The Burden of Otolaryngologic Symptoms in Patients with Autoimmune Diseases

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Abstract

Introduction
Otolaryngologic (ORL) manifestations are not often considered in the diagnosis and management of autoimmune diseases (AIMD). This study aimed to quantify the prevalence of common ORL manifestations in AIMD patients to improve treatment strategies and approaches.

Methods
Using the NIH's All of Us database, this retrospective cohort study analyzed U.S. adults diagnosed with AIMD between 1981 and 2022. Patients were stratified by AIMD status and condition to evaluate ORL manifestation rates. Outcomes of interest included hearing loss, dysphagia, tinnitus, vertigo, and mouth ulcers, analyzed via logistic regression with demographic controls, including self-reported race, gender, ethnicity, and socioeconomic status.

Results
The cohort included patients with multiple sclerosis (MS) (n = 2502), rheumatoid arthritis (n = 7485), type 1 diabetes (T1D) (n = 5987), systemic lupus erythematosus (n = 3519), Sjogren's syndrome (n = 3697), and patients without AIMD (non-AIMD) (n = 299,221). Investigated manifestations were hearing loss (n = 24,799), dysphagia (n = 23,110), tinnitus (n = 16,682), vertigo (n = 10,237), and mouth ulcers (n = 3796). Significant associations were found between AIMD presence and hearing loss (OR 1.68 [1.60–1.77], p < 0.0001), mouth ulcers (1.95 [1.78–2.13], p < 0.0001), tinnitus (1.34 [1.27–1.42], p < 0.0001), vertigo (1.47 [1.38–1.56], p < 0.0001), and dysphagia (2.92 [2.80–3.03], p < 0.0001). Non-AIMD patients had significantly lower odds of these outcomes. These associations persisted within strata with individual disease types, with the exceptions of mouth ulcers in MS and tinnitus in T1D.

Conclusion
This study suggests that all investigated AIMDs exhibit ORL manifestations, with most conditions associated with all five. Further research is needed to explore additional manifestations and their mechanisms to improve the ORL and overall health of AIMD patients.

Introduction

Autoimmune diseases (AIMD) are a diverse group of chronic conditions characterized by abnormal immune responses that target the body's own tissues (Liu et al., 2012; Medscape, 2022). These diseases affect millions of individuals in the United States and represent a leading cause of morbidity because of their broad effects on multiple organ systems (Liu et al., 2012; Medscape, 2022). Over recent decades, the prevalence of AIMD has increased, now impacting about 4.6% of the US population and an estimated 7–10% globally (Medscape, 2022; Liu et al., 2012).

Although many AIMD are managed within rheumatologic, neurologic, or endocrine specialties, their otolaryngologic manifestations—such as hearing loss, dysphagia, tinnitus, vertigo, and mouth ulcers—are often overlooked in both diagnosis and care (Exploration Journal, 2024; Liu et al., 2012). Sensorineural hearing loss is particularly prevalent and may serve as an early indicator or complicate the disease course (Medscape, 2022.).

Large cohort studies and systematic reviews confirm a strong association between AIMD and otolaryngologic symptoms, with affected patients showing higher rates of hearing loss, mouth ulcers, tinnitus, vertigo, and dysphagia compared to healthy controls (Liu et al., 2012; Exploration Journal, 2024). This association persists across major conditions affecting multiple organ systems. Recognizing these symptoms is crucial for early detection and improved patient outcomes, preventing irreversible damage and enabling integrated, multidisciplinary care (Liu et al., 2012; Sage Journals, 2024).

Methods

This retrospective cohort study was performed on the National Institutes of Health's (NIH) *All of Us* database. This study used data from the *All of Us* Research Programs Controlled Tier Dataset, version 7, available to authorized users on the Research Workbench.
Patients diagnosed with AIMDs between 1981 and 2022 were identified, and stratified by their AIMD and a concurrent diagnosis of an ORL symptom. Studied AIMDs were multiple sclerosis, systemic lupus erythematosus, Sjogren's syndrome, rheumatoid arthritis, and type 1 diabetes. ORL symptoms studied were hearing loss, mouth ulcers, tinnitus, vertigo and dysphagia.
Odds ratios were calculated controlling for self-reported race, gender, ethnicity, and socioeconomic status, as well as the diagnosis of a concomitant AIMD or ORL symptom. Odds ratios were adjusted using multivariate logistic regression to give odds ratios of the presence of an ORL symptom in a given AIMD population.

Conclusion

This work indicates significantly higher odds of being diagnosed with common ORL symptoms, hearing loss, mouth ulcers, tinnitus, vertigo and dysphagia, in the populations of autoimmune disease patients when compared to the population without.
These trends persisted in nearly all stratifications of ORL symptom and autoimmune disease further accentuating the strength of this association between AIMDs and the studied ORL symptoms.
However, this study has limitations mainly attributable to the limitations of a database for patient information extraction. The odds ratios were adjusted using common social and structural determinants of health as well as concomitant AIMDs and ORL symptoms to attempt to isolate a connection between the presence of a singular AIMD and having an ORL symptom present, but more detailed patient information, such as family history of ORL symptoms would have further increased the robustness of the statistical analysis. While these factors were present, their representation was not complete across patients.
Next steps for our analysis would exploring the relationship between time of diagnosis of ORL symptom versus AIMD to understand the timelines of these symptoms so that physicians may address the development of these symptoms at the appropriately. Understanding how autoimmune diseases can affect the otolaryngological health of a patient is crucial for the comprehensive care of patients living with autoimmune diseases. Increased awareness of common symptoms to look out for during routine ORL health maintenance can ensure that these symptoms are noticed early and treated to reduce the ORL morbidity experienced by patients with AIMDs.

Results

A diverse sample of 20086 patients with AIMD was obtained from the *All of Us* database. Patients were stratified by the presence of one of the studied otolaryngological manifestations. Overall, within this patient cohort, when compared with non-AIMD patients the odds ratio of having hearing loss, mouth ulcers, tinnitus, vertigo and dysphagia were all significantly higher with the exception of mouth ulcers in multiple sclerosis and tinnitus in type 1 diabetes. (Table 1).
Dysphagia was the most common ORL manifestation followed by hearing loss in all AIMD cohorts Mouth ulcers and vertigo were the least common ORL manifestations across all AIMD cohorts.
Sjogren's Syndrome and Rheumatoid Arthritis had the highest overall rate of ORL manifestation while Multiple Sclerosis had the lowest rate of ORL manifestations across all studied AIMD cohorts. (Table 2)

Table 1: Odds Ratio of Having a Diagnosed Otolaryngological Manifestation Given Autoimmune Disease Diagnosis

Autoimmune Disease	Odds Ratio of the Presence of Otolaryngological Manifestation Compared with Non-Disease Controls [95% Confidence Interval] (p-value)				
	Hearing Loss	Mouth Ulcers	Tinnitus	Vertigo	Dysphagia
Multiple Sclerosis	1.33 [1.15 - 1.54] ** (p = 0.0001)	1.17 [0.89 - 1.52] (p = 0.243)	1.27 [1.08 - 1.49] ** (p = 0.003)	1.29 [1.09 - 1.53] ** (p = 0.003)	2.73 [2.45 - 3.02] *** (p < 0.0001)
Systemic Lupus Erythematosus	1.38 [1.22 - 1.56] *** (p < 0.0001)	2.77 [2.35 - 3.25] *** (p < 0.0001)	1.48 [1.3 - 1.68] *** (p < 0.0001)	1.30 [1.13 - 1.49] ** (p = 0.0002)	3.56 [3.27 - 3.87] *** (p < 0.0001)
Sjogren's Syndrome	1.44 [1.3 - 1.59] *** (p < 0.0001)	2.33 [1.99 - 2.72] *** (p < 0.0001)	1.63 [1.46 - 1.82] *** (p < 0.0001)	1.46 [1.3 - 1.64] *** (p < 0.0001)	3.29 [3.04 - 3.56] *** (p < 0.0001)
Rheumatoid Arthritis	1.54 [1.43 - 1.66] *** (p < 0.0001)	2.14 [1.88 - 2.42] *** (p < 0.0001)	1.37 [1.26 - 1.49] *** (p < 0.0001)	1.32 [1.21 - 1.45] *** (p < 0.0001)	2.72 [2.56 - 2.88] *** (p < 0.0001)
Type 1 Diabetes	2.22 [2.04 - 2.41] *** (p < 0.0001)	1.31 [1.09 - 1.55] ** (p = 0.0024)	1.07 [0.97 - 1.18] (p = 0.171)	1.58 [1.43 - 1.75] *** (p < 0.0001)	2.53 [2.36 - 2.71] *** (p < 0.0001)
All Studied Autoimmune Diseases	1.68 [1.60 - 1.77] *** (p < 0.0001)	1.95 [1.78 - 2.13] *** (p < 0.0001)	1.34 [1.27 - 1.42] *** (p < 0.0001)	1.47 [1.38 - 1.56] *** (p < 0.0001)	2.92 [2.80 - 3.03] *** (p < 0.0001)

* p < 0.05, ** p < 0.01, *** p < 0.0001

Table 2: Rates of Otolaryngological Manifestations with Autoimmune Disease Cohorts

Autoimmune Disease	ORL Manifestation (% of total AIMD patient population)					
	Hearing Loss (n = 24799)	Mouth Ulcers (n = 3796)	Tinnitus (n = 16682)	Vertigo (n = 10237)	Dysphagia (n = 23110)	One or more ORL manifestation
Multiple Sclerosis (n = 2502)	319 (12.7%)	58 (2.3%)	241 (9.6%)	156 (6.2%)	504 (20.1%)	838 (33.5%)
Systemic Lupus Erythematosus (n = 3519)	482 (13.7%)	181 (5.1%)	390 (11.1%)	254 (7.2%)	900 (25.6%)	1439 (40.9%)
Sjogren's Syndrome (n = 3697)	783 (21.2%)	191 (5.2%)	588 (15.9%)	388 (10.5%)	1048 (28.3%)	1778 (48.1%)
Rheumatoid Arthritis (n = 7485)	1421 (19.0%)	308 (4.1%)	977 (13.1%)	644 (8.6%)	1802 (24.1%)	3221 (43.0%)
Type 1 Diabetes (n = 5987)	1236 (20.6%)	146 (2.4%)	713 (11.9%)	508 (8.5%)	1257 (21.0%)	2432 (40.6%)
All studied patients (n = 20086)	3547 (17.7%)	674 (3.4%)	2394 (11.9%)	1606 (8.0%)	4401 (21.9%)	8019 (39.9%)

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References

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