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REVIEW ARTICLES

Otologic manifestations of rheumatoid arthritis: a comprehensive review

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ABSTRACT

Aims: To provide a comprehensive literature review of the otologic manifestations in RA and discuss potential pathogenesis and risk factors.
Methods: We screened the MEDLINE, Scopus, and Embase databases, and Google Scholar for articles involving patients with RA who presented otological manifestations up to May 2025, including meta-analyses, systematic reviews, observational studies, case series, and case reports published in English and/or Spanish.
Results: Rheumatoid arthritis (RA), besides affecting articulations, may be involved in other systems, including the cardiovascular, neurological, ocular, cutaneous, respiratory, renal, and gastrointestinal systems. Otologic manifestations, such as hearing loss, tinnitus, Meniere's disease, and vertigo, are relatively common in patients with RA. Hearing loss shows a notable prevalence, with an average rate of 16.14% among RA patients, an odds ratio of 3.42, and a relative risk of 2.28 when compared to the general population.
Conclusions: Given the high prevalence and impact of otologic manifestations in RA patients, a multidisciplinary approach involving both rheumatologists and otolaryngologists is essential for proper diagnosis and management. Early recognition of hearing loss and other otologic symptoms by rheumatologists may prevent complications and improve patients' quality of life.

Keywords: Hearing loss; Otologic disease; Rheumatoid arthritis; Tinnitus; Vertigo.

INTRODUCTION

Rheumatoid arthritis (RA) is an autoimmune disease characterized by chronic and symmetric joint inflammation, which damages cartilage and bone[1-3]. The worldwide prevalence of RA is estimated at 0.24%[4]. RA can cause extraarticular manifestations, such as cardiovascular, neurological, ocular, cutaneous, respiratory, renal, gastrointestinal, and otologic features[5-7].

Patients with RA may present otologic manifestations during their disease, including hearing loss, tinnitus, vertigo, and Meniere's disease. Several of these have been associated with decreased quality of life, depression, and anxiety[8-11]. There is limited information about RA and otologic manifestations. This comprehensive review aimed to provide an overview of the otologic manifestations reported in RA patients, discussing their pathogenesis and risk factors.

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Search strategy

We conducted a literature search using the MEDLINE, SCOPUS, and EMBASE databases, and Google Scholar until May 2025, focusing on English and/or Spanish-language articles. The search strategy incorporated Boolean operators (AND, OR) using combinations of the following MeSH terms: "Rheumatoid arthritis" AND ("otologic manifestations" OR "hearing loss" OR "audiometry" OR "tinnitus" OR "vertigo" OR "vestibular" OR "dizziness" OR "Meniere's disease" OR "otalgia" OR "labyrinthitis" OR "otitis" OR "chondritis" OR "neuritis" OR "Ramsay Hunt syndrome" OR "relapsing polychondritis" OR "Cogan's syndrome"). The articles reviewed included meta-analysis, systematic reviews, cases and control studies, narrative reviews, case series, and case reports. References within the articles were also screened. Due to the limited literature on the otologic manifestations of RA, articles were not excluded based on publication date. We prioritized recent studies with high evidence levels from the past two decades. EndNote software (v. 20, Clarivate, Philadelphia, USA) was used as the primary tool for managing bibliographic references.

Two independent reviewers screened titles and abstracts for relevance. Full-text articles were assessed for eligibility based on the inclusion of otologic manifes-

tations in RA patients. Disagreements were resolved through discussion or consultation with the corresponding author. Exclusion criteria included articles unrelated to RA or otologic manifestations, not in adult patients, and non-English/Spanish articles.

The information extracted from eligible studies was categorized according to specific otologic manifestations in RA: hearing loss, tinnitus, vertigo, and Meniere's disease. Within each category, the information was sectioned based on pathophysiological mechanisms, prevalence, risk factors, and severity, when available. Other rare manifestations were grouped under a separate section. Priority was given to meta-analyses, systematic reviews, and large cohort studies.

OTOLOGIC MANIFESTATIONS

Hearing Loss

Hearing loss is described as the presence of hearing thresholds in both ears of ≥ 20 dB[12]. In 2013, hearing loss was estimated to affect 1.3 billion people worldwide[13]. Mexico has an estimated 2.3 million individuals with hearing impairment[14].

Pathophysiology

The pathophysiology of otologic involvement in RA remains uncertain[15, 16]. There are multiple theories to elucidate the origin of this involvement. One of these involves the participation of rheumatoid factor in cross-reactions. An Indian case-control study found that 27% of the patients with positive rheumatoid factor reported the absence of distortion product otoacoustic emission[17]. Additionally, RA patients with hearing loss had higher anti-cyclic citrullinated protein antibody levels compared to those without hearing loss[18]. The inflammatory process associated with disease activity in RA is another likely contributor. Elevated cytokines such as tumor necrosis factor-alpha (TNF-α) and matrix metalloproteinases (MMPs) can enter the inner ear via the circulatory or lymphatic systems, potentially causing direct tissue damage[19,20]. MMP-3, in particular, has been linked to the progression of structural damage in RA patients[21-24]. In a cross-sectional study, MMP-3 was significantly higher in RA patients who had hearing loss than in those who did not[25]. This elevated MMP-3 activity may contribute to the degradation of the matrix components of the incudomalleolar and incudostapedial joints, leading to oxidative damage to the inner ear's hair cells. Additionally, MMP-3 can activate other matrix metalloproteinases, such as pro-MMP-1, pro-MMP-8, pro-MMP-9, and pro-MMP-13, which may further exacerbate tissue damage[26].

In addition to antibody-mediated damage, vascular dysfunction is also believed to play a role in hearing impairment in RA. A reduction in blood flow due to subclinical atherosclerosis may impair the circulation to the inner ear, which is particularly vulnerable to hypoxic damage. This could affect the perception of high-frequency sounds, a common characteristic of sensorineural hearing loss. Thickening of the carotid artery's intima-media layer may also disrupt blood flow to the labyrinthine artery, further contributing to SNHL, particularly at higher frequencies[27-29]. A Mexican study demonstrated a positive correlation between the thickness of the carotid intima-media and hearing loss[27]. Recent studies seem to indicate that diarthrodial joints may suffer inflammation of the synovial membrane, including the incudomalleolar and incudostapedial joints of the middle ear[15, 27]. An experimental study from 2016 induced arthritis in male mice. The temporal bones were recollected for posterior analysis with high-resolution micro-computed tomography of the ossicles. The result of the presence of RA on the ears showed a narrowing of the incudostapedial joint space and the presence of multiple closed pores[16].

Prevalence in RA

The prevalence, odds ratio, and additional information are summarized in Table I. Hearing loss has a high prevalence among RA patients, with varying rates across studies. A meta-analysis study published in 2023, reported a prevalence of 16.14% among RA patients[30]. Similarly, a 2020 meta-analysis of 13,389 RA patients found an odds ratio of 3.42 and a relative risk of 2.28 for this condition[31].

Studies from Korea and Taiwan have also demonstrated this association. A Korean research group found a statistically significant correlation between RA and sudden sensorineural hearing loss, with a hazard ratio of 2.22[32]. A Taiwanese study that included 18,267 patients with recently diagnosed RA showed a hearing loss incidence of 3.08 per 1,000 person-years, compared to 1.62 in the control group[33]. A similar Korean study showed a sensorineural hearing loss rate of 0.8% in RA patients[34].

Additional studies from Mexico and Iran have similar findings. An observational study conducted in Mexico evaluating 117 female RA patients, found symmetric bilateral hearing impairment in 91.45% of the patients[35-36]. Another study from the same country, found hearing impairment in 24% of 113 RA patients[37]. A study involving 104 RA patients observed that 23% of the patients had hearing loss at baseline. Among the remaining 80 patients without hearing loss, 6.25% experienced hearing loss after 6 months, and an additional 6.25% developed hearing loss within a year[38]. Similarly, a study in Iran found 71% of 100 RA patients exhibited abnormal audiometry[39]. Another case-control study

TABLE I. Select hearing loss studies in patients with rheumatoid arthritis (RA)

Study	Design	N (RA vs. non-RA)	HR/OR (95% CI) RA vs. non-RA	Prevalence (RA vs non-RA)
Jeong et al[23]	Retrospective: RA vs controls	8,233 vs 66,250	HR: 1.51 (1.20–1.91)	1.19% vs 0.73%
Chung-Ming et al[24]	Retrospective cohort study	18,267 vs 73,068	HR: 1.90 (1.70-2.13)	Not reported
Galarza-Delgado et al[27]	Cross-sectional: RA vs controls	117 vs 251	Not reported	94.9% vs 66.1% at very high frequencies
Lee et al[25]	Retrospective longitudinal: RA vs controls	7,619 vs 30,476	HR: 1.40 (1.05-1.87)	0.8% vs 0.6%
Pascual-Ramos et al[28]	Cross-sectional: RA only	113	Not reported	23.89% RA only
Pascual-Ramos et al[29]	Prospective longitudinal cohort: RA only	104	Not reported	23% at the start, 12.5% additional developed hearing loss at 12-month follow-up
Tsirves et al[31]	Cross-sectional: RA vs controls	60 vs 60	Not reported	66.6% on RA patients
Lasso et al[32]	Cross-sectional: RA vs controls	53 vs 71	Not reported	69.8% on RA patients at high frequency
Rahne et al[33]	Cross-sectional: RA vs controls	22 vs 34	Not reported	36% vs 20%
Oztürk et al [34]	Cross-sectional: RA vs controls	74 vs 45	Not reported	76% vs 32%

Rheumatoid arthritis (RA); hazard ratio (HR); odds ratio (OR)

demonstrated an increase in the average hearing loss value in 66% of 60 Greek RA patients[40].

A Spanish study of 53 RA patients found a prevalence of 69.8% of hearing loss using high-frequency audiometry[41], while a German study of 22 RA patients reported a prevalence of 36%. Exclusively, sensorineural hearing loss was found, and not a single case of conductive hearing loss was reported, although the results were not statistically significant[42]. Another German study found a prevalence of 76% of RA patients (74 patients)[43]. A Turkish study found 15.7% of 35 RA patients with hearing loss [44].

Severity

Moderate hearing loss at very high frequencies was observed in a group of Mexican female RA patients[35]. In another study from the same country, 74% of the patients were classified as having mild hearing loss, while 26% had moderate hearing loss for at least 1 frequency[37]. An Iranian study showed that 52% of their RA patients had slight/mild hearing loss[39]. The same results were obtained from another Iranian case-control study, with the evaluation of 60 RA case patients. The hearing loss was only significant at high and very high frequencies[45]. Mild hearing loss in high frequencies was described in 46.66% of a Greek RA group, meanwhile, moderate hearing loss was found in 20% of the same group[40]. A Spanish study revealed severe hearing loss in RA patients at the age of 50 years at ultra-high frequencies (14,000 Hz)[41].

Diabetes mellitus, hypertension, and hypercholesterolemia demonstrated a significant association with an unfavorable prognosis (lack of recovery) for sudden sensorineural hearing loss in RA patients, as described in a retrospective cohort study based on the records of 663 patients in China[46].

Risk Factors

Risk factors are summarized in Table II. A higher incidence of sudden sensorineural hearing loss was demonstrated in a Korean follow-up study among male RA patients aged over 50 years. Other risk factors were ischemic heart disease and stroke[34]. Additionally, a Chinese cohort described chronic kidney disease, hypertension, diabetes mellitus, hyperlipidemia, and hyperthyroidism as risk factors for hearing loss[33].

Similar risk factors were found in a Mexican study, with the additional risk factor of tobacco use[37]. The primary finding from another Mexican study was that the only predictor of incident hearing loss was the assessment of disease activity using the disease activity score-C reactive protein[38]. Anti-cardiolipin was de-

TABLE II. Risk factors for developing hearing loss in patients with rheumatoid arthritis[24,25,32,35]

Sex (male)
Age >50 years
Ischemic heart disease
Stroke
Chronic kidney disease
Hypertension
Diabetes
Dyslipidemia
Hyperthyroidism

TABLE III. Frequency of otologic manifestations of rheumatoid arthritis

Manifestation	Frequency
Hearing loss	Very frequent
Tinnitus	Frequent
Vertigo	Frequent
Meniere's disease	Infrequent
Relapsing polychondritis	Infrequent
Cogan's syndrome	Very infrequent
Ramsay Hunt syndrome	Very infrequent
Vestibular neuritis	Very infrequent
Otalgia	Very infrequent
Otitis with effusion	Very infrequent

scribed as a risk factor in a Spanish study, along with rheumatoid factor and male gender[41].

Tinnitus

Tinnitus refers to the conscious perception of sound without an external acoustic stimulus[47]. Typically, tinnitus perceptions manifest as indistinct auditory sensations, such as ringing or hissing. It can affect one or both ears and may also be characterized as originating within the head[48]. Data suggest that tinnitus is encountered by over 740 million individuals globally, with a severe form affecting more than 120 million people worldwide[49]. According to data from the American Tinnitus Association, approximately 50 million individuals in the United States are affected by chronic tinnitus[50].

Pathophysiology

There is a lack of conclusive evidence regarding the relationship between tinnitus and RA. However, a link may exist regarding common risk factors for both conditions, like tobacco[51]. This is secondary to vasoconstriction induced by nicotine, leading to a subsequent reduction in oxygen supply, which may damage ear cells[52]. Multiple studies have highlighted a strong association between sensorineural hearing loss and tinnitus[13,53-55]. A systematic review and meta-analysis found that the presence of sensorineural hearing loss is a significant risk factor for tinnitus, suggesting a possible pathophysiological connection between the two in RA patients[56]. In addition, temporomandibular joint (TMJ) disorder has been identified as another important risk factor for tinnitus, which has also been observed as a potential consequence in RA patients (OR 1.08, 95% CI: 1.03-1.13, P = .001)[56-63]. The release of inflammatory mediators, such as histamine, may increase blood flow and vascular permeability in the inner ear[64], potentially contributing to the perception of tinnitus. Additionally, autoimmune diseases like RA, Sjögren's syndrome, and systemic lupus erythematosus are associated with a higher risk of developing tinnitus[65,66]. Autoimmune inner ear disease, which commonly presents with hearing loss, tinnitus, and vestibular symptoms, can occur either as an isolated condition or as part of a systemic autoimmune disease. While the exact mechanism is still not fully understood, several immune-mediated processes have been proposed. These include humoral antibody attacks on inner ear antigens, cell-mediated ototoxicity, immune complex deposition in the small vessels of the inner ear, and both direct and indirect involvement of the neuronal pathways. Connective tissue diseases such as RA, Behçet's syndrome, systemic lupus erythematosus, and Cogan's syndrome can affect the inner ear, leading to disorders in both vestibular and auditory functions[67-70].

Prevalence in RA

In a meta-analysis conducted in 2023, it was discovered that among the comorbidities associated with tinnitus, autoimmune diseases such as RA were notably present. This study categorized factors related to tinnitus into six distinct and broad domains of exposure or occurrence, concluding the nature of this condition and its connections to various health conditions[56]. A systematic review from the year 2020, which explored the relationship of non-auditory factors in the development of tinnitus, discovered significant data in patients with RA[71]. These studies conducted in Korea, including a cross-sectional study from 2015 with 19,290 participants, found an association with an odds ratio of 1.89 for RA. This indicates a higher likelihood of experiencing tinnitus in individuals who previously had RA when compared to the general population surveyed. As a result, a notable prevalence of tinnitus was observed in RA, with a higher occurrence described in older patients[72].

A cross-sectional study performed in a hospital in Mexico analyzed the prevalence of tinnitus in RA. The RA group had a 20.5% prevalence of bilateral tinnitus[36]. In a large prospective population-based cohort study of individuals residing in the northern Netherlands, RA was associated with tinnitus (odds ratio of 1.35)[73].

Meniere's disease

Meniere's disease is an uncommon and persistent condition affecting the inner ear, marked by sensory hearing impairment, occasional episodes of dizziness, ringing in the ears, and a sensation of fullness in the ear[74]. Studies conducted worldwide have reported prevalence rates ranging from as little as 3.5 cases per 100,000 to as high as 513 cases per 100,000. The incidence is 8.2 cases per 100,000[75].

Pathophysiology

The progression of symptoms in Meniere's disease and hearing loss is associated with the accumulation of immune complexes that can lead to inflammation and disrupt the filtering function of the endolymphatic sac. Numerous research studies have shown elevated levels of circulating immune complexes in a significant portion of individuals diagnosed with Meniere's disease[76]. The development of hearing impairment and the onset of vertigo symptoms in individuals with Meniere's disease were found to be associated with increased levels of lymphocytes in systemic autoimmune conditions. This observation suggests a potential association between Meniere's disease, factors of the immune system, and the manifestation of auditory and vestibular symptoms[77].

Prevalence in RA

Several studies have determined a potential autoimmune origin to Meniere's disease and an association with other autoimmune diseases like RA. A systematic review found the prevalence of autoimmune arthritis in individuals diagnosed with Meniere's disease was 4.7% (range 1-10%). This prevalence of autoimmune arthritis among Meniere's disease patients exceeded the occurrence rate of autoimmune arthritis within the broader population, which ranged from 0% to 1.1%[76]. In a case series involving 690 adults diagnosed with Meniere's disease, the observed prevalence of RA exceeded the anticipated rate for the general population[77].

Vertigo

Vertigo is a symptom that can be described as the feeling of movement, usually with a spinning sensation, whether it is perceived as an external, objective experience or an internal, subjective one[78]. The prevalence of vertigo in the general population has been approximated to be in the range of 20% to 30%, with an annual occurrence rate of 7%. This condition is more commonly observed among adults aged 18 to 79. Notably, it has a higher prevalence among females, with an annual ratio of 1:2.7 between men and women[78].

Pathophysiology

As discussed earlier, there is a relationship when vertigo is mentioned as an issue involving the vestibular system. Several probable causes can help us understand the pathophysiology of vertigo related to autoimmune disorders, in this case, RA. The condition of vertigo is associated with various diseases, the main isolated immune-mediated vestibular disorders in which vertigo plays a central role are autoimmune inner ear disease, delayed endolymphatic hydrops, Meniere's disease, and bilateral vestibulopathy[79].

The clinical manifestation of autoimmune inner ear disease typically involves a rapidly advancing bilateral hearing loss that occurs within a few weeks to several months. It is notably linked to symptoms of vertigo as well as tinnitus, with occasional variations in symptom intensity. This condition can either originate as a primary ear disorder or result from an underlying autoimmune systemic disease[80].

There is a recognized association between autoimmune factors and vertigo, similar to the connection observed with tinnitus. Autoimmune diseases, such as RA, can be linked to autoimmune inner ear disease, vasculitis, neuritis, or structural damage to the incudomalleolar and incudostapedial joints of the middle ear[78,40]. An experimental study was conducted to investigate the inner ear's immune response to the KLH antigen in animals with surgically removed endolymphatic sacs and a control group that underwent sham surgery. In the initial immune responses of the inner ear, the obstruction of the endolymphatic sac led to decreased levels of anti-KLH antibodies in the bloodstream compared to the control group. The endolymphatic sac is recognized as an organ with the capability to mount an immune response, and it appears that both cellular and humoral aspects of immunity are involved. This is evident in the presence of circulating antibodies in delayed endolymphatic hydrops[81]. In contrast, a recent study involving RA mouse models found that structural damage may contribute to hearing and vestibular dysfunction in RA patients. The study observed that the tectorial membrane over cochlear hair cells in the RA model was thinner and more fragile compared to normal mice. Additionally, they noted the loss of sensory hair cells and inflammation within the semicircular canal ampulla in RA mice, suggesting that vestibular dysfunction may result from direct damage to the organs of Corti and semicircular canals[82]. These findings underscore

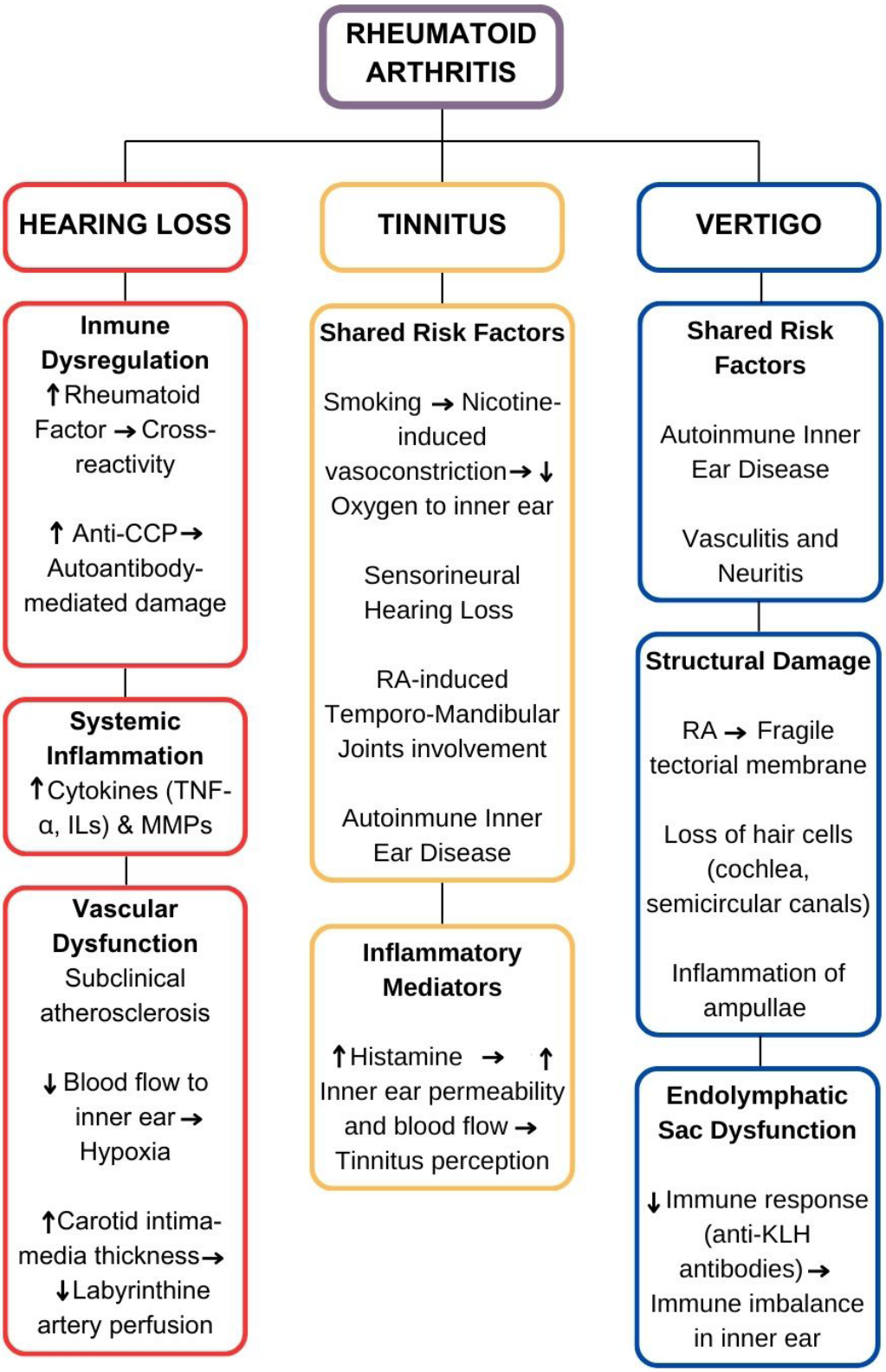

Figure 1. Flowchart of the possible pathophysiological mechanisms involved in the otologic manifestations of Rheumatoid Arthritis (RA) patients

the need for further research to better understand the pathophysiology of vertigo in patients with rheumatoid arthritis, as the exact mechanisms remain unclear.

Prevalence in RA

In a study of 117 RA patients from Mexico, vertigo was reported by 6.8% of patients[36]. In a case-control cohort of 40 patients with RA, videonystagmography revealed central abnormalities in 12 patients and peripheral abnormalities in 9 patients, as well as mixed abnormalities in one patient. Additionally, vertigo was referred by 70% of RA patients vs 0% in the control group[83]. In another report of 60 patients with RA, 61.4% of the patients reported experiencing vertigo[42].

Other manifestations

Cogan's syndrome is an autoimmune disease characterized by interstitial keratitis and vestibulocochlear dysfunction[84]. Few cases have been reported with Cogan's syndrome and RA. One of the cases was a 51-year-old woman with a 10-year history of RA who presented episcleritis, bilateral hearing loss, and unilateral tinnitus[85]. Another case from the United Kingdom reported a 63-year-old woman with a 20-year history of RA who presented bilateral interstitial keratitis and sensorineural hearing loss[84].

Vestibular neuritis, otalgia, and otitis media with effusion (serous otitis media) in patients with RA have been reported in very few case reports[86-88]. The frequency of the otologic manifestations is summarized in Table III. Ramsay Hunt syndrome is characterized by peripheral paralysis of the facial nerve, otologic herpes zoster vesicles, and vestibular-auditory affection. It is caused by the reactivation of the varicella-zoster virus in the geniculate ganglion[89]. Some RA treatments may predispose to herpes zoster[90]. Case reports have been described where these two entities occur concomitantly[89,91,92]. Relapsing polychondritis (RP) is an uncommon disease that primarily affects cartilaginous structures, causing eye and ear inflammation. A few cases of RP with RA have been published[93-97].

DISCUSSION

This study provides a comprehensive analysis of the otologic manifestations that may be present in patients with RA, focusing on the potential physiopathology, prevalence, and risk factors of these conditions.

While multiple theories have been proposed to explain the pathophysiology of otologic manifestations in RA patients, and numerous studies support the higher prevalence of these manifestations in this population[98-100], there is also evidence from studies showing no statistically significant differences in the prevalence of otologic manifestations, specifically hearing loss, between RA patients and control groups[42]. Therefore, future research, particularly prospective studies, is needed to more comprehensively understand the relationship between RA and otologic manifestations, as well as to elucidate their underlying etiology and pathophysiological mechanisms.

This comprehensive review highlights the need to better understand the impact of RA on hearing function and the associated effects on the quality of life in patients living with this condition. It is essential that healthcare providers, especially rheumatologists, consider these potential manifestations in their clinical assessments. Referrals to otolaryngologists should be made when appropriate for further evaluation and management. Moreover, it is crucial to address the current gap in diagnostic and treatment algorithms for these cases. Clinical practice guidelines that specifically address otologic manifestations in RA patients are vital for an early diagnosis and standardized treatment approaches

This review has several limitations. First, the available literature on otologic manifestations in RA is limited. A significant portion of the evidence derives from case reports, cross-sectional studies, or small sample cohorts. Second, the search was limited to articles published in English and/or Spanish, which may have led to the exclusion of relevant studies in other languages. Lastly, there is a lack of prospective studies and randomized controlled trials in this area.

CONCLUSION

Otologic manifestations are a frequent cause of morbidity in RA. However, they remain underdiagnosed even when their presence negatively impacts the quality of life. Hearing loss was the most common otologic manifestation of RA, particularly in men aged over 50 years, with ischemic heart disease, chronic kidney disease, hypertension, diabetes mellitus, hyperlipidemia, or hyperthyroidism. Early recognition of otologic manifestations by physicians may improve quality of life and outcomes.

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