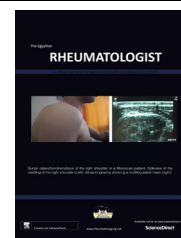




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ORIGINAL ARTICLE

Auditory disorders in patients with systemic lupus erythematosus: Relation to clinical parameters



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KEYWORDS

Systemic lupus erythematosus (SLE);
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 Sensorineural hearing loss (SNHL);
 SLE disease activity index (SLEDAI)

Abstract *Aim of the work:* To evaluate the hearing disorders in SLE patients with particular regard to their frequency and relationship to disease duration and activity.

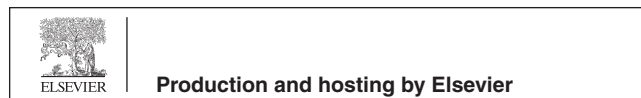
Patients and methods: Twenty female SLE patients were enrolled in the study. Assessment of disease activity was done using the SLE disease activity index (SLEDAI). Another 20 otologically healthy subjects of matched age and sex served as controls. Auditory assessment was performed and included otoscopic examination, pure tone audiometry (PTA), acoustic immittance testing and speech audiometry.

Results: The PTA was abnormal in 13 (65%) patients; 4 had tinnitus and 1 vertigo. The PTA results showed a highly significant statistical difference from the control ($p < 0.001$). Otoscopic examination, acoustic immittance testing and speech audiometry of all patients were normal. A significant difference was found in the age at disease onset between those with and without abnormal PTA ($p = 0.023$). Moreover, there was a significantly lower hearing level (right ear) at 12,000 Hz in juvenile-onset ($N = 6$) (20.83 ± 3.76 db) compared to adult-onset cases (32.5 ± 15.66 db) ($p = 0.02$). No significant difference was present in the audiovestibular manifestations ($p = 0.114$), clinical, laboratory parameters or disease activity between those with or without hearing loss. However, hearing levels were significantly lower in those with lupus nephritis and those receiving hydroxychloroquine.

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Conclusion: Pure tone audiometry revealed SNHL in 65% of SLE patients. Absence of audio-vestibular manifestations does not exclude inner ear affection. Age at disease onset is remarkably associated with hearing loss in SLE. Lupus nephritis and hydroxychloroquine use are associated with lower hearing levels and possible early hearing loss.

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1. Introduction

Systemic lupus erythematosus (SLE) is associated with several comorbidities, including hearing and vestibular disorders [1]. Sensorineural hearing loss (SNHL) is remarkably present in SLE [2]. Different mechanisms leading to SNHL in SLE patients and in those with antiphospholipid syndrome (APS) have been proposed, such as secondary vasculitis, microinfarctions of the capillaries or arterioles in the temporal bone and thrombosis in the otologic region [3]. Hearing loss in SLE may be potentially due to autoimmunity, vasculitis, premature presbycusis and drug ototoxicity [4]. Gazquez et al. [5] showed autoimmunity to be associated with the pathophysiology of Meniere's disease (MD), an inner ear disorder characterized by episodes of vertigo with hearing loss and tinnitus. They found an elevated prevalence of systemic autoimmune disease such as SLE with MD. This finding suggested an autoimmune background in the pathophysiology of hearing loss. In the mouse model of SLE, immunoglobulin G deposits on the thickened basement membranes of capillaries in the stria vascularis and ultimately significant hearing loss (HL) have been reported [6].

In an SLE patient with serous effusion and hemorrhage in both middle ears, the right cochlea, vestibule, semicircular canals and vestibular aqueduct were filled with dense fibrous tissue and new bone formation. The histopathologic examination revealed a dense perivascular accumulation and infiltration of inflammatory cells and vasculitis in the fibrous tissue [7].

Localization of hearing loss in SLE is known as a cochlear lesion but other sites may be also involved. In the work of *Maciaszczyk and his colleagues* [8], an increase of neural conduction was observed in SLE patients compared to controls, which suggested subclinical retrocochlear or central involvement of the auditory pathway.

In the study by *Maciaszczyk et al.* [8] it was found that SLE patients had poorer hearing thresholds than the age-matched controls. Furthermore, *Roverano et al.* [9] showed that 66% of SLE patients revealed an asymptomatic SNHL at high frequencies with statistically significant differences when compared with the control group. Sudden SNHL may be a manifestation of SLE and may have an important impact on the health of these patients [10].

The aim of this study is to evaluate the hearing disorders in patients with SLE with particular regard to their frequency and relationship to disease duration and activity.

2. Patients and methods

Twenty female patients with SLE fulfilling the updated American College of Rheumatology (ACR) revised classification criteria for the SLE [11] were enrolled into the study. Assessment of disease activity was done using the SLE disease activity index (SLEDAI) [12]. The control group consisted of

20 otologically healthy persons matched to the SLE group for age and sex. The patients were selected from the outpatient clinic and inpatient section of Rheumatology and Rehabilitation department, Faculty of Medicine, Cairo University Kasr el Ainy Hospital. An informed consent was obtained from all participants in the study, and the study was approved by the Institutional Review Board (IRB) of faculty of medicine, Cairo University.

Patients or control with any of the following were excluded from the study: Diabetes, uncontrolled hypertension for more than one year duration, history of ototoxicity due to drugs e.g. Aminoglycosides, history of noise exposure e.g. occupational as working in a factory, history of fever which causes affection of hearing e.g. Measles, Mumps, Rubella & Meningitis, history of neurological disease that causes affection of hearing e.g. multiple sclerosis (MS) and a family history of hearing loss.

All patients included in this study were subjected to:

- 1- Comprehensive history taking including auditory symptoms such as hearing loss, tinnitus, vertigo, earache and thorough general and clinical examination of the cardiopulmonary, abdominal, neurological and musculoskeletal systems.
- 2- Routine laboratory investigations including complete blood count (CBC), erythrocyte sedimentation rate (ESR), liver and kidney functions, and urine analysis, in addition to estimation of total albumin in 24 h urine, immunological assays (anti-nuclear antibody; ANA, anti-double stranded deoxyribonucleic acid antibodies; anti-dsDNA, anti-cardiolipin antibodies, and lupus anticoagulants), and serum complement levels (C3 and C4).
- 3- Auditory assessment was done by an audiologist and included the following: otoscopic examination [13], pure tone audiometry (PTA) [14], acoustic immittance testing (tympanometry and acoustic reflex) [15] and speech audiometry [16].

Statistical analysis: Data were statistically described in terms of mean \pm standard deviation (SD), median and range, or frequencies (number of cases) and percentages when appropriate. Comparison of numerical variables between the study groups was done using Student *t* test for independent samples when variables were normally distributed and Mann-Whitney *U* test for independent samples when not normally distributed. For comparing categorical data, Chi square (χ^2) test was performed. Exact test was used instead when the expected frequency is less than 5. *p* values less than 0.05 was considered statistically significant. All statistical calculations were done using computer programs SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 15 for Microsoft Windows.

3. Results

This study included 20 female SLE patients. Their age ranged from 20 to 48 years, with mean age of 28.8 ± 9.36 years. Their age of onset of SLE ranged from 14 to 41 years, with mean age of onset 24.6 ± 9.01 years. Six patients had disease onset before 18. The disease duration ranged from 2 months to 9 years, with mean duration 47.85 ± 34.15 months. The control group included 20 age and sex matched otologically healthy individuals. Their ages ranged from 22 to 49 years, with mean age of 33 ± 8.03 years. There was no statistically significant difference in the median age between the patient and the control groups. The clinical characteristics of the SLE patients are presented in Table 1 and the laboratory features in Table 2.

3.1. Audiovestibular symptoms of SLE patients

4 (20%) patients had tinnitus and 1 (5%) patient had vertigo. 15 (75%) patients had no audiovestibular symptoms. None of the patients complained of earache, ear fullness or hearing loss.

None of the patients gave history of ear infection, occupational exposure to noise or family history of hearing loss.

3.2. Disease activity assessment

The SLEDAI score ranged from 4 to 29 with a mean of 14.8 ± 6.5 .

Table 1 Clinical characteristics of the systemic lupus erythematosus (SLE) patients.

Clinical manifestations	SLE patients (<i>n</i> = 20)	
	No.	%
<i>Constitutional manifestations</i>		
Fever	13	65
Weight loss	8	40
Fatigue	13	65
<i>Mucocutaneous manifestations</i>		
Malar rash	18	90
Oral ulcers	16	80
Maculopapular rash	6	30
Discoid rash	3	15
Photosensitivity	13	65
Alopecia	9	45
Vasculitis	7	35
<i>Musculoskeletal manifestations</i>		
Arthralgia	18	90
Arthritis	14	70
Myalgia	1	5
<i>Neurological manifestations</i>		
Psychosis	1	5
Cranial nerve neuropathy	1	5
Peripheral neuropathy	1	5
Lupus headache	4	20
Cognitive dysfunction	1	5
Pleurisy/pleural effusion	4	20
Pericarditis/pericardial effusion	2	10
Raynaud's phenomenon	4	20
Nephritis	7	35
Autoimmune hepatitis	1	5
Antiphospholipid syndrome	0	0

Table 2 Laboratory features of systemic lupus erythematosus (SLE) patients.

Laboratory data	Range	mean \pm SD
ESR(mm/ 1st h)	10–130	69.05 \pm 40.49
ALT(U/L)	7–44	18.4 \pm 10.71
AST(U/L)	9–129	26.85 \pm 26.32
Creatinine(mg/dl)	0.4–3.5	0.79 \pm 0.65
Urea (mg/dl)	5–201	35.4 \pm 41.19
Urinary protein (gm/24 h)	0.0–3.4	0.58 \pm 0.93
<i>Immune profile</i>		
	No.	%
Positive ANA	20	100
Positive anti-DNA	20	100
swPositive ACL IgM	3	15
Positive ACL IgG	1	5
Positive LAC	2	10
Consumed C3 and C4	2	10

ESR: erythrocyte sedimentation rate, ALT: alanine transaminase, AST: aspartate transaminase, ANA: anti-nuclear antibodies, DNA: deoxy nucleic acid, ACL: anticardiolipin, LAC: lupus anticoagulant, C: complement.

3.3. Medications of the SLE patients

10 (50%) patients were on corticosteroids only and another 10 (50%) were on a combination therapy of corticosteroids, azathioprine and hydroxychloroquine. All patients received steroids in a daily dose ranging from 5 to 45 mg with mean of 19 ± 10.46 , hydroxychloroquine daily dose ranged from 200 to 400 mg with mean of 340 ± 96.6 and azathioprine daily dose ranged from 50 to 150 mg with mean of 85 ± 24.15 .

3.4. Results of auditory assessment

Pure tone audiometry (PTA) was abnormal in 13 (65%) patients and normal in 7 (35%) patients. Results of otoscopic examination, acoustic immittance testing and speech audiometry of all patients (100%) were normal. All patients had 96–100% speech discrimination scores and type A tympanogram. The acoustic reflex showed thresholds consistent with the level of hearing loss.

Pure tone audiometry revealed hearing loss in 13 (65%) of SLE patients, while all controls (100%) showed normal hearing. None of the controls had any hearing loss as their PTA revealed bilaterally normal thresholds, their speech discrimination scores reached 96–100% and the tympanogram did not show any abnormality. There was a highly significant statistical difference between SLE patients and the control group as regards PTA ($p < 0.001$).

Of the thirteen SLE patients who had abnormal pure-tone thresholds, 2 (10%) patients had bilateral symmetrical hearing loss, 8 (40%) patients had bilateral asymmetrical hearing loss, and 3 (15%) patients had unilateral hearing loss.

Two patients had low tone loss and 11 patients had high tone loss. The mean values of the air-conduction hearing thresholds in SLE patients were poorer than in control group for frequencies 250, 8000 and 12,000 Hz (Fig. 1).

The hearing level of the right ear at a frequency of 12,000 Hz was significantly lower in the 6 SLE patients with juvenile onset of the disease (20.83 ± 3.76 db) compared to

the 14 adult onset cases (32.5 ± 15.66 db) ($p = 0.02$). There was no significant difference at other frequencies however there was a tendency to decrease in the left ear (at 12,000 Hz) in the juvenile onset cases (28.33 ± 8.16 db vs. 42.86 ± 22.93 db; $p = 0.052$).

3.5. Relation between audiovestibular symptoms and hearing loss

The 5 patients with auditory manifestations all had hearing loss as determined by PTA. The other 8 patients with abnormal PTA results had no auditory manifestations. The patient with vertigo was one of 2 (15.3%) patients that proved by PTA to have mild low tone loss, while the rest of the patients had high tone loss. There was no significant difference in the audiovestibular manifestations according to the PTA results ($p = 0.114$). Table 3 shows the relation between audiovestibular manifestations and hearing loss.

3.6. Relation between demographic, clinical and laboratory features as well as medications used and hearing level

Comparison of the demographic features, clinical and laboratory characteristics as well as the medications received by the SLE patients according to the hearing state as determined by the pure tone audiometry (PTA) is presented in Table 4.

On comparing the hearing level according to the presence or absence of clinical manifestations, only lupus nephritis showed a significant difference at various PTA frequencies (Table 5).

On comparing the hearing level according to intake of medications, it was significantly lower in those receiving azathioprine and hydroxychloroquine ($N = 10$) in the right (12 ± 4.83 db) and left (13 ± 6.75 db) ears compared to those not receiving ($N = 10$) (19.5 ± 6.85 db and 20 ± 7.07 db; $p = 0.012$ and $p = .036$ respectively) at a frequency of 4000 Hz.

4. Discussion

Hearing loss in systemic lupus erythematosus may be potentially due to autoimmunity, vasculitis, premature presbycusis and drug ototoxicity [4].

Table 3 Relation between audiovestibular manifestations and hearing loss as determined by pure tone audiometry (PTA).

Hearing state	Tinnitus/Vertigo		<i>p</i> Value
	No	Yes	
Normal hearing			0.114
No.	7	0	
%	46.7	0	
Hearing loss			
No.	8	5	
%	53.3	100	

This study, which was performed in Kasr al Aini University Hospitals, included 20 female SLE patients. The 20 SLE patients were subjected to auditory assessment using PTA, tympanometry, acoustic reflexes and speech audiometry. All other tests except PTA were normal. All patients had 96–100% speech discrimination scores and type A tympanogram. Also acoustic reflex showed thresholds consistent with the level of hearing loss.

None of the healthy controls had any kind of hearing loss, their PTA revealed bilaterally normal thresholds, their speech discrimination scores reached 96–100% and the tympanogram did not show any abnormality. As regard PTA in SLE patients, 13 (65%) had abnormal pure tone threshold while 7 (35%) had normal hearing threshold. These results are in accordance with the findings of Roverano *et al.* [9] that showed 20/30 (66%) SLE patients to have SNHL at high frequencies with statistically significant differences when compared with the control. Other studies showed different results, as in the work of Bowman and colleagues, hearing loss was observed in only 2/30 (8%) of the SLE patients and Kastanioudakis *et al.* reported hearing loss in 22.5% (8/43) female SLE patients [17,18]. In the study of Maciaszczyk *et al.* [8] they found that SLE patients had poorer hearing thresholds than the age-matched controls and SNHL was observed in 28.6%.

In spite of different results regarding the auditory affection in SLE patients, auditory system involvement ought to be considered as one of elements of the clinical picture of SLE and an adequate investigation of auditory symptoms is important

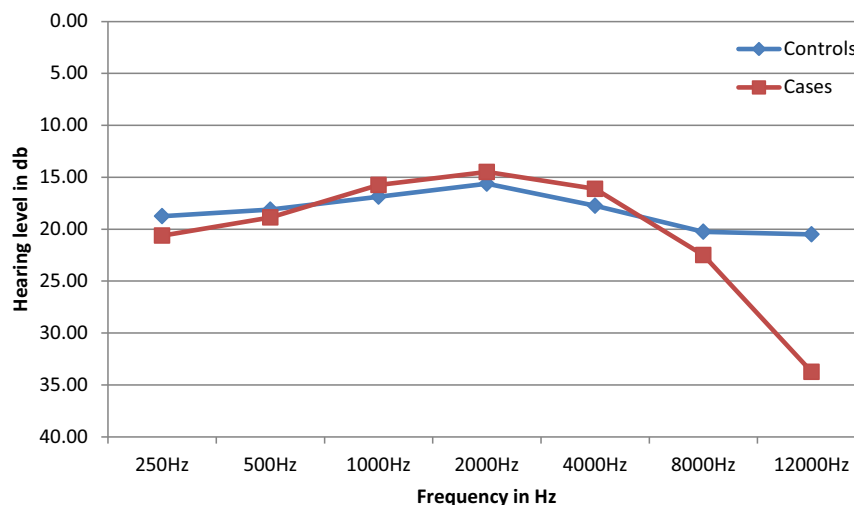


Figure 1 Mean pure tone audiogram of SLE patients (40 ears) compared to control (40 ears).

Table 4 Comparison of the demographic features, clinical and laboratory characteristics as well as medications received by the SLE patients according to the hearing state as determined by pure tone audiometry (PTA).

Feature	Hearing state in SLE patients		p Value
	Normal (n = 7)	Hearing loss (n = 13)	
<i>Demographic features</i>			
Age (years)	24.43 ± 6.6	31.15 ± 9.99	0.621
Age of onset (years)	19.14 ± 5.24	27.54 ± 9.39	0.023*
Disease duration (months)	63.86 ± 38.84	39.23 ± 30.04	0.175
<i>Clinical characteristics</i>			
Vasculitis	1	6	0.329
Cranial neuropathy	0	1	1
Peripheral neuropathy	0	1	1
Cognitive dysfunction	0	1	1
Lupus headache	2	2	0.61
Nephritis	4	3	0.24
SLEDAI (mean ± SD)	14.57 ± 7.52	14.92 ± 6.22	0.92
<i>Laboratory features</i>			
ESR(mean ± SD)	70 ± 46.64	68.54 ± 38.83	0.812
ACL IgM positivity	1	2	0.476
ACL IgG positivity	1	0	0.606
LAC positivity	0	2	0.428
<i>Medications used</i>			
Steroids only	4	6	1
Steroids, HCQ and AZA	3	7	1

* ESR: erythrocyte sedimentation rate, ACL: anticardiolipin, LAC: lupus anticoagulant. HCQ: hydroxychloroquine, AZA: azathioprine. Demographic features, ESR and systemic lupus erythematosus disease activity index (SLEDAI) are presented as mean ± SD while the other characteristics are presented as number of patients.

Table 5 Hearing level according to the presence or absence of lupus nephritis in the right and left ear.

Hearing level (db) mean ± SD (HZ)	SLE patients (N = 20)		p value	
	LN (N = 7)	Without LN (N = 13)		
Right ear	250	16.43 ± 3.78	23.85 ± 5.06	0.002
	500	15 ± 4.08	20.77 ± 5.34	0.016
	1000	13.57 ± 3.78	16.92 ± 4.8	0.11
	2000	12.86 ± 2.67	13.46 ± 4.27	0.7
	4000	12.86 ± 3.93	17.31 ± 7.8	0.11
	8000	16.43 ± 4.76	25 ± 12.42	0.041
	12,000	23.57 ± 9.45	31.92 ± 15.75	0.16
Left ear	250	14.29 ± 3.45	23.08 ± 5.6	0.000
	500	12.86 ± 3.93	22.31 ± 5.63	0.000
	1000	10.71 ± 1.89	18.46 ± 4.27	0.000
	2000	10.71 ± 3.45	18.46 ± 6.58	0.003
	4000	10 ± 0.00	20.0 ± 7.36	0.000
	8000	17.14 ± 6.99	26.15 ± 12.44	0.053
	12,000	32.14 ± 16.29	41.92 ± 22.41	0.28

SLE: Systemic lupus erythematosus, LN: lupus nephritis. Bold values are significant at $p < 0.05$.

during their follow-up, since manifestations of the auditory apparatus and SNHL can affect a significant proportion of patients [19].

None of the patients with abnormal PTA results gave symptoms of hypoacusis and this was in accordance with another study on 40 female SLE patients, all of them asymptomatic in terms of hearing impairment that found that 57.5% presented a subclinical sensorineural hearing abnormality [20]. The study of Roverano et al. [9] also revealed asymptomatic SNHL in 66% of SLE patients. Karatas et al. [2]

stated that PTA showed SNHL in 6/28 (21.4%) SLE patients, yet symptomatic hearing loss was reported in 2 (7%). Moreover, the work of Gad et al. [21] showed that in juvenile SLE, 25% of the SLE children had asymptomatic SNHL.

Only 5 patients reported audiovestibular symptoms including tinnitus in 4 (20%) and vertigo in 1 (5%). The patient with vertigo was one of 2 (15.3%) patients that proved by PTA to have mild low tone loss, while the rest of the patients had high tone loss. There was no significant difference in the

audiovestibular manifestations between those with normal hearing or hearing loss.

In the work of *Batuecas-Caletrio et al.* [1] SNHL was found to be associated with a history of episodic vertigo, but not at time of assessment. *Gomides et al.* [19] observed in their study that 25 (55.5%) SLE patients presented one or more symptoms at the time of assessment, including vertigo, hypoacusis, ear fullness or tinnitus. Analysis of audiometric alterations showed SNHL in 7 (15.6%). The association between audiovestibular symptoms and hearing loss in SLE patients needs further investigations [19]. Vertigo and dizziness are not common symptoms in SLE, but are probably present more often than was formerly thought [22]. The prevalence of vertigo and/or balance disorders reported by SLE patients varies between 13% and 67% [4].

Low tone hearing loss together with the presence of vertigo detected in one of our SLE patients could be attributed to the presence of hydrops. This showed agreement with *Andonopoulus et al.* [20] who reported low frequency hearing loss and supported the possibility of the presence of subclinical hydrops in SLE patients. In contrast *Karatas et al.* [2] reported vertigo in 8 (28%) SLE patients who had significantly more peripheral type vestibular pathology compared with the control. Prevalence of vertigo in SLE was higher in patients with abnormal electro-nystagmography (ENG) results. Abnormal ENG findings and vestibular symptoms are probably present more often than were formerly thought in SLE patients [2].

Gomides et al. [19] observed a marked prevalence of vertigo (31.1%) in SLE patients and *Maciaszczyk et al.* [8] stated that over 70% of SLE patients reported vertigo and dizziness in a questionnaire. The association between audiovestibular symptoms and hearing loss in SLE patients needs further investigations.

The mean values of the air-conduction hearing thresholds in SLE patients were poorer than in control group for frequencies 250, 8000 and 12,000 Hz. The results showed highly significant statistical difference between SLE patients and control as regards PTA. 2 (10%) patients had bilateral symmetrical hearing loss, 8 (40%) had bilateral asymmetrical hearing loss, while 3 (15%) had unilateral hearing loss. 2 (15.3%) had low tone loss and 11 (84.6%) patients had high tone loss.

Most of the patients are typical of autoimmune hearing loss as it is often regarded as bilateral, but asymmetrical. High-frequency hearing loss is often attributed to tonotopic base to apex differences in cochlea like viability of outer hair cells, vascularization, and intrinsic susceptibility of basal hair cells to free radicals, which make a basal turn receptor more sensitive to damage.

Vasculitis processes, excessive generating of free radicals and the cochlear pathology in the stria vascularis seem to dominate in lupus pathology with hearing loss development in the course of the disease [23].

This was in agreement with *Kastanioudakis et al.* [18] who reported that out of 8 patients with hearing loss, 1 (12.5%) had bilateral symmetric and 7 (87.5%) had bilateral asymmetric hearing loss. *Gomides et al.* [19] stated that in most lupus patients, the hearing loss was unilateral and classified as mild or moderate. *Karatas et al.* [2] reported that out of 6 patients with hearing loss, it was unilateral in 3 (50%) and bilateral in 3 (50%). *Batuecas-Caletrio et al.* [1] stated that 19% of the SLE patients showed hearing loss, mainly affecting higher frequencies. In contrast, *Maciaszczyk et al.* [8] stated that in

the SLE patients, hearing loss was mainly bilateral, symmetrical and affecting high frequencies. There were no cases of fluctuating hearing loss. This was frequently not typical of autoimmune hearing loss as it is often regarded as bilateral, but asymmetrical.

In the present study, there was no significant statistical association between disease duration and hearing loss. Previous researches yielded similar results. *Andonopoulus et al.* [20] found no correlation between duration of SLE and the presence of low frequency hearing loss which they attributed to the presence of hydrops. *Sperling et al.* [4] concluded that the disease duration did not have a significant effect on the results of their study. This also coincides with the findings of *Gomides et al.* [19] reporting that there was no association between SNHL and the duration of SLE. In opposition, a significant correlation between values of the mean air-conduction hearing thresholds and SLE duration was proved in the work of *Maciaszczyk et al.* [8].

The present work showed a significant statistical association between age at disease onset and hearing loss in SLE patients with lower hearing levels at higher frequencies. This relation was not previously reported in other studies and should be considered in future longitudinal researches on a larger scale.

Of the twenty patients with SLE in this study 10 (50%), were treated with corticosteroids only and 10 (50%) with a combination of corticosteroids, hydroxychloroquine (HCQ) and azathioprine. There was no significant difference in the medications received between those with and without hearing loss. However, on comparing the hearing level according to intake of medications, there was a significantly lower level in those receiving azathioprine and hydroxychloroquine in the right and left ears compared to those not receiving.

These results are in agreement with *Kastanioudakis et al.* [18] who found that although most SLE patients were exposed to potentially ototoxic medications (HCQ and frusemide), the asymmetric results observed in 15/26 (58%) argue against ototoxicity as the cause of aural symptoms. At the time of the study performed by *Roverano et al.* [8] 25/30 patients (83.3%) were under treatment with HCQ (200 mg/day), and 16 exhibited SNHL. The remaining 5 patients, who had not been treated with HCQ presented with SNHL. Wang and colleagues reported only one SLE patient out of 156 users received 203 courses of antimalarials, to stop the medication due to ototoxicity [24]. Besides the well-known retinal toxicity, its use has been suspected of being associated to ototoxicity. Ototoxicity, SNHL, tinnitus, sense of imbalance and cochleovestibular manifestations have been reported with use of antimalarials. Alterations in hearing related to HCQ have been reported; the reversibility of ototoxicity has been debatable, but there is suggestion that such complication can be corrected if the medication is stopped and appropriate therapy with steroids is instituted [25].

In the present study, there was no association between SNHL and clinical variables or laboratory parameters. However, the hearing level was significantly lower in those with lupus nephritis which could be an early sign before the development of hearing loss. No correlation was found between the hearing level with renal or CNS involvement and presence of antibodies [7]. Also, in the study of *Gomides et al.* [19] no correlation was observed between hearing loss and clinical manifestations or laboratory variables

(complement, anti-DNA, antiphospholipid antibodies). *Batuecas-Caletrio et al.* [1] stated that in SLE patients, SNHL was not associated with kidney disease, ANA or anti-phospholipid positivity. In contrast, *Sperling et al.* [4] observed that aural symptoms, like hearing loss and tinnitus, were more frequent in SLE patients who had higher creatinine and lower C3 levels.

Although, the presence of antiphospholipid antibodies is a proposed etiology for hearing loss in SLE patients [3], in this study no statistical difference was found between the presence of anti-phospholipid antibodies and hearing loss. *Toubi et al.* [26] found that 27% of 30 patients with sudden SNHL were positive for aCL compared to 0% in their control group. *Naa-remdrop and Spiera* [27] also described six patients with SLE or lupus-like syndrome who developed sudden SNHL with elevated aPLs. *Green and Miller* [28] described a case of sudden SNHL in association with aPL as the first manifestation of SLE. In a recent study by *Mouadeb et al.* [29] in a cohort of 168 patients with SNHL of unknown etiology, they found 42 patients (25%) with at least one elevated aPL antibody and 20 patients had two or more positive aPL tests. An interesting case of a 34-year-old pregnant woman with APS with fluctuating bilateral hearing loss was recently reported [30].

In another study, 5 (25%) patients had positive antiphospholipid antibodies and all of them had SNHL (100%), 4 (80%) had abnormal videonystagmography (VNG) results and 3 (60%) had abnormal computerized dynamic posturography (CDP) results [21]. *Kastanioudakis et al.* [18] did not find any correlation between the presences of anti-phospholipid antibodies and hearing loss. In the work of *Roverano et al.* [8] they stated that there was no statistically significant relation between antiphospholipid antibodies and SNHL.

In this work, no significant statistical association between disease activity using SLEDAI score and hearing loss could be detected. This was in agreement with *Gomides et al.* [19] as in their study no correlation was observed between hearing loss in SLE patients and disease activity parameters. Furthermore, in the study of *Gad et al.* [21] there was no significant statistical correlation between SLEDAI scores and hearing loss in SLE patients. *Abbasi and colleagues* [31] performed a case-control study on 45 patients with SLE. The patients were examined and evaluated for auditory and hearing problems as well as parameters related to their disease severity and progression. No statistical significant relationship was found between severity of the disease and hearing loss.

The results of this study should be interpreted in the context of several limitations. First, the small number of the patients was chosen. Second, the study did not exclude patients with juvenile onset disease. Third, none of the patients included fulfilled the criteria of diagnosis of APS which is a claimed cause of auditory affection in SLE.

In conclusion, hearing affection is frequent in SLE patients and since it is commonly asymptomatic, it could be neglected. So regular screening of auditory functions of SLE patients should be done, for better and early management. Age at disease onset is remarkably associated with hearing loss in SLE. Lupus nephritis and hydroxychloroquine use are associated with lower hearing levels and possible early hearing loss. Further studies should work on how often this asymptomatic SNHL progresses to a clinical problem to define the importance that SLE patients undergo audiometric tests as part of their initial investigations.

Conflict of interest

There is no conflict of interest to declare.

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