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Original Article

Fibromyalgia in the Patients With Allergic Rhinitis: Its Prevalence and Impact on the Quality of Life

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Abstract

Background: Allergic rhinitis (AR) is a common allergic diseases which affect a patient's quality of life. Another important disease which has a negative impact on quality of life is fibromyalgia (FM). Some studies have suggested that a probable relationship exists between atopic diseases and FM.

Objectives: This study was designed to determine the prevalence of FM and its impact on quality of life among AR patients.

Methods: One hundred five consecutive adult patients with AR who were between 18 and 57 years old were prospectively recruited in this study between April 2017 and May 2018. All patients were evaluated for the presences of FM. Patients were diagnosed with FM according to the classification criteria of the 2010 American College of Rheumatology. The patients' quality of life was evaluated by Turkish versions of the Rhinoconjunctivitis Quality of Life Questionnaire and the Nottingham Health Profile (NHP).

Results: Thirty-four patients were diagnosed as having FM (32.4%). The percentage of FM was considerably higher than in the general population (2%–5%). Median individual domain scores except practical problems ($P = .108$) and eyes symptoms ($P = .227$) were significantly higher in AR with FM patients ($P < .001$). All median levels of the NHP domains were significantly higher in AR with FM patients ($P < .001$).

Conclusion: We would like to suggest that FM may be considered as one of the overlooked comorbid conditions in AR patients. Physicians should be aware of the occurrence of FM, especially in patients with impaired quality of life.

Keywords

allergic rhinitis, atopy, central sensitization, comorbidity, fibromyalgia, quality of life, prevalence, questionnaire, nasal symptoms, skin prick test

Introduction

Allergic rhinitis (AR) is one of the most common allergic diseases and is characterized by chronic inflammation that affects the upper airways, the nose, and the eyes. It is induced by immunoglobulin E-(IgE) mediated inflammation due to exposure to allergens.[1] The prevalence of AR is increasing due to the rising amount of environmental allergens, less ventilation in homes and offices, dietary factors, the higher concentration of air pollution, and a growth in pet ownership.[1,2] The variations of the clinical presentation of AR and the severity of symptoms experienced affect the patient's quality of life (QoL). The performance of daily activities, quality of sleep, cognitive functions, school or work performance, and psychosocial status can be impaired.[1] The presence of comorbidities of AR such as asthma, rhinosinusitis, sleep disturbances, depression, and anxiety may enhance the effects of the disease on QoL. Besides some well-known comorbid disorders, some conditions may be more common among AR patients than is often

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recognized. One of these conditions could be fibromyalgia (FM). In the literature, there is some evidence regarding the probable relationship between atopic diseases and FM.[3–5]

FM is a chronic pain syndrome characterized by generalized musculoskeletal pain.[6] It is generally accompanied by symptoms such as fatigue, headache, sleep disturbance, and mood disorders.[7,8] Although the exact prevalence of FM is unknown, it affects 2% to 5% of the population, and it is more prevalent in women.[7,9] It has a negative impact on the QoL of patients.[10] In the etiopathogenesis of FM, immune dysregulation, oxidative stress and mitochondrial dysfunction, and hypothalamic–pituitary–adrenal axis abnormalities have been proposed.[11] Currently, it is thought that the central player in the pathogenesis of FM is central sensitization which involves dysfunction in the central nervous system (CNS) involving ascending and descending neural pathways leads to increased response to mechanical stimulus.[12] Central sensitization is a sensitization in the limbic structures, which is an important area for emotional and cognitive processing, and peripheral inflammation and sensitization mutually influence each other.[13]

Indeed, FM is mentioned in conjunction with "central sensitization syndrome" (CSS) which was termed by Yunus et al. as a group of diseases that includes irritable bowel syndrome (IBS), migraines, and chronic fatigue syndrome (CFS) having common clinical features such as pain and fatigue.[3,11,14] In 1 report,[3] the authors suggested that central sensitization may be involved in AR due to the evidence of the comorbidity of allergy and CSS[4] as mentioned above. In the lights of these findings, the main aims of the present study were to identify the prevalence of FM among AR patients and to analyze the impact of the presence of FM on QoL.

Methods

Study Population

One hundred five consecutive adult patients with AR were prospectively recruited in this study between April 2017 and May 2018. The inclusion criteria were signs of AR with exposure to inhaled allergens and a positive skin prick test with standard inhaled allergen extracts (*Dermatophagoides pteronyssinus*, *Dermatophagoides farinea*, grass mix, weed mix, trees mix, *Blatella germenica*, cat dander, and mold mix) (Alk, Denmark). Histamine (10 mg/mL) was used as a positive control and saline was used as a negative control. The participants were required to be able to read and write in Turkish. Being younger than 18 years old, rhinitis patients with negative skin prick test and concomitant autoimmune disease(s), and pregnancy were exclusion criteria. The study was conducted in accordance with the Helsinki Declaration and approved by the local Ethics Committee of the study center. All participants signed an informed consent prior to the initiation of the study.

The patients' demographic data and medical history, additional history of atopic disease, clinical features of concomitant allergic disease(s), and family history of allergy were recorded. All participants were classified into 4 categories according to the Allergic Rhinitis and its Impact on Asthma classification: mild intermittent rhinitis (MIR), moderate/severe intermittent rhinitis (SIR), mild persistent rhinitis (MPR), and moderate/severe persistent rhinitis (SPR). The pattern of symptoms was termed as "intermittent or persistent" considering the persistence of AR, and "mild or moderate to severe" considering the severity of AR.[15]

All patients were investigated for FM. The diagnoses of patients were based on the 2010 American College of Rheumatology classification criteria for FM which includes a clinician administered tool for widespread pain index and a symptom severity scale for FM.[16] The patients were evaluated for FM by the same physical medicine and rehabilitation physician.

Symptoms and Health-Related QoL Assessments

We assessed the health status and QoL of patients by using generic- and disease-specific health-related QoL questionnaires. Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ) is a disease-specific questionnaire which designed to measure the impact of AR on the patient during the previous week. It includes 7 domains as follows: sleep (3 items), nonhay fever symptoms (7 items), practical problems (3 items), nasal symptoms (4 items), eye symptoms (4 items), activities (3 items), and emotions (4 items) for a total of 28 questions. Each item is scored from 0 to 6 using a Likert-type scale (higher scores indicate worse symptoms in patients), and the mean value for each domain was calculated. The overall QoL is expressed as the mean of the 7 dimension score.[17] We used its validated Turkish version for our study.[18]

We also used the validated Turkish version of the Nottingham Health Profile (NHP) as a generic QoL questionnaire.[19] The NHP consists of 2 sections. The first section includes the 6 domains such as pain, sleep, energy level, physical mobility, social isolation, and emotional reactions and 38 yes or no questions. The total scores range from 0 to 600. The second section is associated with the impact of a disease upon daily life; its total score ranges from 0 to 7.[20]

Statistical Analysis. The statistical analysis was performed using the Statistical Package for Social Sciences (SPSS)

for Windows, version 11.5 (SPSS Inc., Chicago, IL). The variables were investigated using both visual (histograms, probability plots) and analytical methods (Kolmogorov–Smirnov/Shapiro–Wilk test) to determine whether or not the data were normally distributed. Normally distributed continuous variables were expressed as mean ± standard deviation, while the continuous variables without a normal distribution were expressed as the median (minimum–maximum). In addition, categorical variables were summarized as counts (percentages). Comparisons of normally distributed continuous variables between the groups were tested using the Student's *t* test. For nonnormally continuous variables, differences between groups were assessed using the Mann–Whiney *U* test. Associations between categorical variables were determined with the Pearson χ^2/Fischer's exact test. A 2-sided *P* value of $<.05$ was considered statistically significant. A multiple linear regression model was used to predict factors of health QoL. The variables with a significance level of $P < .20$ following the univariate analysis were identified as candidate variables for a multiple model. A multiple linear regression was finally created using the stepwise method.

Results

Of the 105 patients with AR, 73 (69.5%) were females and 32 (30.5%) were males. The mean age was 32.9 ± 10.79 years, with a range of 18–57 years. The median (min–max) disease duration was 48 (1–300) months. Fourteen patients (13.3%) had asthma, 6 (5.7%) had a food allergy (banana, peach, kiwi, wheat flour, and fish), 4 (3.8%) had a drug allergy (antibiotics and analgesics), and 4 (3.8%) had atopic dermatitis. The most common allergen was pollen (78.1%). Twenty-seven patients (25.7%) were classified as MIR, 2 patients (1.9%) as SIR, and 76 patients (72.4%) as SPR. There were not any patients in the MPR group.

Thirty-four patients were diagnosed with FM (32.4%). FM was more common among female patients (women: n = 27/34, 79.4%; men: n = 7/34, 20.6%; $P = .128$). Further analyses were performed with the 2 groups separated into patients with or without FM. The mean age of patients both with and without FM were 35.12 ± 10.36 and 31.90 ± 10.90 ($P = .154$), respectively. There was no significant difference regarding the duration time of AR, the presence of additional diseases (whether atopic or not), and the type of sensitized allergen between the 2 groups (*P* values for each analyses are shown in Table 1). The complete clinical and demographic findings are shown in Table 1.

There are significant differences about symptom pattern severity (moderate/severe rhinitis with FM: n = 30 (38.5%) and mild rhinitis with FM: n = 4 (14.8%)) and persistency (persistent rhinitis with FM: n = 29 (38.2%) and intermittant rhinitis with FM: n = 5 (17.2%)) between patients with or without FM ($P = .024$ and $P = .041$, respectively). The number of patients in the total group was not sufficient to analyze statistically (MPR: n = 0; SPR: n = 2), so we compared the SPR and MIR. There was a significant difference between the SPR (n = 29/76; 38.2%) and the MIR (n = 4/27; 14.8%) regarding the presence of FM ($P = .026$).

The mean overall RQLQ score was 4.12 ± 0.81 in patients with FM and 3.21 ± 2.10 in those without FM ($P < .001$). The mean individual domain scores were all significantly higher in AR patients with FM except practical problems and eye symptoms. The mean values of the domains of RQLQ in patients with FM and without FM were as follows: the score of activities was 3.96 ± 1.47 and 3.25 ± 1.62; the score of sleep was 3.74 ± 1.85 and 1.92 ± 1.53; the score of nonhay fever symptoms was 4.73 ± 1.21 and 2.97 ± 1.78; the score of nasal problems was 4.39 ± 1.48 and 3.77 ± 1.53; and the score of emotions was 4.89 ± 1.43 and 2.69 ± 1.85 (*P* values for each domain are shown in Table 2). All mean levels of NHP domains were significantly higher in AR with FM patients ($P < .001$; Table 2). The score of the mean values in patients with FM and without FM in the part of NHP 1 was as follows: the pain scores were 45.94 ± 30.43 and 8.06 ± 15.42, emotional reaction scores were 54.41 ± 31.29 and 14.92 ± 21.16, sleep was 49.96 ± 30.87 and 15.93 ± 25.81, social isolation was 27.15 ± 34.51 and 6.32 ± 21.13, physical mobility was 18.53 ± 17.83 and 4.87 ± 11.12, and energy was 81.6 ± 31.41 and 30.86 ± 38.18.

We evaluated the impact of FM on the RQLQ. When adjusted for both the aria classification and pollen allergy, FM impaired the QoL score by 0.987 units. When adjusted for both the aria classification and FM, pollen allergy impaired the QoL score by 0.642 units. When adjusted for both the FM and pollen allergy, being SPR improved the QoL score by 0.816 units (Table 3).

Discussion

In the present study, we evaluated the prevalence of FM among patients with AR and whether AR patients with FM had a greater unfavorable impact on QoL. One-third of the AR patients also had FM. Age, gender, the duration time of the disease, the presence of any allergic or additional diseases, and types of allergen sensitization were similar in patients with or without FM. AR patients with FM had poorer outcomes regarding their impairment of QoL. To our knowledge, this is the first study to investigate the presence of FM in patients with AR and also to assess its impact on the QoL.

AR and FM are both chronic conditions that present as not only "rhinitis" and "pain" but also cause physical

Table 1. Patients' Characteristics According to the Presence of FM.

	AR With FM (n = 34, 32.4%)	AR Without FM (n = 71, 67.6%)	*P*
Gender (female/male), n (%)	27 (79.4)/7 (20.6)	46 (64.8)/25 (35.2)	.128
Age, mean ± *SD*	35.12 ± 10.36	31.90 ± 10.90	.154
Duration time of AR (month); median (minimum–maximum)	60 (1–204)	48 (6–300)	.173
Occupation, n (%)			.122
Housewife	20 (45.5)	24 (54.5)	
Currently working	8 (23.5)	26 (76.5)	
Student	5 (25)	15 (75)	
Retired	—	1 (100)	
Smoking, n (%)	5 (31.2)	11 (68.8)	.916
Presence of allergic diseases, n (%)			
Asthma	3 (21.4)	11 (78.6)	.541
Drug allergy	1 (25.0)	3 (75.0)	1.000
Atopic dermatitis	3 (75.0)	1 (25.0)	.099
Food allergy	3 (50.0)	3 (50.0)	.386
Venom allergy	2 (66.7)	1 (33.3)	.244
Presence of any additional diseases, n (%)	5 (45.5)	6 (54.5)	.329
Family history of allergy, n (%)	6 (25.0)	18 (75.0)	.379
Skin prick test positivity, n (%)			
Pollens	25 (30.5)	57 (69.5)	.434
House dust mites	21 (35.6)	38 (64.4)	.426
Blatella germenica	7 (26.9)	19 (73.1)	.493
Mold mix	1 (16.7)	5 (83.3)	.661
Cat dander	1 (20.0)	4 (80.0)	1.000

Abbreviations: AR, allergic rhinitis; FM, fibromyalgia; n, number; *SD*, standard deviation.

Table 2. Results of Questionnaires of Rhinoconjonctivitis Quality of Life and Nottingham Health Profile.

	FM+	FM−	*P*
RQLQ activities	3.96 ± 1.47	3.25 ± 1.62	.024*
Sleep	3.74 ± 1.85	1.92 ± 1.53	<.001*
Nonhay fever symptoms	4.73 ± 1.21	2.97 ± 1.78	<.001*
Practical problems	3.93 ± 2.17	3.41 ± 1.75	.108
Nasal problems	4.39 ± 1.48	3.77 ± 1.53	.028*
Eye symptoms	3.72 ± 1.76	3.26 ± 1.80	.227
Emotions	4.89 ± 1.43	2.69 ± 1.85	<.001*
Over all quality of life	4.12 ± 0.81	3.21 ± 2.10	<.001*
NHP part 1			
Pain	45.94 ± 30.43	8.06 ± 15.42	<.001*
Emotional reactions	54.41 ± 31.29	14.92 ± 21.16	<.001*
Sleep	46.96 ± 30.87	15.93 ± 25.81	<.001*
Social isolation	27.15 ± 34.51	7.32 ± 21.13	<.001*
Physical mobility	18.53 ± 17.83	4.87 ± 11.12	<.001*
Energy	81.6 ± 31.41	30.86 ± 38.18	<.001*
NHP part 2	1.74 ± 2.10	0.53 ± 1.33	<.001*

Abbreviations: RQLQ, Rhinoconjunctivitis Quality of Life Questionnaire; NHP, Nottingham Health Profile.

and psychosocial complications, which may be masked or overlooked. Those 2 diseases have important consequences on personal, social, and economic aspects of patients' lives. AR has various comorbid conditions that must be recognized to appropriately manage this disease. FM could contribute to the psychosocial effects of some diseases by as being a comorbid condition.[3,21] Although the exact prevalence of FM in Turkey is

Table 3. Prediction of Factors for Quality of Life.

	Univariate Linear Regression Results				Multiple Linear Regression Results			
	B	95% CI	Standard Error	Sig.	*B*	95% CI	Standard Error	Sig.
FM (absent/present)	1.124	0.697–1.551	.216	<.001	0.987	0.576–1.397	.207	<.001
Pollen (absent/present)	0.547	0.014–1.080	.269	.044	0.642	0.186–1.098	.230	.006
House dust mite (absent/present)	−0.375	−0.822–0.073	.226	.100	–	–	–	–
Aria (MIR/SPR)	1.022	0.547–1.497	.239	<.001	0.816	0.382–1.250	.219	<.001

Abbreviations: CI, confidence interval; FM, fibromyalgia; MIR, mild intermittent rhinitis; SPR, severe persistent rhinitis.
Multiple linear regression R^2: 34.1%; R^2(adj): 32.1%.

unknown, some studies have reported the prevalence of FM as follows; 3.6% in Trabzon (20- to 60-year-old women)[22] and 8.8% were in Diyarbakır.[23] Our results showed that the percentage of FM in AR was considerably higher than that reported by previous studies in Turkey which referred above. It can be interpreted that there is a close relationship between AR and FM. The awareness of the possible coexistence of these 2 diseases should allow clinicians to make the correct differential diagnosis, which leads to more successful management and, improvement in the QoL.

Seventy percent of FM patients complain of rhinitis.[7] Tuncer et al. reported that 47% (n = 15) of FM patients (n = 32) gave a history of atopy which was significantly different from controls. Three of the 32 patients had a history of AR. Skin prick tests were positive in 10 FM patients.[24] Cleveland et al. investigated the presence of FM in 47 patients with rhinitis. Thirty-seven of those (79%) were AR and dust mites were the most commonly sensitized allergen identified using skin tests. In total, the prevalence of FM was 38% (n = 18).[25] The overall prevalence of FM in our study group was 32.4%. In contrast with the study of Cleveland et al., our study group only included AR patients. Pollen was the most common aeroallergen, which is compatible with the rates of general aeroallergen sensitization in Turkey.[26] We found no association with the type of allergen sensitization and FM. We thought that this finding is compatible with the suggestion of Frieri and Argyriou that "rhinitis" is associated with FM instead of atopy.[8]

In our study, AR patients with FM had worse QoLs than patients without FM. We found higher scores on the 5 domains of the RQLQ such as activities, sleep, nonhay fever symptoms, nasal problems, and emotions in AR patients with FM. Remarkably higher scores were achieved on sleep, nonhay fever symptoms (fatigue, headache, exhaustion, etc), nasal problems, and emotions. These symptoms were related and can be seen in both AR and FM patients. Nasal symptoms, such as nasal obstruction, may impair both sleep and cognitive functions. Sleep disturbances are closely related to anxiety and depression.[27] Nasal symptoms may also lead to social isolation in AR patients.[25] Our results indicated that AR and FM contributed to an impaired QoL and AR patients with FM experienced a greater unfavorable impact on QoL than those with either condition in isolation. The positive correlation between a greater decrease in QoL and the coexistence of AR and FM may be explained by central sensitization mechanism. The RQLQ revealed no association between ocular symptoms and the presence of FM. Therefore, FM may be more frequently associated with nasal symptoms instead of ocular symptoms. However, nasal symptoms had more effects on sleep, emotions, and cognitive functions related to FM than ocular symptoms. The NHP questionnaire results of our patients also supported our hypothesis that FM contributes to the impairment of QoL and also the suggestion that AR may be involved in central sensitization by Tsiakiris et al.[3] This suggestion must be supported by further studies.

Based upon the literature, some similar mechanisms as follows were asserted in the pathogenesis of AR and FM. Triggered neurogenic inflammation is one underlying mechanism of AR. Neurogenic inflammation leads to vasodilatation and increased vascular permeability due to the release of neuropeptides by sensory nerve endings.[28] Trigeminal fibers and C-fibers play a role in neurogenic inflammation. It is considered that mast cells and nerve fibers interact. When mast cells stimulate nerves, neuropeptides are released, such as substance P (SP) and calcitonin gene-related peptide (CGRP). It was shown that the concentrations of SP and CGRP were increased after nasal allergen challenge.[29] Some investigators have suggested that neurogenic inflammation in the nasal mucosa has a secretory response rather than a vascular response.[28] Neurogenic inflammation has an important role in FM. Brain-related mechanisms drive neurogenic inflammation in both the peripheral and CNS. Above all, emotional stimuli lead to the release of neuropeptides such as SP, CGRP, and neurokinin A. The effect of neuropeptides on the vascular response as vasodilatation and the increase in local blood flow

shapes the clinical presentation in FM and related diseases. In the skin, SP interacts with immune cells such as mast cells. Mast cells act on sensory nociceptive terminals. After this interaction, pain, swelling, and vasodilatation happen.[30] AR and FM may share a common genetic predisposition. Specific gene polymorphisms in the human leukocyte antigen region of chromosome 6 or others may play a role in both diseases.[12,27,31] Recently, the most emphasized mechanism was central sensitization, which is related to emotional and cognitive processes. It was suggested that central sensitization may be implicated in various diseases such as FM, CFS, IBS, and asthma. Central sensitization and psychiatric disorders including anxiety, panic disorder, and depression are closely connected.[3] Depression and anxiety are considered comorbid disorders in FM and also AR.[10,27]

Our study had some limitations. We did not compare the statistical differences in the study group with the control group. However; even if we had had a control group, it would not have reflected the general population. Second, we did not analyze any other cytokines related to the pathogenesis of FM and AR. Understanding the immunopathological roles of cytokines may clarify the association between FM and AR.

In conclusion, we suggest that FM be considered as an overlooked comorbid condition in AR patients. The presence of FM in AR patients was more likely to lead an impaired QoL. Treating the comorbidities is essential to improve the treatment of underlying diseases. AR may have important impacts on patients' lives and on their social and economic progress if left untreated. Therefore, physicians should be aware of the occurrence of FM, especially in patients with an impaired QoL. Multidisciplinary management programs may be useful for the best management of AR. Further studies might shed light on whether the proper treatment of FM in AR patients would improve the clinical outcomes and QoL of these patients.

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