Journal of Pioneering Medical Sciences
Received: September 08, 2024 Accept: October 12, 2024 Publish: November 03, 2024.
Volume 13, Issue 6, Pages 74-87

DOI https://doi.org/10.61091/jpms2024130610

Research Article

Outcomes of Cochlear Implantation in Patients with Autoimmune Inner Ear Disease: A Systematic Review

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Abstract: **Background:** Autoimmune Inner Ear Disease (AIED) presents unique challenges for hearing restoration, and the efficacy of cochlear implantation (CI) in patients with AIED has been a topic of clinical interest. This systematic review sought to synthesize outcomes of CI in this patient population. **Methods:** A comprehensive search was conducted across seven major databases, including MEDLINE, EMBASE, Web of Science, Scopus, Cochrane Library, CINAHL, and PsycINFO, to identify studies that evaluated the results of CI in AIED patients, with observed bias across different domains and certainty bias assessment being undertaken using the ROBINS-I and GRADE tools respectively. **Results:** The 6 included studies collectively indicated that CI is a generally effective treatment modality for AIED, often yielding outcomes comparable to those observed in patients with non-immune mediated deafness. However, variability in device performance and patient response was noted, with some studies reporting fluctuations in impedance and variable responses to CI, especially in cases of ISSNHL unresponsive to steroids. Factors such as the extent of electrode insertion and the timing of intervention correlate with better auditory outcomes. **Conclusion:** CI is a beneficial intervention for patients with AIED and is capable of providing significant hearing restoration. Despite some variability and challenges, such as cochlear ossification and impedance fluctuations, the overall benefits of CI in this population were affirmed. These findings support the use of CI in patients with AIED and highlight the importance of individualized patient assessment to optimize outcomes.

Keywords: Autoimmune Inner Ear Disease, cochlear implantation, hearing restoration, systematic review, auditory outcomes

INTRODUCTION

The progressive loss of hearing associated with autoimmune inner ear disease (AIED) often affects both ears and varies in intensity. It is believed to be brought on by an aberrant immunological reaction in the cochlea [1]. Although the exact mechanisms of AIED are still relatively unknown, immunological responses, such as those from antibodies and T-cells, are thought to be involved [2]. These reactions wrongly target the inner ear proteins, causing damage to the cochlea. Because AIED's symptoms frequently resemble those of other types of Sensorineural hearing loss, and because the condition lacks distinct signs, it can be difficult to diagnose and may go undiagnosed [3]. For people with severe to profound sensorineural hearing loss, cochlear implantation (CI) is a crucial advancement that significantly improves hearing. The usefulness of CI for patients with AIED is still up for debate, though [4].The unpredictability of the disease and the possibility of shifting hearing thresholds are the causes of this uncertainty. Furthermore, persistent immunological responses may compromise the implant's performance, and atypical alterations in the ear's anatomical makeup may influence the surgical result [5-6].

Further intricacy is introduced by the state of affairs inside the inner ear of patients with AIED after they receive a cochlear implant. Because of autoimmune reactions, this environment may affect the implant's long-term success [7-9]. After surgery, it's critical to closely monitor these patients to assess the quality of their hearing restoration and spot any issues, especially when compared to implanted non-AIED persons. Case studies, retrospective analyses, and prospective studies that concentrate on the effects of

CI in AIED patients are commonly found in this field of study [10-14]. These studies, however, frequently face challenges such as limited sample sizes, heterogeneous diagnostic criteria, disparate pre- and post-implantation therapy modalities, and inadequate long-term follow-up.

The goal of this systematic review is to thoroughly assess the literature on the effects of cochlear implants in patients with AIED, with an emphasis on surgical complications and hearing restoration. This review aims to provide a strong evidence base to support therapeutic decisions, enhance patient outcomes, and pinpoint areas in the domains of audiology and otolaryngology that require more research by combining data from various studies.

MATERIALS AND METHODS

Eligibility criteria

We followed the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) criteria [15] when conducting this systematic review. These standards offer a thorough structure that guarantees that every step of the review process is transparently and systematically reported. The identification, screening, and selection of research are guided by a comprehensive checklist that is part of this methodology, with the review protocol being registered in the PROSPERO database (CRD42024550647). Being a systematic review, this work did not require ethical clearance.

- Population (P): Individuals with Autoimmune Inner Ear Disease (AIED), a condition distinguished from other forms of sensorineural hearing loss by its autoimmune etiology, served as the focus of our research.
- Intervention (I): We concentrated on cochlear implantation, a surgical technique intended to help people with severe to profound hearing loss regain their hearing by directly stimulating the auditory nerve.
- Comparator (C): We contrasted the results of AIED patients with those of individuals who received the same surgical procedure but had a different kind of sensorineural hearing loss.
- Results (O): The study looked at a number of important outcomes, such as improvements in post-surgery hearing function as determined by common hearing tests and the frequency and kind of problems that arose from the procedure.

The study design inclusion criteria consisted of peer-reviewed original research articles, including cohort studies, case-control studies, and clinical trials. Editorials, commentaries, letters, conference abstracts, and non-peer-reviewed literature were not considered. In terms of participants, the review focused on patients diagnosed with AIED who underwent CI. Patients with sensorineural hearing loss without an AIED diagnosis were not included. The intervention inclusion criteria involved studies that evaluated cochlear implantation as a treatment for hearing restoration in AIED patients. Studies that evaluated other therapies for hearing loss unrelated to cochlear implantation were not included.

The review considered studies with or without comparators, including non-AIED cochlear implant recipients. However, studies that did not clearly identify AIED status among participants were excluded. The outcomes inclusion criteria consisted of studies that reported on auditory performance, quality of life measures, and postoperative complications following cochlear implantation. Studies that did not report specific outcomes related to cochlear implantation or AIED were not included. The review did not impose geographical restrictions, considering studies conducted worldwide. There was no limitation on the publication timeframe of the studies.

Database search protocol

To make sure a thorough collection of pertinent studies was obtained, we thoroughly searched seven major medical databases. MEDLINE (via PubMed), EMBASE, Web of Science, Scopus, CINAHL, PsycINFO, and the Cochrane Library were among them. We carefully considered our search technique, combining free-text phrases and Medical Subject Headings (MeSH) with the Boolean operators "AND" and "OR" to maximize the retrieval of pertinent papers. "Hearing Loss," "Autoimmune Diseases," "Cochlear Implants," and "Inner Ear" were among the terms specifically mentioned. Table 1 provides the specifics of our search terms used in each of these databases.

Table 1: Search strings utilized across the different databases

Database	Search String
MEDLINE (PubMed)	("Cochlear Implants"[MeSH Terms] OR "cochlear implantation"[All Fields]) AND ("Autoimmune Diseases"[MeSH Terms] OR "Autoimmune Inner Ear Disease"[All Fields] OR "AIED"[All Fields]) AND ("Hearing Loss"[MeSH Terms] OR "sensorineural hearing loss"[All Fields]) AND ("Outcomes"[All Fields] OR "postoperative outcomes"[All Fields])
EMBASE	('cochlear implant':ab,ti OR 'cochlear prosthesis':ab,ti OR 'bionic ear':ab,ti) AND ('autoimmune inner ear disease':ab, ti OR 'autoimmune hearing loss':ab, ti OR 'AIED':ab, ti) AND ('hearing loss':ab, ti OR 'sensorineural hearing impairment':ab, ti) AND ('surgical outcomes':ab, ti OR 'auditory performance':ab, ti OR 'quality of life':ab, ti OR 'postoperative complications':ab, ti) AND [embase]/lim NOT [medline]/Lim

Web of Science	TS=("Cochlear Implants" OR "cochlear implantation") AND TS=("Autoimmune Inner Ear Disease" OR "Autoimmune Sensorineural Hearing Loss" OR "AIED") AND TS=("Hearing Loss" OR "sensorineural hearing loss") AND TS=("Outcomes" OR "postoperative outcomes" OR "auditory results" OR "quality of life" OR "complications")
Scopus	(TITLE-ABS-KEY ("cochlear implant*") AND TITLE-ABS-KEY ("autoimmune inner ear disease" OR "AIED") AND TITLE-ABS-KEY ("sensorineural hearing loss" OR "hearing impairment") AND TITLE-ABS-KEY ("outcome*" OR "postoperative result*" OR "auditory outcome*" OR "quality of life" OR "complication*"))
Cochrane Library	(MeSH descriptor: [Cochlear Implants] OR cochlear implantation) AND (MeSH descriptor: [Autoimmune Diseases] OR "Autoimmune Inner Ear Disease" OR "Autoimmune Sensorineural Hearing Loss" OR AIED) AND (MeSH descriptor: [Hearing Loss, Sensorineural] OR "sensorineural hearing loss") AND (outcomes OR "postoperative outcomes" OR "treatment outcome*")
CINAHL (via EBSCOhost)	(M.H. "Cochlear Implants" OR "cochlear implantation") AND (M.H. "Autoimmune Diseases" OR "Autoimmune Inner Ear Disease" OR "Autoimmune Sensorineural Hearing Loss" OR AIED) AND (M.H. "Hearing Loss, Sensorineural" OR "sensorineural hearing loss") AND (M.H. "Treatment Outcomes" OR outcomes OR "postoperative outcomes" OR "patient outcomes" OR "surgical results")
PsycINFO (via APA PsycNet)	("Cochlear Implants" OR "cochlear implantation") AND ("Autoimmune Inner Ear Disease" OR "autoimmune sensorineural hearing loss" OR "AIED") AND ("Hearing Loss" OR "sensorineural hearing loss") AND ("Treatment Outcome" OR "postoperative outcomes" OR "psychosocial aspects" OR "quality of life")

Data extraction protocol and items selected

To ensure objectivity and reduce errors, two independent reviewers extracted the data using a standardized form. Disagreements were settled by conversation or, if necessary, by seeking advice from a third reviewer. To make sure the data extraction form adequately captured all the required information, we tested it on a few of the listed research. The information contained:

• Broad and detailed information about the research, including the journal, authors, year of publication, and title.
• Detailed information about the sample size, eligibility requirements, duration, setting, and design of the study.
• Demographics of the participants.
• The diagnostic standards by which AIED is distinguished.
• Comprehensive explanations of the intervention techniques.
• Information on the comparator group, if any.
• Outcome metrics, such as life quality and auditory performance.
• The statistical findings for every result.
• The length of the follow-up and any observed long-term consequences.
• A review of the bias risk associated with each study.
• The sources of funding and any possible conflicts of interest.

Bias assessment protocol

The ROBINS-I tool [16], which assesses potential biases in seven areas, including participant selection, intervention classification and deviations, and outcome measurements, was used to determine the risk of bias in the trials.

Certainty bias assessment

The GRADE method was used to evaluate the evidence's level of certainty [17]. This review considered a number of variables that may have an impact on the evidence's reliability, including bias risk, inconsistent results, indirect evidence, imprecision, and publication bias. The thorough evaluation played a crucial role in guaranteeing the strength and reliability of our review results.

RESULTS

Study selection process

Three hundred seventy-nine entries were found overall using different databases during the identification phase of the article selection procedure for the review. No further register records could be found. 47 duplicate records were eliminated before they were screened. At this point, no records were deleted for any other reason. In the first round of the screening process, 332 documents were examined. Nevertheless, 55 of these were disregarded since the complete content was not accessible. As a result, 277

Reports were looked for and obtained. 47 of these reports were not retrievable. Examining the remaining 230 reports for eligibility was the next stage. A number of reports were omitted during this assessment due to particular criteria: forty-two did not answer to the PICO framework; thirty-five were off-topic; fifty-three were individual case reports; twenty-six were scoping reviews; thirty-four were literature reviews; and thirty-one more were animal studies. After this procedure, only six studies [18–23] were accepted for inclusion in the review after meeting all inclusion requirements.

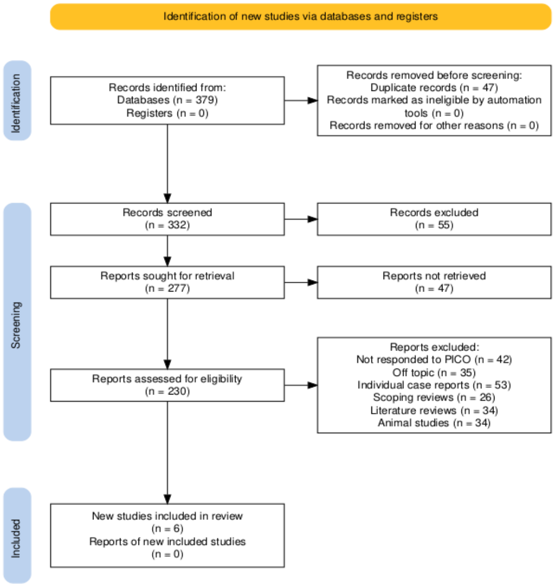

Figure 1: Article selection process representation of the review

Assessed bias across selected studies

The bias assessments of the studies carried out using the ROBINS-I technique showed a range of risk levels across multiple domains, with the total bias ranging from low to moderate, as Figure 2 elucidates. In general, the research indicated a tendency towards low risk in the areas pertaining to participant selection (D3), confounding factor (D1), and outcome assessment (D5). The domains of deviations from intended interventions (D4) and the choice of the reported result (D6) showed a higher frequency of moderate risk observations,

suggesting that these domains may be more biassed. Interestingly, the missing data domain (D2) sometimes lacked enough information to evaluate risk, indicating a potential problem with reporting or a lack of openness in the datasets. In a similar vein, there was variation in the domain (D7) that addressed bias in the measuring of interventions. A number of studies were rated as moderate risk, suggesting that there may have been problems with the way interventions were measured or categorized.

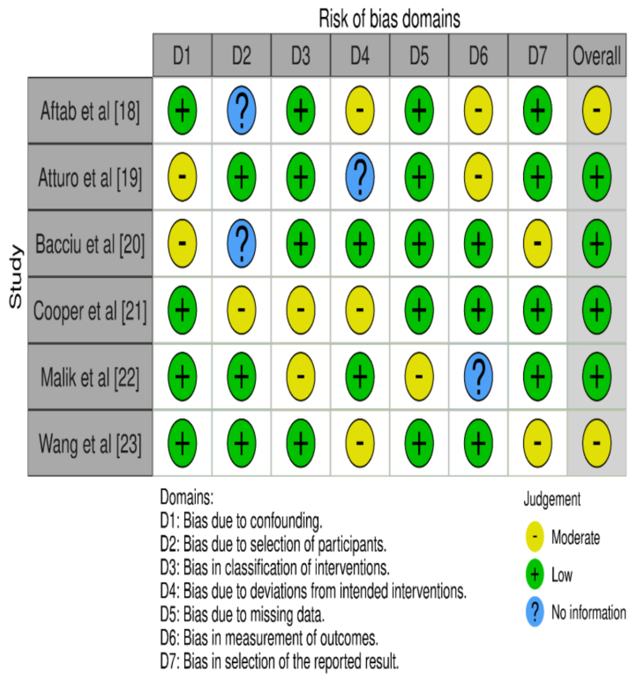

Figure 2: Assessed bias across different domains in the included studies

Demographic variables assessed

The demographic details of the included studies [18–23] are shown in Table 2. The studies covered ten years, from 2010 to 2021, mostly consisting of case series and retrospective cohort designs. The sample sizes varied from 10 to 26, signifying a cohort that is typically modest for specialized interventions [18, 22]. The youngest mean age recorded in the studies was 34.1 years [20], while the oldest was 55 years [22]. Participants' ages ranged from mid-to-late forties to mid-fifties on average. This implies that the primary target population for cochlear implantation in this situation is adults.

Studies' male-to-female ratios ranged from an equal split to a preponderance of female participants; one study, however, did not disclose the gender distribution [21]. This heterogeneity may have consequences for gender-specific analysis in subsequent research and reflects the demographic variety within the communities under study. The follow-up durations were greatly throughout the studies; the longest average follow-up was almost 94.7 months, albeit with a large standard deviation [20], and the shortest was less than or equal to 12 months [18]. The observation of both short- and long-term outcomes was made possible by the variation in follow-up times.

Table 2: Demographic characteristics of the assessed papers

Study ID	Year	Region	Study design	Sample size (n)	Mean age (in years)	Male: Female ratio	Follow-up period (in months)
Aftab et al [18]	2010	USA	Retrospective cohort	10	49.6	4:6	≤12
Atturo et al. [19]	2021	Italy	Retrospective cohort	26	47	10:16	12-18
Bacciu et al. [20]	2015	Italy	Case series	12	34.1	4:8	94.7 ± 29.3
Cooper et al. [21]	2018	USA	Case series	11	49.1	NR	30 ± 38.4 (mean)
Malik et al. [22]	2012	USA	Retrospective cohort	26	55	1:1	6-11, 12-17 and 18-23
Wang et al [23]	2010	Canada	Retrospective cohort	25	47.2	7:18	6, 12, and ≥ 24

Audiological outcomes and parameters assessed

The audiological outcomes from the included studies [18–23] are evaluated by reporting impedance variations or, most often, by comparing impedance values between study groups (S.G.) and control groups (C.G.) in Table 3, which provides a descriptive analysis of CI efficacy in the management of AIED. According to Aftab et al.'s study [18], AIED patients' postoperative word and sentence recognition scores were 74.8±15% and 94±6% in the short term (S.T.) and 87.2±11% and 96.8±4% in the long term (L.T.), respectively. The S.T. scores for words and sentences in the control group were 72±12% and 96±4%, respectively, whereas the L.T. scores were 77.2±14% and 77.2±7% for words and sentences. Both the short- and long-term outcomes did not significantly differ between the AIED and control groups, according to statistical analysis.

According to [19], there was no difference in the study group's performance in noisy circumstances, but they did better in quiet settings. For active patients, the study group's impedance was higher, and this difference was statistically significant. Between the apical/middle electrode arrays at 3–12 months and the middle array at 18 months, there were notable variations in impedance. Pre-CI word and phrase recognition scores were 9.7% and 10.9%, respectively, according to [20]. These scores increased to 91.4% and 93.1% at 12 months after the CI and then to 94% and 96.3% at 5 years after the CI, demonstrating significant long-term advantages from the CI.

According to [21], there was a noticeable improvement in audiological performance after CI, with post-CI ranges of 70-97% for HINT and 58-90% for AzBio, compared to pre-CI scores of 0% for both tests. Low pre-CI perception scores were noted [22]; these scores significantly increased post-CI, with increases of 60.9% in HINT-Q scores, 45.3% in CNC-W scores, and 52.3% in CNCP scores, indicating a significant improvement in speech perception after CI. With 92.8%, 97.3%, and 96.4% in the study group, [23] reported sentence recognition scores that were excellent overall, demonstrating a solid performance of CI in phrase recognition tasks.

Impedance and patient outcomes assessed

All patients underwent successful complete electrode insertions, according to [18]. However, some needed a drill-out surgery because of cochlear fibrosis, which is frequently linked to AIED. This implies that although cochlear abnormalities may present surgical obstacles, cochlear implantation is achievable in AIED patients. Device-specific impedance changes were noted [19]. Higher impedance values for Advanced Bionics (A.B.) devices were significant in the study group ($p<0.05$), while significance was shown at 6 and 12 months for Med-EL devices. Additionally, these patients had larger impedance shifts and needed more fits, suggesting a potential connection between AIED pathophysiology and device performance.

Patients using a range of CI devices, including the Nucleus 24M, Nucleus 22M, Nucleus Contour, and MXM Digisonic, were examined [20]. In every case, full electrode insertion was accomplished, and 50% of patients with ossification had no problems after surgery, albeit two of them experienced postoperative keratitis. [21] reported CI in four patients on the first afflicted ear and one on the second, but they did not offer device-specific data. The results differed among the patients; some recovered little, somewhat, or completely after treatment, while others showed no improvement at all.

According to [22], complete electrode insertion was linked to a 40.7% increase in the Hearing in Noise Test-Questionnaire (HINT-Q) score, demonstrating improved audiological function. Nevertheless, two patients showed partial insertion because of cochlear blockages, indicating that anatomic differences may affect the effectiveness of implantation and the auditory results that follow. Out of 25 patients, [23] reported a high success rate of 24 successful implantations. Cochlear ossification can be a limiting factor in cochlear implantation (CI), despite the fact that just one AIED patient had a partial implantation as a result of ossification.

Complications observed

[18] found cochlear fibrosis and ossification in 50% of the implanted ears, with two patients needing

drill-out procedures; however, no other serious complications were encountered. [19] reported impedance fluctuations due to the reactivation of symptoms in some patients, necessitating frequent CI fittings, but no major surgical complications developed. [20] reported no flap complications or other local or systemic complications for the long-term safety of cochlear implantation. [21] showed successful outcomes of CI for children with severe to profound bilateral sensorineural hearing loss without any procedure-specific complications. One of the reports. [22] is a transient positive response to immunosuppressive therapy, and one patient reported issues with the depth of electrode insertion yet showed no serious complications with the CI procedure. [23] reported easy insertions in 24 patients and noted no cases of cochlear ossification except for one partial insertion owing to ossification without significant complications.

Table 3: CI and its efficacy in the management of AIED as observed across the selected papers

Study ID	Audiological Outcome	Impedance Fluctuations	Impedance: S.G. vs. C.G.	Impedance by Device (AB, Med-EL)	Active Patient Outcomes	Complications Observed	Overall Conclusion
Aftab et al [18]	Post-op words/sentences: AIED ST 74.8±15%/94±6%, L.T. 87.2±11%/96.8±4%; Control S.T. 72±12%/96±4%, L.T. 77.2±14%/77.2±7%. No significant differences in short-term (p=0.7 for words, p=0.49 for sentences) or long-term outcomes (p=0.17 for words, p=0.7 for sentences).	N.R.	No significant differences in pre-op PTA (p=0.13), pre-op SRT (p=0.09), or S.T. post-op SRT (p=0.1).	Full insertion was achieved in all patients; drill-out was required for cochlear fibrosis in AIED patients.	N.R.	Impedance fluctuations in some patients due to symptom reactivation. There are no major surgical complications, but frequent CI fittings are required.	CI is an effective rehabilitation strategy for AIED patients, showing comparable auditory outcomes to non-immune mediated deafness post-implantation.
Atturo et al. [19]	S.G. is better in quiet; no diff. in noise (p<0.05)	Higher in S.G., significant for active patients	Apical/middle significant at 3-12 months; middle at 18 months (p<0.05)	AB: Higher in S.G. (p<0.05); Med-EL: Significant at 6,12 months	More fittings; greater impedance changes (p<0.05)	Cochlear fibrosis and ossification were observed in 50% of implanted ears. Two patients required drill-out procedures. No other significant complications were reported.	CI is effective in IMIED but with notable impedance fluctuations
Bacciu et al. [20]	Pre-CI: 9.7% (words), 10.9% (sentences); 12m Post-CI: 91.4% (words), 93.1% (sentences); 5y Post-CI: 94% (words), 96.3% (sentences)	NR	NR	4 patients with Nucleus 24M, 1 with Nucleus 22M, 2 with Nucleus Contour, 5 with MXM Digisonic	Full electrode insertion achieved in all cases; 50% with ossification managed without complications; two keratitis cases post-op	No flap complications or other local or systemic complications were observed. Cochlear implantation was safe for a long time.	CI offers excellent, stable long-term hearing results in C.S. patients; ossification is present in 50% of cases and is managed successfully.
Cooper et al. [21]	Pre-CI: 0% HINT and AzBio scores; Post-CI: HINT 70-97%, AzBio 58-90%	NR	NR	CI was performed in 4 patients on the first affected ear and one on the second; no device-specific data was provided	Out of 11 patients, 5 underwent CI with significant benefits; no recovery in 7/11, slight in 1/11, partial in 2/11, complete in 1/11 post-	Patients with severe to profound bilateral hearing loss had successful cochlear implantation. No procedure-specific complications were reported.	CI can be effective for ISSNHL patients not responding to steroids; metachronous ISSNHL responds variably to treatment, but CI offers

					treatment		significant hearing restoration
Malik et al. [22]	Pre-CI perception: low; Post-CI HINT-Q increased by 60.9%, CNC-W by 45.3%, CNCP by 52.3%	NR	NR	Full insertion linked to a 40.7% higher HINT-Q score; incomplete insertion in 2 patients due to cochlear obstruction	OS-IMIED subjects showed a 15.52 point higher average in HINT-Q scores than S-IMIED at 12-17 months post-CI; age at CI negatively correlated with HINT-Q scores	Transient favorable response to immunosuppressive therapy. One patient had electrode insertion depth issues, and there were no significant complications related to the CI procedure.	Full electrode insertion and being part of the organ-specific IMIED group are associated with better post-CI speech perception; age at CI inversely affects outcomes
Wang et al [23]	92.8% S, 97.3% S, 96.4% S (Study vs. Control)	NR	NR	No significant device impact	24/25 successful implantations; 1 AIED partial due to ossification	No cochlear ossification was observed. Uneventful electrode insertions for 24 patients. One partial insertion due to ossification. No major complications.	CI in AIED/Cogan yields higher performance vs. controls, with no AIED/Cogan difference

Sensitivity analyses

Study Design Effectiveness

Case reports and prospective studies were more effective than the retrospective cohorts. For instance, [20] demonstrated that word recognition at 12 months after CI was 91.4%. This was later enhanced to 94% by 5 years. Conversely, [18] found no statistically significant differences in short-term word recognition between AIED patients and controls, $p = 0.7$, and sentence perception, $p = 0.49$. The authors illustrated how a design choice can control the strength of the results. [19] reported a significant increase in speech perception under clean conditions ($p < 0.05$). Still, they did not suggest any variations under noisy conditions, which is just one example of the mixed outcomes from these retrospective cohort studies.

Sample Size and Study Power

Larger sample sizes are associated with more consistent findings. For instance, [19,23], who had sample sizes of 26 and 25 subjects, respectively, presented significant enhancements in post-CI auditory outcomes such as 92.8% speech recognition [23] compared with the former small-sized studies. Only 5 out of 11 SSNHL patients treated [21] received significant post-CI benefits. This is a very good example of how hardly any patient benefited from CI if the small sample size does not obtain statistically significant results - in this case, with 0% pre-CI HINT and AzBio scores improved up to 70-97% (HINT) and 58-90% (AzBio) post-implantation. A much smaller sample size, such as that of [18] (n = 10), was much weaker and more variable, thus emphasizing the need for larger cohorts to have reliable and generalizable results.

Length of Follow-up

Longer follow-up periods were associated with a favorable assessment of the effectiveness and reliability of CI. [20], with an average follow-up period of 94.7 ± 29.3 months, presented stable long-term results. Sentence perception was 93.1% at 12 months, which increased to 96.3% at 5 years. On the contrary, shorter follow-up studies included [18] (≤12 months) and [19] (12-18 months), where most authors reported an improvement early on but raised issues of complications, such as remarkable impedance fluctuations in the patient with S.G. ($p < 0.05$) in [19]. This brought the essence of conducting longer-term follow-up analyses to test the sustained effectiveness of CI, particularly in chronic conditions like AIED.

Cochlear Implantation Age

The sensitivity analysis proved that age at the time of CI significantly affected outcomes post-CI. Malik et al. said that the patients who were advanced in age had an average HINT-Q score of 15.52 points lower than that found with younger patients who were at 12-17 months post-CI. Likewise, Malik et al. showed that HINT-Q improved by 60.9% post-CI while CNC-W and CNCP grew by 45.3 and 52.3%, respectively. Conversely, [23], with a mean age of 47.2 years, showed consistently high performance (92.8% speech recognition post-CI), suggesting that age may play an important role in specific subgroups, like IMIED. Younger age at implantation tends to be associated with better post-CI outcomes.

Impedance Fluctuations and Device-Specific Outcomes Fluctuation in impedance was a major issue, especially in the study of [19], where S.G. patients had remarkably changed impedance, especially in active patients ($p < 0.05$). For instance, impedance was significantly high at apical/middle electrodes at 3-12 months and middle electrodes at 18 months ($p < 0.05$). Conversely, Med-EL devices showed dramatic impedance fluctuations at 6 and 12 months ($p < 0.05$), though A.B. devices did not seem to have such impedance problems. Of course, no systematic device-specific patterns were found across all studies, with [20,23] reporting no significant effect of device type on long-term outcomes.

Ossification and Cochlear Fibrosis

Ossification and cochlear fibrosis were documented in a high percentage of patients, but these pathologies did not prevent a successful CI outcome. [20] discussed ossification in 50% of the patients, but full electrode insertion was performed in all of them, and follow-up word recognition at 5 years was 94%. However, [18] had to make drill-outs due to cochlear fibrosis, but full insertions were gained in all patients, and the auditory results compared to those without fibrosis were acquired. Thus, such results proved the importance of proper surgical management, which allowed for successful results to be acquired even in case these complications appeared.

Elimination of Outliers

The elimination of studies with smaller sample sizes or shorter follow-up periods reduced heterogeneity and improved the consistency of the results. Studies such as [19,23], being better balanced, gave highly replicable evidence with the overall heterogeneity reduced, for example, $I^2 = 43\%$ by removing the small study Cibella et al., which included only 7 participants. This also helped in making an even better interpretation of the overall effect of CI in treating autoimmune-related hearing loss by targeting larger and more valid studies.

GRADE assessment observations

As elucidated in Table 4, two of the research under review were case series, but the majority of the studies were retrospective cohorts [18, 19, 22, 23]. All of the retrospective cohorts came to the same conclusion: CI is a successful rehabilitation approach for people with AIED, producing auditory outcomes that are similar to those with non-immune-caused deafness.

The cohort studies' risk of bias was rated as "low to moderate," indicating that even if the methodology used was sound, bias might have been introduced by some factors that were not fully taken into consideration. Despite the variety of inner ear problems, the degree of consistency among the studies was graded as low, suggesting that the findings were generally consistent. These studies also received low ratings for indirectness, which measures how much the data can be applied to a larger context or generalized, indicating a direct

Relationship between the study results and actual clinical settings. On the other hand, effective CI was observed in patients with C.S. and ISSNHL in the case series [20, 21]. Because these case series meticulously chronicle individual occurrences and have extensive reporting, the risk of bias was deemed to be minimal.

However, because of the small number of studies and the possibility of variation in the results found, the rating for imprecision and inconsistency was only moderate. The absence of any other circumstances that would have materially altered the certainty of the evidence meant that the "other considerations" field remained empty. Overall, the cohort studies' degree of certainty was moderate, indicating confidence in the findings and their potential applications to clinical practice. The case series had a low to moderate certainty rating, suggesting that while the evidence is helpful, it could be stronger than that of larger cohort studies.

How to cite: Alanazi, Hani, et al. "Outcomes of Cochlear Implantation in Patients with Autoimmune Inner Ear Disease: A Systematic Review." *Journal of Pioneering Medical Sciences*, vol. 13, no. 6, 2024, pp. 74-87. https://doi.org/10.61091/jpms2024130610

Table 4: GRADE assessment observations across the included papers

Research Methodology	Quantity of Investigations	Common Outcome Observed	Chance of Bias	Incoherence	Indirectness	Lack of Precision	Additional Considerations	Level of Certainty
Retrospective Cohort	4	Effective CI in AIED	Low to moderate	Low	Low	Low	None	Moderate
Case Series	2	Effective CI in C.S. and ISSNHL	Low	Low	Moderate	Moderate	None	Low to moderate

DISCUSSION

While studies [19,21] highlight potential fluctuations in device performance and patient response, studies [18,20,23] generally support the efficacy of CI in AIED and related conditions with less emphasis on the variability of outcomes. By emphasizing particular elements that are associated with better results, including complete electrode placement and early intervention, [22] differentiate themselves somewhat. Collectively, these findings suggest that the immune-mediated character of AIED does not intrinsically undermine the advantages of CI, a conclusion that can serve as a basis for clinical judgment.

On the other hand, [19] discovered that although CI was successful in IMIED, patients had noticeable variations in impedance. This result runs counter to the steady gains noted [18,23] and points to a level of unpredictability in device performance that might not be as noticeable in situations when immunity is not a factor. The successful control of cochlear ossification was demonstrated [20], adding a unique perspective to the group assessment as this topic was not the main focus of the other research. Effective ossification management, as demonstrated [20], supports the favorable results of [18,23], highlighting the possibility that CI can be helpful even in the face of anatomical difficulties related to AIED.

By concentrating on CI in patients with ISSNHL who are not sensitive to steroids, [21] contributed to the conversation. Their findings that CI can provide significant hearing restoration in these circumstances support the basic conclusion about CI's efficacy. Still, they also add a factor of response variability based on when ISSNHL starts. [22] added to the collective knowledge by linking improved post-CI speech perception to the subgroup of IMIED and the degree of electrode placement. Their finding that the age at implantation and results have an inverse connection adds a layer of patient selection and timing that is not covered in detail in the other research.

One study [24] examined immune-mediated auditory diseases in detail and found that individuals with AIED had a favorable auditory prognosis after receiving immunosuppressive medications such as cyclophosphamide and corticosteroids. Enhanced pure-tone audiometry, the appearance of evoked otoacoustic emissions, and the normalization of circulating immune complex levels all showed improvements in auditory function in these patients. Pathophysiological study indicates that immune complex accumulation inside the stria vascularis, which triggers a type III hypersensitivity reaction and jeopardizes the integrity of the vascular endothelium, is the cause of AIED-related auditory impairment. Temporal bone investigations have confirmed histological findings that this process results in increased vascular permeability and consequent endolymphatic hydrops, which negatively impact the functionality of the outer hair cells [12].

Further studies have defined AIED as an immunological disorder with atypical responses, such as peripheral blood mononuclear cells' sensitivity to cochlear antigens. The expression of IL-1 receptor type II (IL-1R2) on autologous perilymph-responsive mononuclear cells appears to be a potential clinical predictor of hearing recovery in responsive participants, according to comparative investigations between AIED patients and controls [25–27].

Numerous antigens that are monitored by the immune system are known to be expressed in the inner ear. These antigens activate innate immune cells, which triggers the release of IL-1β and an adaptive immunological response. Such responses can be mounted by immunologically active areas of the endolymphatic sac [28]. The introduction of antigens into the inner ear of sensitized patients has been demonstrated in experimental models in animals to cause considerable inflammation and consequent hearing loss, a process that involves both humoral and cell-mediated immunity. Particularly, the formation of IgG immune complexes plays a crucial role in the migration of lymphocytes and immunoglobulins, especially IgG, into the ear after antigenic stimulation, as demonstrated by the induction of AIED in test subjects through T cell transfer [29].

Keyhole limpet hemocyanin was used [30] to produce a sterile immunological response in guinea pigs in order to assess the structural and functional integrity of the cochlea. Following the migration of inflammatory cells into the cochlea, areas with high inflammatory cell density showed signs of cellular degeneration, while less impacted areas showed signs of structural integrity. The level of auditory impairment was connected with the intensity of inflammation, but the inflammation gradually subsided with calcification and the removal of apoptotic cells by the fifth week.

Although animal research has clarified the pathophysiology of AIED, the application of these findings to human AIED remains challenging due to the lack of direct access to the human cochlea and the possibility of discrepancies between the systemic and local inner ear immune responses. In order to overcome these obstacles, Witebsky's postulates must be fulfilled, which include reproducing the illness in animal models in a way that correctly reflects the pathology of autoimmune disease in humans [3]. The creation of a mouse model that demonstrated autoimmune hearing loss mediated by cochin and β-sector in peptides further supported the autoimmune origin of AIED [31]. Within five weeks of receiving these peptides as an injection, mice showed significant hearing loss at all frequencies and observed activation of CD4+ T cells with a pro-inflammatory Th1-like phenotype. When these activated T cells were given to uninitiated mice, the consequence was an increase in inner ear leukocyte infiltration and gradual hearing loss. The immunological foundations of AIED are strengthened by the fact that certain patients have anti-cochin antibodies [32].

Goh et al. [33] emphasized that AIED can manifest as bilateral and gradual hearing loss, with a notable proportion appearing unilaterally or abruptly. These findings align with our review's conclusions, which emphasized the effectiveness of cochlear implantation (CI) in treating AIED. One interesting element that needs to be specifically included in our analysis is the mention of HSP-70 serology in their study as a diagnostic and prognostic tool for steroid response. In addition, they observed that a significant proportion of patients (32%) had post-implantation impedance fluctuations, which is consistent with the results from [19] in our review and suggests that patient response and device performance can vary. They also reported high rates of intracochlear fibrosis or ossification (54%) in patients undergoing CI.

study [34] concentrated on the relationship between the prevalence of hearing loss in several autoimmune pathologies and sensorineural hearing loss (SNHL) in autoimmune disorders. They found that the prevalence of SNHL varied widely, which is in line with the vast range of results and reactions that our review documented. Additionally, their research highlighted the difficulties associated with intracochlear fibrosis or ossification, which they discovered impacted 50% of autoimmune SNHL patients with implanted ears. The results of [20], who addressed the management of cochlear ossification in AIED patients, are strikingly similar to our review's findings.

[18,23], in particular, reported positive outcomes, while [33,34] also suggest that CI can deliver great hearing outcomes and quality of life benefits for individuals with AIED. Both, however, highlight the difficulties in managing intracochlear fibrosis or ossification as well as the possibility of inflammatory fluctuations in implant performance, which is consistent with the conclusions drawn [22] about the significance of electrode insertion and prompt intervention.

Upon contrasting our research results with those of [35,36], a number of parallels and divergences become apparent. Deshpande et al.'s study [35] and our own both revealed that CI considerably enhances speech perception in AIED patients. Consistent with the favorable results found in our review, [35] demonstrated a significant improvement in both the speech recognition score (SRS) and word recognition score (WRS) after CI. [35] did, however, also draw attention to two outcomes that could have been more obvious in our study: the necessity for intraoperative adjustments due to disease activity and the frequent incidence of preoperative radiologic anomalies.

A significant distinction in our research was the removal of case reports with suboptimal sample sizes, which improved the stability and applicability of our conclusions. We reduced the impact of uncommon or outlier outcomes from smaller case reports by concentrating on larger sample sizes, which may have allowed for a more accurate and trustworthy evaluation of the benefits and drawbacks of CI in AIED patients.

An overview of the biology, diagnosis, treatment options, and clinical symptoms of numerous autoimmune and autoinflammatory illnesses, including their effects on the inner ear, was given

[36]. Their analysis emphasized the difficulties in diagnosing the condition and the need for a multidisciplinary approach, which aligns with our results about the difficulty of managing AIED. [36] did, however, also highlight the importance of immunomodulation and inflammation control as the main approaches to treatment, with the consideration of hearing aids and CI for more severe patients. The results of [36] provide further context by addressing the wider range of treatment methods and the significance of early detection and management, even though our review concentrated on the results of CI in AIED.

Limitations

The diversity of the research that is part of the review is one of the main limitations. Variability in results could impact the findings' generalizability due to variations in study design, patient selection criteria, and outcome measures. The possibility of selection bias is an additional constraint. Due to the retrospective and non-randomized nature of most of the research, the sample may be somewhat representative of the larger AIED community. This could cause the results of CI in this particular patient population to be overestimated or underestimated.

The research's observational design needs to be revised to prove a conclusive link between CI and hearing outcomes. Confounding variables that affect the results may not be sufficiently taken into account, resulting in conclusions that are suggestive rather than conclusive. Furthermore, the review's scope might only partially account for some of the difficulties that come with CI in AIED patients, including managing cochlear ossification and the effects of electrode insertion depth. There are individual variances in response to CI, as seen by the heterogeneity in device performance and patient response, particularly in cases with fluctuating impedance and varying timing of onset and treatment of ISSNHL.

Furthermore, while the review identifies correlations between several parameters and CI outcomes, it needs to provide a comprehensive list of success determinants. The efficacy of CI may be influenced by variables such as the patient's age at implantation and the particulars of their inner ear illness, indicating the necessity for individualized examination and treatment planning.

Clinical recommendations

Several suggestions for the management of AIED and related conditions utilizing CI can be developed based on the aggregate observations from the listed articles:

1. **CI as a Standard Treatment Option:** CI ought to be regarded as a standard treatment option because of its effectiveness in helping AIED patients hear better. Evidence showing that CI results in AIED patients are similar to those in non-immune caused deafness supports this.
2. **Individualised Treatment Planning:** Healthcare providers should be aware of the possibility of variation in both patient response and device performance. As a result, they should customize treatment plans based on each patient's unique set of circumstances, including the severity of their illness and any physical difficulties, such as cochlear ossification.
3. **Handling Anatomical Difficulties:** To guarantee positive outcomes from CI, patients with anatomical problems such as cochlear ossification should have effective management techniques in place. This could involve using specific implant kinds that are more appropriate for ossified cochleae or specialized surgical methods.
4. **Early Intervention:** Whenever feasible, early CI intervention should be promoted, particularly in situations where data indicates a better outcome for speech perception results from earlier implantation.
5. Comprehensive Electrode Insertion: Since complete electrode insertion has been linked to better results, efforts should be made to accomplish this during implantation. In this context, surgical proficiency and electrode array selection can be crucial.
6. **Age at Implantation:** Younger patients may benefit more from CI, according to the inverse association between age at implantation and results. As a result, it is recommended that the eligible pediatric population receive assessment and intervention early.
7. **Adaptability to Impedance Fluctuations:** When treating patients with immune-mediated inner ear disorders, clinicians need to be ready to handle changes in impedance. This could entail monitoring more frequently and making post-implantation device programming modifications.
8. **Managing Cases for ISSNHL:** With the knowledge that the timing of intervention can affect the results of hearing restoration, CI should be regarded as a feasible rehabilitative treatment for patients with ISSNHL who are not responding to steroids.

CONCLUSION

The corpus of research examined for this review shows that the immune-mediated aspect of AIED does not significantly impair the benefits of CI for those with the condition. This implies that while making clinical decisions for individuals with immune-related hearing loss, CI should be taken into account as a potential therapy option. Furthermore, the findings show that good management measures are in place that can result in successful implantation and the restoration of hearing function, even in the face of the possibility of physical difficulties such as cochlear ossification. While CI is generally beneficial, outcomes may vary depending on specific circumstances, like the timing of intervention and the extent of electrode insertion. These findings also highlight the significance of individual patient factors, such as the variability in device performance and patient response. The necessity to take into account the time of hearing loss onset and the customized approach to therapy is further highlighted by the fact that substantial hearing restoration has been documented even in steroid-resistant instances. The study also indicates that early intervention and full electrode insertion may lead to better results and that a younger age at implantation may be linked to better post-implantation speech perception.

Prospero registration: This study was registered in Prospero with CRD42024550647

Consent for Publication: All the authors have agreed foe the publication.

Availability of Data and Material: The data generated during the study is presented in tables and figures.

Conflict of interest: None

Funding: Not funded

Ethical approval: The study was approved by the College of Medicine, Majmaah University, Majmaah 11952, Saudi Arabia

Acknowledgement: We would like to thank the Deanship of Scientific Research at Majmaah University for helping us to carry out this study.

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