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The relationship between neuropathic pain and lower urinary tract symptom scores in patients with primary Sjögren's syndrome

Nilay Erdik[1*], Anil Erdik[2], Damla Kizil[3], Gokhan Yavuzbilge[4], Sumeyye Merve Turk[1], Cansu Arslanturk Guneysu[1], Abbas Karakurt[5], Sedat Ozmen[6] and Emel Gonullu[1]

Abstract

Objective To evaluate the effect of neuropathic pain on lower urinary tract symptoms (LUTS) scores in patients with primary Sjögren's syndrome (pSS).

Methods Seventy-two patients diagnosed with pSS were included in the study. The patients with pSS were divided into two groups according to the presence/absence of neuropathic pain. The Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) questionnaire was recorded assess neuropathic pain. LUTS was evaluated using the International Prostate Symptom Score (IPSS), International Incontinence Consultation Questionnaire Short Form (ICIQ-SF) and Overactive Bladder Questionnaire (OAB-V8).

Results The mean age of the patients was 52.4 ± 11.2 years. Neuropathic pain was recorded in 21 (29.2%) patients. Among the patients, the number of patients with mild symptoms was recorded as 41 (56.9%), moderate symptoms in 25 (34.7%), and severe symptoms in 6 (8.3%) according to IPSS. IPSS and IPSS voiding subscores were statistically significantly higher in patients with neuropathic pain than non-neuropathic pain group ($p = 0.035$; $p = 0.001$, respectively). Although ICIQ-SF, OAB-V8 and IPSS storage subscores were found to be higher in patients with neuropathic pain group, there was no statistically significant difference between the groups ($p = 0.299$; $p = 0.283$; $p = 0.237$, respectively).

Conclusion Neuropathic pain concomitant with PSS patients may negatively affect bladder voiding functions.

Keywords Lower urinary tract symptoms, Neuropathic pain, Primary Sjögren syndrome

*Correspondence:
Nilay Erdik
nilayerdik@sakarya.edu.tr
[1]Department of Internal Medicine, Division of Rheumatology, Sakarya University Faculty of Medicine, Sakarya, Turkey
[2]Department of Urology, Ministry of Health Karasu State Hospital, Karasu/Sakarya 54500, Turkey
[3]Department of Internal Medicine, Division of Rheumatology, Ministry of Health Yalova State Hospital, Yalova, Turkey
[4]Department of Internal Medicine, Division of Rheumatology, Hatay Training and Research Hospital, Hatay, Turkey
[5]Department of Internal Medicine, Bozuyuk State Hospital, Bilecik, Turkey
[6]Department of Ophthalmology, Sakarya University Faculty of Medicine, Sakarya, Turkey

Introduction

Primary Sjögren's syndrome (pSS) is a rheumatic disorder characterised by lymphocytic infiltration and exocrine insufficiency of salivary and lacrimal glands and frequently described by extraglandular attributes, such as renal tubular acidosis, interstitial nephritis, peripheral neuropathy, and palpable purpura [1]. It has been noted that affect 0.9-6 per thousand individuals, diagnosed 4th-5th decades of life and women are affected more frequently than men [2].

Around half of patients cultivate extraglandular manifestations [3], also bladder disorders could appear in pSS patients [4]. Lower urinary tract symptoms (LUTS) include symptoms of urinary frequency, urgency, nocturia and urinary incontinence (UI) [5]. Several studies have found an association between increased severity of LUTS for pSS compared with control populations [6, 7]. It has been suggested that autoantibodies bind to the M3 muscarinic receptor in the bladder, causing detrusor smooth muscle contraction and exocrine dysfunction in patients with pSS [8].

Neuropathic involvement is another extraglandular manifestations in pSS. The frequency of neuropathic symptoms is estimated to be approximately 8.5–70% among pSS patients [9]. In recent studies, the increase in the frequency of neuropathic pain among pSS is noteable [10, 11]. Pure sensory neuropathies even, more frequently, small fiber neuropathies (SFN) might be responsible for neuropathic pain in pSS [12]. The pSS has an crucial role in the etiology of SFN [13]. SFN occurs with the involvement of thinly myelinated A-delta and unmyelinated C fibers [14]. SFN may leading cause of pSS-related bladder disorders.

Both overactive bladder (OAB) and underactive bladder (UAB) can lead to LUTS. The etiopathogenesis of these conditions involves myogenic, neurogenic and idiopathic factors [15, 16]. It is well established that the physiological contraction of the detrusor muscle is mediated by the M3 muscarinic receptor, and myogenic causes are thought to be related to this pathway [17, 18]. The afferent pathways of the bladder, which include thinly myelinated A-delta and unmyelinated C fibers, play crucial roles in bladder sensation and reflexive contraction. Dysfunction in these afferent pathways has been implicated in both OAB and UAB [15, 16]. Given this, we hypothesized that neuropathic pain in Sjögren's syndrome patients might affect A-delta and unmyelinated C fibers, thereby triggering LUTS.

There is a notable paucity of studies investigating pSS-related bladder disorders. Also, no previous study has evaluated the association of neuropathic pain with symptoms of LUTS in patients with pSS. The primary aim of this paper is to explore the relationship between LUTS with neuropathic pain in pSS patients.

Materials and methods

Cohort

This single-centred study was approved by the Institutional Review Board of the Ethics Committee of Sakarya University (approval number: E-71522473-050.01.04-194545-320). All included patients provided written informed consent. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Data were collected from 82 patients diagnosed with pSS followed in the rheumatology outpatient clinic at our institution between December 2021 and November 2023. Baseline characteristics and laboratory data, such as age, gender, body mass index (BMI), Leeds Assessment of Neuropathic Symptoms and Signs (LANSS), International Prostate Symptom Score (IPSS), International Consultation on Incontinence Questionnaire Short Form (ICIQ-SF) and Overactive bladder questionnaire (OAB-V8) scores were recorded. Three male patients were excluded the study considering the possible effects of infra-vesical obstruction on LUTS. Seven patients who had undergone cystoscopy due to LUTS within the last 3 months, tested urine analysis positive for nitrite and had bacterial growth in urine culture, and/or lacked LANSS and IPSS scores were excluded from the study. The remaining 72 female patients were included the study. To investigate the effects of neuropathic pain on LUTS, patients were divided into two groups: neuropathic pain and non-neuropathic pain. Figure 1 displays an overview of the patient selection and stratification process in this study.

Symptom score questionnaires

LANSS is 7-item pain scale used to identify patients with neuropathic pain. Five items are scored based on symptom inquiry and two items are scored based on the presence of clinical symptoms. The LANSS scoring system combines patient-reported symptoms and clinical signs, with a total possible score of 24. Patients with LANSS scores of ≥12 were included in the neuropathic pain group, as a score of ≥12 is indicative of neuropathic pain mechanisms [19]. In our study, we used this threshold to categorize patients into neuropathic and non-neuropathic pain groups, allowing us to investigate the association between neuropathic pain and LUTS more precisely.

The IPSS is an eight-item questionnaire, consisting of seven symptom questions [20]. The IPSS questionnaire evaluating frequency, nocturia, urgency, intermittency, incomplete voiding, weak urine flow, and hesitancy urination. Each question can be scored between 0 and 5 and the total score can be 35. The IPSS score is categorised

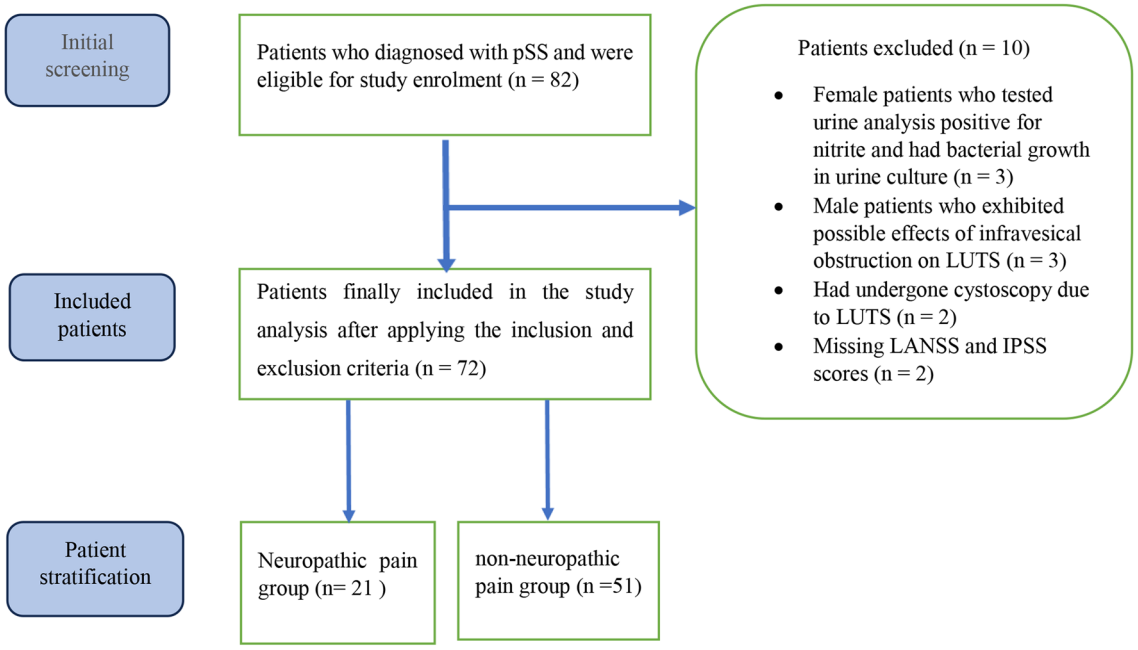

Fig. 1 Flowchart of the patient selection and grouping process in this study

as asymptomatic (0 points), mild (1–7 points), moderate (8–19 points), and severe (20–35 points) [20].

The IPSS is divided into two components: the voiding symptom subscore and the storage symptom subscore. The voiding symptom subscore is calculated by adding responses to question 1 (incomplete emptying), question 3 (intermittency), question 5 (weak stream), and question 6 (straining to urinate). In contrast, the storage symptom subscore combines responses to question 2 (frequency), question 4 (urgency), and question 7 (nocturia). These subscores are useful for assessing symptom severity and tracking treatment outcomes [21].

The OAB-V8 questionnaire is with 8 questions, and each question includes severity of complaint; not at all (0); a little bit (1); somewhat (2); quite a bit (3), a great deal (4) and a very great deal (5) [22]. The total score can vary between 0 and 40. A score of >8 is considered a sign of OAB [23]. The ICIQ-SF questionnaire inquirys urinary frequency or urinary leakage, amount of urinary leakage, type of urinary incontinence and its effects on quality of life. The maximum total score is 21. An increase in score indicates higher symptomatology [24].

Neuropathic pain

Neuropathic pain has been defined by the International Association for the Study of Pain (IASP) as 'pain caused by a lesion or disease of the somatosensory nervous system'. Neuropathic pain is not a diagnosis but a clinical description that requires a demonstrable lesion or a disease that meets established neurological diagnostic criteria [25]. The fact that it is a clinical description and the lack of biomarkers for neuropathic pain make diagnosis challenging. Surveys using pain descriptors such as burning, electric shocks, tingling, stabbing, pricking, numbness, and itching have been developed and validated. Examples of these validated questionnaires include the LANSS, the Neuropathic Pain Questionnaire (NPQ), the Douleur Neuropathique 4 (DN4), PainDetect, and ID Pain. Two of these tools, LANSS and DN4, incorporate a brief sensory examination [26]. In our study, we preferred to use the LANSS due to its inclusion of a sensory examination.

Statistical analysis

For continuous variables, normality criteria evaluated using Kolmogorov-Smirnov test. In cases where normality criteria not existed the Mann–Whitney U test was performed and used median (IQR: Interquartile range) for variables. Significance tests used to examine patients with and without LANSS score positive were the Mann-Whitney U for continuous variables. Data management and analysis were performed using SPSS (version 26, Chicago, IL, USA). All tests were 2-sided, with a p-value<0.05 was considered statistically significant. Further, independent predictors for LUTS patients over 50 years of age was evaluated using multivariate linear and logistic regression analyses.

Results

Cohort

A total of 72 female patients were included in this study. The mean age of the patients was 52.4±11.2 years. Mean

Table 1 LANSS, IPSS, ICIQ-SF and OAB-V8 scores of patients

	Median (IQR)
LANSS	8 (12)
IPSS	6 (10)
IPSS voiding symptom subscore	1 (3)
IPSS storage symptom subscore	4 (7)
ICIQ-SF	2 (8)
OAB-V8	9 (13)

ICIQ-SF: International Consultation on Incontinence Questionnaire Short Form, IPSS: International Prostate Symptom Score, IQR: Interquartille Range, LANSS: Leeds Assessment of Neuropathic Symptoms and Signs, OAB-V8: Overactive bladder questionnaire

Table 2 Symptom scores of the patient cohort with and without neuropathic pain

	Neuropathic pain patients ($n=21$) (Median, IQR)	Non-neuropathic pain patients ($n=51$) (Median, IQR)	*p* value*
IPSS	11 (14)	5 (9)	0.035
IPSS voiding symptom subscore	3 (8)	0 (2)	0.001
IPSS storage symptom subscore	7 (9)	4 (6)	0.237
ICIQ-SF	4 (8)	1 (7)	0.299
OAB-V8	10 (12)	9 (11)	0.283

*Mann Whitney-U test, ICIQ-SF: International Consultation on Incontinence Questionnaire Short Form, IPSS: International Prostate Symptom Score, IQR: Interquartille Range, OAB-V8: Overactive bladder questionnaire

BMI was 29.31±6.58. The median LANSS score of the pSS patients was 8 (IQR 12) and, overall prevalence of LANSS score positive (≥12 points) within the population in the current study was 21 of 72 (29.2%). No CNS involvement was observed in any of the patients. The median IPSS score of the cohort was 6 (IQR 10). Forty-one patients (56.9%) with an IPSS score were below 8, 25 patients (34.7%) were between 7 and 20, 6 patients were (8.3%) 20 and above. Median LANSS, IPSS, ICIQ-SF and OAB-V8 median scores are shown in Table 1.

Relationship between neuropathic pain group and questionnaire forms

Twenty-one patients had LANSS score≥12 and they were included neuropathic pain group. When the questionnaire forms were evaluated, there was a significant difference in IPSS and IPSS voiding symptom subscore between the groups. IPSS and IPSS voiding symptom subscore were higher in the neuropathic pain group. However, no significant difference was found between the groups with other symptom scores. The results of the statistical analysis are presented in Table 2.

In patients above 50 years of age, LUTS might be affected by many factors such as age, BMI, smoking, hypertension, diabetes mellitus and taking hydroxychloroquine. These parameters were examined using multivariate analysis among pSS patients whose IPSS score over 7. There was no evidence that these parameters has an influence on LUTS (Table 3).

Table 3 Multivariate analysis of multiple factors potentially affecting LUTS for in pSS patients above 50 years of age

Variable	OR (95% CI)	*p* value
Age	1.032 (0.980–1.086)	0.231
BMI	1.038 (0.956–1.127)	0.374
Smoking	0.997 (0.310–3.205)	0.997
Hypertension	0.579 (0.143–2.349)	0.444
Diabetes mellitus	0.369 (0.069–1.967)	0.243
Hydroxychloroquine taking	0.868 (0.252–2.994)	0.822
Nitrite-positive urine (ref. presence)	2.670 (0.471–15.117)	0.267

Discussion

A systematic literature review concluded that the prevalence of neuropathic pain in the general population was 6.9–10% [27]. In a study investigating the frequency of neuropathic pain among pSS patients, Segal et al. reported that seropositive pSS patients had %36, seronegative pSS patients had %40 neuropathic pain [10]. In addition, Yolcu et al. reported the presence of neuropathic pain in 36% of 36 pSS patients [28]. In our study, we found that neuropathic pain in our cohort was 29.2%, which is almost similar to prior studies in the literature.

Neuropathic pain associated with peripheral nerve involvement can be occurred by means of various mechanisms [29, 30]. Abnormal or hyperactivity of SFN nociceptive thin myelinated (A delta) and unmyelinated (C) fibers may cause neuropathic pain [31]. Additionally, it has been thought that nociplastic pain might be a component of neuropathic pain or a distinct entity [32]. Neuropathic pain is occurred with central sensitization results from reorganization (plasticity), sensitization (hyperexcitability), or reduced inhibition of nociceptive neurons in the central nervous system by NMDA receptor activation [29]. Fibromyalgia pain may also be secondary to central sensitization (nociplastic pain) [33].

Neuropathic pain can typically present as continuous pain (burning, squeezing, pressure), paroxysmal pain (sensations resembling electric shocks or stabbing pain), triggered pain (allodynia), or paresthetic and dysesthetic sensations (tingling, prickling). Due to the heterogeneity of neuropathic pain, the underlying mechanisms remain unclear. Continuous pain has been associated with both peripheral and central mechanisms, and may be related to the activation of C nociceptor axons in the skin or central hyperactivity resulting from deafferentation [34, 35]. On the other hand, paroxysmal pain originates from peripheral hyperexcitable nociceptive fibers [36]. Allodynia can also arise as a result of central sensitization [37].

Neuropathic complaints are prominent in the presence of SFN in pSS and non-pSS patients [38–40].

However, neuropathic symptoms (such as pricking, tingling, numbness, itching, burning sensations, and electric shocks) could not be differentiated in 30 patients with pSS, regardless of the presence or absence of SFN [40]. A deeper understanding of neuropathic and nociplastic pain might be important in terms of additional symptoms such as urological complaints accompanying in pSS.

LUTS is a description rather than a diagnosis. Voiding and storage symptoms are evaluated by means of some questionnaire forms [41]. For example, LUTS are evaluated with the IPSS form. Three questions in the IPSS form assess storage (frequency, urgency, and nocturia) and four questions assess voiding symptoms (intermittency, incomplete voiding, weak urine flow, and hesitant urination). The OAB-V8 questionnaire form can be used to inquire about OAB symptoms. In addition, urination frequency, amount and quality of life are inquired with the ICIQ-SF questionnaire form. While storage complaints may indicate conditions such as OAB and/or detrusor overactivity, voiding complaints may suggest detrusor underactivity and/or bladder outlet obstruction [16].

A cohort study has found an increased risk of OAB and bladder pain syndrome/interstitial cystitis in patients with pSS [42]. In the etiology of bladder pain syndrome/interstitial cystitis, dysfunction of the bladder urothelium, neurogenic inflammation, and neuropathic pain are discussed. Neurogenic inflammation occurs due to the release of inflammatory mediators by afferent neurons, creating a cycle in which activated inflammatory cells stimulate neurons, leading to increased sensitivity and subsequent release of more inflammatory mediators.

In reviewing the literature, it can be seen that studies conducted to determine the prevalence of LUTS in pSS patients are reported in a wide range. Haarala et al. analysed the data from 36 pSS patients and reported that the frequency of severe LUTS 14% among in pSS patients [43]. In a study including 21 secondary SS patients, severe LUTS was reported in 19% [44]. Another study conducted with 71 pSS patients, showed that the rate of severe LUTS was 61% [6]. The current study found that the prevalence of moderate and severe LUTS in pSS patients was 43.1%. The difference of prevalence rates may be explained due to the various in the number of patients in the studies.

In this study, patients with pSS were divided into two sub-groups according to the presence/absence of neuropathic pain. IPSS and IPSS voiding subscores of neuropathic pain group were significantly higher than non-neuropathic pain group. IPSS storage, OAB-V8 and ICIQ-SF scores were higher in the neuropathic pain group, although there was no statistically significant difference. These results suggest that the presence of neuropathic pain in pSS may be related to detrusor underactivity and/or bladder outlet obstruction.

In our study, 43 patients (59.7%) were postmenopausal. The median IPSS score for premenopausal patients was 5 (IQR 11), compared to 7 (IQR 10) for postmenopausal patients. However, there were no statistically significant differences between these two groups in terms of IPSS or its subgroups. Additionally, out of 56 patients questioned about vaginal dryness, 26 (46.4%) reported experiencing it. The median IPSS score for patients without vaginal dryness was 4.5 (IQR 9), while those with vaginal dryness had a median IPSS score of 6.5 (IQR 12). Again, no statistically significant differences were observed in IPSS or its subgroups between these two groups. While hormonal changes, particularly postmenopausal atrophic changes, are discussed in the literature as potential contributors to LUTS [45], our findings did not support a significant impact in this cohort. This suggests that factors other than hormonal alterations might play a more prominent role in the development of LUTS in pSS patients. Further studies with larger populations may be needed to explore this relationship more thoroughly.

In a study conducted with type 2 diabetic patients, it has revealed that detrusor underactivity was associated with A-delta and C-fiber bladder afferent pathways, which are among the neuropathic pain pathways [46]. The prevalence of SFN is approximately 52.95 per 100,000 population, with diabetes and idiopathic origins being the most common etiologies. Symptoms often present in a length-dependent pattern and include dysesthesia, allodynia, pain, burning sensations, and coldness. Additional autonomic features, affecting urinary, gastrointestinal or cardiovascular systems, are common but often poorly documented [47]. SFN is diagnosed based on intraepidermal nerve fiber density, quantitative sensory and autonomic tests, alongside normal nerve conduction studies [47]. In another study with 51 patients among chronic pelvic pain suggested that detrusor underactivity and/or bladder outlet obstruction may be associated with SFN [48]. In a study involving 39 patients, where skin punch biopsies were performed to detect SFN positivity, SFN positivity was found in 64% of the patients [49]. Patients reported a combination of pain characteristics, including pain when the bladder is full, urethral pain during and after urination, pain on the vulvar or scrotal surface, and deep pain in the vagina, penis, or rectum during sexual activity or at rest [49]. On the other hand, Tarhan et al. found the OAB-V8 score to be 56% positive (>8 points) in 50 pSS patients and stated that the frequency of OAB was high in pSS [4]. In this study, OAB-V8 positivity was found 54.2% among 72 pSS patients.

Limitations of the study

The current study has several limitations. First, there is no healthy control group included. Second, it is possible that the amount and type of fluid ingested by pSS patients could be contribute for their LUTS. However, we were unable to record the amount of fluid intake or caffeine consumption by the patients. Finally, the evaluation of patients with LUTS and neuropathic pain symptoms was limited to symptom score questionnaires, and no invasive procedures were performed.

Conclusion

These findings suggest a potential association between LUTS in pSS and neuropathic pain. It appears that, when considering the IPSS subgroups, OAB-V8, and ICIQ-SF, neuropathic pain may have a more pronounced impact on bladder voiding functions compared to bladder storage functions. This study represents an initial attempt to provide evidence that neuropathic pain could negatively influence bladder voiding functions in pSS patients. However, further research is needed to gain a deeper understanding of the underlying mechanisms of neuropathic pain associated with LUTS in this patient population.

Abbreviations

BMI	Body mass index
DN4	Douleur Neuropathique 4
ICIQ-SF	Intemational Consultation on Incontinence Questionnaire Short Form
IPSS	International Prostate Symptom Score
LANSS	Leeds Assessment of Neuropathic Symptoms and Signs
LUTS	Lower urinary tract symptoms
NPQ	Neuropathic Pain Questionnaire
OAB	Overactive bladder
OAB-V8	Overactive bladder questionnaire
pSS	Primary Sjögren's syndrome
SFN	Small fiber neuropathies
UAB	Underactive bladder
UI	Urinary incontinence

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Author contributions

Research conception and design: Nilay Erdik, Abbas Karakurt, Emel Gonullu. Data acquisition: Nilay Erdik, Damla Kizil, Gokhan Yavuzbilge, Sumeyye Merve Turk, Cansu Arslanturk Guneysu, Abbas Karakurt. Statistical analysis: Nilay Erdik, Anil Erdik. Data analysis and interpretation: Nilay Erdik, Anil Erdik, Damla Kizil, Abbas Karakurt. Drafting of the manuscript: Nilay Erdik, Anil Erdik, Sumeyye Merve Turk, Emel Gonullu. Critical revision of the manuscript: Anil Erdik, Emel Gonullu. Administrative, technical, or material support: Gokhan Yavuzbilge, Sumeyye Merve Turk, Cansu Arslanturk Guneysu. Supervision: Sedat Ozmen, Emel Gonullu. Approval of the final manuscript: Emel Gonullu. All authors have read and approved the manuscript.

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Data availability

Data are available on reasonable request. Deidentified participant data are available on reasonable request from the Sakarya University School of Medicine via the department of rheumatology. Reuse is permitted with reasonable rationale, after discussion. Additional information (protocols, statistical analysis plans) are available.

Declarations

Ethics approval and consent to participate

The present study protocol was reviewed and approved by the Institutional Review Board of Sakarya University College of Medicine (approval number: E-71522473-050.01.04-194545-320). The study followed the ethical principles of the Declaration of Helsinki. Informed consent was obtained by all subjects when they were enrolled.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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References

1. Jonsson R, Haga H, Gordon T. Sjögren's syndrome. In: Koopman W, editor. in Arthritis and allied conditions. 14th ed. Philadelphia: Lippincott Williams & Wilkins; 2001;1736–59.
2. Seror R, Ravaud P, Mariette X, et al. EULAR Sjogren's Syndrome Patient Reported Index (ESSPRI): development of a consensus patient index for primary Sjogren's syndrome. Ann Rheum Dis. 2011;70(6):968-72. https://doi.org/10.1136/ard.2010.143743
3. Stefanski A-L, Tomiak C, Pleyer U, Dietrich T, Burmester GR, Dörner T. The diagnosis and treatment of Sjögren's syndrome. Dtsch Arztebl Int. May 2017;114(20):354–61. https://doi.org/10.3238/arztebl.2017.0354.
4. Tarhan F, Tarhan H, Keser G, Mertoglu O, Yildirim U. Increased overactive bladder symptoms in primary Sjogren's syndrome. World J Nephrol Urol. 2013. https://doi.org/10.4021/wjnu85w.
5. Maserejian NN, Chen S, Chiu GR, Wager CG, Kupelian V, Araujo AB, McKinlay JB. Incidence of lower urinary tract symptoms in a population-based study of men and women. Urology. 2013 Sep;82(3):560-4. https://doi.org/10.1016/j.urology.2013.05.009
6. Walker J, Gordon T, Lester S, Downie-Doyle S, McEvoy D, Pile K, Waterman S, Rischmueller M. Increased severity of lower urinary tract symptoms and daytime somnolence in primary Sjögren's syndrome. J Rheumatol. 2003 Nov;30(11):2406-12.
7. Leppilahti M, Tammela TLJ, Huhtala H, Kiilholma P, Leppilahti K, Auvinen A. Interstitial cystitis-like urinary symptoms among patients with Sjögren's syndrome: a population-based study in Finland. Am. J. Med. 2003;115(1):62–5. https://doi.org/10.1016/s0002-9343(03)00257-2
8. Van De Merwe JP, Arendsen HJ. Interstitial cystitis: a review of immunological aspects of the aetiology and pathogenesis, with a hypothesis. BJU Int. 2000;85(8):995-9. https://doi.org/10.1046/j.1464-410x.2000.00646.x
9. Fauchais A-L, Magy L, Vidal E. Central and peripheral neurological complications of primary Sjögren's syndrome. Presse Med. Sep. 2012;41(9):e485–93. https://doi.org/10.1016/j.lpm.2012.06.002.
10. Segal BM, Pogatchnik B, Henn L, Rudser K, Sivils KM. Pain Severity and Neuropathic Pain Symptoms in Primary Sjögren's Syndrome: A Comparison Study of Seropositive and Seronegative Sjögren's Syndrome Patients. Arthritis Care Res. (Hoboken). 2013;65(8):1291-8. https://doi.org/10.1002/acr.21956
11. Birnbaum J, Duncan T, Owoyemi K, Wang KC, Carrino J, Chhabra A. Use of a novel high-resolution magnetic resonance neurography protocol to detect abnormal dorsal root ganglia in Sjögren patients with neuropathic pain: case series of 10 patients and review of the literature. Med (Baltim). May 2014;93(3):121–34. https://doi.org/10.1097/MD.0000000000000024.
12. Vitali C, Papa ND. Pain in primary Sjögren's syndrome. Best Pract Res Clin Rheumatol. Feb. 2015;29(1):63–70. https://doi.org/10.1016/j.berh.2015.05.002.
13. Johnson SA, Shouman K, Shelly S, Sandroni P, Berini SE, Dyck PJB, Hoffman EM, Mandrekar J, Niu Z, Lamb CJ, Low PA, Singer W, Mauermann ML, Mills J, Dubey D, Staff NP, Klein CJ. Small Fiber Neuropathy Incidence, Prevalence, Longitudinal Impairments, and Disability. Neurology. 2021 Nov 30;97(22):e2236-e2247. https://doi.org/10.1212/WNL.0000000000012894
14. Hovaguimian A, Gibbons CH. Diagnosis and treatment of pain in small-fiber neuropathy. Curr Pain Headache Rep. Jun. 2011;15(3):193–200. https://doi.org/10.1007/s11916-011-0181-7.

15. Banakhar MA, Al-Shaiji TF, Hassouna MM. Pathophysiology of overactive bladder. Int. Urogynecol. J. 2012;23(8):975-82. https://doi.org/10.1007/s00192-012-1682-6
16. Osman NI, Chapple CR, Abrams P, Dmochowski R, Haab F, Nitti V, Koelbl H, van Kerrebroeck P, Wein AJ. Detrusor underactivity and the underactive bladder: a new clinical entity? A review of current terminology, definitions, epidemiology, aetiology, and diagnosis. Eur Urol. Feb. 2014;65(2):389–98. https://doi.org/10.1016/j.eururo.2013.10.015.
17. Smith PP, Birder LA, Abrams P, Wein AJ, Chapple CR. Detrusor underactivity and the underactive bladder: symptoms, function, cause-what do we mean? ICI-RS think tank 2014. Neurourol Urodyn. Feb. 2016;35(2):312–7. https://doi.org/10.1002/nau.22807.
18. Brading AF, Turner WH. The unstable bladder: towards a common mechanism. Br J Urol. Jan. 1994;73(1):3–8. https://doi.org/10.1111/j.1464-410x.1994.tb07447.x.
19. Bennett MI, Smith BH, Torrance N, Potter J. The S-LANSS score for identifying pain of predominantly neuropathic origin: Validation for use in clinical and postal research. J. Pain. 2005;6(3):149-58. https://doi.org/10.1016/j.jpain.2004.11.007
20. Barry MJ, Fowler FJ Jr, O'Leary MP, Bruskewitz RC, Holtgrewe HL, Mebust WK, Cockett AT. The American Urological Association symptom index for benign prostatic hyperplasia. The Measurement Committee of the American Urological Association. J Urol. 1992;148(5):1549–57. https://doi.org/10.1016/s0022-5347(17)36966-5. discussion 1564, Nov.
21. Liao C-H, Kuo H-C. Use of the international prostate symptom score voiding-to-storage subscore ratio in assessing lower urinary tract symptoms. Tzu Chi Med J. 2014;26(2):61–3. https://doi.org/10.1016/j.tcmj.2014.05.008.
22. Tarcan T, Mangır N, Ozgur O, Akbal C. OAB-V8 Aşırı Aktif Mesane Sorgulama Formu validasyon çalışması. Üroloji Bülteni. 2012;21(21):113–6.
23. Basra RK, Cortes E, Khullar V, Kelleher C. A comparison study of two lower urinary tract symptoms screening tools in clinical practice: The B-SAQ and OAB-V8 questionnaires, J. Obstet. Gynaecol. (Lahore)., vol. 32, no. 7, pp. 666 -671, Oct. 2012, https://doi.org/10.3109/01443615.2012.696158
24. Çetinel B, Ozkan B, Can G. The validation study of ICIQ-SF Turkish version. Turk J Urol. 2003;30(3):332–8.
25. Scholz J, et al. The IASP classification of chronic pain for ICD-11: chronic neuropathic pain. Pain. Jan. 2019;160(1):53–9. https://doi.org/10.1097/j.pain.0000000000001365.
26. Jensen TS, Baron R, Haanpää M, Kalso E, Loeser JD, Rice ASC, Treede RD. A new definition of neuropathic pain. Pain. Oct. 2011;152(10):2204–5. https://doi.org/10.1016/j.pain.2011.06.017.
27. van Hecke O, Austin SK, Khan RA, Smith BH, Torrance N. Neuropathic pain in the general population: a systematic review of epidemiological studies. Pain. Apr. 2014;155(4):654–62. https://doi.org/10.1016/j.pain.2013.11.013.
28. Yolcu G, Abacar KY, Kenis-Coskun O, Nevsun-Inanc G, Karadag-Saygi E, Gunduz OH. Comparison of cutaneous silent period parameters in patients with primary Sjögren's syndrome with the healthy population and determination of ıts relationship with clinical parameters. Rheumatol. Int. 2022;43(2):355-62. https://doi.org/10.1007/s00296-022-05198-x
29. Baron R, Supplement. S12–20, Jun. 2000. https://doi.org/10.1097/00002508-200006001-00004.
30. Attal N, Bouhassira D. Mechanisms of pain in peripheral neuropathy. Acta Neurol Scand. Oct. 1999;100:12–24. https://doi.org/10.1111/j.1600-0404.1999.tb07386.x.
31. Lefaucheur J-P. Neuropathies douloureuses et atteinte des petites fibres. Rev Neurol (Paris). Dec. 2014;170(12):825–36. https://doi.org/10.1016/j.neurol.2014.10.008.
32. Kosek E, Cohen M, Baron R, Gebhart GF, Mico JA, Rice ASC, Rief W, Sluka AK. Do we need a third mechanistic descriptor for chronic pain states? Pain. Jul. 2016;157(7):1382–6. https://doi.org/10.1097/j.pain.0000000000000507.
33. Bailly F. The challenge of differentiating fibromyalgia from small-fiber neuropathy in clinical practice. Jt Bone Spine. Dec. 2021;88(6):105232. https://doi.org/10.1016/j.jbspin.2021.105232.
34. Ochoa JL, Campero M, Serra J, Bostock H. Hyperexcitable polymodal and insensitive nociceptors in painful human neuropathy. Muscle Nerve. 2005;32(4):459-72. https://doi.org/10.1002/mus.20367
35. Willis WD. Long-term potentiation in spinothalamic neurons. Brain Res Brain Res Rev. Oct. 2002;40:1–3. https://doi.org/10.1016/s0165-0173(02)00202-3.
36. Jensen TS, Baron R. Translation of symptoms and signs into mechanisms in neuropathic pain. Pain. 2003;102(1–2):1–8. https://doi.org/10.1016/s0304-3959(03)00006-x
37. Ji R-R, Kohno T, Moore KA, Woolf CJ. Central sensitization and LTP: do pain and memory share similar mechanisms? Trends Neurosci. 2003;26(12):696-705. https://doi.org/10.1016/j.tins.2003.09.017
38. Gorson KC, Herrmann DN, Thiagarajan R, Brannagan TH, Chin RL, Kinsella LJ, Ropper AH. Non-length dependent small fibre neuropathy/ganglionopathy. J Neurol Neurosurg Psychiatry. Feb. 2008;79(2):163–9. https://doi.org/10.1136/jnnp.2007.128801.
39. Khan S, Zhou L. Characterization of non–length-dependent small-fiber sensory neuropathy. Muscle Nerve. Jan. 2012;45(1):86–91. https://doi.org/10.1002/mus.22255.
40. Tin SNW, Zouari HG, Wahab A, Sène D, Lefaucheur J-P. Characterization of Neuropathic Pain in Primary Sjögren's syndrome with respect to Neurophysiological evidence of small-Fiber neuropathy. Pain Med. May 2019;20(5):979–87. https://doi.org/10.1093/pm/pny183.
41. Abrams P, Cardozo L, Fall M, Griffiths D, Rosier P, Ulmsten U, Van Kerrebroeck P, Victor A, Wein A. The standardisation of terminology in lower urinary tract function: report from the standardisation sub-committee of the International Continence Society. Urology. Jan. 2003;61(1):37–49. https://doi.org/10.1016/s0090-4295(02)02243-4.
42. Lee CK, Tsai CP, Liao TL, Huang WN, Chen YH, Lin CH, Chen YM. Overactive bladder and bladder pain syndrome/interstitial cystitis in primary Sjögren's syndrome patients: a nationwide population-based study. PLoS ONE. 2019;14(11):e0225455. https://doi.org/10.1371/journal.pone.0225455.
43. Haarala M, Alanen A, Hietarinta M, Kiilholma P. Lower Urinary Tract Symptoms in Patients with Sjögren's Syndrome and Systemic Lupus Erythematosus. Int. Urogynecol. J. Pelvic Floor Dysfunct. 2000;11(2):84-6. https://doi.org/10.1007/s001920050075
44. Lee K, Chen M, Yeh J, Huang S, Tai H, Yu H. Lower urinary tract symptoms in female patients with rheumatoid arthritis, Scand. J. Rheumatol., vol. 35, no. 2, pp. 96 -101, Jan. 2006, https://doi.org/10.1080/03009740500395278
45. Robinson D, Cardozo LD. The role of estrogens in female lower urinary tract dysfunction. Urology. 2005;62(4)Suppl 1:45-51. https://doi.org/10.1016/s0090-4295(03)00676-9
46. Lee W-C, Wu H-P, Tai T-Y, Yu H-J, Chiang P-H. Investigation of urodynamic characteristics and bladder sensory function in the early stages of Diabetic bladder dysfunction in women with type 2 diabetes. J Urol. Jan. 2009;181(1):198–203. https://doi.org/10.1016/j.juro.2008.09.021.
47. Chan ACY, Wilder-Smith EP. Small fiber neuropathy: getting bigger! Muscle Nerve. May 2016;53(5):671–82. https://doi.org/10.1002/mus.25082.
48. Mozafarpour S, Chen A, Paredes Mogica JA, Nwaoha N, Farhad K, Morrison SM, De EJB. Urodynamic autonomic bladder dysfunction in women with complex chronic pelvic pain is associated with small fiber polyneuropathy. Neurourol. Urodyn. 2022;41(1):482–9. https://doi.org/10.1002/nau.24858
49. Chen A, De E, Argoff C. Small Fiber Polyneuropathy Is Prevalent in Patients Experiencing Complex Chronic Pelvic Pain. Pain Med. 2019:20(3):521-27. https://doi.org/10.1093/pm/pny001

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