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Original Article

# Role of Otoacoustic Emission Test in Active Rheumatoid Arthritis Patients

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## Abstract

**Introduction:** Rheumatoid arthritis (RA) is an autoimmune, chronic systemic inflammatory disease affecting the small joints and also has extra-articular manifestations. The early active stage of RA shows increased titer of anticyclic citrullinated protein antibodies in serum. Cochlear involvement resulting in Sensorineural hearing loss is one of the extra-articular manifestations in its active stage which can be identified at its subclinical level by screening with otoacoustic emission (OAE) test. OAE are sounds produced by healthy hair cells of the cochlea which shows a decrease or disappearance in active RA.

**Materials and Methods: Thirty** RA patients in active stage satisfying 2010 American College of Rheumatism/European League Against Rheumatism and Disease Activity Score IV criteria with normal hearing ability between 25 and 45 years of age and 30 age- and sex-matched controls were subjected to OAE test. Both males and females were included in the study.

**Results:** Statistical analysis was done using software SPSS version 21. All controls PASSed the test indicating normal hair cell function in both ears (60 ears). Thirty active stage patients were tested for both ears (60 ears). Out of 60, 19 PASSed the test and 41 showed REFER indicating subclinical hair cell dysfunction.

**Conclusion:** Study revealed subclinical hair cell dysfunction in 2/3rd of cases. Thus, OAE has a key role in screening, diagnosing and in preventing hearing disability in RA patients.

**Key words:** Anticyclic citrullinated protein antibodies, Otoacoustic emissions, PASS, REFER, Rheumatoid arthritis

## INTRODUCTION

Rheumatoid arthritis (RA) is a multifactorial, chronic systemic inflammatory disease affecting the small joints of the body in a symmetrical manner and also affects the other systems of the body in 15–25% of individuals[1] resulting in extra-articular manifestations. The auditory system can be affected in active stage of the disease. The active disease is defined according to Disease Activity Score of 28 joints (DAS 28 score) >5.1, increased titer of Anticyclic Citrullinated Protein Antibodies (ACPA). ACPA's in the serum are the powerful biomarker in the diagnosis of RA at an early active stage.[2]

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The healthy cochlear hair cells are damaged by the expression of antigens such as 58Kda protein and 68 Kda protein immune complex deposition[3] and by pro-inflammatory cytokines such as interleukin-6 (IL-6) resulting in sensorineural hearing loss (SNHL) ranging from undetectable degree of disability to profound loss of hearing ability. The early subclinical involvement of hair cells can be identified by screening with otoacoustic emissions (OAE) test. Early assault to the hair cells are identified by screening for OAE.[4]

OAE are sounds produced by healthy hair cells of the cochlea which shows a decrease or disappearance in hearing dysfunction. OAE is a biomarker of cochlear hearing impairment at an early stage.[5] Those with abnormal OAE may be subjected to diagnostic OAE

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and the severity of hearing deficit is determined and intervened early.

### Aim and Objectives

The aim of the study is to evaluate the role of OAE in active RA patients in comparison with age- and sex-matched controls. The objective of the study is to identify the subclinical hair cell damage and measures instituted early aiming at preserving the functional integrity of hair cells thus preventing the hearing impairment and improving the quality of life in these patients.

## MATERIALS AND METHODS

The study was conducted at the Institute of Physiology and Experimental Medicine, Madras Medical College, Chennai-3, after ethical approval from the Institutional Ethics Committee, Madras Medical College, Chennai.

### Inclusion Criteria

Thirty active RA patients 25–45 years of age with duration of illness <1 year diagnosed according to 2010 American College of Rheumatism/European League Against Rheumatism criteria with normal hearing ability confirmed by Pure Tone Audiometry participated in my study. The active disease is confirmed by increased titer of ACPA's by ELISA method and with DAS 28 score >5.1.

Thirty age- and sex-matched controls were included in the study.

### Exclusion Criteria

Children, pregnant women, subjects with diabetes, hypertension, tumors, and hearing abnormalities including presbyacusis were excluded from the study.

After obtaining informed and written consent, they were subjected to OAE test at the Institute of Audiology, Rajiv Gandhi Government General Hospital, Chennai-3.

### Principle

OAE screening is a sensitive and specific tool in the evaluation of subclinical hair cell damage in early active RA. It was first reported by Kemp in 1978. When the inner ear is stimulated by the sounds, the hair cells vibrate and produce an inaudible sound, echoed to the middle ear and measured by the probe placed in the external auditory canal. OAE are not generated with a hearing loss of 25–30 decibels. PASS indicates normal hair cell function and REFER abnormal hair cell function with increased risk of hearing impairment in future that recommends early diagnostic OAE.[6]

### Procedure

After a preliminary general and ENT examination, the microphone of the device is inserted into the external auditory meatus of the subject and click stimulus given with PORTABLE LABAT machine and screened for Transient Evoked OAE. The results are displayed as PASS or REFER.

## RESULTS

Statistical analysis was done using the software SPSS version 21. The mean age in the study group is 38.47 ± 5.06 in cases and 38.30 ± 4.41.

Study showed highly significant titer of ACPA in active RA patients when compared to controls, $P$ <0.0001 [Table 1 and Graph 1] with student $t$-test confirming active disease. Both the ears of controls and cases were subjected to OAE screening test. Control ears PASSed the test indicating normal hair cell function. Out of 60 ears of cases, ten right ears and nine left ears PASSed the test and 41 ears showed REFER [Graphs 2 and 3].

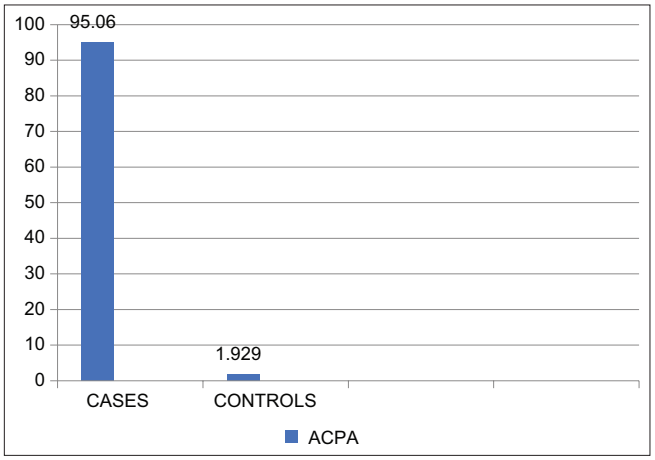
## DISCUSSION

Study shows significant reduction in OAE in 41 ears out of 60 ears of active RA patients who had normal hearing

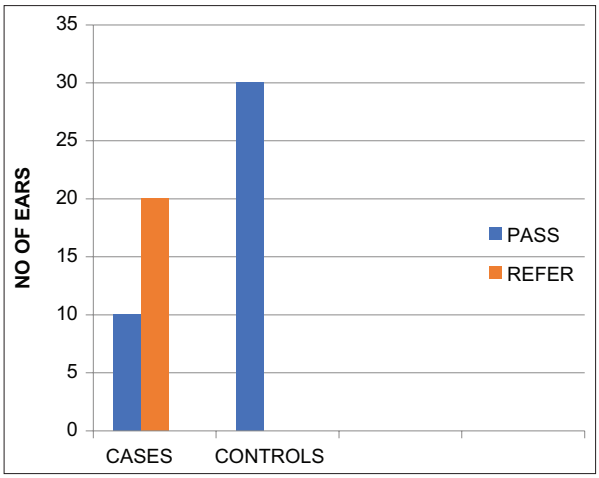
**Table 1: Comparison of mean values of ACPA (RU/ml) between active RA patients and controls**

| ACPA | MEAN | SD | *P*-value |
|---|---|---|---|
| Cases | 95.060 | 50.3 | 0.0001*** |
| Controls | 1.929 | 0.76 | |

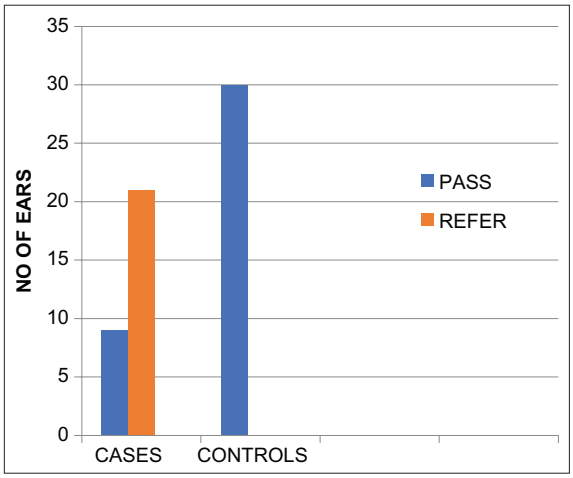
ACPA: Anticyclic citrullinated protein antibodies, RA: Rheumatoid arthritis. Table shows highly significant titer of ACPA in active RA patients when compared to controls ($P$ < 0.0001)




**GRAPH 1: Comparison of mean values of ACPA between active RA patients and controls**




**GRAPH 2: Comparison of PASS & REFER in right ears of active RA patients between cases and controls. Graph indicates that ten right ears and all controlsPASSed the OAE indicating normal hair cell function. 20 right ears had REFER indicating subclinical hair cell dysfunction**




**GRAPH 3: Comparison of PASS & REFER in left ears of active RA patients between cases and controls. Graph indicates that nine left ears and all controls PASSed the otoacoustic emissions indicating normal hair cell function. Twenty-one left ears had REFER indicating subclinical hair cell dysfunction**

in Pure Tone Audiometry. This goes in line with studies by Emamifar *et a1*.,[7] Murdin *et al*.,[8] Bayazit *et al*.,[9] Dikici *et al*.,[10] Baradaranfar and Doosti[11] who reported the decrease in OAE's are seen in patients with normal hearing status in active RA indicating an early stage of hearing impairment.

The present study showed a significant increase in the titer of ACPA's confirming the active stage of the disease which coincides with the work done by Aggarwal *et al*., 2009,[12] where he pointed out that ACPA remains the specific and sensitive biomarker of the active stage of the disease. Aletaha *et al*.,[13] Virginia *et al*.,[14] Shyam *et al*.,[15] and Yunye *et al*.[16] recruited patients with active disease of <1 year duration with DAS 28 >5.1 and explained that SNHL with cochlear involvement is very common.[13] This study is similar to our study which included active disease of <1 year. Emamifar *et al*.[7] have explained that patients with active RA are more prone to develop SNHL and also revealed that the hair cells are affected sub clinically in active disease with the risk of hearing impairment in future. Similar trend was observed in our study proved by OAE test. Takatsu *et al*. and [3] Kumar *et al*.[17] have described that the hair cells are damaged by the oxidative process in RA by the deposition of immune complexes and inflammatory cytokines like IL-6 which are released during active disease and results in SNHL. Immune-mediated SNHL occurs in 25.2–60% as defined by Magaro *et al*.[18]

OAE is an important test for the evaluation of cochlear function.[19] Kemp has explained that OAE's play an important role in screening and diagnosis of hearing loss due to hair cell dysfunction at an earlier stage to prevent functional disability.

## CONCLUSION

The study shows that cochlear hair cells are affected in the active stage of RA, which is confirmed by ACPA titer. Screening with OAE test can identify subclinical hearing defects. Early diagnosis and intervention with antioxidants, intratympanic steroids, vasodilators, etc., may preserve the hair cells thus preventing hearing disability promising a better quality of life in the society for these patients.

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