

Subject Area: Rheumatology and Rehabilitation

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Abeer H. Ismaiel

*Mataria Teaching Hospital, abeerhussein2@yahoo.com*

Ahmad M. A. Gawad

*Mataria Teaching Hospital*

Amany F. Hakim

*Mataria Teaching Hospital*

Soha S. Shaaban

*Mataria Teaching Hospital*

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### Recommended Citation

Ismaiel, Abeer H.; A. Gawad, Ahmad M.; Hakim, Amany F.; and Shaaban, Soha S. (2021) "Assessment of auditory dysfunction as an extra-articular manifestation in rheumatoid arthritis using brainstem auditory-evoked potential," *Journal of Medicine in Scientific Research*: Vol. 4: Iss. 4, Article 14.

DOI: [https://doi.org/10.4103/jmisr.jmisr\\_29\\_21](https://doi.org/10.4103/jmisr.jmisr_29_21)

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# Assessment of auditory dysfunction as an extra-articular manifestation in rheumatoid arthritis using brainstem auditory-evoked potential

Abeer H. Ismaiel<sup>a</sup>, Soha S. Shaaban<sup>a</sup>, Amany F. Hakim<sup>a</sup>, Ahmad M.A. Gawad<sup>b</sup>

<sup>a</sup>Department of Physical Medicine Rheumatology and Rehabilitation, Mataria Teaching Hospital, Cairo, Egypt <sup>b</sup>Department of Ear, Nose and Throat, Mataria Teaching Hospital, Cairo, Egypt

## Abstract

### Objectives

The paper aims to study brainstem auditory-evoked potential parameter changes in rheumatoid arthritis (RA) patients, and their relation to the duration of illness, degree of disease activity, functional stage of the disease, and intensity of pain.

### Materials and methods

Control (group 1) comprised 25 healthy female patients of age 50–60 years, while the study group (group 2) comprised 25 female patients with RA of more than 5 years. Proven cases of RA (according to american college of rheumatology (ACR) 2010 criteria) underwent brainstem auditory-evoked potentials. The recording was carried out by using RMS EMG EPMK2. In the RA group, the following parameters were collected: number of painful and swollen joints, intensity of pain in the joints of patients evaluated by a visual analog scale (VAS) of 0–100 mm, speed sedimentation rate, a disease activity index, and functional disability of patients.

### Results

In this study, we found in the right ear, a highly significant difference in mean peak latency of wave I between groups 1 and 2 with ( $P < 0.01$ ); also, there was a significant difference in the mean peak latency of waves IV and V between groups 1 and 2 with ( $P < 0.05$ ). As regards the mean interpeak latency from I to III, there were highly significant differences between groups 1 and 2 with ( $P < 0.01$ ). For the left ear, there was a highly significant difference in mean peak latencies of waves I and V between groups 1 and 2 with ( $P < 0.01$ ), while there was a significant difference in mean peak latency of wave II between groups 1 and 2 with ( $P < 0.05$ ). The mean differences in interpeak latencies of waves I and II and III–V between groups 1 and 2 were highly significant ( $P < 0.00$ ). Estimation of the correlation coefficients for the parameters of brainstem auditory-evoked potential, and the indices of disease activity, showed statistically significant correlations with the functional class and intensity of pain by the VAS. Also, there was a significant correlation between the absolute peak latency of wave I and interpeak latency of waves I–III and disease duration with  $P < 0.05$ .

### Conclusion

The authors conclude that RA causes delayed latencies and alteration of the waves of brainstem auditory-evoked potentials due to hearing affection.

**Keywords:** Autoimmune inner-ear disease, brainstem auditory-evoked potential, rheumatoid arthritis

## INTRODUCTION

Rheumatoid arthritis (RA) is a chronic multisystem disease characterized by inflammatory synovitis, causing progressive irreversible damage to the articular and periarticular structures, usually involving peripheral joints in a symmetric

**Correspondence to:** Abeer H. Ismaiel, MD,  
Department of Physical Medicine Rheumatology and Rehabilitation, Mataria  
Teaching Hospital, Cairo 11762, Egypt  
Tel: 01100765612;  
E-mail: Abeerhussein2@yahoo.com

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Submitted: 07-Apr-2021 Revised: 15-Apr-2021 Accepted: 21-Apr-2021 Published: 11-Dec-2021

**How to cite this article:** Ismaiel AH, Shaaban SS, Hakim AF, A. Gawad AM. Assessment of auditory dysfunction as an extra-articular manifestation in rheumatoid arthritis using brainstem auditory-evoked potential. J Med Sci Res 2021;4:362-8.

### Access this article online

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DOI:  
10.4103/jmsr.jmsr\_29\_21

distribution [1]. The disease onset is most frequent during the fourth and fifth decades of life, with 80% of patients developing the disease between 35 and 50 years of age [2].

Many organ systems could be affected in RA patients, including the auditory system. Sensorineural hearing loss (SNHL), conductive hearing loss (CHL), or mixed type has been recorded in RA patients. Currently, the pathogenesis of hearing disability in RA is not distinctly recognized [3]. RA can involve the incudomalleolar and incudostapedial joints altering the ossicular mechanics in response to static air-pressure modifications. These joints are true diarthroses and therefore subject to the same rheumatic lesions as any other articulation in the body and could make CHL [4].

In addition, RA can produce an autoimmune response to the sensitive cells of the inner ear; the inflammatory cells can enter the cochlea from the circulatory system through the spiral modiolar vein leading to SNHL. SNHL is a collection of common auditory disorders resulting from dysfunction of the inner ear, auditory nerve, or the auditory-processing pathway in the central nervous system [5].

Brainstem auditory-evoked potential (BAEP) is a sensitive and specific method to diagnose retrocochlear hearing loss, demyelination, and other diseases of brain stem, so it is important to be used for early detection of auditory defects associated with RA patients. BAEP are potentials recorded from the ear and vertex in response to a brief auditory stimulation to assess the conduction through the auditory pathway up to the midbrain [6]. Sound is converted into an electrical impulse and passes from the cochlea to the auditory cortex. Any type of hearing alteration, such as conductive or sensorineural, for instance, results in changes on record of this potential. RA is thought to affect the auditory system through different mechanisms causing these different types of Hearing defects (7).

According to the literature, the alterations occur on BAEP record in cases of CHL, where an increase of latency values of waves I, III, and V with normal interpeaks I–III, III–V, and I–V can occur [8]. Also, in other studies, SNHLs in high frequencies of cochlear origin affect the morphology of BAEP waves and retro-cochlear dysfunction [9].

The BAEP is formed by seven waves. I, III, and V are the most visible ones. In relation to the place of origin of these waves, the most accepted classification nowadays is I—distal portion at the brainstem of the hearing nerve, II—proximal portion at the brainstem of the hearing nerve, III—cochlear nucleus, IV—superior olivar complex, V—lateral lemniscus, VI—inferior colliculus, and VII—medial geniculate body [10].

Severe hearing impairment in RA patients is significantly associated with having a hearing-related disability and self-reported communication difficulties [11]. Social and psychological well-being in those patients may be profoundly affected. The auditory system manifestations and complications of RA disease may be prevented or reduced with early detection and effective treatment [12].

## Aim

The paper aims to study BAEP changes in RA patients, and their relation to the duration of illness, degree of disease activity, functional disability, and intensity of pain.

## PATIENTS AND METHODS

The study protocol was approved by the Ethnic Committee of GOTH. Our prospective study included 50 patients selected from an outpatient clinic in Mataria Teaching Hospital. Our participants were divided into two groups: one group that included 25 RA patients was diagnosed on clinical and radiological basis according to ACR/EULAR 2010 classification criteria [13], with mean age of  $50.58 \pm 0.93$  years and disease duration of more than 5 years, and the second group included 25 healthy individuals with mean age of  $49.41 \pm 1.08$  years as the control group. Patients with history of the intake of drugs with known ototoxicity, patients with history of ear discharge and deafness, renal diseases, hepatic diseases, chronic respiratory diseases, diabetes mellitus, uncontrolled hypertension, and pregnant or lactating mothers were excluded.

Full history and clinical examination were done. In the RA group, the following parameters were collected: number of tender and swollen joints, intensity of joint pain evaluated by a visual analog scale (VAS) of 0–100 mm, a disease activity index using Disease Activity Score (DAS28) calculated from number of swollen joints (out of 28) and number of tender joints (out of 28), and erythrocyte sedimentation rate. The score may range from 0 to 9.3, where a DAS28 score less than or equal to 3.2 is mild disease activity; greater than or equal to 3.2 and less than or equal to 5.1 is moderate disease activity; and greater than or equal to 5.1 is severe disease activity [14]. Functional activity of patients was assessed using Health Assessment Questionnaire (HAQ) score [15].

Otological examination in the outpatient clinic in Mataria Teaching Hospital included examination of preauricular region, ear pinna, postauricular region, external acoustic canal, and tympanic membrane.

Both studied groups underwent the study of BAEP.

### Brainstem auditory-evoked potential test (BAEP)

It was conducted using the Intelligent Hearing System (Smart EP windows USB version 3.91) with insert earphones ER-3A. Responses were collected with silver chloride electrodes and were differentially recorded from Cz (active) to the ipsilateral mastoid (reference), with a common grounding electrode placed on the forehead. The patients were instructed to lie comfortably in the supine position and relax to promote a passive recording condition. No other stimulus was used during the tests. Frequency following response recording: the frequency following response was evoked by 1024 sweeps and 60 dBHL tone bursts at 500 Hz using rarefaction polarity, with a 5000- $\mu$ s rise and fall time in a trapezoidal envelope and a 15 000- $\mu$ s duration at a rate of 5.1 per sec. The response

was filtered between 30 and 3000 Hz in a graduated analysis window of 50 msec. The response cycles obtained for the study group were compared with those obtained for the control group. Auditory brainstem response recording: the auditory brainstem response was evoked by 1024 clicks with a 100- $\mu$ s duration using a rarefaction polarity and a rate of 37.1 clicks per sec. A high-pass filter of 100 Hz and a low-pass filter of 3000 Hz were used on a 12.5-msec graduated window of analysis. Waveforms were obtained in both ears at 70 dBHL, and waves I, III, and V were identified. The absolute latencies of waves I, III, and V and interpeak latencies I–III, III–V, and I–V were obtained and compared between the study and control groups.

**Statistical analysis**

All tabulated data were expressed as mean  $\pm$  SD. Comparisons between patients and control groups were done by using Student’s *t* test. For all statistical tests, significance was done using the correlation coefficient (*r*) test in which significance is defined as the level of probability “*P*” value of < 0.05. Computations were done using an SPSS statistical program version 12 and graphs were assessed using Microsoft excel XP version.

**RESULTS**

We studied 25 healthy females as a control group and 25 rheumatoid patient groups (23 were females and 2 were males) with mean disease duration of 11.2  $\pm$  3.6. Both groups were with mean age of 54.1  $\pm$  2.4 and 54.0  $\pm$  3.1 years, respectively, with no statistically significant difference (*P* = 0.091).

The results of tests of functional ability of the patients (RA group) using the HAQ showed average values of 2.82  $\pm$  0.56, and the average disease activity (DAS28) was 3.18  $\pm$  0.85 [Table 1]. Sixteen (64%) patients had moderately active disease, while nine (36%) had highly active disease. In total, 12 (48%) RA patients had pain intensity on the VAS scale greater than 50 mm [Table 1].

In our study, we found that the frequency of altered BEAP is 45 ears (90%) of RA patients studied with delayed latency of wave I in 22 (44%), of wave II in 8 (16%), of wave III in 8 (16%), of wave IV in 7 (14%), and of wave V in 9 (16%). It decreased the amplitude of wave Ia in 24 (48%) and of wave Va in 45 (90%) of RA patients. It also increased interpeak latency between III and V in 25 (50%) and in 10 (20%) of RA patients. There is a statistically significant difference in the frequencies of all BEAP parameters between control and RA groups with *P* > 0.05.

In our study, we found in the right ear, a highly significant difference in peak latency of wave I in groups 1 and 2 with (*P* < 0.01), as seen in Table 1. Also, there was a significant difference in the peak latency of waves IV and V of groups 1 and 2 with (*P* < 0.05). While for the rest of the waves, it was insignificant with (*P* > 0.05). There were significant differences in the amplitudes of waves I—aI and V—aV in groups 1 and 2, with *P* < 0.05 [Table 2].

**Table 1: Values of the estimates of disease activity in the rheumatoid arthritis group**

Indices of disease activity	Mean $\pm$ SD
Disease duration (y)	11.2 $\pm$ 3.6
Disease activity (DAS28)	4.18 $\pm$ 0.85
HAQ	2.82 $\pm$ 0.56
Intensity of pain (VAS) mm	46.51 $\pm$ 11.92

DAS28, Disease Activity Score; HAQ, Health Assessment Questionnaire; VAS, visual analog scale.

**Table 2: Comparison between rheumatoid arthritis patients and controls according to the latencies of right (RT) ear**

RT ear latency	Control group <i>n</i> = 25	Patients’ group <i>n</i> = 25	<i>P</i>	Sig.
Wave I				
Mean $\pm$ SD	1.38 $\pm$ 0.39	1.82 $\pm$ 0.28	0.000	HS
Range	1-1.88	1.5-2.15		
Wave II				
Mean $\pm$ SD	2.85 $\pm$ 0.06	2.77 $\pm$ 0.23	0.089	NS
Range	2.8-3	2.2-3.08		
Wave III				
Mean $\pm$ SD	3.92 $\pm$ 0.11	4.00 $\pm$ 0.49	0.449	NS
Range	3.8-4.08	3-5.2		
Wave IV				
Mean $\pm$ SD	5.11 $\pm$ 0.06	5.30 $\pm$ 0.44	0.030	S
Range	5-5.1	4.72-6.1		
Wave V				
Mean $\pm$ SD	5.75 $\pm$ 0.04	6.06 $\pm$ 0.63	0.018	S
Range	5.7-5.8	5.43-6.7		
Amplitude I—Ia ( $\mu$ v)				
Mean $\pm$ SD	0.28 $\pm$ 0.14	0.18 $\pm$ 0.03	0.04	S
Range	0.14-0.42	0.15-0.21		
Amplitude V—Va ( $\mu$ v)				
Mean $\pm$ SD	0.47 $\pm$ 0.2	0.32 $\pm$ 0.23	0.03	S
Range	0.27-0.67	0.09-0.55		

*P* > 0.05: nonsignificant (NS). *P* < 0.05: significant (S). *P* < 0.01: highly significant (HS). \*Independent t-test.

The mean differences in interpeak latencies of waves (I–III) of groups 1 and 2 were highly significant (*P* < 0.00) (Table 3, Figs 1 and 2).

In the left ear, there was a highly significant difference in mean peak latencies of waves I and V of groups 1 and 2 with (*P* < 0.01), while there was a significant difference in mean peak latency of wave II of groups 1 and 2 with (*P* < 0.05), but for rest of the waves, there was an insignificant difference in the mean peak latencies with (*P* > 0.05). There were insignificant differences in the amplitudes of all waves I—aI and V—aV in groups 1 and 2 with *P* > 0.05 (Table 4, Fig. 3).

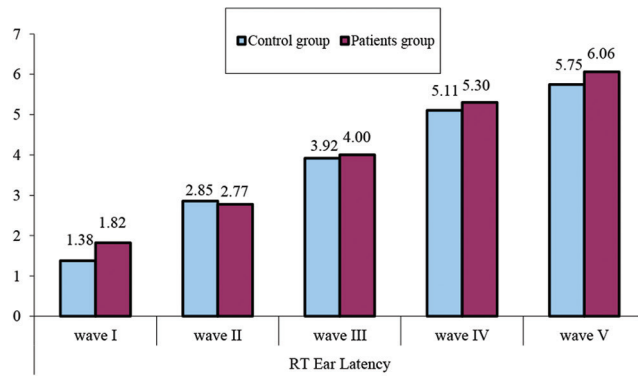
The mean differences in interpeak latencies of waves (I–III) and (III–V) of groups 1 and 2 were highly significant (*P* < 0.00) (Table 5, Fig. 4).

There is a significant positive correlation between disease duration and peak latency of wave I and interpeak latency

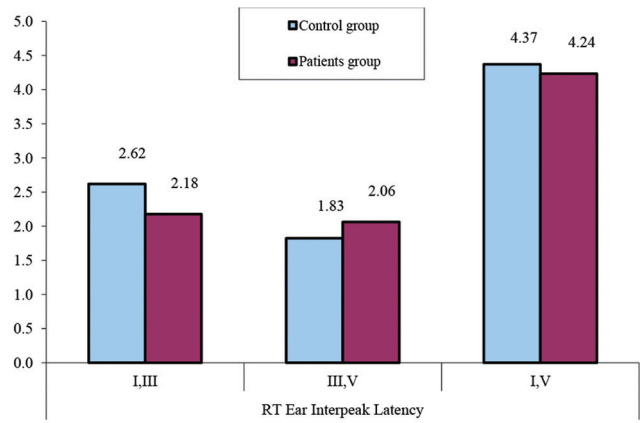
**Table 3: Comparison between rheumatoid arthritis patients and controls according to the interpeak latencies of right (RT) ear**

RT ear interpeak latency	Control group n=25	Patients' group n=25	P	Sig.
I, III				
Mean±SD	2.18±0.47	2.62±0.53	0.003	HS*
Range	1.9-3.87	1.7-3.45		
III, V				
Mean±SD	1.83±0.14	2.06±0.75	0.129	NS
Range	1.62-1.95	1.1-3.5		
I, V				
Mean±SD	4.37±0.40	4.24±0.76	0.430	NS
Range	3.87-4.8	3.1-5.8		

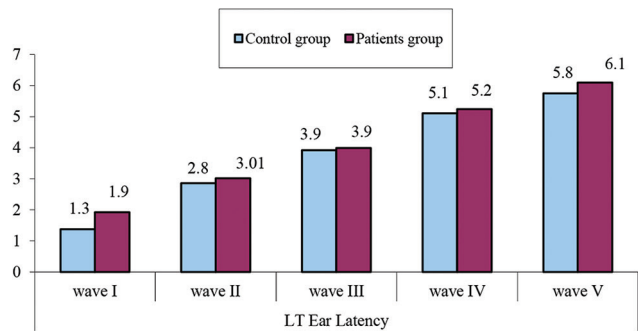
\*High significant correlation. P>0.05: nonsignificant (NS). P<0.05: significant (S). P<0.01: highly significant (HS).



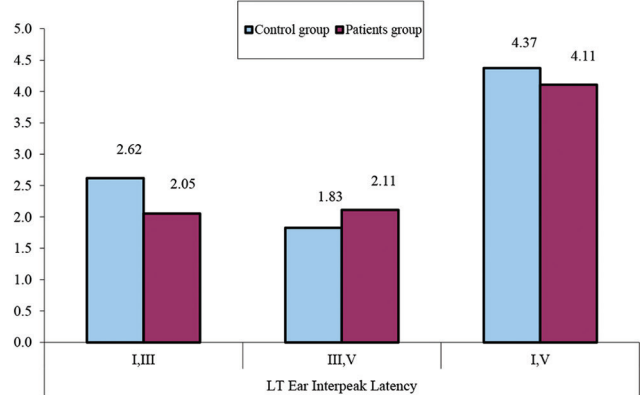
**Figure 1:** Comparison between rheumatoid arthritis patients and controls according to the latencies of right ear.



**Figure 2:** Comparison between interpeak latencies of RT ear in RA patients.



**Figure 3:** Comparison between rheumatoid arthritis patients and controls according to the latencies of left ear.



**Figure 4:** Comparison between interpeak latencies of LT ear RA patients.

of waves I–III with ( $r = 0.47^*$  and  $-0.65^*$ , respectively, and  $P > 0.05$ ). Also, there are statistical significant correlations between BEAP-studied parameters and DAS28, functional activity (HAQ), and pain severity (VAS), with  $P > 0.05$ , as shown in Table 6.

**DISCUSSION**

RA is a systemic inflammatory autoimmune disease of unknown etiology that affects ~ 1% of the worldwide population. Females are more commonly affected than males, usually between 30 and 50 years of age [16]. RA

is characterized by the presence of chronic symmetric polyarthritis of mainly the small joints that leads to progressive irreversible damage of articular and periarticular structures, deformities, and functional impairment, and inversely affect the quality of life [17].

RA may affect many-body systems, including heart, lung, skin, and eye. In this regard, the possibility of auditory system

contention in RA has been one of the domains with great concern. Raut *et al.*[18] studied 35 patients with RA with 35 age- and sex-matched controls to assess the relation between RA and hearing disability; the finding revealed a considerable hearing disability at 500 Hz, 1.0 kHz, and 2.0 kHz in patients with RA.

**Table 4: Comparison between rheumatoid arthritis patients and controls according to the latencies and amplitudes of left (LT) ear**

LT ear latency	Control group	Patients' group	P	Sig.
Wave I				
Mean±SD	1.3±0.39	1.92±0.25	0.00	HS
Range	1-1.88	1.45-2.2		
Wave II				
Mean±SD	2.86±0.06	3.01±0.30	0.01	S
Range	2.8-3	2.4-3.5		
Wave III				
Mean±SD	3.92±0.11	3.99±0.37	0.38	NS
Range	3.8-4.08	3.55-5.08		
Wave IV				
Mean±SD	5.11±0.06	5.24±0.41	0.11	NS
Range	5-5.2	4.72-6.1		
Wave V				
Mean±SD	5.8±0.04	6.10±0.50	0.00	HS
Range	5.7-5.8	5.33-6.60		
Amplitude I—Ia (µV)				
Mean±SD	0.29±0.11	0.25±0.10	0.06	NS
Range	0.18-0.40	0.15-0.35		
Amplitude V—Va (µV)				
Mean±SD	0.43±0.23	0.39±0.23	0.23	NS
Range	0.20-0.66	0.17-0.62		

P>0.05: nonsignificant (NS). P<0.05: significant (S). P<0.01: highly significant (HS). \*Independent t-test.

After exposure of the inner ear in RA patients to either local or systemic immunization of the antigen, this will generate immune responses through the inflammatory cells entering the scala tympani through the spiral modiolar vein and causing labyrinthitis. The ensuing labyrinthitis results in physiologic dysfunction, loss of sensory cells, and ultimately fibrosis and osteoneogenesis within the cochlea [19].

The incudomalleolar and incudostapedial joints are synovial in type. These joints can be affected by rheumatoid changes. Autoimmune ear injury can involve the auricle, external auditory canal, middle ear, and the inner ear. Inner-ear involvement is termed autoimmune inner-ear disease (AIED) [20].

McCabe defined AIED as a rapidly progressive (weeks to months) bilateral SNHL that responds to the administration of immunosuppressive agents [21].

The aim of our study is to study the role of BAEP in early detection of the sub clinical cases of auditory dysfunction in RA patients and the correlation between BAEP parameters and disease duration and activity.

In our study, we found that the frequency of altered BEAP is detected in 45 ears (90%) of RA patients studied with delayed latency of wave I in 22 (44%), of wave II in 8 (16%), of wave III in 8 (16%), of wave IV in 7 (14%), and of wave V in 9 (16%). It decreased the amplitude of wave Ia in 24 (48%) and of wave Va in 45 (90%) of RA patients. It increased the interpeak latency between III and V in 25 (50%), and in 10 (20%) of RA patients. There is a statistically significant difference in the frequencies of all BEAP parameters between control and RA groups with P > 0.05.

Our results were in agreement with those of other studies where they confirmed that SNHL has been reported as the

**Table 5: Comparison between rheumatoid arthritis patients and controls according to interpeak latencies of left (LT) ear**

LT ear interpeak latency	Control group		Patients' group	Test value	P	Sig.
	N=25					
I-III	Mean±SD	2.62±0.53	2.05±0.38	4.366	0.000	HS
	Range	1.9-3.87	1.55-3			
III-V	Mean±SD	1.83±0.14	2.11±0.39	-3.487	0.001	HS
	Range	1.6-2	1.4-2.8			
I-V	Mean±SD	4.37±0.40	4.11±0.71	1.623	0.111	NS
	Range	3.87-4.8	1.68-5.45			

P>0.05: nonsignificant (NS). P<0.05: significant (S). P<0.01: highly significant (HS). \*Independent t-test.

**Table 6: Correlation of disease duration, disease activity index, functional activity, and VAS scores with the BAEP studied parameters**

Indices of disease activity	Wave I r P		Wave III r P		Wave V r P		I-III r P		III-V r P		I-V r P	
Duration	0.47*	0.01	-0.25	0.21	-0.16	0.42	-0.65*	0.0	0.03	0.8	-0.3	0.07
DAS28	0.44	0.02	0.47	0.01	-0.38	0.05	0.031	0.88	-0.38	0.05	0.47	0.01
HAQ	-0.42	0.02	-0.231	0.26	-0.16	0.43	0.47	0.01	0.03	0.88	-0.6*	0.0
VAS	-0.38	0.05	0.44	0.02	-0.38	0.05	-0.14	0.48	0.42	0.02	-0.6*	0.0

0.05+significant. BAEP, brainstem auditory-evoked potential; DAS28, Disease Activity Score; HAQ, Health Assessment Questionnaire; VAS, visual analog scale.

most common hearing impairment in RA, with a prevalence of ~12–80%, following by CHL and mixed hearing loss [22].

Özcan *et al.* [23] investigated hearing- and middle-ear functions in 37 patients with RA and 35 controls to study the prevalence and the nature of hearing loss in RA. The results of this study showed a higher prevalence of an abnormal tympanogram in RA patients. In 1980, Reiter *et al.* [24] measured the middle-ear immittance in RA patients. In their study, immittance data disclosed abnormal discoveries in 59% of the patients. The discrepancies between these findings may be due to differences in the mean age and the number of samples.

In our study of the right ear, we observed significant delay in absolute peak latency of waves I, II, and V of BAEP with ( $P < 0.00$ ), and in the left ear, we observed significant delay in absolute peak latency of waves I, IV, and V when RA patients were compared with controls, which is in agreement with the study of Shelja *et al.* [25], who showed that in the right ear, the difference in the absolute peak latency of wave III of groups 1 and 2 was significant, while for the rest of the waves, it was insignificant. In the left ear, the difference in absolute peak latency of waves I, IV, and V of groups 1 and 2 was significant, while for the rest of the waves, it was insignificant ( $P > 0.05$ ). The differences in interpeak latencies (I–III, III–V, and I–V) were insignificant ( $P > 0.05$ ), when controls were compared with RA patients.

Our findings were confirmed by other authors, where auditory brainstem responses (ABRs) were recorded using 105-dB click stimulation, they found a statistically significant increase in the wave I latency of ABRs in RA patients compared with controls. They evaluated the prevalence and features of hearing impairment in 28 RA patients [26].

In our study of the right ear, there were significant differences in the amplitudes of waves I—aI and V—aV in RA patients compared with controls, with  $P < 0.05$ . The mean differences in the interpeak latencies of waves (I–III) between both groups were statistically significant. In the left ear, there were insignificant differences in the amplitudes of all waves I—aI and V—aV between both groups with  $P > 0.05$ . The mean differences in the interpeak latencies of waves (I–III) and (III–V) between both groups were highly significant ( $P < 0.00$ ).

Similar results were observed in other studies where they found that in the right ear, there was no significant ( $P > 0.05$ ) change in interpeak latencies I–III, III–V, and I–V when controls were compared with RA patients. There was no significant ( $P > 0.05$ ) change in the amplitude of I—Ia and V—Va when controls were compared with RA patients. In the left ear, there was a significant ( $P < 0.05$ ) change in the amplitude of I—Ia in the left ear when controls were compared with RA patients. There was an insignificant ( $P > 0.05$ ) change in the amplitude of V—Va when controls were compared with RA patients [25].

In our study, there was a significant correlation between the disease duration of RA patients and hearing affection, which is

similar to the study of Ozturk *et al.* [3], where they determine a positive significant correlation between disease duration and mean hearing threshold value in the left-ear studies.

Controversially, Arslan *et al.* in 2011 [27] examined the relation between the incidence of hearing loss and duration of disease in 44 RA patients with mean age of  $47.2 \pm 11.2$ . The results of this study showed no relation between the incidence of hearing loss and duration of disease.

Also, in 2016, the authors investigated hearing in RA population. They carried out their study on fifty-three patients with RA and 71 patients with an indigenous condition of health who were matched for age and sex. In their study, no correlation was found between those diagnosed with SNHL using PTA and the duration of the disease [20]. The discrepancies between these findings may be due to differences in the mean age and the number of samples.

In our study, there are statistical significant correlations between BEAP-studied parameters and disease-activity score DAS28, functional activity (HAQ), and pain severity (VAS), with  $P > 0.05$ .

A significant association, especially at high frequencies, between hearing impairment and disease activity, was detected in a study by Yildirim *et al.* [28], where the audiometric results of 62 patients with active disease were compared with 26 patients in remission. DAS28-C-Reactive Protein (DAS28-CRP) was measured based on a count of 28 tender joints, 28 swollen joints, patients' global assessment, and laboratory results of CRP, which is widely used in clinics.

## CONCLUSION

In conclusion, the present study showed that the frequency of hearing affection in the RA group was significantly more than the control group. RA causes increased latencies of the waves of BAEP. Therefore, the disease could directly interfere in neurotransmission of the auditory pathway or indirectly through altering certain processes that modulate brainstem auditory activity. Accordingly, audiological assessment should be considered in routine evaluation of patients with RA, to prevent hearing-related handicap.

## Conflicts of interest

None.

## REFERENCES

1. Lipsky PE. Rheumatoid arthritis. In: Fauci AS, Kasper DL, Braunwald E, Hauser SL, Longo DL, Jameson JL, editors. *Harrison's principles of internal medicine*. 17<sup>th</sup> ed. New Delhi: McGraw Hill; 2008. pp. 2083-2088.
2. Colletti V, Fiorino FG, Bruni L, Biasi D. Middle ear mechanics in subjects with rheumatoid arthritis. *Audiology* 1997; 36:136-146.
3. Oztürk A, Yalçın S, Kaygusuz I, Sahin S, Gök U, Karlıdağ T, *et al.* *Am J Otolaryngol*. 2004;25:411-7.
4. Emamifar A, Hansen IM. An update on hearing impairment in patients with rheumatoid arthritis. *J Otol* 2018; 13:1-4.
5. Hurley RM, Sells JP. Autoimmune inner ear disease. *Am J Audiol* 1997; 6:22-30.

6. Martini WH, Pratt H, Schwegler JW. The origin of the human auditory brainstem response wave II. *Electroencephalogr Clin Neurophysiol* 1995; 96:357-370.
7. Huang CM, Chen Hg, Huang DH, Tsay GI, Lan JI, Sung FC, *et al.* Retrospective cohort study on risk of hearing loss in patients with rheumatoid arthritis using claims data. *BMJ Open* 2018; 8:e018134.
8. Matas CG. Medidas eletrofisiológicas da audição. Audiometria de tronco encefálico. Em: Carvalho RMM, organizadora. Fonoaudiologia informação para a formação – Procedimentos em Audiologia. 1<sup>st</sup> ed. Rio de Janeiro: Guanabara Koogan; 2003. pp. 43–57
9. Watson DR. A study of the effects of cochlear loss on the auditory brainstem response (ABR) specificity and false positive rate in retrocochlear assessment. *Audiology* 1999; 38:155-164.
10. Möller AR, Janneta P, Bennet M, Möller MB. Intracranially recorded responses from human auditory nerve: new insights into the origin of brainstem evoked potentials. *Electroencephalogr Clin Neurophysiol* 1981; 52:18-27.
11. Dalton DS, Crwckshanks KJ, Klein BG, Klein R, Wiley TL, Nondahl DM, *et al.* The impact of hearing loss on quality of life in older adults. *Gerontologist* 2003; 43:661-668.
12. Theander L, Nyhall- Wahlin BM, Nilsson JA, Willim M, Jacobsson LT, Petersson IF, *et al.* Severe extra-articular manifestations in a community- based cohort of patients with rheumatoid arthritis. Risk factors and incidence in relation to treatment with tumor necrosis factor inhibitors. *J Rheumatology* 2017; 44:981-987.
13. Aletaha D, Neogi T, Silman A, Fanovites J, Felson DT, Bingham CO III, *et al.* 2010 rheumatoid arthritis classification criteria: an American college of Rheumatology/European League Against Rheumatism Collaborative Initiative. *Arthritis Rheum* 2010; 62:2569-2581.
14. Bruce B, Fries JF. The Stanford Health Assessment Questionnaire: a review, history, issues, progress, and documentation. *J Rheumatol* 2003; 30:167-178.
15. Prevo ML, van't Hof MA, Kuper HH, van Leeuwen MA, van de Putte LB, van Riel PL. Modified disease activity scores that include twenty-eight-joint counts. Development and validation in a prospective longitudinal study of patients with rheumatoid arthritis. *Arthritis Rheum* 1995; 38:44–48.
16. Lipsky PE. Rheumatoid Arthritis. In: Fauci AS, Kasper DL, Braunwald E, Hauser SL, Longo DL, Jameson JL, editors. *Harrison's principles of internal medicine*. 17<sup>th</sup> ed. New Delhi McGraw Hill; 2008. p. 2083-8.
17. Alamanos Y, Drosos AA. Epidemiology of adult rheumatoid arthritis. *Autoimmun Rev* 2005; 4:130-136.
18. Raut VV, Cullen J, Cathers G. Hearing loss in rheumatoid arthritis. *J Otolaryngol* 2001; 30:289-294.
19. Harris JP, Woolf NK, Ryan AF. Elaboration of systemic immunity following inner ear immunization. *Am J Otolaryngol* 1985; 6:148.
20. Lasso de la Vega M, Villarreal IM, Lopez-Moya J, Garcia-Berco J. Examination of hearing in a rheumatoid arthritis population: role of extended-high-frequency audiometry in the diagnosis of subclinical involvement. *Scientifica* 2016; 2016:571383.
21. McCabe BF. Autoimmune sensorineural hearing loss. *Ann Otol Rhinol Laryngol* 1979; 88:585-589.
22. Kiakojuri K, UousefGhahari B, Soltanparast S, Monadi M. Hearing status in patients with rheumatoid arthritis. *Caspian J Intern Med* 2019; 10:447-451.
23. Özcan M, Karakuş FM, Gündüz O, Tuncel Ü, Şahin H. Hearing loss and middle ear involvement in rheumatoid arthritis. *Rheumatol Int* 2002; 22:16-19.
24. Reiter D, Konkle DF, Myers AR, Schimmer B, Sugar JO. Middle ear immittance in rheumatoid arthritis. *Arch Otolaryngol* 1980; 106:114-117.
25. Shelja D, J Yadav., J Gulia., H Singh, A Arvind. Rheumatoid arthritis affects brainstem auditory evoked potential. *Int J Basic Appl Physiol* 2015; 4:1.
26. Salvinelli F, D'Ascanio L, Casale M, Vadacca M, Rigon A, Afeltra A. Auditory pathway in rheumatoid arthritis. A comparative study and surgical perspectives. *Acta Otolaryngol* 2006; 126:32-36.
27. Arslan N, Cicek Y, Islam A, Ureten K, Safak MA, Oguz H. Involvement of ear in rheumatoid arthritis. Prospective Clinical Study. *Int Adv Otol* 2011;7:208-14.
28. Yildirim A, Surucu G, Dogan S, Karabiber M. Relationship between disease activity and hearing impairment in patients with rheumatoid arthritis compared with controls. *Clin Rheumatol* 2016; 35:309e314.