

Hearing Loss and the Affecting Factors in Patients with Fibromyalgia

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ABSTRACT

Objective: To find the frequency of hearing loss in newly diagnosed patients with fibromyalgia (FM), and the factors affecting it.

Study Design: Descriptive study.

Place and Duration of the Study: Department of Physical Medicine and Rehabilitation and Department of Otorhinolaryngology Head and Neck Surgery, Istanbul Medeniyet University, Goztepe Prof. Dr. Suleyman Yalcin City Hospital, Turkey, from March 2021 to November 2022.

Methodology: Patients with FM and gender/age matched controls were compared with pure-tone audiometric (PTA), and transient evoked otoacoustic emissions (TEOE) tests after standardised otorhinolaryngologic assessment. The subjects were questioned for NSAID uptake and scored with ASAS-NSAID score.

Results: There were 33 patients with FM and 32 healthy volunteers. Subjective tinnitus, dizziness, and hearing loss rate in the FM group were 12%, 18%, and 15%, respectively. PTA air and bone conduction studies yielded significant differences between the control and FM group ($p < 0.05$). The statistical difference was pronounced in higher frequencies. TEOE tests showed the FM group had significantly lower scores when compared to the control group at 3000 Hz and 4000 Hz ($p < 0.05$). The median ASAS-NSAID scores were 0 for the control group and 7.78 for the FM group ($p < 0.001$).

Conclusion: Patients with FM had high rate of audiometric hearing loss of the sensorineural type. The abnormalities were more prominent in the high frequencies but also present in the low frequencies.

Key Words: Fibromyalgia syndrome, Hearing loss, Audiometry, Ototoxicity, Central sensitisation.

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INTRODUCTION

Fibromyalgia syndrome (FM) is a common syndrome with chronic widespread pain, fatigue, sleep disturbances, and various symptoms. The aetiopathogenesis of FM is unclear. Sensitisation created by the dysregulation of the central nervous system (CNS) and peripheral nervous system (PNS) had been regarded as the cause.¹ Patients with FM can become hypersensitive to any stimuli like other central sensitivity syndromes. Apart from widespread pain, patients with FM often have a variety of symptoms. Moreover, patients with FM have an increased risk of many comorbidities and diseases.² The disease can significantly reduce quality of life, with widespread pain and other symptoms, and cause a great burden on the health system.³

There is no specific diagnostic test for diagnosing FM. Diagnosis is largely based on the amount of widespread pain. Additionally, fatigue, increased sensitivity to sound, light or ambient temperature, widespread tenderness on clinical examination, longevity of symptoms, history of ineffective treatments, feeling overwhelmed by patients, and expansive symptomatology are well-known characteristics of the syndrome.^{4,5}

The various classification criteria of FM use widespread pain and symptoms for diagnosis. In the American College of Rheumatology (ACR) 2010 Criteria, generalised pain is defined by the widespread pain index (WPI) and symptoms are assessed using a symptom severity scale score (SSS). The WPI probes how many of the 19 body regions are painful. In the SSS, fatigue, waking unrefreshed, and cognitive symptoms are examined. Additionally, the presence of headache, pain or cramps in the lower abdomen, and depression are scored. Symptoms could be present at a similar level for at least 3 months. Patients with WPI ≥ 7 and SSS ≥ 5 or WPI of 4–6 and SSS score ≥ 9 can be classified as having FM.⁶

As other central sensitisation disorders, many symptoms that are not included in the ACR criteria can be seen in patients with FM. Migraine, irritable bowel syndrome, chronic fatigue syndrome, chronic pelvic pain, and temporomandibular joint

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disorder are also believed to have common central nervous system mechanisms, and the term chronic overlapping pain conditions (COPC) has also been used for central sensitivity syndromes.⁷ Otological symptoms can be seen in a significant number of patients. Dizziness is the most frequent otologic symptom followed by tinnitus and hearing loss.⁸ Epidemiologic studies have suggested that patients with FM may have hearing loss.⁹⁻¹¹ A few studies with audiometric tests also confirmed the epidemiological studies.^{9,12,13} However, there may be several reasons for hearing loss in patients with FM including the use of ototoxic drugs and comorbidities.

In this study, the primary aim was to determine the frequency of subjective and audiometric hearing loss in newly diagnosed patients with FM. The secondary aim was to find the factors affecting hearing loss. The hypothesis of the study was that hearing loss was not more common than in healthy controls after excluding confounding factors.

METHODOLOGY

The study started after an approval from the Medeniyet University Ethics Committee on November 2021 (No. 2021/0117). All patients signed an informed consent form to participate in the study according to the Declaration of Helsinki. The sample size was estimated with the G Power V.3.1.7 program (University of Kiel, Kiel, Germany) for the primary outcome measure. According to the literature, the mean values of pure-tone audiometric tests were determined as 30.14 ± 9.11 Hz in the patient group and 17.2 ± 8.8 Hz in healthy controls.⁷ The sample size was calculated at a significance level of 0.1 and 95% power. For each group, 23 participants were enrolled according to the sample size analysis.

A clinical assessment of the patients were performed. In the newly-diagnosed FM group, 20-50 years of female patients with FM according to the ACR 2010 criteria were included in the study. Patients who had previously received anti-depressants including duloxetine and pregabalin for FM were excluded from the study. All subjects were questioned about the use of non-steroidal anti-inflammatory drugs (NSAID) for the previous three months and evaluated with an ASAS-NSAID score.¹⁴ The control group consisted of healthy women aged 20-50 years.

All patients and healthy controls were referred to an experienced otologist for otoscopic examination of both ears. An otoscopic examination was performed to prove a healthy tympanic membrane. All subjects were questioned about tinnitus, vertigo, facial nerve function, and family history of hearing loss. The possible aetiological factors that could lead to hearing loss such as use of ototoxic medicine, noise exposure, previous ear surgery, the presence of Meniere's disease, cranial trauma, and metabolic and systemic diseases were assessed with a standardised assessment form. The exclusion criteria was ototoxic drug use other than NSAIDs, prior ear surgery, head or ear trauma, tympanic membrane perforation, acquired hearing loss and congenital ear disorder, and participants with

diabetes, hypertension, cardiovascular disease, infectious diseases, neurological deficits, autoimmune diseases, pulmonary diseases, endocrine disorders, and malignancies.

After assessment by the otologist, the patients and healthy controls underwent pure-tone audiometric (PTA), and transient evoked otoacoustic emissions (TEOE) tests. The same audiologist performed PTA measurements with airway and bone conduction measurements in an Industrial Acoustic Company (IAC) standard double-walled soundproof audiology booth. Audiometry measurements were performed using the Madsen Astera, test battery (Denmark) for frequencies of 250, 500, 1,000, 2,000, 4,000, 6,000, and 8,000 Hz. High-frequency test measurements including 9,000, 10,000, 11,200, 12,500, 14,000, 16,000, 18,000, and 20,000 Hz frequencies were carried out using Sennheiser HDA 300 circumaural headphones. Hearing loss was defined as being present when the audiometric tests disclosed pure-tone thresholds ≥ 25 dB HL in the audiogram.¹⁵

TEOE measurements were performed with an Echoport ILO292 (United Kingdom) instrument. Measurements were made in a quiet room according to the IAC standard, and the patient was in a sitting position during the test. During the test, the stimulus intensity used was 84 dB. The resulting transient impulses averaged 260 times, and the results were recorded.¹⁶

IBM SPSS Statistics for Windows (Version 25.0. Armonk, NY: IBM Corp) was used for statistical analysis. Frequency, percentage, mean, median, and standard deviation values were obtained using descriptive statistical methods. The conformity of the data to the normal distribution was evaluated using the Shapiro-Wilk test. The Pearson Chi-square test was used to compare the categorical data. The Mann-Whitney U test with a significance level of 0.05 was used for statistical analysis of continuous variables.

RESULTS

Initially, 45 newly diagnosed patients with FM and 40 healthy controls were enrolled for the study. Ten patients from the FM group were excluded due to the use of anti-epileptics or anti-depressants as revealed in their history during the clinical assessment. Two patients from the FM group and seven patients from the control group were excluded after otoscopic assessment. The study was completed with 33 patients with FM and 32 healthy volunteers.

According to Shapiro-Wilk's test, only age and body mass index variables were distributed normally. The other variables had a skewed distribution and were analysed with Mann-Whitney test. The demographic data of the patients are summarised in Table I. There was statistical significance in education and occupation ($\chi^2 = 21.8$; $p = 0.001$, $\chi^2 = 39.4$; $p = 0.001$). The age, body mass index, and smoking variables were similar between groups ($p = 0.17$, $p = 0.24$, $\chi^2 = 1.09$, and $p = 0.33$, consecutively).

Table I: Demographic data.

		Control (n=32)		Fibromyalgia (n=33)	
Education	Primary school	2	6.3%	20	60.6%
	High school	15	46.9%	8	24.2%
	University	15	46.9%	5	15.2%
Occupation	None	0	0%	25	75.8%
	Body	7	21.9%	2	6.1%
	Office worker	25	78.1%	6	18.1%
Smoking	-	25	78%	29	87.9%
	+	7	22%	4	12.1%
Age (years)		38.53±6.01		40.51±5.64	
Body mass index (kg/m ²)		25.59±3.06		26.63±4.01	

Table II: Pure-tone audiogram air conduction (PTAC) and pure tone bone conduction (PTBC) results.

	Group	Mean	Median	Range	z	p-value*
PTAC- Right 250Hz	Control	6.2500	5	20	-2.34	0.01
	FM	10.4545	10	30		
PTAC-Right 500Hz	Control	9.0625	10	20	-0.79	0.42
	FM	10.6061	10	25		
PTAC-Right 1000Hz	Control	8.5938	10	20	-1.28	0.2
	FM	10.4545	10	20		
PTAC-Right 2000Hz	Control	5.3125	5	15	-2.96	0.003
	FM	9.6970	10	30		
PTAC-Right 4000Hz	Control	6.8750	5	20	-4.44	0.001
	FM	17.4242	15	45		
PTAC-Right 6000Hz	Control	9.2188	5	25	-4.53	0.001
	FM	22.1212	20	35		
PTAC-Right 8000Hz	Control	5.0000	5	15	-5.67	0.001
	FM	22.1212	20	50		
PTAC-Right high frequency mean	Control	16.9375	14.5	38	-4.69	0.001
	FM	36.1818	36	59		
PTAC-Right mean	Control	7.5313	8	17	-2.4	0.04
	FM	10.1515	10	23		
PTAC-Left 250Hz	Control	6.0938	5	20	-2.08	0.04
	FM	10.0000	10	25		
PTAC-Left 500Hz	Control	7.9688	7.5	20	-1.81	0.07
	FM	11.2121	10	25		
PTAC-Left 1000Hz	Control	7.5000	5	20	-0.852	0.39
	FM	8.9394	10	25		
PTAC-Left 2000Hz	Control	5.3125	5	15	-3.55	0.001
	FM	11.2121	10	30		
PTAC-Left 4000Hz	Control	7.1875	5	20	-3.78	0.001
	FM	16.3636	15	50		
PTAC-Left 6000Hz	Control	10.0000	10	25	-3.9	0.001
	FM	22.5758	20	60		
PTAC-Left 8000Hz	Control	8.4375	10	30	-4.35	0.001
	FM	23.3333	20	60		
PTAC-Left high frequency mean	Control	16.7500	10.5	50	-4.740	0.001
	FM	35.9091	35	60		
PTAC-Left mean	Control	6.2500	7	13	-3.16	0.002
	FM	10.3333	10	22		
PTBC-Right 250Hz	Control	5.93	5	20	-2.65	0.008
	FM	10.6	10	30		
PTBC-Right 500Hz	Control	3.59	0	10	-1.32	0.18
	FM	5.6	5	25		
PTBC-Right 1000Hz	Control	3.43	5	10	-2.09	0.04
	FM	6.06	5	20		
PTBC-Right 2000Hz	Control	2.18	0	15	-3.38	0.001
	FM	5.9	5	30		
PTBC-Right 4000Hz	Control	3.12	2.5	15	-4.72	0.001
	FM	11.96	10	45		
PTBC-Right 6000Hz	Control	9.68	7.5	25	-4.39	0.001
	FM	21.81	20	35		
PTBC-Right 8000Hz	Control	5.78	5	30	-5.37	0.001
	FM	21.21	20	50		
PTBC-Right mean	Control	2.81	2	10	-3	0.003
	FM	5.75	5	25		

Continued.

	Group	Mean	Median	Range	z	p-value*
PTBC-Left 250Hz	Control	5.78	5	20	-2.02	0.04
	FM	9.84	10	25		
PTBC-Left 500Hz	Control	3.12	0	15	-2.05	0.04
	FM	5.60	5	20		
PTBC-Left 1000Hz	Control	2.5	0	10	-2.76	0.006
	FM	5.9	5	25		
PTBC-Left 2000Hz	Control	1.71	0	15	-3.62	0.001
	FM	5.9	5	10		
PTBC-Left 4000Hz	Control	2.65	0	10	-4.48	0.001
	FM	11.06	10	50		
PTBC-Left 6000Hz	Control	10.78	10	25	-3.69	0.001
	FM	25.57	20	60		
PTBC-Left 8000Hz	Control	9.21	10	30	-3.99	0.001
	FM	22.42	20	60		
PTBC-Left mean	Control	2.53	2	10	-3.3	0.001
	FM	5.87	5	25		

*Mann-Whitney U test.

Table III: Transient evoked otoacoustic emissions results.

	Group	Mean	Median	Range	z	p-value*
Right 1000Hz	Control	8.39	7.5	18.8	-1.6	0.1
	FM	10.82	10	21		
Right 1500Hz	Control	11.97	11.6	20	-0.63	0.5
	FM	13.47	13.2	28.7		
Right 2000Hz	Control	9.41	8.45	17.8	-1.37	0.16
	FM	11.79	9.9	39.9		
Right 3000Hz	Control	7.02	5.6	18.5	-1.155	0.24
	FM	5.27	4.3	14.8		
Right 4000Hz	Control	7.32	5.8	24.8	-3.73	0.001
	FM	2.56	2.2	9.4		
Left 1000Hz	Control	10.66	11.25	21.1	-0.51	0.6
	FM	9.96	9.8	23.9		
Left 1500Hz	Control	12.08	12.05	19.1	-0.59	0.55
	FM	13.06	12.3	27.1		
Left 2000Hz	Control	9.68	9.95	17.4	-1.44	0.14
	FM	8.3	7.2	23.4		
Left 3000Hz	Control	7.71	6.7	21	-2.153	0.03
	FM	4.66	3.5	12.6		
Left 4000Hz	Control	6.75	5.05	24	-2.58	0.01
	FM	4.06	2.6	14.9		

*Mann-Whitney U test.

All audiometric results are summarised in Tables II and III. The values of the audiometric tests yielded significant differences between the control and FM groups at all frequencies. However, it was found that the statistical difference was more pronounced at higher frequencies. The results of the bone conduction audiometric studies were in the same pattern as those of the air conduction studies. The TEOE studies showed that the FM group was significantly at lower scores when compared to the control group at 3.000 Hz and 4.000 Hz.

Subjective tinnitus, dizziness, and hearing loss rate in the FM group were 12%, 18%, and 15%, respectively. According to the audiometric results, hearing loss was found in four of the 32 patients in the healthy group (12.1%) and 29 of the 33 patients in the FM group (87.5%). The Chi-square analysis showed statistical significance between patient and control groups ($\chi^2 = 36.93$ and $p = 0.001$). All patients were regarded as having sensorial-type hearing loss.

The subjects were questioned for NSAID uptake and scored with ASAS-NSAID score; 12 of the 32 control subjects and 29 of the 33 patients with FM had used NSAIDs in the previous 3 months. The median ASAS-NSAID scores were 0 for the control group and 7.78 for the FM group. Results of the Mann-Whitney U test indicated a statistical difference ($z = -5.44$, $p < 0.001$).

DISCUSSION

This study confirmed that patients with FM had a high rate of hearing loss after controlling most confounding factors. A nationwide population-based study suggested that overall hearing loss was 1.46-fold higher in the FM group than in the non-FM group.¹⁰ In a study, Wolfe *et al.* compared hearing loss in patients with FM, osteoarthritis, and rheumatoid arthritis. They found that there was a high amount of hearing problems in FM than in other rheumatic diseases. The authors emphasised the role of central sensitisation in FM.¹¹ Stranden *et al.* Compared patients with FM, patients with other musculoskeletal pain, and a reference group.

They found increased subjective hearing loss in FM when compared to the other groups. The authors also pointed out the role of central mechanisms and explained hearing loss with the experience of auditory stimuli and cognitive dysfunction.⁹ In this study, the most subjective otologic symptom was dizziness, and only five patients suffered from hearing loss. However, it was found that 87.5% of the patients with FM had abnormalities in audiometry, according to the previously defined criteria. The rate of hearing loss in this study was extremely high, despite excluding subjects with potentially confounding factors. This finding led to the rejection of the hypothesis of the study.

Gencer *et al.* compared the PTA results of FM to control subjects and found statistical significance at high frequencies. The authors suggested that the difference in high frequencies was dependent on the effects of phospholipid antibodies, serotonin, and ganglioside antibodies.¹² Koca *et al.* also showed a statistical difference between 25 and 12.000 Hz independent of the disease activity.¹⁷ This study showed that the abnormalities were more prominent at high frequencies but were also present at low frequencies. All of the hearing loss was sensorineural (SNHL). This finding was in line with the previous studies.⁹ Sensorineural hearing loss can occur with an immune-mediated mechanism or might be caused by the use of ototoxic agents.¹³ More than 150 drugs including loop diuretics, aminoglycosides, anti-cancer drugs, quinine, macrolide antibiotics and salicylate analgesics are defined as ototoxic drugs.¹⁸ In this study, patients using ototoxic anti-depressants or anti-epileptic agents were excluded which have might affected central sensitivity. However, patients with FM used NSAIDs excessively. The overuse of NSAIDs might induce hearing loss in patients with FM. The ototoxic drugs led to hearing loss primarily at high frequencies according to PTA.¹⁹ One of the important results of this study were the findings obtained with TEOE. The hearing loss at high frequencies in the FM group also suggested the ototoxic effect of NSAIDs.

Another possible mechanism for hearing loss is central sensitivity. Sensorineural hearing loss may result from the cochlea, auditory nerve, or central auditory areas.²⁰ There is a lack of research that might explain the relationship between hearing loss and central sensitivity in patients with fibromyalgia. Functional MRI studies in fibromyalgia are usually related to the main symptom which is pain. In patients with FM, activity changes have been identified in insula, anterior cingulate cortex, and prefrontal cortex which are non-specific for pain. These areas can be activated by auditory stimuli.²¹ It can be said that central sensitivity may play a role in causing hearing loss in patients with FM but this relationship has not been fully investigated.

This study had both strengths and limitations. A sufficient sample size and homogenous patient group with strict exclusion criteria strengthened the study. However, the lack of assessment of central sensitivity was a limitation. Addition-

ally, since it was a cross-sectional research, it was not possible to establish a cause-effect relationship, especially in terms of drug toxicity.

CONCLUSION

This study confirmed the high rate of audiometric hearing loss in patients with FM. Statistically significant results were found at all frequencies but more prominent at higher frequencies. Excessive use of NSAIDs and central sensitivity may be the causes of hearing loss.

ETHICAL APPROVAL:

An approval was obtained from the Istanbul Medeniyet University Clinical Research Ethics Committee on 10.02.2021 with the registration No. 2021/0117.

PATIENTS' CONSENT:

All participants provided written informed consent prior to participation.

COMPETING INTEREST:

The authors declared no competing interest with respect to the authorship and/or publication of this article.

AUTHORS' CONTRIBUTION:

HCY: Concept, literature review, and writing.

OIO: Concept, literature review, and critical review.

IY: Design, analysis and interpretation, and literature review.

CTS, OE: Data collection.

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