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Hearing disorders in lupus patients: correlation with duration and severity of the disease

Saad Mahmoud Alzokm^{1*} and Soliman S. Ghanem²

Abstract

Background: Hearing loss can greatly affect the overall quality of life. Several studies have reported that patients with SLE may suffer from audio-vestibular manifestations. The aim of this study is to evaluate the influence of systemic lupus erythematosus (SLE) on hearing and association of hearing impairment with severity and duration of SLE.

Results: Pure-tone audiometry (PTA) (air conduction and bone conduction) thresholds showed significant elevation in SLE group than controls ($P \leq 0.05$). It was observed also that there is a significant association between SLE severity and duration with sensorineural hearing loss (SNHL) and its degree.

Conclusion: SLE can lead to hearing loss, and there is a positive association of SLE severity and duration with degree of hearing loss.

Keywords: Systemic lupus, Audiometry, Hearing loss

Background

Hearing is a vital sensation for people. It assists with getting the general climate and can alarm of any approaching risk around us. Hearing is a fundamental method for communication. Hearing loss can affect learning and advancement in kids, including speech and language. In adults, hearing loss can incredibly influence the general personal satisfaction. In conductive hearing loss (CHL), vibrations cannot pass from the external ear to the inner ear. In sensorineural hearing loss (SNHL), there is brokenness in the internal ear. In mixed hearing loss, there is a mix of conductive and sensorineural parts. Toward the end of the internal ear (cochlea), a great many auditory nerve strands distinguish the high and low sound frequencies and send action potentials to the cerebrum, which deciphers the sign as sound [1] (Table 1).

Systemic lupus erythematosus (SLE) is an autoimmune disease that affects more than one organ (non-organ specific) with incidence of up to 39 per 100,000 people in general [3]. SLE affect mainly female; female to male ratio is 9: 1 [4], more common in Asians and Africans than Europeans (3:1) and commonly affect age group from 20 to 45 years old [5].

It has been suggested that immunologic processes may involve inner ear [6, 7]. It is also true for SLE too. Several studies have also shown the effect of SLE in the inner ear [3, 8, 9]. Kastanioudakis et al. [10] and Sperling et al. [11] have reported that patients with SLE may suffer from audio-vestibular manifestations. In the majority of cases, hearing loss is unilateral. The pathophysiology is unclear, genetic predisposition; exogenous factors as drug, virus, or ultraviolet rays may initiate the disease. Vascular or autoimmune etiology has been proposed in 10% of cases [12].

Some studies proposed a number of mechanisms as vasculitis, drugs toxicity, free radical formation in vessels of cochlea, and thrombosis in the vessels of the ear due to anti-phospholipid syndrome [13, 14].

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Table 1 Degree of hearing loss based on the hearing threshold

| Degree of hearing loss | Hearing threshold (dB HL) |
|------------------------|---------------------------|
| Normal hearing | −10–15 |
| Slight | 16–25 |
| Mild | 26–40 |
| Moderate | 41–55 |
| Moderately severe | 56–70 |
| Severe | 71–90 |
| Profound | > 91 |

Source [2]: Clark JG: Uses and abuses of hearing loss classification. *ASHA*. 1981, 23:493–500

The aim of this study was to evaluate the influence of SLE, duration, and severity on hearing in patients with SLE.

Methods

This cross-sectional survey design study was conducted on ninety-eight (98) patients diagnosed with SLE according to Systemic Lupus International Collaborating Clinics (SLICC) classification criteria 2012 [11]. These patients represent the study group (1). Another group consisted of twenty (20) normal healthy adult subjects with normal hearing threshold according to the American National Standards Institute (ANSI) (1969) was selected from relatives accompanying patients represent the control group. The age of both groups ranged from 20 to 40 years and represented both genders.

All patients and controls were selected from patients attending the internal medicine and rheumatology clinics, university hospital from May 2018 to August 2019.

The study protocol was approved in 13/4/2018, by the local ethics and research committee of Faculty of Medicine (registration number IRB 00012367-18-04-002), and an informed written consent was signed by each patient before inclusion in the study.

Normal otoscopic finding, normal hearing threshold, and normal middle ear functions as evidenced by tympanometry and acoustic reflex were included, while patients with history of ear diseases (hearing loss, noise exposure, ototoxic drug intake, head trauma, and others), and history of medical systemic diseases, e.g., any rheumatic diseases, diabetes mellitus, hypertension, smoking, renal, and cardiovascular diseases, were excluded from the study.

Instrumentation

1. Sound treated room locally made according to international specifications

2. Audiometry, Interacoustics, Model AD229b, Denmark, calibrated according to ANSI standards
3. Immittance meter, Interacoustics, model AT 235 middle ear analyzer, Denmark, ISO standards

Methods

Participants of both groups were subjected to the following:

1. Full history taking to exclude history of systemic diseases, noise exposure, ototoxic drug intake, and family history of hearing impairment
2. Otological examination
3. Basic audiological evaluation of both ears for every participant in the study, which includes the following:

- a. Pure-tone audiometry (PTA) from 250 to 8000 Hz for air conduction and from 500 to 4000 Hz for bone conduction in octave steps. The air conduction stimulus was delivered via supra-aural headphone model TDH 39P. The bone conduction was delivered via bone conduction vibrator model B71. Accordingly, the three main types of hearing loss are classified as conductive (CHL), sensorineural (SNHL), and mixed hearing losses. CHL is usually associated with dysfunction located in the outer and/or middle ear while having a normal inner ear function. In CHL, the audiogram typically shows normal bone conduction (0–25 dB) and abnormal air conduction threshold levels (higher than 25 dB) [15]. SNHL is a hearing loss that occurs as a result of damage in the cochlea or beyond, that is, either along the 8th cranial nerve or in the brain. SNHL can cause complete loss of hearing, despite the outer ear and middle ear being normal. Individuals with SNHL demonstrate similar air and bone conduction thresholds [1]. Mixed hearing loss is a type of hearing loss that has a combination of conductive and sensorineural damage in the same ear [1].

Hearing loss can be classified according to the severity or degree of the disease. Hearing losses between 26 and 40 dB are considered mild, 41 and 55 dB moderate, 56 and 70 dB moderately severe, 71 and 90 dB severe, and greater than 91 dB profound [2, 16].

- b. Speech audiometry includes the following:
 - Speech reception threshold (SRT) using Arabic spondee words

Table 2 Demographic characteristics of the studied groups

| | SLE group (1) N = 98 | | Control group (2) N = 20 | | Test of significance | |
|-----------------|-------------------------|----------|-----------------------------|----------|----------------------|--------|
| | No. | % | No. | % | χ^2 | P |
| Gender | | | | | | |
| Males | 16 | 16.33 | 5 | 25.0 | 0.632 | 0.002* |
| Females | 82 | 83.67 | 15 | 75.0 | 0.293 | 0.042* |
| Total | 98 | 100 | 20 | 100 | | |
| Age (years): | Mean | \pm SD | Mean | \pm SD | t-test | P |
| • Mean \pm SD | 34.8 | 5.69 | 33.8 | 4.97 | 0.0015 | 0.869 |
| • Range | Min | Max | Min | Max | | |
| | 20 | 40 | 20 | 40 | χ^2 | P |
| Smoking: N (%) | 38 | 38.77 | 7 | 35 | 0.056 | 0.164 |

χ^2 , chi-square test; $P \leq 0.05$, significant. SLE systemic lupus erythematosus

- Speech discrimination scores using Arabic phonetically balanced words (PB words)
- c. Impedancemetry which includes the following:
- Tympanometry which was done at pressure range from +200 to –400 mm H₂O)
 - Acoustic reflex threshold elicited ipsilaterally and contra-laterally using frequency range of 500 up to 400 0Hz).
4. Laboratory studies that help in diagnosis and classification of SLE including erythrocyte sedimentation rate (ESR), rheumatoid factor (RF), antinuclear antibody (ANA), anti-double stranded nuclear antibody (anti-DNA), anti-Smith, complete blood count (CBC), urine analysis, aspartate aminotransferase (AST), serum glutamic pyruvic transaminase (SGPT), anticardiolipin, and lupus anticoagulant.
5. The disease severity index was determined for the patients according to the standard criteria with systemic lupus disease activity index (SLEDAI). Mild SLE, SLEDAI 0–5; moderate SLE, SLEDAI 6–12, and severe SLE, > 12 [17].

Statistical analysis

Statistical analyses were completed using SPSS v23 statistical software (SPSS, Inc, Chicago, Illinois). Descriptive statistics (means, standard deviations, frequencies, and correlation coefficients) were calculated for all measures. To compare the two groups, a paired *t*-test was carried out to determine *P*-values using the Pearson's correlation test and a χ^2 test and a one-sample *t*-test and Wilcoxon test performed when appropriate.

F test by analysis of variance(ANOVA) was used to compare between more than two groups. *P* equal or less than 0.05 was considered statistically significant.

Results

The study included 98 SLE patients, 16 males and 82 females represent the patients' group, their ages ranged from 20 to 40 years with a mean \pm SD of 34.8 ± 5.69 years and another 20 apparently healthy subjects, and 5 males and 15 females represent the control group with age ranged from 20 to 40 years and mean \pm SD of 33.8 ± 4.97 years. There is predominance of females in the patients' group ($P = 0.012$), as shown in Table 2. Mean duration of the disease was 6.4 ± 4.4 years.

Measurement of air conduction hearing thresholds of both right and left ears showed significant elevation in SLE compared to control subjects in all frequencies ($P \leq 0.05$) as shown in Table 3.

Measurement of bone conduction hearing thresholds of both right and left ears showed significant elevation in SLE compared to control subjects in all frequencies, and their mains showed ($P \leq 0.05$) as shown in Table 4.

So, the prevalence of hearing loss in SLE patients by air conduction threshold, and bone conduction threshold, were 36.7% and 33.7%, respectively, with an average of 35.7% as reported in Table 5.

Comparison between the SLE disease activity index (SLEDAI) and hearing loss in patients of SLE group showed a significant association between hearing loss and severity of SLE disease ($P = 0.39$) as shown in Tables 6 and 7.

As regard association between duration of SLE disease and SNHL, there is a strong positive association ($r = 0.6395$, $p \leq 0.001$) as shown in Fig. 1.

Table 3 Air conduction hearing thresholds in both groups

| Frequency (Hertz) | SLE group (mean ± SD) | Control group (mean ± SD) | Significance | |
|-------------------|-----------------------|---------------------------|--------------|--------|
| | | | T | P |
| Right ear | | | | |
| 250 | 5.96 ± 3.23 | 1.84 ± 3.47 | 0.5241 | 0.004* |
| 500 | 7.19 ± 2.54 | 1.91 ± 4.61 | 0.6035 | 0.003* |
| 1000 | 9.97 ± 5.24 | 2.24 ± 2.16 | 0.8037 | 0.001* |
| 2000 | 10.67 ± 6.18 | 2.83 ± 3.11 | 0.8122 | 0.001* |
| 4000 | 12.84 ± 6.41 | 3.12 ± 3.09 | 0.9108 | 0.001* |
| 8000 | 14.68 ± 8.44 | 3.69 ± 3.52 | 0.9535 | 0.001* |
| Left ear | | | | |
| 250 | 6.11 ± 4.67 | 1.73 ± 4.75 | 0.5512 | 0.004* |
| 500 | 8.41 ± 7.45 | 2.19 ± 4.13 | 0.6997 | 0.003* |
| 1000 | 9.57 ± 7.18 | 2.95 ± 5.33 | 0.7279 | 0.002* |
| 2000 | 11.92 ± 8.12 | 4.35 ± 5.47 | 0.7989 | 0.002* |
| 4000 | 14.78 ± 6.48 | 4.48 ± 5.19 | 0.9382 | 0.001* |
| 8000 | 15.54 ± 9.21 | 4.79 ± 4.96 | 0.9458 | 0.001* |

*P ≤ 0.05 = significant. SLE systemic lupus erythematosus

Table 4 Bone conduction hearing thresholds in both groups

| Frequency (Hertz) | SLE group (mean ± SD) | Control group (mean ± SD) | Significance | |
|-------------------|-----------------------|---------------------------|--------------|--------|
| | | | t | P |
| Right ear | | | | |
| 250 | 4.72 ± 8.22 | 0.37 ± 3.64 | 0.5362 | 0.004* |
| 500 | 4.24 ± 4.98 | 1.19 ± 4.14 | 0.4564 | 0.005* |
| 1000 | 3.55 ± 3.62 | 2.11 ± 3.95 | 0.2392 | 0.012* |
| 2000 | 2.89 ± 4.41 | 1.67 ± 2.18 | 0.2084 | 0.014* |
| 4000 | 5.12 ± 3.26 | 2.24 ± 3.45 | 0.4391 | 0.005* |
| Mean ± SD | 3.51 ± 3.36 | 1.25 ± 2.64 | 0.4008 | 0.007* |
| Left ear | | | | |
| 250 | 3.53 ± 5.15 | 1.22 ± 4.18 | 0.3769 | 0.008* |
| 500 | 4.11 ± 4.19 | 1.41 ± 7.45 | 0.4282 | 0.006* |
| 1000 | 4.21 ± 5.13 | 2.12 ± 6.68 | 0.3367 | 0.009* |
| 2000 | 4.25 ± 5.44 | 2.23 ± 6.12 | 0.3284 | 0.009* |
| 4000 | 4.44 ± 5.18 | 3.18 ± 7.05 | 0.2174 | 0.013* |
| Mean ± SD | 4.18 ± 4.94 | 2.13 ± 6.65 | 0.3311 | 0.009* |

*P ≤ 0.05 = significant. SLE systemic lupus erythematosus

Discussion

Systemic lupus erythematosus affects mainly females which was presented in our study; this is agreed by many studies [17, 18]. It can affect the inner ear by disrupting either the hearing or balance system. Affection of hearing can be anatomically categorized into conductive, SNHL, and mixed [1].

Auditory disturbance has been reported in 8–66% of patients with SLE [12, 19, 20]. Because of those differences in the reported related studies, the current study was conducted to evaluate auditory disturbance in patients with SLE and its association with severity and duration of the disease.

The current study reported SNHL in all studied frequencies with different degrees (more observed in high frequency) which was observed also by Roverano et al. [18], and Maciaszczyk et al. [19] described bilateral, SNHL in air conduction high frequencies. Khalidi et al. [17] described unilateral SNHL in mid and high frequencies (500 to 3000 Hz) associated with a 16% of word discrimination score recognized by speech audiometry.

In this study, air conduction hearing thresholds showed significant elevation in SLE compared to control subjects in all frequencies. Also, bone conduction hearing thresholds had a significant elevation in SLE compared to control subjects in all frequencies and their mains (P ≤ 0.05). This indicates that there is a great prevalence of hearing loss in SLE patients which was proved by air conduction threshold, and bone conduction threshold was 36.7% and 33.7%, respectively, with an average of 35.7%.

These results were slightly higher than Karatas et al. [17] who reported incidence of hearing loss in 21% of SLE patients, Kastanioudakis et al. [10] reported 21.5%, Abbasi et al. [21] reported incidence of 26.7%, and Maciaszczyk and colleagues [19] reported 28.6% and lower than Roverano et al. [18] who reported an incidence of 66% hearing loss in SLE patients; this big difference may be because Roverano et al. conduct their study on low number of patient, 30 only, but this study is conducted on a higher number, 98 patients. All these studies and this study were opposed by the study of Polanski et al. [22]; although they reported that SLE patients had more SNHL than controls, no conductive

Table 5 Prevalence of SNHL in SLE patients (N = 98)

| Prevalence of SNHL | Yes | | No | | Significance | |
|---------------------------|-----|------|----|------|----------------|---------|
| | N | % | N | % | χ ² | P-value |
| Air conduction threshold | 36 | 36.7 | 62 | 63.3 | 11.713 | 0.000* |
| Bone conduction threshold | 33 | 33.7 | 65 | 66.3 | 14.249 | 0.000* |
| Prevalence of SNHL | 35 | 35.7 | 63 | 67.3 | 14.249 | 0.000* |

χ², chi-square test, *P ≤ 0.05 = significant. SNHL sensorineural hearing loss. SLE systemic lupus erythematosus

Table 6 Comparison between the SLE disease activity index (SLEDAI) and SNHL in SLE patients ($N = 98$)

| SNHL | Mild SLEDAI (≤ 6) = 34 | | Moderate SLEDAI (7–12) = 35 | | Severe SLEDAI (> 12) = 29 | | F-test | P-value |
|------|-------------------------------|-------|-----------------------------|-------|-------------------------------|-------|--------|---------|
| | N | % | N | % | N | % | | |
| Yes | 0 | 0.0 | 12 | 34.28 | 23 | 79.31 | 0.193 | 0.039* |
| No | 34 | 100.0 | 23 | 65.71 | 6 | 20.68 | | |

* $P \leq 0.05$ = significant. SLEDAI systemic lupus erythematosus disease activity index. SNHL sensorineural hearing loss

Table 7 Degree of hearing loss in SLE and control groups

| Degree of hearing loss | SLE group $N = 98$ | | | | | | Control group $N = 20$ | |
|---------------------------------|-------------------------------|-------|-----------------------------|-------|-------------------------------|-------|------------------------|------|
| | Mild SLEDAI (≤ 6) = 34 | | Moderate SLEDAI (7–12) = 35 | | Severe SLEDAI (> 12) = 29 | | N | % |
| | N | % | N | % | N | % | | |
| Normal hearing (–10–15 dB HL) | 34 | 100.0 | 16 | 45.71 | 4 | 13.79 | 18 | 90.0 |
| Slight (16–25 dB HL) | 0 | 0.0 | 7 | 20.0 | 2 | 6.89 | 1 | 5.0 |
| Mild (26–40 dB HL) | 0 | 0.0 | 4 | 11.42 | 6 | 20.68 | 1 | 5.0 |
| Moderate (41–55 dB HL) | 0 | 0.0 | 4 | 11.42 | 11 | 37.93 | 0 | 0.0 |
| Moderately severe (56–70 dB HL) | 0 | 0.0 | 2 | 5.71 | 3 | 10.34 | 0 | 0.0 |
| Severe (71–90 dB HL) | 0 | 0.0 | 1 | 2.85 | 2 | 6.89 | 0 | 0.0 |
| Profound (> 91 dB HL) | 0 | 0.0 | 1 | 2.85 | 1 | 3.44 | 0 | 0.0 |

SLE systemic lupus erythematosus. dBHL decibels hearing level. SLEDAI systemic lupus erythematosus disease activity index

hearing loss was detected in their study. They depend on clinical and serological lupus profile on their study.

It is not conceivable to recognize the patients with hearing loss by the clinical or serological lupus profile. Gad and Abdulateef [23] studied the association between antiphospholipid antibody syndrome and hearing loss in children with SLE. In addition, many case studies associate sudden SNHL in SLE with the presence of autoantibodies [24].

This study compared between the SLEDAI and SNHL in patients of SLE group and found that there is a significant association between SNHL and severity of SLE disease ($P = 0.39$). So, results of current study may imply that SNHL is directly related to the disease severity, which was opposed by Abbasi et al. [21], since SNHL is not related to the severity of the disease. Other mechanism should be taken in mind. More detailed study ought to be designed about the matter to explain the mechanism. If audiologic examination is conducted as soon as the diagnosis was done, more conclusive come about the mechanism and pathophysiology

of SNHL may be achieved. Roverano et al. [22] and Maciaszczyk et al. [19] have found similar results.

SNHL was significantly associated with duration of SLE disease ($r = 0.6395$, $p \leq 0.001$) in this study. This was in agreement with the study of Maciaszczyk et al. [19] which had reported significant positive association between air conduction hearing loss and duration of SLE. Abbasi et al. [21] study was in contrary to these results. They found no association between duration of the disease and hearing threshold; this difference may be that the mean duration of the disease was short duration (4.4 ± 3.3 years) in their study, but in the current study, the mean duration of the disease was longer (6.4 ± 4.4 years). It was emphasized that early detection of hearing loss in SLE is important for proper treatment [22], as the autoimmune etiology may respond to glucocorticoid and immunosuppressive treatment [8].

The limitation of this study was the small sample size of studied patients, so in the future study, we recommend this research to be conducted on more number of patients. Also, auditory evoked potentials to detect

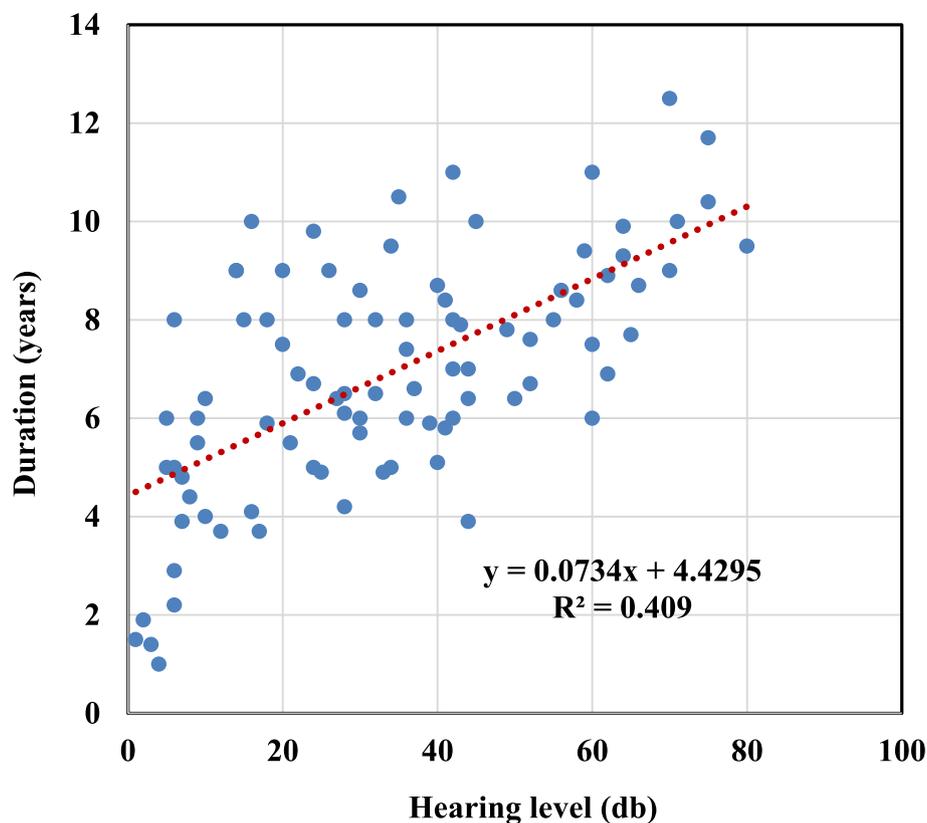


Fig. 1 Correlation coefficient (r) and regression line between duration of systemic lupus erythematosus (SLE) and sensorineural hearing loss (SNHL). There is a strong positive association ($r = 0.6395$, $p < 0.001$)

any demyelinating cause and use MRI and MRA study of temporal area and petrus bone not used in this study because of the high cost, so we recommend in the future study to introduce these investigations to make more evaluations of hearing impairment in cases of SLE.

Conclusions

SLE can lead to hearing loss, and there was positive association of SLE severity and duration with SNHL, so that it is recommended that E.N.T examination and audiometry become a part of routine follow-up visits of SLE patients.

Abbreviations

SLE: Systemic lupus erythematosus; SLICC: Systemic Lupus International Collaborating Clinics; ANSI: American National Standards Institute; PTA: Pure-tone audiometry; SNHL: Sensorineural hearing loss; SRT: Speech reception threshold; SLEDAI: Systemic lupus disease activity index; RF: Rheumatoid factor; ANA: Antinuclear antibody; Anti-DNA: Anti-double stranded DNA; ESR: Erythrocyte sedimentation rate.

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Authors' contributions

SG performed otological examination, pure tone audiometry, speech audiometry, and tympanometry and contributes in writing the manuscript. SZ selected SLE patients from rheumatology clinic, analyzed and interpreted the patient's data, and shared in writing the methods and discussion. All authors read and approved the final manuscript.

Availability of data and materials

The data and materials are all available.

Declarations

Ethics approval and consent to participate

The study protocol was approved in 13/4/2018, by the local ethics and research committee of Al-Azhar Faculty of Medicine, New Damietta (registration number: IRB 00012367-18-04-002), and an informed written consent was signed by each patient before inclusion in the study.

Consent for publication

Not applicable in this research.

Competing interests

The authors declare that they have no competing interests.

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