the conceptual and psychometric integrity of the original questionnaire. Although urinary symptoms are frequently linked to acute cystitis, they are not exclusive to this condition; they may also be present in individuals with other urological disorders. Therefore, both the presence and the severity of these symptoms must be considered. The test-retest reliability analysis further confirmed the robustness of the Persian ACSS, with an ICC of 0.75 (95% CI, 0.62–0.85), reflecting good stability of the scores over time. This value is consistent with previous validation studies of the ACSS in other languages, which reported ICCs ranging from 0.70 to 0.85. Moreover, EFA revealed a 4-factor structure corresponding to the conceptual domains of the original ACSS (Typical, Differential, QoL, and Additional), explaining approximately 71% of the total variance. Visual inspection of the scree plot further supported the 4-factor structure of the Persian ACSS, consistent with the original conceptual model. The distinct elbow after the fourth component confirmed that most of the explained variance was concentrated within these domains, reinforcing the factorial stability and construct validity of the instrument. These findings demonstrate that the Persian version maintains both the conceptual integrity and the psychometric validity of the original questionnaire, ensuring its suitability for both clinical and research settings. The excellent content validity results further strengthen the psychometric robustness of the Persian ACSS. All items achieved CVR and CVI values above the recommended thresholds, confirming that the experts perceived each question as both essential and relevant to the construct of acute cystitis. The high S-CVI/Ave (0.94) demonstrates strong interexpert consensus, consistent with international ACSS validation studies in other languages. Collectively, these results support the conclusion that the Persian version adequately captures the conceptual and clinical dimensions of acute cystitis symptoms and their related impacts on quality of life.

A notable aspect of the ACSS is its emphasis on evaluating symptom severity and its effects on quality of life and on differentiating cystitis from other urogenital conditions.[6] Some women in the control group reported mild to moderate urinary symptoms, such as frequency, urgency, and painful urination; however, their urine cultures showed no significant bacteriuria ($>10^5$ CFU/mL). Nevertheless, significant bacteriuria of $\geq 10^5$ CFU/mL in adults was originally defined for the diagnosis of pyelonephritis.[16] Traditional diagnostic methods, including urine culture and dipstick urinalysis, have well-recognized limitations. Although the specificity of urine culture at $\geq 10^5$ CFU/mL is high, its sensitivity is low (approximately 51%).[17] Dipstick tests similarly demonstrate variable performance, with nitrites showing high specificity but low sensitivity and leukocyte esterase demonstrating the opposite pattern.[19,20] In contrast, the Persian ACSS achieved balanced, high diagnostic accuracy (sensitivity, 96%; specificity, 96%), underscoring its utility as a rapid, symptom-based diagnostic tool. This is particularly relevant in clinical settings where immediate laboratory testing is unavailable or where antibiotic stewardship initiatives encourage more precise identification of symptomatic infections. Hooton et al. confirmed that Escherichia coli counts as low as 10^1 to 10^2 CFU/mL were sensitive and specific for the diagnosis of uAC in symptomatic women.[18] Our previous studies, however, did not reveal a significant association between CFU levels and symptom severity.[8]

Leman evaluated the diagnostic validity of urinalysis, urine microscopy, and physical findings for the early detection of UTI in emergency departments.[19] According to the study results, the leukocyte esterase test demonstrated high sensitivity (0.88) but low specificity (0.42). In contrast, the nitrite test was the most specific of all urinalysis parameters (0.94) but had low sensitivity (0.48). Combining positive leukocyte esterase and nitrite tests improved specificity to 1.00 but at the cost of markedly reduced sensitivity (0.38).[19] In the same study, the highest calculated balanced accuracy of 0.76 was observed for a urinary red blood cell (RBC) count greater than 250 RBC/mL, corresponding to a sensitivity of 0.63 and a specificity of 0.90.[19]

A systematic review by St John et al. reported similar findings, indicating that the highest diagnostic values were achieved when either the leukocyte esterase or the nitrite test was positive.[20] The reported sensitivity in these instances was 0.82 (95% CI, 0.70–0.93), and the specificity was 0.80 (95% CI, 0.70–0.90).[20] We calculated the overall diagnostic balance for these values to be 0.81 (95% CI, 0.70–0.95).

These findings align with our previous research, which showed that the sensitivity and specificity of detecting uAC based on the presence of pyuria were 0.85 (95% CI, 0.80–0.89) and 0.72 (95% CI, 0.66–0.78), respectively. These values varied significantly depending on the presence and severity of the symptoms defined in the "Typical" domain of the ACSS, highlighting the importance of typical complaints in diagnostic deci-

sion-making.[21]

The ACSS may also help distinguish individuals with uAC from those with conditions such as painful bladder syndrome/interstitial cystitis, vulvodynia, overactive bladder, or other nonbacterial disorders in all cases, underscoring its practical clinical value. In a retrospective study of 442 patients, 44.8% of patients with vulvodynia had a history of UTIs.[22]

The analysis also highlighted significant differences between the first and second visits in female patients diagnosed with uAC ($P < .05$). The impact of uAC on quality of life is further illustrated by the significant differences in scores across the QoL domain. The severity of symptoms related to uAC directly correlates with diminished quality of life, as evidenced by the ACSS results. Figures 3 and 4 depict the severity of both typical and differential symptoms, emphasizing that patients experience considerable discomfort and functional impairment.

Given the current challenges related to the antibiotic crisis and bacterial resistance, there is an urgent need for a straightforward and dependable tool that can enhance diagnostic accuracy and guide antibiotic prescribing.[23] International guidelines on urological infections advocate empirical treatment based on local bacterial resistance patterns and antibiotic stewardship initiatives. However, the initial and most crucial step is the accurate diagnosis of uAC. The EAU guidelines advocate a comprehensive assessment of all patient symptoms and risk factors.[4] However, until now, there has been no validated self-administered questionnaire in Farsi for clinical diagnosis. Such a tool would enable self-diagnosis and self-evaluation of patient-reported outcomes, facilitating comparisons of the effectiveness of various treatment methods, including both antibiotic and nonantibiotic therapies.

The newly validated Farsi version of the ACSS is now available for diagnosing and managing women with uAC and can be incorporated into routine clinical practice to improve adherence to antibiotic stewardship principles, as well as used in clinical and epidemiological research. The findings of this study provide valuable insights into the differences in symptomatology and quality of life between patients diagnosed with uAC and the control group. The statistically significant differences observed across the Typical, Differential, and QoL domains underscore the impact of uAC on patients' health and well-being.

A post hoc power analysis was conducted in the current study to evaluate its ability to identify significant differences between the patient and control groups across the 3 domains of the Persian ACSS. Using Cohen's d for effect size calculation, the analysis showed a power of 97.7% to 100% for detecting differences in symptom severity. The largest effect size was observed in the "Typical" domain, indicating the most pronounced differences between the groups. These findings support the sufficient power of the current study and justify the reliability of the Persian ACSS in assessing symptom severity in women with uAC.

Although the results of the current study offer valuable and critical insights into the symptomatology of uAC, a few limitations must be acknowledged. The cross-sectional design precludes causal inferences regarding symptom progression and changes in quality of life over time. Additionally, the exclusive focus on female patients may limit the generalizability of the findings to male populations and other demographic groups. Future research should use longitudinal study designs to monitor symptom progression and assess the efficacy of various treatment modalities in improving the quality of life of patients with uAC. Expanding the participant pool to include more diverse demographic groups would also provide a more comprehensive understanding of the broader implications of uAC.

Some participants in the control group reported mild urinary symptoms attributable to other urological conditions, such as overactive bladder, urinary stones, or interstitial cystitis. Although these individuals did not have pyuria or bacteriuria, their inclusion may have slightly reduced the specificity estimate. However, this approach reflects real-world clinical overlap and supports the robustness of the ACSS in differentiating uAC from other symptomatic conditions.

The primary aim of this study was the linguistic and clinical validation of the Persian ACSS. Therefore, we chose not to publish the results of laboratory analyses, physical examinations, and urine cultures in order to maintain focus and adhere to the word limit requirements of the journal. Furthermore, the exclusion of the 10 patients lost to FU was necessary to minimize potential bias and ensure the integrity of our results.

This study was conducted at a single center, which may limit the external validity of our findings; multicenter validation studies are needed to confirm generalizability across diverse populations and health care settings. The Persian ACSS was validated exclusively in women with uAC, and its performance in complicated UTIs or overlapping urological conditions remains to be established. Although educational attainment differed significantly between the groups (eg, 2-year diploma: 8% of controls vs 34% of patients; $P = .005$), other sociodemographic factors, such as urban/rural residence and socioeconomic status, were not analyzed in depth; the possibility that educational level influenced questionnaire comprehension or response patterns cannot be excluded and warrants dedicated investigation, as does the performance of the ACSS across educational strata. The post hoc power calculations are presented for descriptive completeness only and should be interpreted with caution, as they are mathematically related to the observed P values and add little beyond the CIs already reported; the sample size for this study was not determined by an a priori power calculation. Looking ahead, longitudinal studies, integration of the Persian ACSS into routine clinical practice, and its evaluation within antibiotic stewardship and surveillance programs represent important next steps for this line of research. A formal statistical comparison of AUC values was performed using the DeLong test for both the domain-level ROC analyses (Typical Symptoms, Differential, QoL, and total ACSS scores) and the individual items in **Table 4** (**Supplementary Figure S4**). The 5 Typical-domain items and the 3 QoL items formed a block of high, largely statistically indistinguishable AUCs (all $\geq$0.86), whereas the 5 Differential-domain items formed a separate block of lower AUCs (all $\leq$0.68) that likewise did not differ significantly from one another but differed highly significantly ($P < .001$) from every Typical/QoL item. This pattern is consistent with the intended clinical role of the Differential domain, which is designed to help exclude alternative diagnoses rather than to inde-

pendently diagnose uAC, and supports the conceptual item-domain structure of the ACSS.

Clinical Implications

The validated Persian ACSS provides clinicians with a practical, standardized instrument that can be used to:

- Support the clinical diagnosis of uAC by quantifying the severity and pattern of typical symptoms.
- Guide treatment decisions, including determining when empirical antibiotic therapy is warranted.
- Monitor symptom trajectories and evaluate treatment response using the follow-up/"Dynamics" domain.
- Differentiate uAC from other causes of lower urinary tract symptoms, such as overactive bladder (OAB), interstitial cystitis/bladder pain syndrome (IC/BPS), vulvodynia, and urethral syndrome.
- Enhance patient-clinician communication by providing a structured format for symptom reporting. This tool can therefore contribute directly to improved diagnostic accuracy and more judicious antibiotic use in alignment with antibiotic stewardship principles.

CONCLUSIONS

The Persian ACSS is a psychometrically sound and clinically valuable instrument for diagnosing and monitoring uAC in Farsi-speaking women. Its excellent diagnostic accuracy, strong internal consistency, construct validity, and practical follow-up capabilities make it uniquely suited for both clinical practice and research. By providing a standardized approach to symptom assessment, the Persian ACSS has the potential to improve diagnostic precision, support antibiotic stewardship, and enhance patient-reported outcome measurement in both routine care and epidemiological studies.

SUMMARY

A new Persian questionnaire for diagnosing bladder infections in women was tested and found to be highly accurate and reliable, helping doctors identify urinary infections quickly.

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The authors thank the copyright holders for permission to use the ACSS and for reviewing the manuscript. The ACSS is copyrighted by the Certificate of Deposit of Intellectual Property in the Fundamental Library of the Academy of Sciences of the Republic of Uzbekistan, Tashkent (Registration No. 2463; August 26, 2015), and the Certificate of the International Online Copyright Office, European Depository, Berlin, Germany (No. EU-01-000764; October 21, 2015). The rightsholders are Jakhongir Fatikhovich Alidjanov (Uzbekistan), Ozoda Takhirovna Alidjanova (Uzbekistan), Adrian Martin Erich Pilatz (Germany), Kurt Guenther Naber (Germany), and Florian Martin Erich Wagenlehner (Germany). The e-USQOLAT is copyrighted by the Authorship Certificate of the International Online Copyright Office, European Depository, Berlin, Germany (No. EC-01-001179; May 18, 2017). Translations of the ACSS into other languages are available at https://acss.world/downloads/. We also appreciate the cooperation of the Clinical Research Development Unit of Imam Reza General Hospital, Tabriz, Iran, in conducting this research.

CONFLICT OF INTEREST

The authors declare no conflicts of interest relevant to the content of this article. This study did not receive external funding.

DECLARATIONS

Ethics Approval

This project was performed in accordance with the ethical principles and the national norms and standards for conducting medical research in Iran and was approved on April 22, 2024, by the Research Ethics Committee of Tabriz University of Medical Sciences (approval number: IR.TBZMED.REC.1403.065). The study is an MD thesis with an ethics code from Tabriz University of Medical Sciences.

Informed Consent

Informed consent was obtained from each patient before participation in the study.

Data Availability

The original contributions presented in this study are included in the article and its supplementary material. Further inquiries can be directed to the corresponding authors.

Author Contributions

Conceptualization, H.S., K.H., N.Sh., M.M., and S.H.; methodology, K.G.N., J.A., H.S., A.P., and F.M.W.; software, J.A.; validation, K.G.N., J.A., and H.S.; formal analysis, J.A. and H.S.; investigation, N.Sh., M.M., and K.Sh.; resources, K.H., N.Sh., M.M., H.S., and K.Sh.; data curation, N.Sh., M.M., J.A., and H.S.; writing—original draft preparation, K.Sh., M.M., K.H., N.Sh., and H.S.; writing—review and editing, K.G.N., J.A., H.S., A.P., F.M.W., and S.H.; visualization, J.A.; supervision, K.G.N., J.A., H.S., A.P., F.M.W., and S.H.; project administration, K.G.N. and H.S.; funding acquisition, K.G.N. and H.S. All authors have read and agreed to the published version of the manuscript.

Statement on Affiliations

We, the authors of this manuscript, hereby confirm that none of us is employed by any government agency whose primary function is other than research and/or education. Additionally, we affirm that this manuscript is not being submitted as an official representative or on behalf of any government entity.

On behalf of all authors, we declare that we are affiliated with Tabriz University of Medical Sciences, where we serve as academic staff or employees. Our roles are exclusively focused on research, education, and the provision of health care within the framework of the medical sciences universities in Iran. We confirm that none of us holds a position that diverts from these primary functions.

This statement serves to clarify our affiliations and to ensure transparency regarding our roles and responsibilities in relation to this manuscript.

APPENDIX

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