



ASSOCIATIONS OF DISEASE DURATION, RHEUMATOID FACTOR, AND DISEASE ACTIVITY WITH HEARING LOSS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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ABSTRACT

Rheumatoid arthritis (RA) is a systemic autoimmune inflammatory disease that may involve extra-articular organs, including the auditory system. This study investigated the associations of disease duration, rheumatoid factor (RF) status, and disease activity level with hearing loss in patients with RA at Adam Malik Hospital, Medan. This analytic observational study employed a cross-sectional design and was conducted at the Otorhinolaryngology and Internal Medicine outpatient clinics of Adam Malik General Hospital, Medan, from February 2025 to October 2025. The study population consisted of patients with rheumatoid arthritis (RA) diagnosed by a consultant rheumatologist. A total of 47 patients who met the inclusion and exclusion criteria were enrolled using a non-probability consecutive sampling technique. After obtaining informed consent, demographic and clinical data, including rheumatoid factor (RF) levels and DAS28-ESR scores, were obtained from interviews and medical records. Hearing function was assessed using tympanometry and pure-tone audiometry. The collected data were analyzed using univariate, bivariate, and receiver operating characteristic (ROC) analyses. Most patients were female (93.6%), with a mean age of 40.02 ± 6.75 years. The most frequent clinical characteristics were disease duration ≤ 5 years (53.2%), low disease activity (53.2%), and RF positivity (85.1%). Type A tympanograms predominated (93.6%). Mean hearing thresholds increased at higher frequencies, indicating predominant high-frequency involvement. Sensorineural hearing loss was the most common type, and the degree of hearing loss was generally mild to moderate. Disease duration, disease activity level, and RF status were significantly associated with the type of hearing loss ($p < 0.005$). Disease duration and RF status were significantly associated with the degree of hearing loss ($p \leq 0.005$), whereas disease activity level was not ($p \geq 0.05$). A disease duration of ≥ 5 years was associated with hearing loss. Patients with RA, particularly those with disease duration ≥ 5 years, RF positivity, or high disease activity, should be prioritized for periodic audiological screening to enable early detection of hearing loss.

Keywords: disease activity; disease duration; hearing loss; rheumatoid arthritis; rheumatoid factor

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INTRODUCTION

Rheumatoid arthritis (RA) is a chronic systemic autoimmune inflammatory disease characterized by persistent synovial inflammation and potential extra-articular involvement. Beyond joint damage, RA may affect multiple organs and systems, including the cardiovascular, renal, pulmonary, gastrointestinal, ocular, cutaneous, nervous, and auditory systems. Extra-articular manifestations have been reported in up to 40% of patients with RA. (Elnagdy O.H. et al., 2022; Jahid M et al., 2023; Radu AF et al., 2021) Hearing loss is clinically important because it adversely affects communication, social functioning, psychological well-being, and quality of life. In patients with RA, auditory involvement has been reported as a relatively frequent extra-articular manifestation and may interfere with daily activities. (Chaitidis N et al., 2020; Jeong H et al., 2016; Sadek et al., 2022)

Previous studies have reported a higher prevalence of hearing loss among patients with RA than among controls. Chaitidis et al. reported prevalence estimates of up to 40% for sensorineural hearing loss and 20% for conductive or mixed hearing loss. In a systematic review, Skare and Carvalho found that hearing loss in RA was generally sensorineural, predominantly affected high frequencies, and resembled a presbycusis-like pattern. Jabbar et al. reported hearing loss in 59.5% of patients with RA; sensorineural hearing loss was the most common type, and mild-to-moderate severity was most frequently observed. (Chaitidis N et al., 2020; Jabbar M et al., 2022; Skare TL et al., 2025) Conductive hearing loss in RA may result from synovial involvement of the incudostapedial and incudomalleolar joints. Because these ossicular joints are true diarthrodial joints, they may be affected by inflammatory processes similar to those involving peripheral joints. Mononuclear cell infiltration and synovial accumulation on the articular surfaces may increase ossicular-chain stiffness and impair sound conduction. (Demir S et al., 2024; Emamifar A et al., 2016; Ramesh S et al., 2018)

Sensorineural hearing loss is the most frequently reported audiological manifestation in RA. Immune dysregulation and autoantibody formation may contribute to cochlear injury through autoantibody-antigen reactions or direct cytotoxic mechanisms affecting hair cells. Rheumatoid vasculitis, particularly in seropositive patients with severe and long-standing disease, may also compromise the labyrinthine artery. Because the cochlea has limited collateral circulation, even minor vascular disturbances may result in hair-cell injury, stria vascularis atrophy, and spiral ganglion degeneration. Vasculitis affecting the vasa nervorum may further cause peripheral nerve ischemia, neuritis, and neuropathy. (Torere BE et al., 2023; Upreti S et al., 2019) Disease duration, disease activity, and RF status have been implicated in auditory involvement in RA. Chen et al. reported that longer disease duration was associated with progressive hearing deterioration, beginning at extended high frequencies and subsequently involving lower frequencies. Gamal et al. found that hearing loss was associated with older age, longer disease duration, and higher Disease Activity Score 28 (DAS28), which incorporates tender and swollen joint counts, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and patient global assessment. Munjal et al. also reported a significant correlation between RF and pure-tone audiometric thresholds. (Chen JJ et al., 2024; Gamal NM et al., 2024; Munjal SK et al., 2017) This study aimed to evaluate the associations of disease duration, RF status, and disease activity level with hearing loss in patients with RA at Adam Malik Hospital, Medan.

METHOD

This analytic observational study used a cross-sectional design. The study was conducted at the Otorhinolaryngology and Internal Medicine outpatient clinics of Adam Malik Hospital, Medan, from February 2025 to October 2025. The study population consisted of patients with rheumatoid arthritis (RA) attending the Rheumatology Clinic of the Department of Internal Medicine during the study period. A total of 47 patients who met the inclusion and exclusion criteria were enrolled using a non-probability consecutive sampling technique. Data were summarized using univariate analysis; associations between variables were assessed using bivariate analysis; and ROC analysis was performed to evaluate disease duration as a predictor of hearing loss. This study was conducted after obtaining ethical approval from the Health Research Ethics Committee of the Faculty of Medicine, Universitas Sumatera Utara, Medan, with approval number 508/KEPK/USU/2025.

RESULT

Baseline Characteristics

The demographic and clinical characteristics of the 47 patients with RA are summarized in table 1. The study population was predominantly female (93.6%), with a mean age of 40.02 ± 6.75 years. More than half of the patients had a disease duration of ≤ 5 years (53.2%) and low disease activity (53.2%). Rheumatoid factor (RF) was positive in the majority of patients (85.1%). Tympanometry findings were predominantly Type A (93.6%), with only 6.4% showing Type As tympanograms. These results indicate generally normal middle-ear function, suggesting that any hearing impairment observed in this cohort was more likely sensorineural rather than conductive in origin.

Table 1.
Baseline characteristics of patients with rheumatoid arthritis

Characteristic	n = 47
Sex, n (%)	
Male	3 (6.5)
Female	44 (93.6)
Age, years	
Mean $\pm$ SD	40.02 $\pm$ 6.75
Median (min–max)	40 (25–50)
Disease duration, n (%)	
≤ 5 years	25 (53.2)
6–10 years	12 (25.5)
11–15 years	10 (21.3)
ESR-based disease activity level, n (%)	
Low	25 (53.2)
Moderate	10 (21.3)
High	12 (25.5)
Rheumatoid factor, n (%)	
Positive	40 (85.1)
Negative	7 (14.9)
Tympanogram	
Type A	44 (93.6)
Type As	3 (6.4)

Associations of Disease Duration, Disease Activity, and Rheumatoid Factor with Type of Hearing Loss

The associations of disease duration, disease activity level, and RF status with type of hearing loss are presented in Table 2.

Table 2.
Associations of disease duration, disease activity, and rheumatoid factor with type of hearing loss

Variable	Conductive	Sensorineural	None	p*
Disease Duration, f (%)				< 0.001 ^a
≤ 5 years	0	24 (48)	26 (52)	
6 – 10 years	0	4 (16.7)	20 (83.3)	
11 – 15 years	6 (30)	14 (70)	0	
Rheumatoid Factor, f (%)				0.003 ^b
Positive	6 (7.5)	40 (50)	34 (42.5)	
Negative	0	2 (14.3)	12 (85.7)	
Disease Activity level, f (%)				< 0.001 ^a
Low	6 (12)	14 (28)	30 (60)	
Moderate	0	4 (20)	16 (80)	
High	0	24 (100)	0	

^aKruskal-Wallis test; ^bMann-Whitney test.

Disease duration, RF positivity, and disease activity were significantly associated with hearing loss ($p < 0.05$). Hearing loss was most prevalent among patients with a disease duration of 11–15 years, all of whom were affected, predominantly with sensorineural hearing loss (70%). RF-positive patients had a higher frequency of hearing loss (57.5%), mainly sensorineural, whereas most RF-negative patients (85.7%) had normal hearing. Additionally, all patients with high disease activity exhibited sensorineural hearing loss, while the majority of those with low disease activity (60%) had no hearing impairment.

Associations of Disease Duration, Disease Activity, and Rheumatoid Factor with Degree of Hearing Loss

The distribution of hearing loss severity according to disease duration, RF status, and disease activity level is shown in Table 3.

Table 3.

Associations of disease duration, disease activity, and rheumatoid factor with degree of hearing loss

Variable	Normal	Mild	Moderate	p*	γ
Disease Duration, f (%)				< 0.001 ^a	0.507
≤ 5 years	26 (52)	20 (40)	4 (8)		
6 – 10 years	20 (83.3)	3 (12.5)	1 (4.2)		
11 – 15 years	0	0	20 (100)		
Rheumatoid Factor, f (%)				0.012	0.658
Positive	34 (42.5)	23 (28.7)	23 (28.7)		
Negative	12 (85.7)	0	2 (14.3)		
Disease Activity level, f (%)				< 0.097	0.214
Low	30 (60)	0	20 (40)		
Moderate	16 (80)	3 (15)	1 (5)		
High	0	20 (83.3)	4 (16.7)		

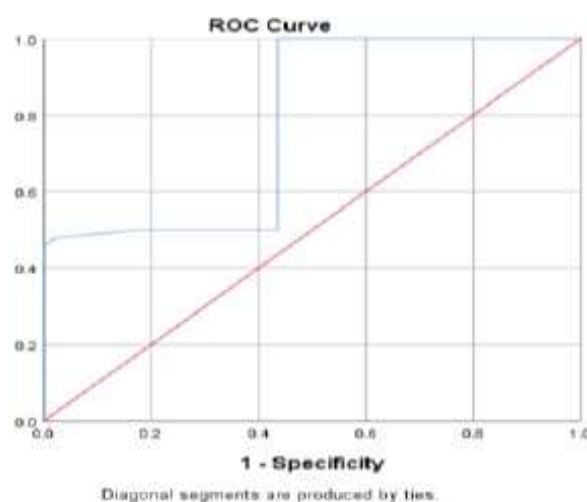
 γ = Gamma Coefficient

Disease duration was significantly associated with degree of hearing loss ($p < 0.001$), with a moderate-to-strong association ($\gamma = 0.507$). Among patients with disease duration ≤ 5 years, hearing status was distributed across normal hearing (52%), mild hearing loss (40%), and moderate hearing loss (8%). Most patients in the 6-10-year group had normal hearing (83.3%). In contrast, all patients in the 11-15-year group had moderate hearing loss. RF status was also significantly associated with degree of hearing loss ($p = 0.012$), with a stronger association ($\gamma = 0.658$). Most RF-negative patients had normal hearing (85.7%), whereas only 14.3% had moderate hearing loss. Among RF-positive patients, hearing status was more evenly distributed: 42.5% had normal hearing, 28.7% had mild hearing loss, and 28.7% had moderate hearing loss.

These findings suggest that RF seropositivity, which is commonly associated with a more aggressive disease phenotype and broader systemic involvement, may contribute to the risk of hearing loss in RA. Disease activity level was not significantly associated with degree of hearing loss ($p = 0.097$), and the strength of association was weak ($\gamma = 0.214$). Although all patients in the moderate disease-activity group had hearing loss (83.3% mild and 16.7% moderate), variability across categories and the limited sample size may have reduced statistical power. These findings suggest that current inflammatory activity may be less predictive of hearing loss severity than cumulative disease burden.

Disease Duration as a Predictor of Hearing Loss

ROC analysis was performed to assess the ability of RA disease duration to predict hearing loss. Hearing-loss status was used as the state variable, with longer disease duration assumed to indicate



a higher probability of hearing loss.

Figure 1. ROC curve for disease duration as a predictor of hearing loss in patients with rheumatoid arthritis

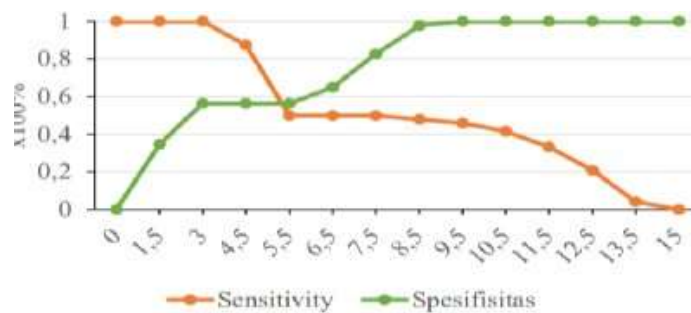


Figure 2. Line plot for determining the optimal disease-duration cut-off point for predicting hearing loss in patients with rheumatoid arthritis

Disease duration demonstrated acceptable discriminative ability for predicting hearing loss. The AUC was 0.780 (SE = 0.049; $p < 0.001$; 95% CI, 0.685-0.876), indicating a 78% probability that a patient with hearing loss had a longer disease duration than a patient with normal hearing. Based on commonly used diagnostic-accuracy criteria, this AUC indicates acceptable-to-good discrimination. The statistically significant result and the 95% confidence interval, which did not include 0.5, support the predictive value of disease duration beyond chance. These findings indicate that longer RA duration is associated with a higher likelihood of hearing loss. Clinically, disease duration may serve as a simple preliminary marker for identifying patients who require audiological evaluation. Patients whose disease duration exceeds the optimal ROC-derived threshold should be prioritized for comprehensive hearing assessment and timely rehabilitative intervention.

DISCUSSION

Baseline Characteristics

The predominance of women in this study (93.6%) and the mean age of 40.02 ± 6.75 years are consistent with the epidemiology of RA, which occurs more frequently in women and commonly begins between 30 and 50 years of age. The female predominance may reflect hormonal, reproductive, and genetic influences on RA susceptibility. Sex hormones modulate immune responses; testosterone and progesterone generally suppress immune activity, whereas estrogen, particularly 17-beta estradiol, and prolactin enhance humoral immunity. Genetic factors, including X chromosome-related microRNA expression, may also contribute to sex-related differences in disease susceptibility. Gamal et al. reported 85 female and 10 male patients with a mean age of 46.5 years, and Almasi et al. reported that 78% of their subjects were female, with a mean age of 53.95 years. Thus, the present cohort is broadly consistent with the demographic profile of RA, although it represents a relatively young to middle-aged adult population. (Gamal NM et al., 2021; Almasi S et al., 2023; Carmona et al., 2024; Tancer S et al., 2025) More than half of the patients in this study had RA for ≤ 5 years, which differs from several previous studies of hearing loss in RA that enrolled patients with longer disease duration. Gamal et al. reported a mean disease duration of 9.57 ± 0.61 years, whereas Almasi et al. reported a mean duration of 12.74 years. This distinction is clinically relevant because longer disease duration has been associated with higher hearing thresholds, impaired cochlear function, and greater risk of hearing loss. (Chen JJ et al., 2024; Gamal NM et al 2021; Almasi S et al., 2023)

Most patients in this study had low disease activity, although moderate and high disease activity remained common. This suggests that some patients had achieved relatively good inflammatory control, but not all had reached remission. Almasi et al. reported a distribution more strongly weighted toward remission, with 58% in remission, 20% with low activity, 20% with moderate activity, and 2% with high activity. RF positivity was observed in 85.1% of patients, consistent with reports that approximately 75-90% of patients with RA are seropositive. RF seropositivity is clinically relevant because it has been associated with a more aggressive disease phenotype, greater joint damage, and more frequent extra-articular manifestations. Therefore, the high proportion of RF-positive patients in this study may indicate a population with a greater

immunological disease burden. (Almasi S et al., 2023; Handa R et al., 2019; Togashi T et al., 2025) Tympanometry demonstrated normal middle-ear function in most patients, as reflected by the predominance of Type A tympanograms (93.6%). This finding is consistent with Kiakojuri et al., who reported abnormal Type As tympanograms in only approximately 5% of patients with RA. Although RA may theoretically involve the incudomalleolar and incudostapedial joints because both are synovial joints, clinically apparent middle-ear involvement appears uncommon. The predominance of Type A tympanograms in this study therefore supports the interpretation that hearing loss in this cohort was more likely sensorineural than conductive. (Chen JJ et al., 2024; Kiakojuri K et al., 2019)

Associations of Disease Duration, Disease Activity, and Rheumatoid Factor with Type of Hearing Loss

Disease duration was significantly associated with type of hearing loss ($p < 0.001$). Patients with shorter disease duration (≤ 5 years) were more likely to have normal hearing, whereas all patients in the 11-15-year group had hearing loss, predominantly sensorineural. The proportion of sensorineural hearing loss was higher in the ≤ 5 -year group than in the 6-10-year group, which may reflect the higher proportion of patients with severe disease activity in the shorter-duration group. This finding suggests that severe inflammatory activity may contribute to sensorineural hearing loss even early in the disease course.

The association between longer RA duration and hearing loss is consistent with previous studies. Kiakojuri et al. studied patients with RA of more than 5 years duration, reported a mean disease duration of 12.51 ± 6.09 years, and found a significant positive correlation between disease duration and hearing loss. In that study, all affected patients had sensorineural hearing loss, particularly at 4,000 and 8,000 Hz bilaterally. Gamal et al. also reported that hearing loss was associated with RA duration and was most commonly symmetrical and sensorineural. (Gamal NM et al., 2021) Similarly, Chen et al. reported that longer disease duration was associated with progressive deterioration of hearing function, beginning at 10,000 Hz during 1-5 years of disease duration, extending to 4,000 Hz at 6-10 years, and involving all frequencies at 11-15 years. Sensorineural hearing loss was the most frequently observed type. These findings support the concept that longer RA duration increases the likelihood of auditory involvement, particularly sensorineural hearing loss. (Chen JJ et al., 2024; Kiakojuri K et al., 2019)

Associations of Disease Duration, Disease Activity, and Rheumatoid Factor with Degree of Hearing Loss

Disease duration was significantly associated with hearing loss severity ($p < 0.001$; $\gamma = 0.507$). All patients with 11-15 years of disease duration had moderate hearing loss, suggesting that cumulative inflammatory exposure may contribute to progressive cochlear dysfunction. Direct evidence linking RA duration with categorical hearing-loss severity remains limited. Deswal et al. reported that 36% of patients with RA of more than 5 years duration had hearing thresholds >25 dB, particularly at 4,000 and 8,000 Hz, but did not categorize hearing loss severity or test its correlation with disease duration. Other studies, including those by Kiakojuri et al., Gamal et al., and Chen et al., support this relationship primarily through elevated hearing thresholds rather than clinical severity categories. (Chen JJ et al., 2024; Gamal NM et al., 2021; Kiakojuri K et al., 2019; Deswal S et al 2021) RF status showed the strongest association with hearing loss severity ($p = 0.012$; $\gamma = 0.658$). RF-positive patients had a more even distribution across normal, mild, and moderate hearing categories, whereas RF-negative patients mostly had normal hearing. This finding is biologically plausible because RF seropositivity is associated with more aggressive and systemic RA. Possible mechanisms include immune-complex deposition in the cochlear microvasculature and systemic vasculitis. However, evidence remains mixed. Elnagdy et al. found no significant correlation between RF positivity and conventional audiometric severity, although RF positivity was significantly associated with extended high-frequency audiometry abnormalities, absent acoustic reflexes, and abnormal transient evoked otoacoustic emission findings. (Elnagdy OH et al., 2022)

Disease activity level was not significantly associated with hearing loss severity ($p = 0.097$; $\gamma = 0.214$). Although descriptive trends were observed, the limited sample size and variability across activity categories may have reduced the ability to detect a significant association. Previous studies have generally assessed hearing impairment using threshold values rather than clinical severity categories. Rkain et al. reported lower mean hearing thresholds in patients in remission than in those not in remission (12.8 ± 5.2 dB vs 18.8 ± 6.9 dB), while Gamal et al. found a significant correlation between DAS28 and high-frequency hearing thresholds. (Gamal NM et al., 2021; Rkain I et al., 2016)

Disease Duration as a Predictor of Hearing Loss

Evidence supporting a >5-year disease-duration cut-off as a formal predictor of hearing loss in RA remains limited. Iskander et al. classified patients according to disease duration (≤ 5 years vs > 5 years) and found that hearing loss increased from 40% in the ≤ 5 -year group to 85% in the > 5 -year group. Although this supports an association between longer disease duration and hearing loss, the study did not use ROC analysis or a formal prediction model. Deswal et al. included only patients with RA of > 5 years duration and found that 36% had hearing thresholds > 25 dB; however, the absence of a ≤ 5 -year comparison group limits interpretation. Taken together, available evidence supports a relationship between longer disease duration and greater auditory involvement, but external validation is required before the > 5 -year threshold can be considered a definitive predictive cut-off. (Deswal S et al 2021; Iskandar M et al 2023)

CONCLUSION

This study demonstrated that hearing loss is a common extra-articular manifestation in patients with rheumatoid arthritis (RA), predominantly presenting as sensorineural hearing loss with greater involvement at high frequencies. Disease duration, rheumatoid factor (RF) status, and disease activity level were significantly associated with the type of hearing loss, whereas disease duration and RF status were significantly associated with hearing-loss severity. Patients with longer disease duration, particularly those with RA duration of ≥ 5 years, and those with positive RF status were more likely to develop hearing loss and experience greater hearing-loss severity. Furthermore, disease duration showed acceptable discriminative ability for predicting hearing loss.

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