

# Hearing Loss in Acromegaly - A Review

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## Abstract

### Keywords

- ▶ deafness
- ▶ acromegaly
- ▶ hearing loss

**Introduction** Acromegaly is a chronic disease caused by growth hormone (GH) excess due to a GH-secreting pituitary adenoma in most cases. There is reasonable data to presume the possible influence of chronic GH and insulin-like growth factor I (IGF-I) hyperproduction on the anatomical structures involved in normal sound perception, and on its conductive and/or sensorineural part.

**Objectives** To review the literature about acromegaly and hearing loss.

**Data Synthesis** A systematic literature search was performed using the MEDLINE database, including hand-searching reference lists from original articles. The search was performed using the terms *hearing loss* and *acromegaly*, and only 5 studies were found.

**Conclusion** The results are not consistent, but led to different conclusions. Therefore, more studies with greater numbers of patients with acromegaly are needed.

## Introduction

Acromegaly is a chronic disease caused by growth hormone (GH) excess due to a GH-secreting pituitary adenoma in most cases.<sup>1</sup> It is associated with an increase in mortality and morbidity, especially due to cardiovascular complications.<sup>2</sup> Among other consequences, it is characterized by the overgrowth of bone, including the **skull** and soft tissues.

Although usually presenting an indolent, slow evolution, diagnosed 5 years after the first signs of acromegaly, cardiovascular and metabolic comorbidities are accompanied with an increased mortality in untreated patients. Without an appropriate therapy, the life of patients with acromegaly can be shortened by ten years. Before the current therapies became available, the standard mortality rate for these patients was reported to be of **2–3 years**. However, in some studies there are meta-analyses reporting mortality rates similar to those of the general population in patients with normal GH after successful therapy, and even normal insulin-like growth factor 1 (IGF-1).

Using sensitive assays, the cut-off level for “safe” GH is still a matter of debate, but a recent consensus suggested it could be of 1 ng/mL.<sup>3,4</sup>

Pituitary adenomas are common benign monoclonal neoplasms accounting for ~ 15% of intracranial neoplasms. Some pituitary adenomas (mainly microadenomas that have a diameter of less than 1 cm) are exceedingly common, and are incidentally diagnosed on magnetic resonance imaging (MRI) performed for an unrelated reason (headache, vertigo, head trauma). Most microadenomas remain clinically occult and stable in size, without an increase in tumor cells, and without local mass effects. However, some pituitary adenomas grow slowly, enlarged by expansion, and become demarcated on the normal pituitary gland (macroadenomas have a diameter greater than 1 cm). They may be clinically silent or secrete anterior pituitary hormones in excess, such as prolactin, GH, or adrenocorticotrophic hormone (ACTH), causing diseases like prolactinoma, acromegaly, Cushing’s disease, or rarely, diseases

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involving the thyroid-stimulating hormone (TSH) or gonadotropins (luteinizing hormone [LH], follicle-stimulating hormone [FSH]).<sup>5</sup>

There is reasonable data to presume the possible influence of chronic GH and IGF-1 hyperproduction on the anatomical structures involved in normal sound perception, and on its conductive and/or sensorineural part.<sup>3</sup> Additionally, there is a possibility of inferior pituitary tumor invasion of the epipharynx with impact on the Eustachian tubes. Although it received some attention in the past, this problem has not been investigated frequently.

Deafness, in all of its forms, affects 1 in every 1,000 newborns in the United States, and progressively afflicts larger numbers of individuals with advancing age. Some studies have described that by the age of 60, 1 out of every 3 individuals in the United States experiences communication difficulties as a consequence of **hearing loss**, and by 85 years of age, half of the population has some degree of hearing disability. Significantly, most peripheral auditory diseases involve some form of cochlear abnormality that disrupts sensory transduction. The variety of conditions that produce such disabilities include genetic abnormalities, trauma (acoustic and mechanical), ototoxic agents, bacterial and viral infections, and disturbances in other organ systems that influence cochlear physiology indirectly.<sup>4,5</sup>

Acromegaly-related soft tissue expansion and bone hypertrophy are thought to cause ear problems; however, such an association has yet to be confirmed. Graham and Brackmann observed hypertrophy of the mastoid cortical bone and posterior bony wall in three patients with acromegaly during middle ear surgery.<sup>6</sup>

Little is known about hearing loss in patients with acromegaly. As it is a scarcely studied subject, it is important to start investigating it. The best way to do it would be to go over everything on the subject, in order to get ideas about it.

Due to the impact of deafness in society, and to the supposed pathophysiological relationship that can exist between acromegaly and hearing loss, we performed a review of the literature on this subject.

## Review of Literature

The search strategy employed in this literature review was guided by the combination of two descriptors indexed in the Medical Subject Headings (MeSH): *acromegaly* and *hearing loss*. Therefore, we performed a systematic review using the same descriptors in the PubMed library, and analyzed all articles published. The last manual search conducted in electronic databases occurred in **July 2016**.

The entire search process, the selection of articles, and data extraction were conducted in pairs. After the search, the articles were selected based on their titles and abstracts. Subsequently, the texts of all selected articles were obtained in full.

A systematic literature search was performed using MEDLINE database, including hand-searching reference lists from original articles. We identified five studies.

Each study was reviewed by two separate authors (L.S.T and I.B.O), **who independently** screened abstracts and titles using the following inclusion criteria: 1) the articles had to be written in English; and 2) they had to be studies on acromegaly and hearing loss. The exclusion criteria were: 1) articles not written in English; and 2) studies that did not correlate hearing loss with acromegaly.

The relevant data for each article found are listed in ► **Table 1**. The evaluated items included author and origin, number of patients (N), journal, study design, and subject. ► **Table 2** shows the type of hearing loss (conductive, sensorineural or mixed) found in the articles, and the percentage of each one. A complete analysis of the articles was performed,

**Table 1** Characterization of the Studies

Author and origin	N	Journal	Study design	Subject
Doig and Gatehouse <sup>7</sup> USA	56	<i>The Journal of Laryngology &amp; Otology</i> , v. 98, 1984	Transversal	Comparison of the audiometry and clinic examinations of an acromegaly group and a control one
Carvalho et al <sup>8</sup> Brazil	34	<i>Brazilian Journal of Otorhinolaryngology</i> , v. 78, 2012	Cross-sectional	A metabolic evaluation, tonal audiometry and brainstem auditory evoked potential study in acromegalic patients.
Aydin et al <sup>6</sup> Turkey	44	<i>Clinical Endocrinology</i> , v. 76, 2012	Transversal	Pure tone audiometry, speech audiometry, tympanometry, otoacoustic emissions testing, computed tomography of the temporal bone and magnetic resonance imaging of the ear performed in acromegalic and healthy patients.
Graham and Brackmann <sup>9</sup> USA	3	<i>The Journal of Laryngology &amp; Otology</i> , v. 92, 1978	Series of cases	Review of the cases of three patients with acromegaly
Babic et al <sup>10</sup> Serbia	30	<i>Otology &amp; Neurotology</i> , v. 27, 2006	Prospective	A prospective study in a tertiary referral center, because of rare conflicting results reported concerning a possible higher frequency of hearing loss in acromegalic patients.

**Table 2** Hearing loss characterization in acromegalic patients

Author	Type of Hearing Loss	Percentage of Hearing Loss
Doig and Gatehouse <sup>7</sup>	Conductive hearing loss	There is no significant difference between the air-bone gaps in the acromegalic patients and those of the controls
Carvalho et al <sup>8</sup>	Sensorineural hearing loss: 8 bilateral and 4 unilateral.	38.9%
Aydin et al <sup>6</sup>	Conductive, sensorineural and mixed hearing losses in at least one ear	9%; 30%, 18%
Graham and Brackmann <sup>9</sup>	Case 1: findings typical of Meniere's disease Case 2: cholesteatoma with a 40 dB conductive hearing loss Case 3: recurrent episodes of purulent drainage	33%, 33%, 33%
Babic et al <sup>10</sup>	Conductive hearing loss; middle ear ventilation problem	23%

and encountered computed tomography (CT) findings in only two of them, as shown in ► **Table 3**.

## Discussion

**Doig and Gatehouse (1978)**<sup>7</sup> evaluated 56 patients with acromegaly through audiometry and clinical examinations. Those patients were compared with a healthy control group. In this study, there were no significant differences between the case and control groups in terms of the audiometric evaluation.

**Carvalho et al (2012)**<sup>8</sup> conducted the first study in acromegalic patients in which the evaluation was performed with auditory brainstem response besides audiometry. This exam is more objective, and, therefore, allows for a more reliable analysis. In this study, only sensorineural hearing loss (SNHL) was found (35.3%), and it was most prevalent in higher frequencies and bilaterally. The researchers noticed that lower levels of GH and IGF-1 were found in higher prevalence in patients with hearing loss, but there was no significant association between these variables, or between hearing loss and the clinical parameters.

The present study may have been the first to make the comparison model of the brainstem auditory evoked potential among acromegalic patients with and without SNHL.

**Aydin et al (2012)**<sup>6</sup> conducted a study to profile the audiological and structural function in patients with acromegaly. The evaluated group was composed of 44 patients with

acromegaly and 36 healthy patients. All of the patients underwent a CT of the mastoids, an MRI of the inner ear, tonal and vocal audiometries and **impedancemetry**. A clinical research focused on auditory symptoms was also conducted. The patients with acromegaly were divided into 3 groups: those who had controlled the disease, those who had partially controlled it, and those with uncontrolled diseases. From the viewpoint of the structure, the significant finding was the presence of degeneration of the temporomandibular joint. In this study, three types of hearing loss were found: conductive, sensorineural and mixed. The elevated hearing thresholds in the patients with acromegaly were not correlated with disease activity in this study, suggesting that acromegaly – whether or not controlled – caused hearing loss.

This study shows that acromegaly is commonly associated with heterogeneous ear problems.<sup>6</sup>

**Graham and Brackmann (1978)**<sup>9</sup> reviewed 3 patients with acromegaly and clinical characteristics. In all patients, the gross clinical features of acromegaly were present, and considerable difficulty was encountered in clearly demonstrating the radiographic features of the temporal bone due to marked bone hypertrophy. However, the internal auditory canal, the cochlea and the vestibule appeared normal. Prior to the surgical intervention, whether or not the facial nerve would be in the normal position due to excessive bone overgrowth was initially a considerable concern. However, in spite of a massive mastoid cortex bone and generally heavy posterior bony canal wall with secondary lengthening of the

**Table 3** Computed Tomography Findings

Author	Computed tomography findings
Doig and Gatehouse <sup>7</sup>	No CT results
Carvalho et al <sup>8</sup>	No CT results
Aydin et al <sup>6</sup>	Auditory imaging showed that 50% of the patients had temporomandibular joint degeneration. The most common abnormality in the patients with acromegaly was mastoid sclerosis.
Graham and Brackmann <sup>9</sup>	In all three patients, considerable difficulty was encountered in clearly demonstrating the radiographic features of the temporal bone due to marked bone hypertrophy. However, in all patients, the internal auditory canal, the cochlea and the vestibule appeared normal.
Babic et al <sup>10</sup>	No CT results

bony external auditory canal, the structures of the otic capsule, horizontal semicircular canal, oval window, round window, and facial nerve were in perfectly normal relationships. Surgery performed on two patients confirmed these findings. Despite the small number of patients in the study, it was very important to evaluate the temporal bone alterations that may occur in patients with acromegaly.

**Babic et al (2006)**<sup>10</sup> performed a prospective study in a tertiary referral center because of rare conflicting results reported concerning a possible higher frequency of hearing loss in acromegalic patients. The goal was to determine whether there is a higher frequency of conductive hearing loss in acromegalic patients. Thirty previously untreated patients with acromegaly were compared with 20 age- and sex-matched healthy control subjects. The interventions in all subjects included: otomicroscopy, tuning fork tests, audiometry, tympanometry, cochleostapedial reflex, and otoacoustic emissions. In the acromegalic patients, endocrinological assessments, MRIs, and, if necessary, epipharyngoscopies were performed. The only statistically significant difference between the untreated acromegalic patients and the healthy subjects was the presence of middle ear ventilation problem: it occurred in 7/30 acromegalic patients (23%), and in none of the 20 healthy controls (0%),  $p = 0.033$ . The acromegalic patients with middle ear ventilation problem were significantly older, with diseases of longer duration, and with lower mean growth hormone (GH) levels in comparison with the acromegalic patients without this problem.

Opinions concerning the presence of conductive hearing loss in acromegaly in the literature are contradictory. Therefore, this study has the goal of investigating possible conductive hearing disturbances in acromegalic patients.

Issues as to the real cause-and-effect relationship between acromegaly and hearing loss require longitudinal studies. However, because of the rarity of this disease, we cannot expect to have studies with larger groups of individuals.

## Final Comments

According to the literature discussed, we can infer that there are no consistent results, and that they lead to different conclusions. This probably occurred due to the significant prevalence of hearing loss in the world, which would require a larger amount of acromegaly patients to be studied.

We conclude that a study with a greater number of patients with acromegaly is needed **to achieve** more confident results.

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