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ORIGINAL RESEARCH

Lower Urinary Tract Symptoms Among Females with Rheumatoid Arthritis: A Prospective Cross-Sectional Study

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Purpose: To assess the presence of lower urinary tract symptoms (LUTS) in rheumatoid arthritis (RA) female patients with assessment of LUTS and its impact on quality of life (QoL).

Patients and Methods: A prospective, cross-sectional study of female patients with RA was conducted. Demographics and clinical data, Bristol Female Lower Urinary Tract Symptoms questionnaire (BFLUTS), and the RA Disease Activity Score 28 (DAS28) were all collected. A correlation has been made between all variables to assess the factors that induce LUTS in RA and the impact on QoL.

Results: Eighty-nine patients were enrolled. About 94.4% of RA patients had at least one symptom of LUTS. Concerning DAS28, 55.1% had moderate disease activity and 16.9% had high disease activity, which was not significantly associated with BFLUTS or QoL. The prevalence of overactive bladder syndrome symptoms (OAB: frequency, urgency, nocturia, and urgency incontinence) were found to be 65.2%, 59.6%, 56.2%, and 30.3%, respectively. Stress incontinence was prevalent in 40.4% of patients. The overall interference with life was evident in 27 (30.3%) patients secondary to LUTS. Body mass index (BMI) was positively and significantly correlated with the presence of storage symptoms ($r = 0.306$, $p = 0.004$) and with the total BFLUTS ($r = 0.251$, $p = 0.018$). BFLUTS subdomains and total scores were significantly correlated to poor QoL. The correlation of the BFLUTS QoL was found to be $r = 0.584$, $p < 0.001$ with storage symptoms, $r = 0.399$, $p < 0.001$ with voiding symptoms, and $r = 0.757$, $p < 0.001$ with incontinence.

Conclusion: LUTS is a prominent and significant disability that directly affects QoL in RA. BMI is an independent factor that is linked to LUTS in RA patients.

Keywords: lower urinary tract symptoms, rheumatoid arthritis, quality of life, DAS28, BFLUTS, overactive bladder

Introduction

Rheumatoid arthritis (RA) is a common type of inflammatory arthritis in women.[1] It is an autoimmune disease that may present with extra-articular manifestations, such as pulmonary complications and Sjögren's syndrome.[2] Rarely, RA may affect the urinary tract and has different clinical presentations, such as urinary tract infections (UTI), urolithiasis, and even de-novo lower urinary tract symptoms (LUTS).[3] The combination of joint pain, stiffness, and other potential systematic involvement may directly negatively impact the quality of life (QoL) of such patients.[4] LUTS is a broad category of symptoms that include storage, voiding, and post-micturition

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symptoms.[5] It commonly affects women and causes significant distress.[6] LUTS in females is either pathological or non-pathological, albeit both affect QoL negatively. For instance, the pregnant female can predominantly have non-pathological LUTS, especially towards the third trimester, and it affects QoL causing prominent stress and embarrassment.[7,8] On the other hand, diabetic and spinal cord injury patients may present with LUTS secondary to a pathological insult to the urinary tract, such as UTIs and urolithiasis.[9,10]

The correlation between RA and LUTS is not well established, which creates a challenge to clinicians as both entities directly negatively impact the patient's QoL.[11] Also, the factors that create or exacerbate LUTS in RA are still debatable and not yet discovered. Few published articles have studied the frequency of LUTS among patients with seropositive systemic inflammatory disease, which showed a high prevalence of voiding dysfunction among such a cohort.[12–14] Furthermore, it is unclear whether RA directly causes LUTS or is part of the natural history of LUTS. Moreover, several factors need to be investigated in RA with LUTS, such as smoking, body mass index (BMI), and coffee intake, as these factors are correlated with the presence and severity of LUTS.[15,16] RA disease activity is another valid question as it is unclear if disease status directly affects the presence and severity of LUTS among RA patients.

In this study, we recruited female patients with RA to evaluate the presence of lower urinary tract dysfunction in them. LUTS (storage, voiding, and incontinence), sexual function and their impact on QoL were explored in detail using the BFLUTS questionnaire. RA disease activity has also been studied in addition to different independent variables to describe the factors that may be related to LUTS in RA patients.

Methods

Study Design

This is a prospective and cross-sectional study that recruited adult female patients who have been diagnosed with RA.

Study Setting

This study was held at four different primary care clinics with rheumatology services, covering a population of 1.5 million, between December 2020 and April 2021.

Inclusion and Exclusion Criteria

Females diagnosed with RA and aged more than 18 years old were included. Patients with previous urological problems, previous urinary tract surgery, or recent documented or symptomatic UTIS were all excluded. Figure 1 shows consort diagram for including RA patients.

Study Population and Sampling

In this study, we included all female patients who had been diagnosed with RA. We performed a questionnaire survey using a judgmental sampling method to reach the patients. Based on the expected population during the research period and a 50% response distribution, the needed sample size was about 90 with a confidence level of 95% and a margin of error of 5%.

Data Collection

The first set was the demographics and clinical data including age, BMI, the presence of DM, smoking, coffee intake, and duration of RA disease, which later was divided into four main categories: ≤1 year, >1–5 years, >5–10 years, and more than ten years.

The second part included a self-administered Bristol Female Lower Urinary Tract Symptoms (BFLUTS) questionnaire. BFLUTS is an instrument created by Jackson et al in 1996 and used to assess a wide range of urinary symptoms.[17,18] It consists of nineteen questions, which are divided into 5 domains as follows: four questions for filling domain (score range 0–15), three for voiding (score range 0–12), five for incontinence (score range 0–20), and the remaining seven questions are distributed with two questions to assess sexual function (score range 0–6) and five for quality of life (score range 0–18). The respondents have to answer each question with a score from "0" to "3" or "0" to "4", which indicates the frequency or severity of the symptoms. The resulting total score ranges between 0 and 71. Higher scores represent more severe symptoms.

In the last part, the RA disease was assessed by applying Rheumatologic Disease Activity Score 28 (DAS28), which is a continuous measure of RA disease activity that combines information from swollen joints, tender joints, and acute-phase response. Accordingly, the output is categorized into four main groups, those who are in remission, where the DAS28 score is ≤2.6, low disease activity when DAS28 between 2.6 and ≤3.2, moderate disease activity with DAS28 score between 3.2 and ≤5.1, and lastly, high

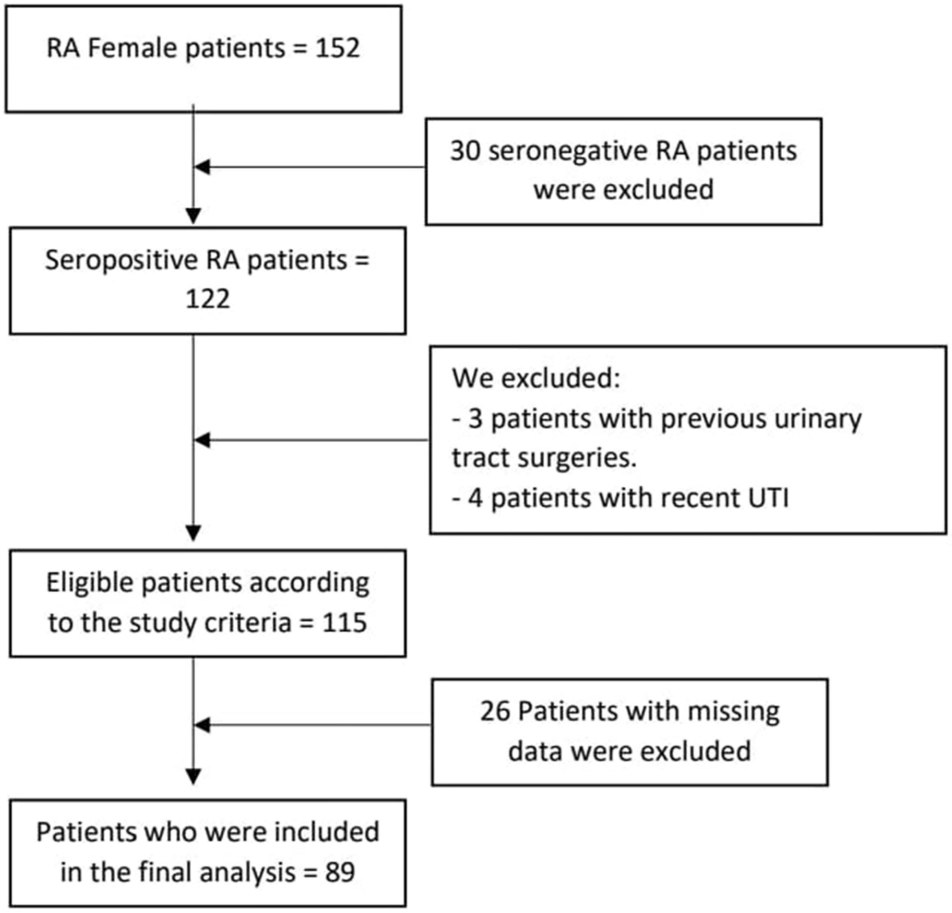

Figure 1 CONSORT diagram for including RA patients.
Notes: Adapted from: Schulz KF, Altman DG, Moher D, CONSORT Group. CONSORT 2010 Statement: Updated Guidelines for Reporting Parallel Group Randomised Trials. *PLoS Med*. 2010;7(3):e1000251.[34] Copyright: © 2010 Schulz et al. Creative Commons Attribution License.

disease activity with DAS28 score above 5.1. The primary outcome was RA disease activity, and the secondary outcomes were LUTS and QoL.

Statistical Analysis

Data were entered and analysed using the Statistical Package for Social Sciences program (SPSS) version 21. Data were expressed as means ± SD and median [Q1-Q3] for continuous variables, and as frequencies and percentages for categorical variables. We used the Pearson test to assess the correlations between BFLUTS, demographics and QoL. Kruskal Wallis and Mann Whitney *U*-test was used to analyse the patients' characteristics according to BFLUTS total score and sub-scores. The significance level was set at a p-value < 0.05.

Ethical Approval and Confidentiality

All aspects of the study protocol, including access to and using patient clinical information, were authorized by An-Najah National University Institutional Review Board (IRB), Nablus, Palestine. Before administering the survey or conducting interviews, each participant provided verbal informed consent. The IRB accepted the study protocol, including the verbal consent process, and there was no need for written consent. All participants were notified that their information will be coded and anonymized. The study was conducted according to the Declaration of Helsinki.

Results

Patients' Demographics and Clinical Presentation

Eighty-nine patients met the inclusion criteria. Patients' demographics and clinical presentation were collected. Majority of women were over 40 years old, and the majority had BMI over 30. Around half of the patients have been diagnosed with RA within one year. Using

DAS28, 13 (14.6%) of the patients were in remission, 12 (13.5%) had low disease activity, 49 (55.1%) had moderate disease activity, and 15 (16.9%) had high disease activity. Table 1 shows the patients' demographics and clinical presentation.

Self-Administered BFLUTS

We found that 94.4% of RA patients had at least one symptom of LUTS according to the BFLUTS questionnaire. The mean total BFLUTS score was 10.75 ±10.38 (range 0–43). The mean score of filling symptoms was 4.82 ± 3.19 (range: 0–13). The mean score of voiding symptoms was 0.61 ± 1.35 (range 0–8). The mean score of incontinence was 2.31 ±3.50 (range 0–16). The mean score of QoL among the cohort was 3.01 ± 4.57 (range 0–16). Table 2 shows the BFLUTS score in each domain.

Table 1 Characteristics of the Participants (N = 89)

Variable	Frequency (%)
Age	
< 40	19 (21.3)
≥ 40	70 (78.7)
Body mass index	
Normal (20–24.9)	20 (22.5)
Overweight (25–29.9)	30 (33.7)
Obese (30–34.9)	39 (43.8)
Disease duration (years)	
≤ 1	41 (46.1)
> 1–5	27 (30.3)
> 5–10	10 (11.2)
> 10	11 (12.4)
Diabetes mellitus type 2	
Yes	11 (12.4)
No	78 (87.6)
Smoking	
Yes	8 (9.0)
No	81 (91.0)
Daily Coffee intake	
Yes	73 (82.0)
No	16 (18.0)
Rheumatoid Arthritis Disease activity	
Remission	13 (14.6)
Low	12 (13.5)
Moderate	49 (55.1)
High	15 (16.9)

BFLUTS Subdomains

Table 3 shows the frequency of each symptom in the BFLUTS subdomain. The most prevalent symptoms are those of the overactive bladder syndrome.

Storage Domain

The storage symptoms were found to be as following: nocturia (>1 times): 50 (56.2%), urgency: 53 (59.6%), and frequency: 58 (65.2%).

Voiding Domain

The voiding symptoms were documented as following: hesitancy: 8 (9%), straining: 8 (9%), and intermittency: 14 (15.7%)

Incontinence Domain

Urinary incontinence is highly prevalent in our cohort with urgency incontinence found in 27 (30.3%) patients, and stress incontinence found in 36 (40.4%) patients.

QoL Domain

The overall interference with life was evident in 27 (30%) patients secondary to LUTS.

Correlation Between BFLUTS Subdomains and Patients' Demographics

BMI is positively and significantly correlated to the presence of storage symptoms (r = 0.306, p = 0.004) and to the total BFLUTS score (r = 0.251, p = 0.018). Age is not correlated with the BFLUTS total score or subdomains.

Table 2 BFLUTS Scores of the Participants (N = 89)

Domain	BFLUTS Range	BFLUTS Mean ± SD	BFLUTS Median [Q1-Q3]
Filling	0.0–13.0	4.82 ±3.19	5.0 [2.0–7.0]
Voiding	0.0–8.0	0.61 ± 1.35	0.0 [0.0–0.5]
Incontinence	0.0–16.0	2.31 ± 3.50	1.0 [0.0–3.5]
Quality of life	0.0–16.0	3.01 ± 4.57	1.0 [0.0–4.0]
Total BFLUTS	0.0–43.0	10.75 ± 10.38	7.0 [3.0–14.0]

Table 3 Frequencies of Each BFLUTS Symptom for Each Domain (N = 89)

Symptoms	Frequency (%)
Storage	
Nocturia (> 1 time)	50 (56.2)
Urgency	53 (59.6)
Bladder pain	17 (19.1)
Frequency	58 (65.2)
Voiding	
Hesitancy	8 (9.0)
Strain to urinate	8 (9.0)
Intermittency (stop and start more than once)	14 (15.7)
Incontinence	
Leaking before getting to the toilet (urge incontinence)	27 (30.3)
Frequency of incontinence	29 (32.6)
Stress incontinence (when physically active, cough, etc.)	36 (40.4)
Unpredictable incontinence (no reason and feeling)	14 (15.7)
Nocturnal incontinence (leaking when asleep)	3 (3.4)
Sexual function	
Sex life spoiled by urinary symptoms	0 (0.0)
Leaking during intercourse	0 (0.0)
Quality of life	
Change outer clothing	28(31.5)
Cut down fluid	25(28.1)
Affect daily tasks	23(25.8)
Avoid situations where no toilet	25(28.1)
Overall interference with life	27 (30.3)

BFLUTS subdomains and total score are significantly correlated with poor QoL. The correlation between the BFLUTS QoL was found to be r = 0.584, $p < 0.001$ with storage symptoms, r = 0.399, $p < 0.001$ with voiding symptoms, and r = 0.757, $p < 0.001$ with incontinence. Table 4 shows the correlations between BFLUTS, demographics, and QoL.

Impact of RA on LUTS and QoL

The disease activity of RA measured by DAS 28 was not found to be associated with any domains of LUTS (filling, voiding, and incontinence), OoL, or total BFLUTS score. For example, the median (Q1-Q3) BFLUTS filling score for patients in remission was 4.0 (2.0–4.5), while 5.5 (3.3–7.8) was for patients with low disease activity, 5.0 (2.5–7.5) was for the moderate activity category, and 4.0 (1.0–5.0) was for high disease activity, with an insignificant *p*-value (0.275). Another important RA-related parameter was the duration of disease, which also was not significantly associated with any domains of BFLUTS or QoL. As an example, the median [Q1-Q3] scores of the BFLUTS incontinence score were as follows: 1.0 [0.0–3.5] for disease duration of ≤1 year, 0.0 [0.0–2.0] for >1–5 years, 3.5 [1.5–6.3] for >5–10 years, and 0.0 [0.0–5.0] for >10 years, with an insignificant *p* value (0.091). Figure 2 shows the distribution of LUTS subdomains among DAS 28 categories. Table 5 shows the clinical variables and BFLUTS subdomain correlation.

Discussion

This study shows that RA patients frequently complain of LUTS, which affects their QoL. A previously published article describes a wide range of urological diseases more prevalent in RA patients, such as UTIs, urolithiasis, and urine retention.[3] However, this study focused on LUTS, which had no obvious underlying cause and led to a negative impact on the patient's QoL. The detailed LUTS analysis which we have done allows us to conclude that the majority of RA patients complain of LUTS, which

Table 4 Correlations Between BFLUTS, Demographics, and QoL

		BFLUTS-FS (Storage)	BFLUTS-VS (Voiding)	BFLUTS-IS (Incontinence)	BFLUTS-Total
Age	Pearson Correlation	0.062	−0.071	0.187	0.185
	Sig. (2-tailed)	0.566	0.508	0.08	0.082
BMI	Pearson Correlation	0.306**	0.073	0.167	0.251*
	Sig. (2-tailed)	**0.004**	0.497	0.117	**0.018**
BFLUTS-QoL	Pearson Correlation	0.584**	0.399**	0.757**	0.927**
	Sig. (2-tailed)	**<0.001**	**<0.001**	**<0.001**	**<0.001**

Notes: **Correlation is significant at the 0.01 level (2-tailed). *Correlation is significant at the 0.05 level (2-tailed). Bold figures indicate a significant *p* value (< 0.05).
Abbreviations: FS, Filling symptoms; VS, Voiding symptoms; IS, Incontinence symptoms.

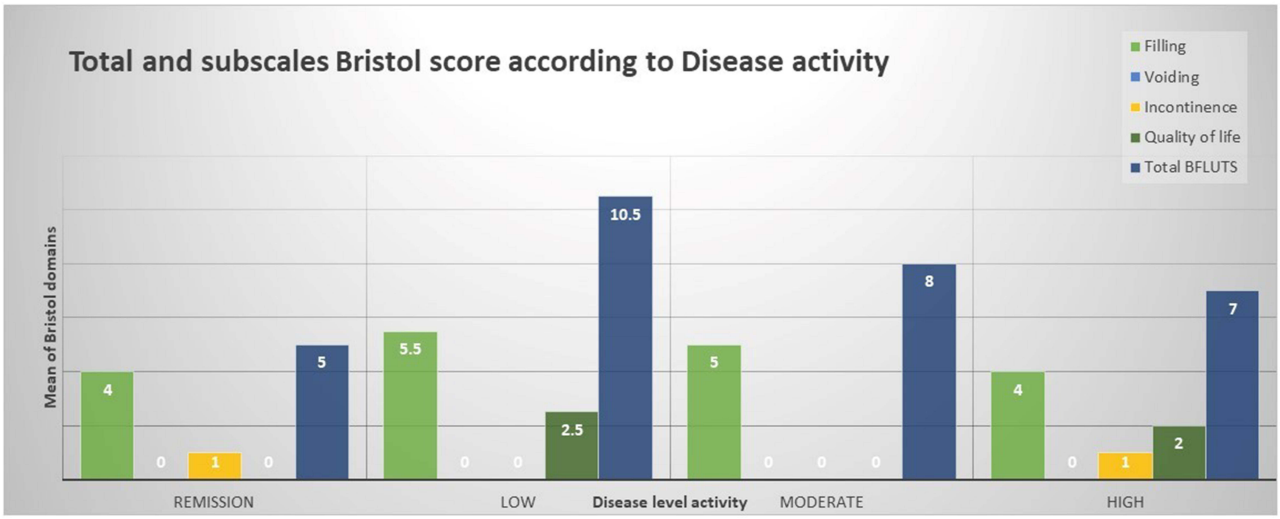

Figure 2 Subscales Bristol scores according to disease activity.

were overlooked by their treating physician and caused noticeable anxiety and interference with their daily activities.

The most prevalent group of symptoms were of overactive bladder syndrome (OAB). The presence of OAB in seropositive systemic inflammatory disease was previously studied and showed significantly worse OAB in this group with a direct negative impact on QoL.[19,20] Nocturia (56.2%), urgency (59.6%), and daytime frequency (65.2%) were the most frequent symptoms in RA patients, according to our results, and these symptoms cause a direct negative impact on QoL ($p < 0.001$). The concept of the negative impact of OAB on QoL is well established in the literature in different cohorts of patients and the general population as well.[7,21–23] The new finding in this study is that the detailed analysis of LUTS uncovered significant OAB in RA that patients and physicians usually overlook. Thus, a routine assessment of such symptoms is paramount for RA disease activity evaluation during RA follow-up clinics.

Furthermore, treatment of OAB should be offered to all symptomatic patients with idiopathic OAB to improve their QoL. The treatment entails primarily either behavioral treatment and/or medication, which can be offered at primary care centers.[24,25] To conclude, a detailed assessment of LUTS and treatment counseling is essential for all RA patients and should be offered during follow-up.

Incontinence is another frequently encountered problem in this study. It was previously published that urinary incontinence is underreported in arthritis.[26] However, in our study, stress incontinence (40.4%) and urgency incontinence (30.3%) are frequently seen in RA patients. This creates a new challenge as urinary incontinence had the highest correlation with QoL in this group. Thus, further studies are required to assess and analyze urinary incontinence to find factors that exacerbate such symptoms and establish treatment strategies.[16,27]

BMI is positively and significantly correlated to OAB symptoms and urinary incontinence in RA and is the main factor that may be responsible for LUTS in RA patients. BMI is well known as an independent variable to exacerbate OAB and urinary incontinence.[28,29] Furthermore, weight reduction strategy is well known to improve LUTS and urinary incontinence.[15] Thus, RA patients with LUTS have to be counseled regarding obesity, especially that obesity was previously linked to RA disease activity, poor response to treatment, and risk for long-term adverse outcomes.

Disease activity was not found to be correlated with LUTS. DAS 28 showed no significant difference between the four categories with respect to LUTS or LUTS-related poor QoL. Furthermore, DM is also not linked directly to LUTS in RA patients despite the available evidence to conclude that DM, in general, is linked to LUTS.[30,31] Further analysis and studies are required to compare controlled DM and poorly controlled DM in view of LUTS, LUTS severity, and QoL.

Smoking and caffeine intake are not directly linked to LUTS in RA. However, smoking is weakly associated with improving LUTS.[32] A recent review showed that the evidence is low regarding the impact of reduction

Table 5 Patients' Characteristics According to Total BRISTOL Score and Subscores

	N (%)	BFLUTS-FS Median[Q1-Q3]	BFLUTS-VS Median[Q1-Q3]	BFLUTS-IS Median[Q1-Q3]	BFLUTS-QoL Median[Q1-Q3]	BFLUTS-SF Median[Q1-Q3]
Disease duration (yrs)						
≤ 1	41 (46.1)	5.0 [3.0–7.0]	0.0 [0.0–1.5]	1.0 [0.0–3.5]	1.0 [0.0–6.5]	9.0 [3.0–19.0]
> 1–5	27 (30.3)	4.0 [1.0–6.0]	0.0 [0.0–0.0]	0.0 [0.0–2.0]	0.0 [0.0–2.0]	5.0 [3.0–11.0]
> 5–10	10 (11.2)	4.5 [2.8–8.5]	0.0 [0.0–0.5]	3.5 [1.5–6.3]	1.5 [0.0–8.8]	11.5 [5.0–19.0]
> 10	11 (12.4)	4.0 [2.0–6.0]	0.0 [0.0–0.0]	0.0 [0.0–5.0]	0.0 [0.0–1.0]	5.0 [2.0–10.0]
	***P*-value**	0.602	0.378	0.091	0.384	0.193
Diabetes mellitus						
Yes	11 (12.4)	6.0 [1.0–8.0]	0.0 [0.0–1.0]	0.0 [0.0–1.0]	0.0 [0.0–9.0]	7.0 [1.0–21.0]
No	78 (87.6)	4.5 [2.0–7.0]	0.0 [0.0–0.3]	1.0 [0.0–4.0]	1.0 [0.0–4.0]	7.0 [3.0–14.0]
	***P*-value**	0.764	0.863	0.187	0.931	0.896
Smoking						
Yes	8 (9.0)	5.0 [3.0–8.8]	0.0 [0.0–1.8]	1.0 [0.0–4.0]	0.5 [0.0–7.5]	8.5 [4.3–20.0]
No	81 (91.0)	4.0 [2.0–7.0]	0.0 [0.0–0.0]	1.0 [0.0–3.0]	1.0 [0.0–4.0]	7.0 [3.0–13.5]
	***P*-value**	0.681	0.477	0.902	0.988	0.575
Caffeine intake						
Yes	73 (82.0)	5.0 [2.5–7.0]	0.0 [0.0–0.5]	0.0 [0.0–3.5]	1.0 [0.0–5.0]	7.0 [3.5–14.5]
No	16 (18.0)	4.0 [1.3–6.0]	0.0 [0.0–0.8]	1.5 [0.0–3.8]	0.0 [0.0–1.0]	7.0 [2.3–12.8]
	***P*-value**	0.516	0.966	0.648	0.132	0.514
Disease activity						
Remission	13 (14.6)	4.0 (2.0–4.5)	0.0 (0.0–0.0)	1.0 (0.0–3.0)	0.0 (0.0–1.0)	5.0 (3.5–8.5)
Low	12 (13.5)	5.5 (3.3–7.8)	0.0 (0.0–1.0)	0.0 (0.0–3.8)	2.5 (0.0–5.5)	10.5 (4.8–14.8)
Moderate	49 (55.1)	5.0 (2.5–7.5)	0.0 (0.0–0.5)	0.0 (0.0–3.5)	0.0 (0.0–5.5)	8.0 (3.0–17.5)
High	15 (16.9)	4.0 (1.0–5.0)	0.0 (0.0–2.0)	1.0 (0.0–4.0)	2.0 (0.0–7.0)	7.0 (3.0–15.0)
	***P*-value**	0.275	0.746	0.899	0.168	0.563

caffeine on improving LUTS. However, urgency is improved with a decrease in coffee intake[33] and fluid intake in general.

Surprisingly, we found that RA patients had no sexual symptoms. This may be due to social embarrassment that prevents patients from disclosing this information.

Strengths and Limitations

This is the first study to assess LUTS in RA using a detailed patient-reported outcome measure questionnaire. However, the absence of a control group (women with no RA) and the small sample size are the main limitations of this study. Small sample size of the subgroups made comparison analysis to be problematic. Certain variables, such as medication use and specifically RA medications, were not addressed in this study, which may have had an impact on developing LUTS. Furthermore, the impact on sexual function may have suffered reporting bias due to social embarrassment.

Conclusions

LUTS are a prominent and significant disability that directly affects QoL in RA. BMI is an independent risk factor that is linked to LUTS in RA patients. OAB and urinary incontinence are the main forms of LUTS in such a cohort of patients. Furthermore, amendable factors that may exacerbate LUTS among female patients with RA should be identified and targeted to improve such symptoms, directly impacting the patient's QoL.

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Author Contributions

All authors made substantial contributions to the conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published, and agreed to be accountable for all aspects of the work.

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