

EXPLORING THE ASSOCIATION BETWEEN RHEUMATOID ARTHRITIS AND THE OCCURRENCE OF SUDDEN-ONSET SENSORINEURAL HEARING LOSS: A REVIEW

Kerry-Lee Bekker

SAERA. School of Advanced Education Research and Accreditation

ABSTRACT

Objective: The aim of this study was to better understand the association between rheumatoid arthritis and sudden-onset sensorineural hearing loss.

Methods: In accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) protocols guidelines this systematic review was conducted (Page et al., 2021). A search of Cochrane Central and PubMed databases was conducted to find primary research papers published in English until 31/01/2024. No lower time limit was set for this search. This search was conducted by one independent investigator (KB), using the following keywords in all possible combinations: sensorineural, sudden-onset, hearing impairment, hearing loss, deafness, rheumatoid arthritis, rheumatic, rheumatoid.

Results: Several studies have indicated a heightened prevalence of sensorineural hearing loss among individuals diagnosed with rheumatoid arthritis, relative to age-matched control cohorts.

Conclusion: Hearing loss is a common issue among individuals diagnosed with rheumatoid arthritis, necessitating consistent monitoring and care for their auditory health. It is imperative that healthcare providers conduct comprehensive assessments, including thorough patient history-taking, routine audiometry examinations, and impedance testing, at regular intervals throughout the progression of the disease. This proactive approach enables early detection of any changes in auditory function, allowing for timely interventions and appropriate management strategies to mitigate the impact of hearing loss on the individual's overall quality of life. By closely monitoring aural health in patients with rheumatoid arthritis, healthcare professionals can optimize treatment plans and provide necessary support to improve patient outcomes and enhance their well-being.

Keywords: *Rheumatoid arthritis, sudden-onset, hearing loss, sensorineural, rheumatic, deafness.*

INTRODUCTION

Rheumatoid arthritis is a multisystemic chronic autoimmune disease-causing inflammation of the synovial membranes of diarthrodial joints, this disease affects approximately 1% of the population (Yildirim et al., 2016). Rheumatoid arthritis is the most prevalent form of arthritis, characterised by symmetric peripheral polyarthritis (Ahmadzadeh et al., 2017). The small joints of the hands and feet are typically the first to be involved, causing joint damage and physical disability. Bone and joint damage can lead to premature death and impose significant socioeconomic challenges. Rheumatoid arthritis patients often experience complications in the head and neck region, encompassing issues such as laryngeal, cervical, and temporomandibular joint involvement (Almasi et al., 2023). The course of rheumatoid arthritis is chronic, progressive, and symmetric. Rheumatoid arthritis manifestations can be affected by factors such as race, genetics, nutrition and environment (Ahmadzadeh et al., 2017). Women and individuals of advanced age tend to have a higher incidence of rheumatoid arthritis compared to other demographic groups. Furthermore, genetic predisposition is implicated in approximately half of all cases (Almasi et al., 2023).

The aetiology of rheumatoid arthritis is characterised by the enlistment of white blood cells, mainly CD4+T cells and monocytes from the vasculature into inflamed synovial tissue and fluid. These antigen activated CD4+T cells stimulate fibroblasts and macrophages to secrete factors that lead to synovial cell

proliferation, bone and cartilage destruction, and weakening and destruction of the ligaments, tendons and joint capsules (Öztürk et al., 2004; Takatsu et al., 2005). This results in chronic inflammation and progressive destruction of articular and periarticular tissue. Extra-articular features of rheumatoid arthritis include systemic features such as cardiovascular, pulmonary, psychological, skeletal, eye disorders, and auditory system disturbances (McInnes & Schett, 2011). Copeman (1963) was the first to report on hearing loss in rheumatoid arthritis patients, he then coined the term 'rheumatoid osteoarthritis'. His initial report included three patients whose hearing was temporarily impaired when the severity of their arthritis aggravated. Patients who have existing concurrent medical conditions should undergo invasive treatments and prioritize the management of risk factors like smoking, dyslipidaemia, diabetes, and hypertension. Extra-articular manifestations could impact as many as 40% of individuals with rheumatoid arthritis. The existence of extra-articular manifestations may substantially elevate both morbidity and mortality rates among rheumatoid arthritis patients, consequently diminishing their overall quality of life (Almasi et al., 2023; Chaitidis et al., 2020).

Cases of sensorineural, conductive and mixed hearing loss have been reported in patients with rheumatoid arthritis. Sensorineural hearing loss associated with rheumatoid arthritis may stem from various factors impacting the inner ear. These may include inflammation of the small blood vessels (vasculitis) supplying the inner ear, nerve inflammation (neuritis), adverse effects of medications used to manage rheumatoid arthritis (such as NSAIDs, steroids, and disease-modifying anti-

rheumatic drugs) that can be harmful to auditory function, and autoimmune reactions targeting the delicate hair cells of the cochlea or leading to the deposition of immune complexes (Ahmadzadeh et al., 2017).

Sensorineural hearing loss is characterised by damage to the cochlear hair cells, auditory nerve or the brain's central processing centres. Sensorineural hearing loss differs from conductive hearing loss in that this is characterised by a middle ear pathology whereby the sound is unable to reach the inner ear. Sensorineural hearing loss and conductive hearing loss have both been reported in patients with rheumatoid arthritis. Studies reporting conductive hearing loss attribute it to the inflammation of the intra-auricular joints, in contrast studies reporting sensorineural hearing loss attribute it to the medications prescribed as treatment for rheumatoid arthritis.

One of the most cited mechanisms in the literature regarding the impact of rheumatoid arthritis on hearing is cochlear damage. Rheumatoid arthritis, being an autoimmune disorder, is characterized by the malfunctioning of the host's adaptive immune system, leading to the production of various auto-antibodies (Li et al., 2016; Zhu & Feng, 2013). These autoantibodies can directly harm cochlear hair cells through reactions with antigens or cytotoxic effects. Additionally, in the context of rheumatoid vasculitis - a well-documented complication of rheumatoid arthritis - immune complexes may accumulate in the labyrinthine artery. This vasculitis tends to occur more frequently in seropositive patients with longstanding and severe disease, affecting blood vessels throughout the body (Makol et al., 2014; Voskuyl et al., 1996).

The cochlea, a vital component of the inner ear responsible for converting sound vibrations into electrical signals that the brain can interpret, possesses a unique vulnerability compared to many other organs in the human body. Unlike organs with robust collateral circulation, which can compensate for minor disruptions in blood supply, the cochlea relies on a relatively limited vascular network, rendering it highly susceptible to ischemic damage even from minor interruptions in blood flow.

When the blood supply to the cochlea is compromised, even temporarily, the consequences can be severe. One of the primary effects is damage to the delicate hair cells that line the cochlear duct. These hair cells play a crucial role in detecting sound vibrations and transmitting auditory signals to the brain. Disruption of blood flow can lead to the death or dysfunction of these hair cells, resulting in hearing impairment or loss.

Furthermore, the stria vascularis, a specialized region of the cochlear duct responsible for maintaining the unique ionic composition of the fluid within the inner ear, is particularly vulnerable to ischemic injury. Decreased blood flow can lead to atrophy of the stria vascularis, compromising its ability to regulate the fluid environment essential for proper auditory function.

Additionally, insufficient blood supply to the cochlea can result in degeneration of the spiral ganglion, a cluster of nerve cells located within the cochlea that transmit auditory information from the hair cells to the brain. Damage to the spiral ganglion can disrupt the transmission of auditory signals, further contributing to hearing loss.

The cochlea's reliance on a limited vascular supply renders it susceptible to damage from

even minor disruptions in blood flow. Ischemic injury can lead to a cascade of detrimental effects, including damage to hair cells, atrophy of the stria vascularis, and degeneration of the spiral ganglion, ultimately resulting in hearing impairment or loss. Understanding the vulnerability of the cochlea to ischemic damage is crucial for developing interventions aimed at preserving auditory function and mitigating the impact of hearing disorders.

The origin of sensorineural hearing loss in rheumatoid arthritis patients appears to involve the cochlea, as suggested by Murthy & Kumar (2012), who observed significantly higher rates of abnormal distortion product otoacoustic emissions in rheumatoid arthritis patients compared to healthy controls.

Sudden onset sensorineural hearing loss or 'idiopathic sudden sensorineural hearing loss' refers to rapid, unexplained hearing loss of more than 30dB across all pure tone frequencies. Hearing loss, tinnitus, ear blockage, dizziness, nausea and/or vomiting are the main clinical symptoms of sudden onset sensorineural hearing loss (Li et al., 2018). Therefore, the concept of autoimmune or, more precisely, immune-mediated inner ear disease has been introduced. This condition is believed to arise from antibodies or immune cells targeting the inner ear, manifesting either as a localized primary ailment or in conjunction with a systemic autoimmune condition (Atturo et al., 2017). Patients with progressive and/or sudden sensorineural hearing loss have been described to present with elevated levels of sera immune complexes and anti-inner ear antibodies.

McCabe (1979) was the first to describe the link between hearing loss and autoimmune disease. Since this initial report, multiple

studies have shown that the inner ear is a susceptible target of an autoimmune response, and that a complication of various autoimmune diseases including rheumatoid arthritis, psoriatic arthritis, systemic lupus erythematosus, and Behcet's disease is sensorineural hearing loss (Jeong et al., 2016). The association between rheumatoid arthritis and hearing loss has been widely reported. The aim of this study was to better understand the association between rheumatoid arthritis and sudden-onset sensorineural hearing loss.

METHOD

Aim of the study

The primary aim of this study was to better understand the association between rheumatoid arthritis and sudden-onset sensorineural hearing loss. Within the medical field, the issue of hearing impairment among individuals with afflicted with rheumatoid arthritis continues to be a subject of significant debate and uncertainty, marked by questions regarding its aetiology and extent.

Inclusion criteria

In accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) protocols guidelines this systematic review was conducted (Page et al., 2021). A search of Cochrane Central and Pubmed databases was conducted to find primary research papers published in English until 31/01/2024. No lower time limit was set for this search. This search was conducted by one independent investigator (KB), using the following keywords in all possible combinations: sensorineural, sudden-onset, hearing impairment, hearing loss, deafness,

rheumatoid arthritis, rheumatic, rheumatoid. In order to be deemed eligible for this review each study had to fulfil the following criteria: published in English until 31/01/2024, investigated association between rheumatoid arthritis and sensorineural and sudden-onset hearing loss, reported quantitative data on outcomes of interest, included a group of patients with rheumatoid arthritis and a group without.

Exclusion criteria

Exclusion criteria included the following: data from sources other than full original publications (abstracts, reviews and oral presentations), articles not published in English, animal studies and studies not reporting results on the outcomes of interest.

Procedure

A total of 67 studies were identified through the initial database search. After removing 25 duplicates, 53 unique studies remained. These studies underwent title and abstract screening, where 20 studies were excluded based on predefined inclusion and exclusion criteria. This left 33 studies for full-text assessment.

During the full-text review, an additional 11 studies were excluded for the following reasons: did not meet inclusion criteria, insufficient data, inappropriate study design'. Consequently, 22 studies met all the inclusion criteria and were included in the final analysis. A manual review was conducted of all previously identified studies' reference lists for additional relevant publications. In the occurrence of overlapping studies, the most recent were included, except when the earlier version reported more relevant outcomes.

RESULTS

Many studies have shown an increased prevalence of hearing loss, specifically the sensorineural type, in rheumatoid arthritis patients. When Öztürk et al. (2004) and Dikici et al. (2009) evaluated patients according to disease duration, they found that hearing impairment increased with disease duration. In a study conducted by Heyworth & Liyanage (1972), it was observed that sensorineural hearing loss was present in 36.4% of cases contrastingly, Reiter et al., (1986) observed a higher prevalence of sensorineural hearing loss in 48% of cases. More recently Raut et al. (2001) reported sensorineural hearing loss in 60% of the cases observed, Magaro et al. (1990) reported a prevalence of 55% sensorineural hearing loss, whereas Elwany et al. (1986) reported only a 29.4% prevalence of sensorineural hearing loss in the observed cases.

Yildirim et al. (2016) found that with pure tone audiometric testing patients with rheumatoid arthritis had thresholds significantly higher at 2000 Hz and 4000 Hz compared to the control group for both ears, the bone conduction thresholds at 1000Hz were also significantly higher in the rheumatoid arthritis group than the control. There was found to be no significance in the air bone gap.

In a study conducted by Takatsu et al. (2005) sensorineural hearing loss was observed in 36.1% of the patients with rheumatoid arthritis, and in the control group 13.9% of participants presented with sensorineural hearing loss. They found that three quarters of rheumatoid arthritis patients with sensorineural hearing loss had bilateral, mild, symmetric hearing loss. Additionally,

their results showed that patients present with cochlear-type sensorineural hearing loss affecting mid to high frequencies, namely: 1000 Hz, 2000 Hz, and 4000 Hz. These results support previous studies that report sensorineural hearing loss ranging from 24% to 60% in patients with rheumatoid arthritis.

In a prospective case-control study performed by Raut et al. (2001), to determine the association between rheumatoid arthritis and hearing loss, a significant hearing impairment at 500Hz, 1000 Hz, and 2000 Hz was seen in participants with rheumatoid arthritis. Ozcan et al. (2002), also reported in a case-control study that the presence of hearing loss in rheumatoid arthritis patients was significantly higher.

In a cohort study conducted by Pascual-Ramos et al. (2012), 80 patients with rheumatoid arthritis and without hearing loss were evaluated. Within 1 year 12.5% of the subjects developed hearing loss, 90% of which was sensorineural and 10% was conductive. Normal type A curves were seen in 89% of rheumatoid arthritis patients, As and B curves 2% each, and type C curves 5% in a study by Rahne et al. (2017). In a previous study with 117 rheumatoid arthritis patients Galarza-Delgado et al. (2018) found a prevalence of 94.9% sensorineural hearing loss in the extended high frequencies, 68.4% in high frequencies, and 36.8% in mid frequencies. A study conducted by Arslan et al. (2011) hearing loss presented at a rate 27.3% in rheumatoid arthritis patients. No significant correlation between sensorineural hearing loss, age, sex, duration and stage of disease, acoustic reflexes, and the anti-rheumatic drugs could be seen.

DISCUSSION

The primary objective of this review was to delve into the intricate relationship between rheumatoid arthritis and sudden-onset sensorineural hearing loss. Within the realm of medical discourse, the issue of hearing impairment among individuals afflicted with rheumatoid arthritis continues to be a subject of significant debate and uncertainty, marked by questions regarding its aetiology and extent. This state of ambiguity arises from a lack of complete understanding surrounding the pathophysiological mechanisms that contribute to hearing loss in the context of rheumatoid arthritis.

In the discourse surrounding the relationship between rheumatoid arthritis and hearing loss, certain authors emphasize the sensorineural aspect of the impairment, highlighting the involvement of the inner ear structures and auditory nerve. Conversely, alternative viewpoints suggest that the middle ear, including components such as the ossicles and tympanic membrane, serves as the principal site affected by rheumatoid arthritis related pathology. The sensorineural damage observed in individuals with rheumatoid arthritis can be attributed to various factors, including neuritis, inflammation of the nerve tissue, which may occur as a consequence of the autoimmune processes characteristic of rheumatoid arthritis. Additionally, vasculitis, the inflammation of blood vessels, can lead to compromised blood flow to the inner ear structures, exacerbating sensorineural hearing loss (Öztürk et al., 2004).

The administration of ototoxic medications, prescribed to manage the symptoms and progression of rheumatoid arthritis, can contribute to sensorineural hearing

impairment. These medications, while efficacious in treating rheumatoid arthritis, may inadvertently damage the delicate structures of the inner ear, thereby compromising auditory function. Overall, the multifaceted nature of rheumatoid arthritis related sensorineural hearing loss underscores the complex interplay of autoimmune processes, vascular pathology, and medication-induced ototoxicity in its pathogenesis.

As rheumatoid arthritis advances and reaches its later stages, the manifestation of sensorineural hearing loss becomes increasingly evident, reflecting a complex interplay of various contributing factors. Among these, a notable mechanism involves the progressive impact of rheumatoid arthritis on the labyrinth, a delicate and intricately structured component nestled within the inner ear, responsible for both auditory perception and maintaining equilibrium. Chronic inflammation and autoimmune processes characteristic of rheumatoid arthritis can lead to degenerative changes within the labyrinth, resulting in compromised auditory function (Ferrara et al., 1988; Magaro et al., 1990).

The labyrinth comprises the cochlea, responsible for hearing, and the vestibular system, responsible for balance. In individuals with rheumatoid arthritis, chronic inflammation and autoimmune processes can infiltrate the labyrinth, leading to structural changes and functional impairments. This infiltration can result in damage to the delicate sensory hair cells within the cochlea, which are essential for detecting sound vibrations and transmitting auditory signals to the brain. Additionally, inflammation within the vestibular system can disrupt the intricate mechanisms

responsible for maintaining balance, potentially leading to symptoms such as dizziness and vertigo.

As rheumatoid arthritis progresses, the cumulative effects of inflammation and tissue damage can compromise the blood supply to the labyrinth, further exacerbating its vulnerability. Decreased blood flow deprives the labyrinth of essential nutrients and oxygen, leading to cellular dysfunction and, ultimately, sensorineural hearing loss.

Moreover, the labyrinth's susceptibility to rheumatoid arthritis related pathology is compounded by the presence of autoimmune reactions targeting specific structures within the inner ear. Autoimmune processes can lead to the production of antibodies that attack healthy tissue, contributing to the destruction of the labyrinth and exacerbating sensory deficits.

Overall, the progression of rheumatoid arthritis into its later stages precipitates a cascade of pathological changes within the labyrinth, culminating in sensorineural hearing loss. Understanding the multifaceted mechanisms underlying this phenomenon is crucial for developing targeted interventions aimed at preserving auditory function and improving the quality of life for individuals living with rheumatoid arthritis.

As rheumatoid arthritis advances, there is often a reduction in the compliance of the ossicular chain, a series of tiny bones within the middle ear responsible for transmitting sound vibrations from the eardrum to the inner ear. The decreased flexibility and mobility of these ossicles can impede the efficient transmission of sound waves, contributing to sensorineural hearing loss. Organic damage may occur within the stapedo-ovalar joint, a crucial junction

within the middle ear involved in sound transmission. Inflammatory mediators released during the course of rheumatoid arthritis can target and damage the tissues surrounding this joint, leading to structural alterations that disrupt the normal functioning of the auditory system.

The culmination of these processes underscores the complex interplay between inflammatory cascades, structural changes, and functional impairment in the development of sensorineural hearing loss in later stages of rheumatoid arthritis. Understanding these intricate mechanisms is crucial for devising effective management strategies aimed at mitigating the impact of hearing impairment in individuals with advanced rheumatoid arthritis.

There are two true diarthrodial joints in the middle ear - the incudo-malleolar and incudo-stapedial joints. The first between the malleus' head and the incus, and the second between the long process of the incus and the head of the stapes. These may be subject to inflammation leading to decreased compliance of the ossicular system leading to hearing loss (Pascual-Ramos et al., 2012). Inflammatory involvement similar to the one observed in other appendicular joints of patients with rheumatoid have been seen in the incudo-malleolar and incudo-stapedial joints (Salvinelli et al., 2004).

The majority of studies report that the origin in hearing loss in rheumatoid arthritis patients is cochlear in its origin, due to the influence of vasculitis, neuritis and ototoxic medication used to treat rheumatoid arthritis on the inner ear structures (Arslan et al., 2011). According to Öztürk et al. (2004), extra-articular manifestations of rheumatoid arthritis, such as vasculitis and neuritis, may theoretically affect the cochlea

and the cochlear nerve thus resulting in a sensorineural hearing loss.

Despite several theories regarding hearing loss in rheumatoid arthritis being proposed, the pathological cause of ear involvement is not fully understood. Inflammatory arthritis of the incudo-stapedial and incudo-malleolar joints leading to conductive hearing loss, auditory neuropathy induced by vasculitis, inflammation of the vestibulocochlear nerve, inflammatory destruction of the cochlear hair cells or inner ear with immune complex deposition due to autoimmune processes, and the effects of medications used to treat rheumatoid arthritis (non-steroidal anti-inflammatory drugs, salicylates), and disease modifying anti-rheumatic drugs, are theories regarding the pathophysiology of hearing loss linked with rheumatoid arthritis (Yildirim et al., 2016). Medications such as non-steroidal anti-inflammatory drugs, and glucocorticoids that are used for the control and treatment of autoimmune diseases have known ototoxic effects (Galarza-Delgado et al., 2018). Over the past decades since McCabe first treated sudden onset sensorineural hearing loss with glucocorticoids, and achieved significant symptom improvement they have remained the go-to treatment. Due to the systemic side effects of extended glucocorticoid treatments, other therapeutic methods have also been investigated (Li et al., 2018).

Conventionally, the inner ear and brain are viewed as being immune privileged due to the blood-labyrinthine barriers that acts in a similar way as the blood-brain barrier, very few macrophages are present in these organs (Juhn et al., 1981). Since McCabe first identified patients with auto-immune associated sudden-onset sensorineural

hearing loss, and treated them successfully with glucocorticoids and vincristine, increasing evidence suggesting an autoimmune component in the pathology of sudden-onset sensorineural hearing loss has emerged. The immune system plays a vital role in guarding the inner ear against harm caused by bacteria, viruses, and other pathogenic micro-organisms. In the pathogenesis of autoimmune hearing loss, contrastingly however, the immune system itself damages the inner ear.

Studies in patients with sudden-onset sensorineural hearing loss and in experimental animal models have identified several factors that are involved in the autoimmune mechanism of its pathogenesis (Li et al., 2018). The immune response in the inner ear relies on cytokines, that play important roles in regulating the immune response of the inner ear. Some inflammatory cells in the inner ear are also involved, including macrophages, T lymphocytes, and leukocytes (Li et al., 2018). Due to the degenerative changes in the organ of Corti, autoimmune diseases can result in perceptive hearing loss (Öztürk et al., 2004).

Further research is needed in this area, and we hope to encourage new research teams to follow up on these groups of patients to identify potential audiological complications associated with autoimmune diseases.

CONCLUSION

The present study enhances our comprehension of the existing research concerning the impact of rheumatoid arthritis on the auditory system. A significant link between rheumatoid arthritis and sensorineural hearing loss was observed. It

should be considered that hearing loss is an important symptom in patients with autoimmune diseases. This study provides compelling evidence underscoring the importance for healthcare professionals to acknowledge the correlation between rheumatoid arthritis and sensorineural hearing loss. Recognizing this association is paramount, as hearing impairment can have far-reaching consequences, potentially exacerbating cognitive decline and significantly affecting the quality of life for individuals with rheumatoid arthritis. Given these implications, it is imperative that clinicians adopt a proactive approach by incorporating early screening measures into the standard care protocol for rheumatoid arthritis patients.

Upon diagnosis of rheumatoid arthritis, clinicians should contemplate initiating routine pure tone audiometry assessments as part of the comprehensive evaluation process. This proactive screening strategy allows for the timely identification of any changes in auditory function, facilitating early intervention and appropriate management of hearing-related issues. Furthermore, the inclusion of extended high-frequency audiometry in the diagnostic protocol can offer additional benefits by enhancing the sensitivity of detection for subtle changes in hearing thresholds.

By implementing these screening measures early in the management of rheumatoid arthritis, healthcare providers can optimize patient care and potentially mitigate the adverse effects of hearing loss on cognitive function and overall well-being. This proactive approach aligns with the principles of patient-centred care, ensuring that individuals with RA receive comprehensive support tailored to their unique needs,

thereby promoting better health outcomes and improving their overall quality of life.

Additionally, the utilization of extended high-frequency audiometry may serve as a valuable tool for achieving earlier detection. Observational studies and literature reviews were used, which were assessed to have a moderate level of bias.

REFERENCES

- Ahmadzadeh, A., Daraei, M., Peyvandi, A. A., Amini, E., Ranibar, L. A., & Daneshi, A. (2017). Hearing status in patients with rheumatoid arthritis. *Journal of Laryngology and Otology*, 131(10), 895-899. <https://doi.org/10.1017/S0022215117001670>
- Almasi, S. Mehrabian, F., Rahbar, N., & Delarestaghi, M. M. (2023). Prevalence rate of hearing loss in patients with rheumatoid arthritis. *Advanced Biomedical Research*, 12, 80
- Arslan, N., Cicek, Y., Islam, A., Ureten, K., Safak, M. A., & Oguz, H. (2011). Involvement of ear in rheumatoid arthritis. Prospective clinical study. *The Journal of International Advanced Otology*, 7(2), 208–2014.
- Ashok Murthy, V., & Mohan Kumar, J. (2012). Rheumatoid factor and hearing loss. *Indian Journal of Otolaryngology and Head & Neck Surgery*, 64(4), 364-365. <https://doi.org/10.1007/s12070-011-0401-9>
- Atturo, F., Colangeli, R., Bandiera, D., Barbara, M., & Monini, S. (2017). Can unilateral, progressive or sudden hearing loss be immune-mediated in origin? *Acta Oto-laryngologica*, 137(8), 823-828. <https://doi.org/10.1080/00016489.2017.1286035>
- Chaitidis, N., Theocharis, P., Festas, C., & Aritzi, I. (2020). Association of rheumatoid arthritis with hearing loss: a systemic review and meta-analysis. In *Rheumatology International* (Vol. 40, Issue 11, pp 1771-1779). Springer Science and Business Media Deutschland GmbH. <https://doi.org/10.1007/s00296-020-04609-1>
- Copeman, W. S. (1963). Rheumatoid otitis arthritis. *British Medical Journal*, 2, 1526–1527.
- Dikici, O., Muluk, N. B., Tosun, A. K., & Ünlüsoy, I. (2009). Subjective audiological tests and transient evoked otoacoustic emissions in patients with rheumatoid arthritis: Analysis of the factors affecting hearing levels. *European Archives of Oto-Rhino-Laryngology*, 266(11), 1719–1726. <https://doi.org/10.1007/s00405-009-0975-y>
- Elwany, S., El-Garf, A., & Kamel, T. (1986). Hearing and middle ear function in rheumatoid arthritis. *Journal of Rheumatology*, 13, 878–881.
- Ferrara, P., Modica, A., & Adelfio, M. (1988). Audiovestibular changes in patients with rheumatoid arthritis. *Minerva Medica*, 79, 1043–1047.
- Galarza-Delgado, D. A., Villegas Gonzalez, M. J., Riega Torres, J., Soto-Galindo,

- G. A., Mendoza Flores, L., & Treviño González, J. L. (2018). Early hearing loss detection in rheumatoid arthritis and primary Sjögren syndrome using extended high frequency audiometry. *Clinical Rheumatology*, 37(2), 367–373. <https://doi.org/10.1007/s10067-017-3959-0>
- Heyworth, T., & Liyanage, S. P. (1972). A pilot survey of hearing loss in patient with rheumatoid arthritis. *Scandinavian Journal of Rheumatology*, 1, 81–83.
- Jeong, H., Chang, Y. S., Baek, S. Y., Kim, S. W., Eun, Y. H., Kim, I. Y., Lee, J., Koh, E. M., & Cha, H. S. (2016). Evaluation of audiometric test results to determine hearing impairment in patients with rheumatoid arthritis: Analysis of data from the Korean national health and nutrition examination survey. *PLoS ONE*, 11(10). <https://doi.org/10.1371/journal.pone.0164591>
- Juhn, S. K., Rybak, L. P., & Prado, S. (1981). Nature of blood-labyrinth barrier in experimental conditions. *Annals of Otolaryngology, Rhinology, and Laryngology*, 90(2), 135–141.
- Li, G., You, D., Ma, J., Li, W., Li, H., & Sun, S. (2018). The role of autoimmunity in the pathogenesis of sudden sensorineural hearing loss. *Neural Plasticity*, 2018. <https://doi.org/10.1155/2018/7691473>
- Li, L., Deng, C., Chen, S., Zhang, S., Wu, Z., Hu, C., Zhang, F., & Li, Y. (2016). Meta-Analysis: Diagnostic Accuracy of Anti-Carbamylated Protein Antibody for Rheumatoid Arthritis. *PLOS ONE*, 11(7), e0159000. <https://doi.org/10.1371/journal.pone.0159000>
- Magaro, M., Altomonte, L., & et al. (1990). Sensorineural hearing loss in rheumatoid arthritis. *Clinical and Experimental Rheumatology*, 8(13), 487–490.
- Makol, A., Crowson, C. S., Wetter, D. A., Sokumbi, O., Matteson, E. L., & Warrington, K. J. (2014). Vasculitis associated with rheumatoid arthritis: a case-control study. *Rheumatology*, 53(5), 890–899. <https://doi.org/10.1093/rheumatology/ket475>
- McCabe, B. (1979). Autoimmune sensorineural hearing loss. *Annals of Otolaryngology, Rhinology, Laryngology*, 88, 585–589.
- McInnes, I. B., & Schett, G. (2011). The Pathogenesis of Rheumatoid Arthritis. *The New England Journal of Medicine*, 365(23), 2205–2219.
- Ozcan, M., Karaku, M. F., & Gunduz, O. H. (2002). Hearing loss and middle ear involvement in rheumatoid arthritis. *Rheumatology International*, 1, 16–19.
- Öztürk, A., Yalçın, Ş., Kaygusuz, I., Şahin, S., Gök, Ü., Karlidağ, T., & Ardiçoğlu, Ö. (2004). High-frequency hearing loss and middle ear involvement in rheumatoid arthritis. *American Journal of Otolaryngology - Head and Neck Medicine and Surgery*, 25(6), 411–417.

<https://doi.org/10.1016/j.amjoto.2004.06.001>

- Page, M., McKenzie, J., Bossuyt, P., Boutron, I., Hoffman, T., & Mulrow, C. (2021). The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. In *BMJ* (p. 372). <https://doi.org/10.1136/bmj.n71>
- Pascual-Ramos, V., Contreras-Yáñez, I., Enríquez, L., Valdés, S., & Ramírez-Anguiano, J. (2012). Hearing impairment in a tertiary-care-level population of Mexican rheumatoid arthritis patients. *Journal of Clinical Rheumatology*, 18(8), 393–398. <https://doi.org/10.1097/RHU.0b013e31827732d3>
- Rahne, T., Clauß, F., Plontke, S. K., & Keyßer, G. (2017). Prevalence of hearing impairment in patients with rheumatoid arthritis, granulomatosis with polyangiitis (GPA, Wegener's granulomatosis), or systemic lupus erythematosus. *Clinical Rheumatology*, 36(7), 1501–1510. <https://doi.org/10.1007/s10067-017-3651-4>
- Raut, V. V., Cullen, J., & Cathers, G. (2001). Hearing loss in rheumatoid arthritis. *Journal of Otolaryngology*, 289–294.
- Reiter, D., Konkle, D., & Myers, A. (1986). Middle ear immittance in rheumatoid arthritis. *Archives of Otolaryngology*, 106, 114–117.
- Salvinelli, F., Cancilleri, Æ. F., Casale, M., Luccarelli, Æ. V, Di Peco, Æ. V, D'ascanio, Æ. L., De Martinoy, Æ. A., Denaroy, V., & Casale, M. (2004). Hearing thresholds in patients affected by rheumatoid arthritis. *Clinical Otolaryngology*, 29, 75–79.
- Takatsu, M., Higaki, M., Kinoshita, H., Mizushima, Y., & Koizuka, I. (2005). Ear Involvement in Patients with Rheumatoid Arthritis. *Otology & Neurology*, 26(4), 755–761.
- Voskuyl, A. E., Zwinderman, A. H., Westedt, M. L., Vandenbroucke, J. P., Breedveld, F. C., & Hazes, J. M. (1996). Factors associated with the development of vasculitis in rheumatoid arthritis: results of a case-control study. *Annals of the Rheumatic Diseases*, 55(3), 190–192. <https://doi.org/10.1136/ard.55.3.190>
- Yildirim, A., Surucu, G., Dogan, S., & Karabiber, M. (2016). Relationship between disease activity and hearing impairment in patients with rheumatoid arthritis compared with controls. *Clinical Rheumatology*, 35(2), 309–314. <https://doi.org/10.1007/s10067-015-3129-1>
- Zhu, T., & Feng, L. (2013). Comparison of anti-mutated citrullinated vimentin, anti-cyclic citrullinated peptides, anti-glucose-6-phosphate isomerase and anti-keratin antibodies and rheumatoid factor in the diagnosis of rheumatoid arthritis in Chinese patients. *International Journal of Rheumatic Diseases*, 16(2), 157–161. <https://doi.org/10.1111/1756-185X.12040>