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RESEARCH ARTICLE

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Comparison of functionality, mood, and biopsychosocial status in rheumatic patients with and without self-reported bowel problems and the evaluation of BETY's impact on these factors: a retrospective study

Nur Banu Karaca[a], Aysu Kahraman[a], Sinan Buran[a], Orkun Tüfekçi[a], Fatma Birgül Kumbaroğlu[a], Zeynep İrem Bulut[b], Senem Bulut[a], Aysima Barlak[a], Atalay Doğru[c], Umut Kalyoncu[d], Ali Akdoğan[d], Şule Apraş Bilgen[d], Sedat Kiraz[d] and Edibe Ünal[a]

[a]Faculty of Physical Therapy and Rehabilitation, Hacettepe University, Ankara, Turkey; [b]Faculty of Health Sciences, Department of Physical Therapy and Rehabilitation, Hasan Kalyoncu University, Gaziantep, Turkey; [c]Faculty of Medicine, Department of Internal Medicine, Division of Rheumatology, Süleyman Demirel University, Isparta, Turkey; [d]Faculty of Medicine, Department of Internal Medicine, Division of Rheumatology, Hacettepe University, Ankara, Turkey

ABSTRACT

Objective: This retrospective study aimed to evaluate the comparison of functionality, mood, and biopsychosocial status in rheumatic patients with and without self-reported bowel problems and the evaluation of *Bilişsel Egzersiz Terapi Yaklaşımı (BETY) – (Cognitive Exercise Therapy Approach in English)*'s impact on these factors.

Methods: The study included 718 patients with eight different diagnoses of rheumatism. The presence of self-reported bowel problems in rheumatic patients was assessed with item 10 of the BETY-Biopsychosocial Questionnaire (BETY-BQ), functionality with the Health Assessment Questionnaire (HAQ), emotional status with the Hospital Anxiety and Depression Scale (HADS), and biopsychosocial status (BPS) with the BETY-BQ. Sixty-five rheumatic patients were included in BETY group exercise sessions for 3 months, 3 days a week.

Results: The rate of self-reporting bowel problems in the total cohort was 61.6%. Among all BPS parameters examined, a significant difference was found in favor of rheumatic individuals who did not report bowel symptoms ($p < .005$). All patients included in the BETY sessions achieved improvement in all parameters, including bowel symptoms ($p < .005$).

Conclusions: Many patients suffered from bowel problems. The investigated parameters of rheumatic patients with bowel symptoms were negatively affected. BETY improved all parameters, including bowel symptoms. BPS features should be considered in disease management in rheumatic patients reporting bowel problems. BETY should be used as an exercise intervention based on the BPS model in these patients.

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Introduction

Rheumatic diseases are complex disorders with various pathophysiological mechanisms and a broad clinical spectrum[1,2]. There are more than 200 defined rheumatic diseases, including Ankylosing Spondylitis (AS), Rheumatoid Arthritis (RA), Psoriatic Arthritis (PsA), Systemic Lupus Erythematosus (SLE), Systemic Sclerosis (SSc), Sjögren's Syndrome (SS), Osteoarthritis (OA), and Fibromyalgia (FM)[1,3]. Patients may have musculoskeletal involvement and extra-articular symptoms impacting the cardiovascular, pulmonary, neurological, and gastrointestinal systems (GIS)[4,5]. Additionally, patients with rheumatic diseases typically self-report symptoms such as pain, decreased functionality, fatigue, emotional distress, anxiety, sleep disturbances, and a decline in quality-of-life[1]. On the other hand, bowel problems are also noteworthy in patients with rheumatism[6].

Increasing evidence suggests that dysbiosis, an imbalance in the gut microbiota, may contribute to the onset or progression of rheumatic diseases[7]. Variability in GIS can arise from both the pathogenesis of these conditions and the ability of certain medication therapies to activate existing bowel symptoms. Non-specific symptoms such as abdominal pain, bloating, indigestion, nausea, diarrhea, and constipation are commonly reported by patients[8]. However, diagnosing GIS involvement can be challenging due to the insidious onset of symptoms and fluctuating severity, which can delay accurate diagnosis[5]. Therefore, evaluating GIS is crucial for establishing correct diagnoses[9]. Furthermore, studies have reported that individuals with high levels of GIS experience worsened psychosocial symptoms such as depression, anxiety, pain interaction, fatigue, social satisfaction, and sleep disorders, both among those with and without a rheumatic diagnosis[10].

CONTACT Edibe Ünal edibeunal@yahoo.com Faculty of Physical Therapy and Rehabilitation, Hacettepe University, 06100 Altındağ/Ankara, Turkey
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Recent studies have highlighted that exercise may enhance microbiota diversity and thus potentially reduce GIS-related disorders. Due to their broad impact, the European Alliance of Associations for Rheumatology (EULAR) guidelines emphasize implementing pharmacological and non-pharmacological treatments and the biopsychosocial (BPS) model in managing rheumatic diseases[11]. Non-pharmacological treatment is an important component that includes patient education and BPS-based exercise interventions[12,13]. There is a growing body of evidence in the literature supporting the necessity and benefits of exercise therapy in managing rheumatic diseases; however, very few studies have examined the effectiveness of exercise in GIS in rheumatic diseases.

The remission of joint inflammation has been linked to a decrease in inflammation in the gut[14]. Exercise programs that last a minimum of 4 weeks are reported to affect gastrointestinal symptoms positively[15]. In another study, the potential effects of exercise training on GIS, recognized for its anti-inflammatory properties[16], were discussed as a worthwhile topic[17].

The Cognitive Exercise Therapy Approach (Bilişsel Egzersiz Terapi Yaklaşımı-BETY) is an innovative method designed to support patients with rheumatic diseases from a BPS perspective. It aims to improve various health domains, such as chronic pain, fatigue, functionality, mood, sexuality, and sociability[18–21]. However, limited information is available regarding the effects of BETY on GIS and related BPS factors in patients with rheumatic diseases. Therefore, this retrospective study aimed to (1) compare functionality, mood, and BPS status in rheumatic patients with and without self-reported bowel problems and (2) examine the effectiveness of BETY, a structured biopsychosocial-based exercise program, on bowel problems, functionality, mood, and BPS status.

Methods

Participants

This retrospective cohort study included adult patients diagnosed with AS, RA, PsA, SLE, SSc, SS, OA, or FM who were followed by rheumatologists and referred to our clinic between April 2018 and April 2023. All patients with neurological diseases, malignancies, or severe mental disorders were excluded from this study. The diagnostic criteria followed for AS, RA, PsA, SLE, SSc, SS, OA, and FM were as follows: 1984 modified New York criteria, 2010 ACR/EULAR criteria, 2006 CASPAR criteria, 2012 Systemic Lupus International Collaborating Clinics criteria, 2013 ACR/EULAR criteria, American–European Consensus Group criteria, 1986 ACR criteria, and 2016 ACR criteria, respectively[22–30]. Hacettepe University Non-Interventional Clinical Research Ethics Committee reviewed and approved this retrospective cohort study protocol (GO 23/519).

Data collection

Demographic information about the patients, such as age, gender, body mass index, and data on disease characteristics, was obtained from the health records kept by the Rheumatological Rehabilitation Unit of Hacettepe University Faculty of Physical Therapy and Rehabilitation. The following patient-reported outcomes measurements (PROMs) were used.

Health Assessment Questionnaire (HAQ): The HAQ consists of 20 questions assessing eight activities, including dressing, rising, eating, walking, hygiene, reaching, gripping, and daily tasks. The patient rates each question on a scale of 0–3 (0; No difficulty, 1; Mild difficulty, 2; Moderate difficulty, 3; Unable to perform). The total score ranges from 0 to 3, with higher scores indicating worse functional levels. HAQ scores greater than 1 indicate the presence of disability[31].

Hospital Anxiety and Depression Scale (HADS): The HADS comprises 14 questions requiring the patient to reflect on the last few days, with each question offering four response options. Odd-numbered questions create the anxiety score (HADS-A), while even-numbered questions create the depression score (HADS-D). The cut-off values of HADS, which are scored between 0–21 in total, were determined as 10 for anxiety and 7 for depression. A higher score signifies elevated levels of anxiety and depression[32].

BETY-Biopsychosocial Questionnaire (BETY-BQ): The BETY-BQ, developed for individuals with rheumatic diseases, consists of 30 items assessing the last week. BETY-BQ comprehensively assesses BPS features, including pain, functionality, fatigue, mood, social participation, sexuality, and sleep. Each item is scored from 0 to 4 (4: Always, 3: Often, 2: Sometimes, 1: Rarely, 0: Never) for a total score ranging from 0 to 120. Higher scores indicate worse biopsychosocial conditions. The BETY-BQ's validity, reliability, and sensitivity have been demonstrated in patients with AS, RA, PsA, SLE, FM, pSS, SSc, and OA[33–41].

Item 10 of the BETY-BQ states, 'I think my bowel function is not regular'. This study used it as an independent measure apart from the scale's total score.

Intervention

BETY is an exercise-based biopsychosocial approach developed for patients with rheumatic diseases that emphasizes active patient involvement in treatment and focuses on resolving complaints. The innovative parameters include four main components: function-oriented core stabilization exercises, dance therapy-authentic movement, chronic pain management, and sexual information management. It can be implemented in individual and group sessions. The BETY process applied is shown in Supplementary Appendix S1[18–21].

Procedure

In this study, item 10 of the BETY-BQ was considered a determinant of the frequency of existing bowel problems. Since the questionnaire assesses the previous week, responses to item 10 of 'Yes, Rarely; Yes, Sometimes; Yes, Often; and Yes, Always' indicated bowel problems, while a response of 'No, Never' indicated no bowel problems. Demographic information and scores for HAQ, HADS, and BETY-BQ were obtained from the health records kept by the patient files. To evaluate the effectiveness of the exercise

intervention, a subgroup of patients who regularly attended group exercise sessions of BETY three times a week for 3 months, with no changes in medication regimens during this period, was also assessed using the same scales after the BETY sessions.

Statistical analysis

Statistical analyses were performed using SPSS software (version 23, SPSS Inc., Chicago, IL). Descriptive statistics for numerical data included mean, standard deviation (SD), median, and interquartile range (IQR), while categorical variables were expressed as counts and percentages (%). Kruskal-Wallis Test was used to analyze the differences in bowel problem frequencies according to different rheumatic disease diagnoses. Mann-Whitney U test was used to analyze differences between groups for numerical data, and the Chi-square test was used for categorical data. Changes in the exercise training group were analyzed using the Wilcoxon test. Effect size (r) was calculated for changes in the exercise training group using the Wilcoxon test, with the formula $r = Z/\sqrt{N}$, where Z is the Wilcoxon Z score and N is the sample size. The Z value can be used to calculate an effect size, such as the r proposed by Cohen[42]. According to Cohen's guidelines, an r value of 0.1 indicates a small effect, 0.3 indicates a medium effect, and 0.5 indicates a large effect[43]. In the analysis conducted before and after treatment, the effect size was determined to be 0.88 based on the total BETY-BQ score. The power of this study was determined to be 98% for 65 individuals. Statistical significance was set at $p < .05$ for all analyses.

Results

A total of 718 patients with rheumatic diseases participated in the study. The mean age of the participants was 47.56 ± 12.25 years, with 586 (81.6%) being female and 132 (18.4%) being male. Demographic information is detailed by diagnosis in Table 1.

Of the rheumatic patients, 61.6% reported experiencing bowel issues. Rates based on diagnoses are presented in Table 2. The reporting rate of bowel problems was statistically similar across diagnoses ($p = .06$). The HAQ, HADS-depression, HADS-anxiety, and BETY-BQ scores for the 718 patients with rheumatic diseases are presented in Table 2.

The HAQ, HADS-A, HADS-D, and BETY-BQ scores of rheumatic patients reporting bowel problems were significantly higher than those reporting no bowel problems ($p < .001$) (Table 3). Considering the cut-off values for these PROMs, 32.6% of patients with bowel problems exhibited

Table 1. Demographic information for patients with rheumatic diseases.

Disease	Total n (female %)	Age (years)		Body Mass Index (kg/m^2)		Duration (years)	
		Median (IQR)	Mean ± SD	Median (IQR)	Mean ± SD	Median (IQR)	Mean ± SD
Ankylosing Spondylitis	105 (47.6%)	38 (31–45)	38.90 ± 9.93	26.61 (22.96–29.30)	26.64 ± 4.30	2 (0–6)	4.06 ± 5.14
Rheumatoid Arthritis	93 (84.9%)	53 (46–59)	50.87 ± 9.46	26.69 (23.57–30.46)	27.79 ± 6.10	10 (4–20)	12.97 ± 11.69
Psoriatic Arthritis	76 (73.7%)	42 (37–54)	43.41 ± 10.91	26.29 (21.69–31.43)	26.93 ± 6.20	6 (2–14)	8.94 ± 8.46
Systemic Lupus Erythematosus	71 (85.9%)	37 (28–49)	38.61 ± 12.88	25.65 (21.88–30.46)	26.04 ± 5.12	8 (4–13)	9.88 ± 7.34
Sytemic Sclerosis	54 (88.9%)	52 (38–59)	49.30 ± 11.63	24.37 (22.41–28.0)	24.93 ± 5.25	12 (6–18)	13.21 ± 8.38
Sjögren's Syndrome	85 (95.3%)	56 (50–61)	54.84 ± 10.34	27.80 (25.06–32.69)	29.26 ± 7.25	8 (3–12)	8.36 ± 6.67
Osteoarthritis	121 (86%)	58 (53–65)	58.37 ± 8.03	31.98 (28.23–35.16)	32.54 ± 5.93	4 (3–8)	5.98 ± 5.83
Fibromyalgia	113 (94.7%)	44 (38–50)	43.51 ± 8.53	25.65 (22.96–29.76)	26.96 ± 5.40	15 (6–18)	12.83 ± 6.46

Data are shown as means with standard deviation or medians (25th, 75th percentiles).

Table 2. Baseline assessment scores categorized by diagnosis in patients with rheumatic diseases.

Diagnosis	HAQ (0–3)	HADS-Anxiety (0–21)	HADS-Depression (0–21)	BETY-BQ (0–120)	Frequency of self-reported bowel problems n (%)					
	Median (IQR)				Never	Rarely	Sometimes	Often	Always	p^*
	Mean ± SD									
Ankylosing spondylitis	0.750 (0.375–1.250)	8 (5–12)	7 (4–10)	53 (28–69)	40 (38.1)	9 (8.6)	21 (20)	16 (15.2)	19 (18.1)	.06
	0.85 ± 0.63	8.91 ± 4.64	7.24 ± 4.17	51.39 ± 26.18						
Rheumatoid arthritis	1.0 (0.5–1.5)	6 (3–9)	5 (2–7)	54 (37–72)	47 (50.5)	6 (6.5)	10 (10.8)	5 (5.4)	25 (26.9)	
	1.04 ± 0.71	6.53 ± 4.53	5.19 ± 4.07	55.61 ± 27.96						
Psoriatic arthritis	0.375 (0.125–0.750)	8 (6–11)	7 (4–10)	44 (27–63)	31 (40.8)	7 (9.2)	19 (25)	11 (14.5)	8 (10.5)	
	0.49 ± 0.45	8.32 ± 4.04	7.12 ± 3.94	45.95 ± 25.44						
Systemic lupus erythematosus	0.2 (0.0–0.5)	6 (3–9)	7 (5–12)	50 (27–65)	25 (35.2)	9 (12.7)	16 (22.5)	15 (21.1)	6 (8.5)	
	0.35 ± 0.42	6.04 ± 3.41	8.27 ± 4.58	48.30 ± 25.97						
Sytemic sclerosis	0.438 (0.125–1.0)	7 (6–11)	7 (4–9)	46 (23–67)	19 (35.2)	11 (20.4)	6 (11.1)	6 (11.1)	12 (22.2)	
	0.71 ± 0.73	8.09 ± 4.72	6.44 ± 3.77	47.06 ± 28.24						
Sjögren's syndrome	0.125 (0.0–0.5)	7 (4–9)	6 (3–10)	43 (27–63)	36 (42.4)	6 (7.1)	20 (23.5)	9 (10.6)	14 (16.5)	
	0.40 ± 0.55	7.09 ± 4.0	6.55 ± 4.72	44.76 ± 23.57						
Osteoarthritis	0.875 (0.5–1.250)	9 (6–12)	7 (5–10)	67 (52–84)	48 (39.7)	15 (12.4)	22 (18.2)	12 (9.9)	24 (19.8)	
	0.96 ± 0.62	9.28 ± 4.64	7.58 ± 3.89	66.97 ± 23.17						
Fibromyalgia	0.750 (0.5–1.125)	10 (6–13)	9 (6–12)	65 (51–83)	30 (26.5)	7 (6.2)	16 (14.2)	18 (15.9)	42 (37.2)	
	0.84 ± 0.54	9.74 ± 4.81	9.07 ± 4.41	66.24 ± 22.42						

Abbreviations. HAQ, Health Assessment Questionnaire; HADS, Hospital Anxiety and Depression Scale; BETY-BQ, BETY-Biopsychosocial Questionnaire.
*Kruskal-Wallis Test.
Data are shown as means with standard deviations or medians (25th–75th percentiles).

Table 3. Comparison of outcome measures in patients with rheumatic diseases with and without self-reported bowel problems.

	Patients reporting bowel problems $n = 442$		Patients not reporting bowel problems $n = 276$		Mann-Whitney U test
	Median (IQR)	Mean ± SD	Median (IQR)	Mean ± SD	*p*-value
HAQ (0–3)	0.750 (0.350–1.250)	0.84 ± 0.66	0.475 (0.125–0.875)	0.57 ± 0.55	<.001
HADS-Anxiety (0–21)	9 (6–12)	9.09 ± 4.42	6 (3–9)	6.71 ± 4.45	<.001
HADS-Depression (0–21)	8 (5–11)	8.14 ± 4.29	6 (3–8)	5.86 ± 4.04	<.001
BETY-BQ (0–120)	62.5 (45–82)	62.66 ± 25.25	41 (23–59)	42.49 ± 23.59	<.001

Abbreviations. HAQ, Health Assessment Questionnaire; HADS, Hospital Anxiety and Depression Scale; BETY-BQ, BETY-Biopsychosocial Questionnaire.
Data are shown as means with standard deviations or medians (25th–75th percentiles).

Table 4. Comparison of pre- and post-BETY session measurement outcomes in rheumatic patients.

$N = 65$		Before BETY sessions		After BETY sessions		Chi-Square		
Item 10	Yes, Always	11 (16.9)		4 (6.2)		0.001		
n (%)	Yes, Often	8 (12.3)		10 (15.4)				
	Yes, Sometimes	15 (23.1)		10 (15.4)				
	Yes, Rarely	8 (12.3)		13 (20)				
	No, Never	23 (35.4)		28 (43.1)				
	Mean ± SD	**Median (IQR)**	**Mean ± SD**	**Median (IQR)**	**Wilcoxon Test**	**Z**	**Effect Size**	
Item 10 (0–4)	1.63 ± 1.50	2 (0–3)	1.21 ± 1.32	1 (0–2)	.006	−2.765	.343	
HAQ (0–3)	0.828 ± 0.49	0.750 (0.5–1.125)	0.546 ± 0.41	0.500 (0.25–0.812)	<.001	−3.927	.487	
HADS-Anxiety (0–21)	8.85 ± 4.64	8 (6–12)	5.71 ± 3.71	5 (3–8)	<.001	−5.086	.631	
HADS-Depression (0–21)	7.02 ± 4.32	7 (3.5–10)	4.66 ± 3.82	4 (1–6.5)	<.001	−3.979	.493	
BETY-BQ (0–120)	57.06 ± 22.07	53 (43.5–69)	37.41 ± 20.08	36 (22.5–50)	<.001	−5.991	.743	

Abbreviations. HAQ, Health Assessment Questionnaire; HADS, Hospital Anxiety and Depression Scale; BETY-BQ, BETY-Biopsychosocial Questionnaire.
Data are shown as means with standard deviation or medians (25th–75th percentiles).

functional disability (HAQ > 1), 35.3% had high anxiety (HADS-*A* > 10), and 53.4% had high depression (HADS-*D* > 7). However, among those without bowel problems, these proportions were 17.4%, 18.1%, and 27.9%, respectively.

Sixty-five patients participated in BETY group exercise sessions, including 17 with AS, 15 with RA, nine with SSc, five with SS, seven with OA, and 12 with FM. There was a statistically significant difference in the prevalence of bowel problems and scores on item 10, HAQ, HADS-A, HADS-D, and BETY-BQ before and after the BETY sessions ($p = .001$, $p = .006$, $p < .001$, $p < .001$, $p < .001$, $p < .001$, respectively). After the BETY, all scale scores were lower, and the reporting rates of bowel problems among patients were also reduced. The effect sizes indicated medium effects for item 10, HAQ, and HADS-Depression, while HADS-Anxiety and BETY-BQ showed large effects (Table 4).

Discussion

In this retrospective study, 61.6% of patients diagnosed with various rheumatic diseases reported bowel problems in the past week. These patients had higher levels of anxiety and depression compared to those who did not report any problems, and their functional levels were poorer. Biopsychosocial characteristics of rheumatic patients with self-reporting bowel problems were negatively affected compared to those without self-reporting bowel problems. BETY improved functionality, mood, and BPS in rheumatic patients reporting bowel problems, including item 10 of BETY-BQ.

The literature includes studies reporting the rates of patient-reported GIS in patients with rheumatic diseases[9]. In our study, the number of patients with rheumatism who reported bowel problems were 61.9% AS, 49.5% RA, 59.2% PsA, 64.8% SLE, 64.8% SSc, 57.6% pSS, 60.3% OA, and 73.5% FM. The patients who reported bowel problems 'always' to the relevant item at the highest rate were FM (37.2%), RA (26.9%), and SSc (22.2%). According to disease diagnoses, bowel problems reported by rheumatic individuals were interpreted as a situation to be considered in disease management.

In addition, while recording problems based on the responses to item 10 of the BETY-BQ ('I think my bowel function is not regular'), no questions were specifically asked about individual complaints. We do not know whether these patients have organic or functional bowel problems. It is also reported in the literature that it is difficult to distinguish functional and organic problems. Validated scales in this field can be used in a clinical setting to evaluate their reflections on disease management[9]. The fact that more than half of the population in our study responded to item 10 shows the importance of the patient's self-perceived bowel problems. BETY-BQ was created from the feedback of rheumatic individuals who participated in BETY exercise sessions, an exercise model based on the BPS model, for many years, describing their recovery. One of these recovery features is improving the bowel problems they described. When we look at the literature, there are studies that mention the relationship between exercise and intestinal effects. Since dysbiosis in the gut microbiota is potentially modifiable, it may serve as a promising therapeutic target for rheumatic diseases[7]. Recent studies have highlighted that exercise may enhance microbiota diversity and thus have the potential to reduce GI disorders. The remission of joint inflammation has been linked to a decrease in inflammation in the gut[14]. Therefore, investigating the potential effects of exercise training on GI symptoms, which is recognized for its anti-inflammatory properties[16], is a worthwhile topic[17]. However, no study has been found that examines the relationship

between an exercise approach based on the BPS model and the patient's cognitive expression. In our study, rheumatic individuals who reported bowel problems were included in BETY exercise sessions and showed improvement in their response to item 10. This improvement also resulted in improvements in functionality, mood, and BPS features.

Different physical exercise protocols can affect the brain–gut axis and change some physiological functions in the brain. Therefore, it is reported that this cycle, created by the communication between the brain and the body, can be clarified by considering the details of some exercise protocols[17]. Considering the positive results obtained in this study, BETY was presented to the literature as an exercise approach contributing to this field, the potential effects of which should be investigated with further studies.

This study has both strengths and limitations. This retrospective study is important in reporting the prevalence and frequency of bowel function complaints among patients with various rheumatic conditions without considering specific diagnoses. However, our study has limitations. The patients included in our study were rheumatic individuals who applied to our unit for exercise recommendations. The information we obtained about the patients consisted of details from scales other than their diagnoses. We were not aware of their organic or functional GIS diagnoses. We learned about their bowel problems from the relevant item of BETY-BQ. Therefore, a study examining the effects of exercise according to GIS diagnoses could not be created from the retrospective data we examined in this study. Given the GIS-related diagnostic limitations of our study, future research should investigate the biopsychosocial characteristics of individuals diagnosed with rheumatism who are monitored in gastroenterology clinics, alongside patient reporting. Furthermore, future research could explore the effectiveness of exercise for individuals with rheumatism and GIS, incorporating both objective and patient perspectives. On the other hand, while we were able to see the rheumatic individuals who reported bowel problems and who we included in the exercise sessions 3 months later, the records were not created to re-evaluate the rheumatic individuals who reported bowel problems and who applied only for exercise advice 3 months later. For this reason, a controlled study design could not be presented between those who participated in the exercise and those who did not with the data obtained from the records.

Conclusion

In conclusion, this study revealed the reported bowel problems in patients with various rheumatic diseases and emphasized that these complaints affect the functionality, mood, and BPS of rheumatic patients. Furthermore, this study highlighted the positive effect of the biopsychosocial-based exercise approach called BETY on all these parameters. Therefore, BETY should be used as an exercise intervention based on the BPS model in rheumatic patients with self-reported bowel problems. The results of this study emphasize the importance of exercise in managing bowel problems reported by rheumatic individuals, and it was interpreted that controlled exercise studies are needed according to different gastrointestinal diagnoses.

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Author contributions

Nur Banu Karaca: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Writing – original draft, Writing – review and editing. Aysu Kahraman: Conceptualization, Formal analysis, Methodology, Writing – original draft, Writing – review and editing. Sinan Buran: Conceptualization, Data curation, Investigation, Methodology, Writing – original draft, Writing – review and editing. Orkun Tüfekçi: Conceptualization, Investigation, Data curation, Methodology, Writing – original draft, Writing – review and editing. Fatma Birgül Kumbaroğlu: Conceptualization, Investigation, Data curation, Writing – review and editing. Zeynep İrem Bulut: Conceptualization, Investigation, Data curation, Writing – review and editing. Senem Bulut: Conceptualization, Investigation, Data curation, Writing – review and editing. Aysima Barlak: Conceptualization, Investigation, Data curation, Writing – review and editing. Atalay Doğru: Conceptualization, Methodology, Resources, Supervision, Writing – review and editing. Umut Kalyoncu: Conceptualization, Methodology, Resources, Supervision, Writing – review and editing. Ali Akdoğan: Conceptualization, Methodology, Resources, Supervision, Writing – review and editing. Şule Apraş Bilgen: Conceptualization, Methodology, Resources, Supervision, Writing – review and editing. Sedat Kiraz: Conceptualization, Methodology, Resources, Supervision, Writing – review and editing. Edibe Ünal: Conceptualization, Investigation, Methodology, Supervision, Writing – original draft, Writing – review and editing. All authors have approved the final version of the manuscript.

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ORCID

Nur Banu Karaca http://orcid.org/0000-0001-9025-4722
Aysu Kahraman http://orcid.org/0000-0001-5132-2534
Sinan Buran http://orcid.org/0000-0003-1378-9584
Orkun Tüfekçi http://orcid.org/0000-0001-7913-2580
Fatma Birgül Kumbaroğlu http://orcid.org/0000-0002-6105-2483
Zeynep İrem Bulut http://orcid.org/0000-0002-3547-1350
Senem Bulut http://orcid.org/0000-0002-6572-825X
Aysima Barlak http://orcid.org/0009-0007-9021-7156
Atalay Doğru http://orcid.org/0000-0002-9797-1182
Umut Kalyoncu http://orcid.org/0000-0001-7129-2109
Ali Akdoğan http://orcid.org/0000-0002-8064-0766
Şule Apraş Bilgen http://orcid.org/0000-0001-8208-1585
Sedat Kiraz http://orcid.org/0000-0003-2802-6061
Edibe Ünal http://orcid.org/0000-0003-2992-0698

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