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Original article

Therapeutic Effect of Combined Oral Zinc and Co-Enzyme Q10 in Cases of Sudden Sensorineural Hearing Loss

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Abstract:

Background: Sudden sensorineural hearing loss (SSNHL) is a distressing condition with various etiologies and a limited array of treatment options. This study aimed to determine the effectiveness of a treatment regimen involving oral zinc and co-enzyme Q10 in improving hearing outcomes in patients diagnosed with SSNHL. **Methods:** This prospective interventional study was conducted with 30 eligible patients aged 20 to 60 years. Comprehensive clinical evaluations, laboratory investigations, and audiometric assessments were performed. Patients received a one-month course of oral zinc and co-enzyme Q10, with the option to extend the treatment to three months in the absence of improvement. Audiological follow-up assessments were conducted at one and three months after treatment initiation. **Results:** The mean age was 48.61 ± 10.27 years. Twentysix point seven percent of the patients had a positive family history. Sixty-six-point seven percent of the patients had hearing loss on the left side, 33.3% were on right side with mean hearing loss duration of 4.12 ± 2.53 days. Moreover, 76.7% of the patients presented with tinnitus. The study revealed a significant decrease in Pure Tone Audiometry (PTA) threshold at various frequencies, as well as improvements in speech audiometry after treatment. The recovery rate increased from 70% after one month to 76. 6% after three months. Factors associated with a higher recovery rate included younger age, the absence of diabetes, a shorter duration of hearing loss, and a significant decrease in PTA threshold. **Conclusion:** The combination of oral zinc and co-enzyme Q10- demonstrated promise as a therapeutic approach for SSNHL.

Keywords: Sudden sensorineural hearing loss; zinc; co-enzyme Q10; audiometry; therapeutic effect.

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Introduction

Sudden Sensorineural Hearing Loss (SSNHL) is defined as any sensorineural hearing loss exceeding 30 dB in three contiguous frequencies occurring over a period of less than three days. It accounts for approximately one percent of all cases of sensorineural hearing loss, posing both diagnostic and therapeutic challenges [(1)].

Sudden sensorineural hearing loss typically affects one ear unilaterally, and the underlying cause is often unidentified. However, various infective, vascular, and immunological factors are proposed, requiring careful evaluation [(2)].

Numerous treatment modalities are available for SSNHL, primarily focused on addressing the underlying cause when identified. Other treatment options may involve the use of anti-inflammatory agents, mainly corticosteroids, vasodilator drugs, antimicrobial therapies, such as antiviral treatment, calcium antagonists, vitamins, essential minerals, volume expanders, defibrinogenators, diuretics, hyperbaric oxygen, and bed rest [(3)].

Oral steroids remain the most commonly used treatment by otolaryngologists for SSNHL. Corticosteroids are believed to improve the condition by reducing inflammation and edema in the inner ear [(4)].

Systemic steroid therapy is associated with numerous complications, even in short-term use, including exacerbation of glaucoma, increased coagulability, intravascular thrombosis, avascular hip necrosis, and insomnia. Moreover, there are several contraindications for systemic steroid therapy, limiting its use in various medical conditions [(5)].

Intratympanic injection of steroids is employed in refractory cases with variable success rates, and its use is limited in cases diagnosed early. It can lead to complications such as permanent perforation, ear infection, post-injection vertigo, and tongue numbness [(6)].

Coenzyme Q10 is a vitamin-like substance used in the treatment of various disorders primarily related to suboptimal cellular energy metabolism and oxidative injury. Between 2007 and 2008, a controlled prospective study was conducted to assess the effect of adding coenzyme Q10 to steroid treatment for SSNHL. The study revealed a significant improvement in speech discrimination with the use of coenzyme Q10, suggesting a potential beneficial effect in treating SSNHL [(7)].

Zinc is a trace element that plays a crucial role in various physiological functions. It exhibits antioxidant effects by modulating oxidative stress at the cellular level and functions as a synaptic modulator in the central nervous and auditory systems. Cochlear tissues contain high levels of zinc in the form of Cu/Zn superoxide dismutase. Zinc supplementation may enhance hearing recovery in patients with SSNHL, offering a new approach to treating this condition [(8)].

The purpose of this study was to determine the effect of oral zinc combined with co-enzyme Q10 in treatment of SSNHL as a new effective and safe line of treatment for those patients.

Patients and methods

This prospective, interventional study was conducted in the ENT department of Benha Teaching Hospital from March 2022 to September 2022. The study population consisted of 30 patients who presented with SSNHL and met the inclusion criteria during the study period.

An informed written consent was obtained from the patients. Every patient received an explanation of the purpose of the study and had a secret code number. The study was done after being approved by the Research Ethics Committee, Faculty of Medicine, Benha University. Approval code: MS 6-3-2022.

Inclusion criteria were patients aged between 20 and 60 years who were diagnosed with SSNHL.

Exclusion criteria were patients with History of ear surgery or with conductive hearing loss or vertigo.

Methods:

All patients underwent a comprehensive clinical evaluation. This included a thorough history-taking process, which gathered personal information such; as name, age, gender, occupation, residence, social status, and the date of examination. The history also encompassed details about; the complaint, specifically the onset, course, duration, and severity of hearing loss, along with any associated symptoms like tinnitus, ear discharge, and vertigo. Past medical conditions and any previous instances of similar issues- were recorded. Furthermore, a family history of positive consanguinity or hearing loss was documented.

Clinical examination was performed, starting with a general examination to assess vital signs (blood pressure, temperature, heart rate, and respiratory rate) and signs of conditions like pallor, cyanosis, jaundice, and lymph node enlargement.

A comprehensive ENT examination followed, which included the inspection of the nose and throat for signs of infection or inflammation. The auricular, pre-auricular, and post-auricular areas- were examined, both visually and through palpation. Otoscopic examination- using a Richter otoscope- was conducted, and tuning fork tests (Rinne and Weber) were administered using a 512 Hz tuning fork.

Laboratory investigations were carried out, consisting of a Complete Blood Count (CBC) and an ESR (Erythrocyte Sedimentation Rate) measurement.

Audiological evaluations included the following tests:

Pure Tone Audiometry: This involved presenting pure tones to the ears through earphones and measuring the lowest intensity (in decibels) at which the tone was perceived 50% of the time. This threshold measurement was recorded for specific frequencies ranging from 250 to 8000 hertz (Hz) for each ear, and the results were plotted on an audiogram.

Speech Audiometry: The Speech Reception Threshold (SRT) test was administered using Arabic Bisyllabic Words for adults. Additionally, the Word Discrimination score (WD) test was conducted using Arabic Phonetically Balanced Words for adults.

Tympanometry: After an otoscopy to ensure the ear canal's clear and undamaged, this test involved inserting a tympanometer probe into the ear canal. The instrument altered the ear's pressure, generated a pure tone, and measured the eardrum's responses at various pressures, producing a tympanogram. Tympanograms were categorized according to their shape, which included normal and abnormal patterns, but this categorization was not used as a diagnostic indicator, **Figure (1).**

Procedure:

Patients were administered a one-month course of treatment, involving an oral dose of 1.3 mg/kg of zinc and 2.2 mg/kg of co-enzyme Q10, as a single daily dose. If no improvement was observed, this treatment regimen continued for three months. Audiological follow-up assessments were conducted one month and three months after the initiation of treatment to evaluate its effectiveness.

Statistical analysis

All data collected in this study were processed, tabulated, and subjected to statistical analysis using SPSS 22.0 for Windows (SPSS Inc., Chicago, IL, USA) and MedCalc 13 for Windows (MedCalc Software bvba, Ostend, Belgium). Prior to analysis, the data were tested for normal distribution using the Shapiro-Wilk test. Qualitative data were presented as frequencies and relative percentages, and the Chi-square test ($\chi 2$) and Fisher exact test were employed to assess differences between qualitative variables as appropriate. Quantitative data were expressed as mean ± SD (Standard Deviation) for parametric data and median with range for non-parametric data. Independent T-tests and Mann-Whitney

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tests were utilized to determine differences between quantitative variables in two groups for parametric and non-parametric variables, respectively. All statistical comparisons were two-tailed, and a significance level of a p-value ≤ 0.05 indicated a significant difference, p < 0.001 indicated a highly significant difference, while p > 0.05 indicated a non-significant difference.

Results

The mean age was 48.61 ± 10.27 years, with mean BMI of 26.83 ± 2.79 kg/m^2. About sixty percent of the patients were females and 40% were males. The most prevalent comorbid was smoking (36.7%) followed by hypertension (16.7%). Forty six point seven percent of the patients had a middle socioeconomic status, 30% had a high socioeconomic status, and 23.3% had a low socioeconomic status. Forty six point seven percent of the patients were rural and 53.3% of the patients were urban. Twenty six point seven percent of the patients had a positive family history.

Sixtysix point seven percent of the patients had hearing loss on the left side, 33.3% were on right side with mean hearing loss duration of 4.12 ± 2.53 days. Moreover, 76.7% of the patients presented with tinnitus **Table (1).**

There is a significant decrease in air conduction PTA after management at every frequency. There is a significant decrease in bone conduction PTA after management at every frequency, **Table (2).**

Table (1): Disease characteristics and routine laboratory parameters of the Studied patients' group.

Variable	**Studied patients** (n=30)	
	N	%
Side		
Right	10	33.3%
Left	20	66.7%
Tinnitus		
Yes	23	76.7%
No	7	23.3%
Duration (days) Mean ± SD	4.12 ± 2.53	
Hemoglobin (g/dl) Mean ± SD	12.86 ± 1.11	
PLT (x103/L) Mean ± SD	227.38 ± 34.39	
TLC (x103/L) Mean ± SD	6.45 ± 0.888	
ALT (U/L) Mean ± SD	26.67 ± 18.13	
AST (U/L) Mean ± SD	35.17 ± 7.42	
Creatinine (mg/dl) Mean ± SD	0.821 ± 0.151	
Urea (mg/dl) Mean ± SD	42.35 ± 10.5	

SD: Standard Deviation; g/dl: grams per deciliter; PLT: Platelets; TLC: Total Leukocyte Count; ALT: Alanine Aminotransferase; AST: Aspartate Aminotransferase; mg/dl: milligrams per deciliter; U/L: Units per Liter.

Table (2): Average pure tone audiometry (PTA) air conduction parameters and Average pure tone audiometry (PTA) bone conduction parameters of the studied patients

Air conduction audiometry	**Studied patients**(n=30)		**pt**	**P**
	Before	**After**		
250Hz (dB) Mean ± SD	33.2 ± 5.37	26.1 ± 4.89	**2.3**	**.021**
500Hz (dB) Mean ± SD	40.4 ± 5.48	21.2 ± 6.77	**2.1**	**.037**
1k Hz (dB) Mean ± SD	44.5 ± 6.45	18.25 ± 6.19	**2.4**	**.019**
2k Hz (dB) Mean ± SD	49.67 ± 7.5	24.3 ± 6.43	**4.8**	**<0.001**
4k Hz (dB) Mean ± SD	59.12 ± 7.11	32.42 ± 6.81	**5.1**	**<0.001**
8k Hz (dB) Mean ± SD	66.51 ± 9.3	43.3 ± 6.35	**5.3**	**<0.001**
Bone Conduction				
500Hz (dB) Mean ± SD	31.54 ± 7.81	21.4 ± 6.63	.802	.425
1k Hz (dB) Mean ± SD	39.6 ± 7.65	18.52 ± 6.48	1.48	.145
2k Hz (dB) Mean ± SD	55.1 ± 6.52	24.3 ± 6.43	**3.43**	**.001**
4k Hz (dB) Mean ± SD	57.82 ± 8.72	31.93 ± 6.72	**5.2**	**<0.001**

Hz: Hertz; dB: Decibels, SD: Standard Deviation; pt: Patient; P: P-value (statistical significance).

There is a significant decrease in speech audiometry after management at every frequency, **Table (3).**

There is a significant decrease in average PTA after treatment to follow up, **Table (4).**

The recovery rate after one was 70% and after 3 months was 76.6%, **Figure (2).**

Young age, no DM, shorter duration and significant decrease in PTA- were found to be significantly associated with higher recovery rate (P value< 0.05).

Idiopathic sudden sensorineural hearing loss (ISSNHL) is characterized by a rapid decline in hearing, often affecting at least three consecutive frequencies by 30 decibels or more within 72 hours (9).

Table (3): Average speech audiometry parameters of the studied patients.

Speech audiometry	**Studied patients**(n=30)		**pt**	**P**
	Before	**After**		
SRT (dB) Mean ± SD	46.15 ± 4.2	18.45 ± 3.19	**2.39**	**.020**
Intensity (dB) Mean ± SD	85.5 ± 4.2	60.1 ± 3.39	**2.4**	**.019**
Discrimination (%) Mean ± SD	71.2 ± 1.62	93.7 ± 1.64	.558	.578
Masking (dB) Mean ± SD	75.5 ± 4.19	50.2 ± 3.5	**2.45**	**.018**

SRT: Speech Reception Threshold; dB: Decibels; SD: Standard Deviation; pt: Patient; P: P-value (statistical significance); %: Percentage.

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Table (4): Average PTA before and after treatment among the studied patients.

	Studied patients (n=30)
Pre-PTA (dB) Mean ± SD	49.91 ± 11.2
Post-PTA (dB) Mean ± SD	29.35 ± 7.6
3 months follow up PTA (dB) Mean ± SD	27.75 ± 5.52
P-value	**<0.001**

Pre-PTA: Preoperative Pure Tone Audiometry; Post-PTA: Postoperative Pure Tone Audiometry; PTA: Pure Tone Audiometry; dB: Decibels; SD: Standard Deviation; P-value: Statistical Significance.

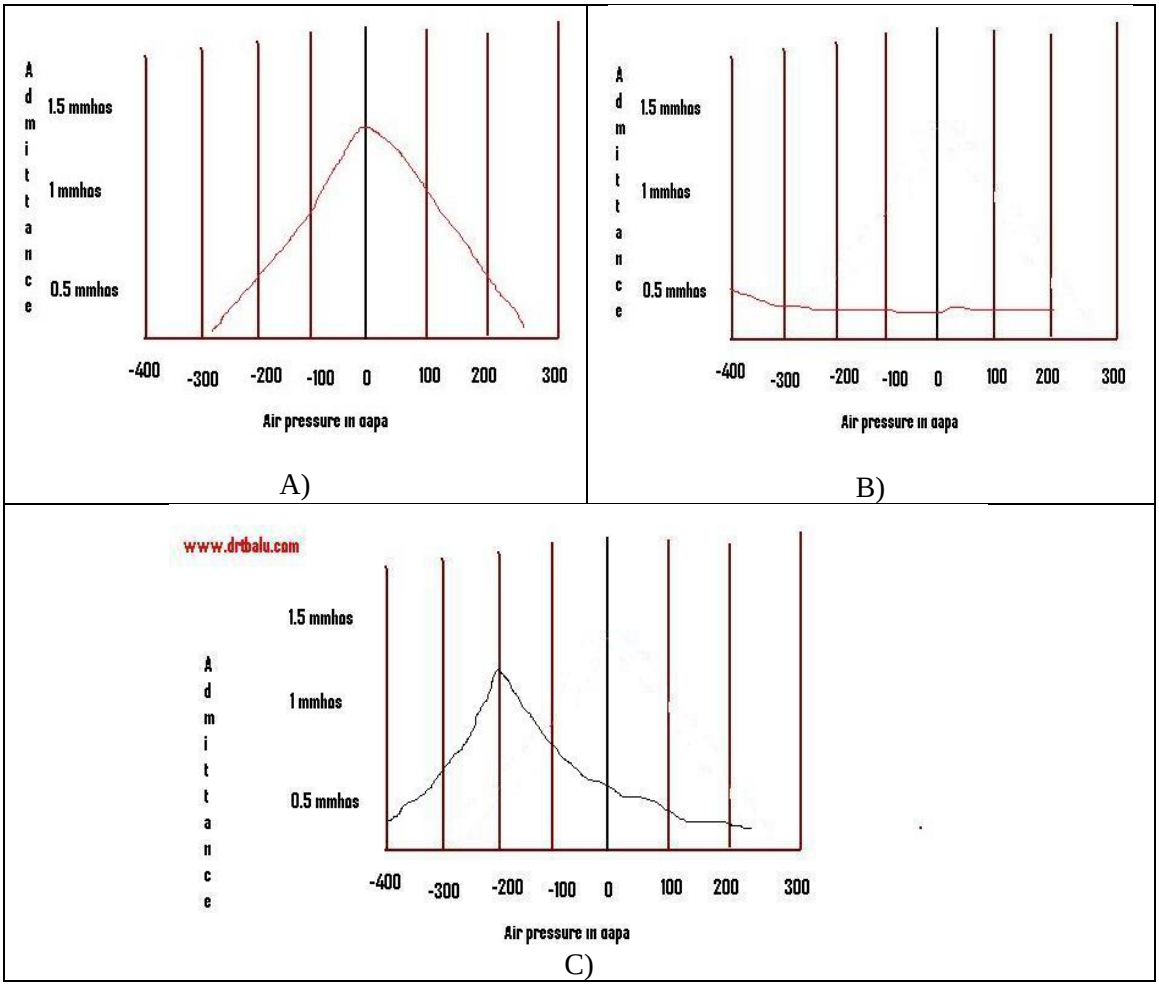

Figure (1): A) Type A tympanogram, B) Type B tympanogram and C) Type C tympanogram

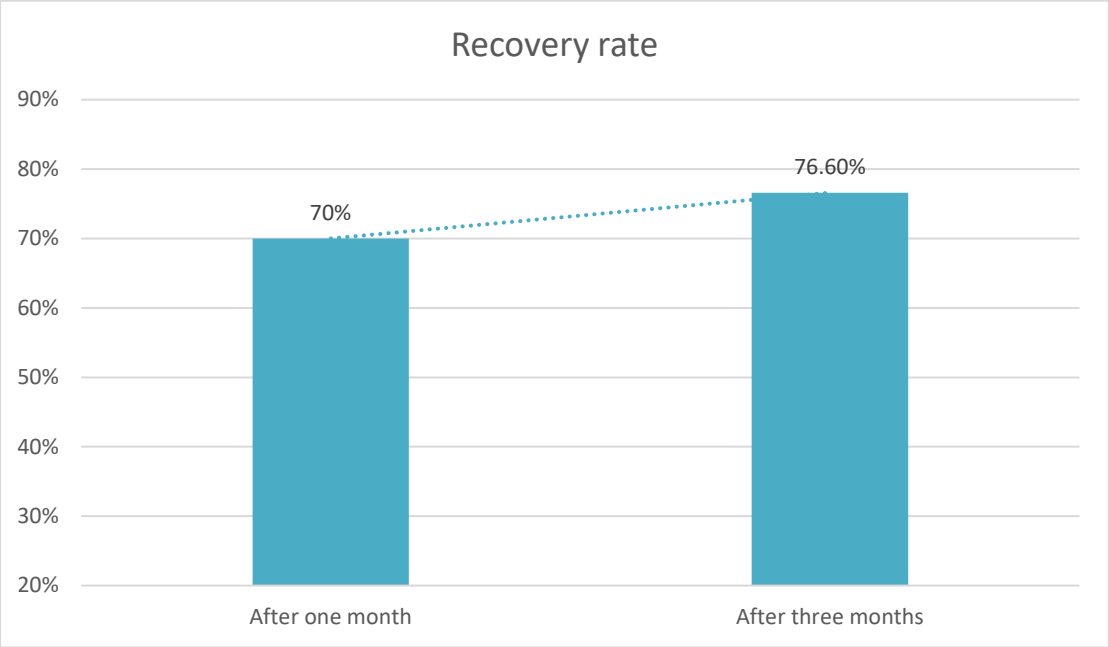

Figure (2): Recovery rate after one and three months

Discussion:

The incidence of ISSNHL is estimated to be 5-20 cases per 100,000 people annually, with a spontaneous recovery rate of 32-65% [(10)]. Although prevalence rates do not differ by sex, side, season, or geographic region, ISSNHL predominantly affects individuals in their 30s to 50s and is often idiopathic and unilateral. While viral infection and vascular dysfunction- are considered primary causes, other factors such as bacterial infection, trauma, autoimmune diseases, tumors, and ototoxicity- can contribute. Early detection and treatment are crucial for a better prognosis [(11)]. Oxidative stress, driven by reactive oxygen species (ROS) and reactive nitrogen species (RNS), has been implicated in ISSNHL, though the initial triggers are unclear. Free radical scavengers like vitamin E, magnesium, and coenzyme Q10 have shown promise in reducing hearing impairment in animal models. Coenzyme Q10- a vital mitochondrial electron carrier and antioxidant- has been associated with low serum levels in ISSNHL patients [(12)]. Additionally, zinc deficiency can contribute to hearing loss, highlighting the significance of nutrition [(13)].

This study aims to investigate the combined effects of Co-Q10 and zinc in treating ISSNHL, offering a potentially effective and safe treatment approach. The prospective interventional study was conducted at the ENT department of Benha Teaching Hospital from March 2022 to September 2022, involving 30 patients with SSNHL.

The main results of this study were as follows:

The current study showed that the mean age was 48.61 ± 10.27 years, with mean BMI of 26.83 ± 2.79 kg/m2. Sixty percent of the patients were females and 40% were males.

A study [(14)] showed that higher BMI was a risk factor for sudden sensory neural hearing loss but neither age nor sex was identified to be associated with the

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incidence of sudden sensory neural hearing loss. So, a weight loss strategy was recommended. Also, a study [15] revealed that there was no association between sex and the incidence of SSNHL.

In the current study we found that the most prevalent comorbid was smoking (36.7%) followed by hypertension (16.7%). A systematic review and meta-analysis [16] showed that cardiovascular risk factors (smoking, increased alcohol consumption) appeared to be associated with a higher risk of developing SSNHL.

The current study showed that 26.7% of the patients had a positive family history. This was comparable with a study [17] revealed that 21.4% affirmed a positive family history. The results indicated that patients with positive family history tend to have an aggravated course of ISSNHL.

Higher than our results, a study [15] revealed that (33.6%) of patients had a family medical history of ISSNHL, whereas 83 (66.4%) did not. A statistically significant association between the development of ISSNHL and a family history of ISSNHL- was observed ($p<0.05$).

Among the studied patients, 66.7% of the patients had hearing loss on left side, 33.3% were on right side with mean hearing loss duration of 4.12 ± 2.53 days. Moreover, 76.7% of the patients presented with tinnitus. A study [11] stated that there was no association between side and the development of ISSNHL. Also, a study [18] stated that ISSNHL is often accompanied by tinnitus, dizziness, and nausea. A study 2015 [14] revealed that there were 68.2% of the patients presented with tinnitus.

In this study, the administration of combined oral zinc and co-enzyme Q10 in SSNHL cases resulted in a significant reduction in air conduction PTA at all frequencies after treatment, as well as a noteworthy decrease in bone conduction PTA and speech audiometry results. Additionally, the study showed a significant decrease in the average PTA from treatment to follow-up, with a 70% recovery rate after one month and a further improvement to 76.6% after three months. Notably, no previous literature has assessed the effectiveness of the combined therapy of oral zinc and co-enzyme Q10 in SSNHL cases, as both nutrients have been studied individually in this context.

In a randomized controlled trial, a study [19] assessed the therapeutic efficacy of coenzyme Q10 in combination with systemic steroids for patients with idiopathic SSNHL, with 75% experiencing a total hearing improvement rate, and the coenzyme Q10 group demonstrating significantly better speech discrimination score improvement.

A study [20] conducted an animal study and found that high-dose coenzyme Q10 protected against cisplatin-induced ototoxicity, particularly at high frequencies.

A study [21] conducted a randomized clinical trial involving 143 patients with SSNHL and found that oral zinc supplementation, when combined with corticosteroid treatment, led to a significantly larger hearing gain, especially at 2000 and 8000 Hz frequencies.

A study [14] aimed to enhance the treatment of idiopathic sudden hearing loss by utilizing zinc and lipoprostaglandin E1 in addition to systemic steroid therapy, showing that zinc supplementation was effective for patients with mild hearing loss, while lipoprostaglandin E1 was beneficial for those with profound hearing loss.

In contrast, A study [22] on the combination of zinc supplementation and standard treatment for idiopathic sudden sensorineural hearing loss and found that zinc supplementation did not confer additional benefits when combined with standard treatment, as both groups showed hearing improvement with no significant difference.

Multivariate regression analysis was performed to determine the potential factors associated with recovery. It was revealed that young age, no DM, shorter

duration and significant decrease in PTA were found to be significantly associated with higher recovery rate.

In agreement with the current study age has been the most consistent adverse factor, with the elderly patients having significantly lower rates of recovery [23, 24]. Also, in concordance with the current study the presence of diabetes mellitus, have been variably associated with a poorer outcome in various studies [25, 26]. Moreover, metabolic syndrome has been documented to be an independent risk factor for SSNHL [27]. The rate of recovery has been shown to be lower in patients with metabolic syndrome, with poorer results associated with four or more features of the syndrome [28].

Regarding the duration of hearing loss literature showed that the patients presenting to the physician within a week are more likely to have a better recovery rate compared to the late presenters [23, 24]. This occurrence may not be related to early onset of treatment, but rather to the fact that a longer duration of hearing loss lessens the chances of recovery.

Also, regarding the pattern of hearing loss, literature showed that among the patients with a mild-severe degree of hearing loss, the prospects of hearing recovery are lesser for the flat audiogram configuration. For the non-flat configuration, an ascending audiogram has a better prognosis than the descending type [23, 24].

However, A study [29] showed that there was a significant correlation between serum zinc level changes and posttreatment hearing thresholds by correlation analysis ($P < .05$), as well as between changes of serum zinc levels and percentage of recovery in the zinc group ($P < .05$). But there was no association between recovery with age pretreatment pure-tone average and Hearing gain.

Also, A study [14] revealed that better hearing gain was associated with low tone hearing loss ($p<0.001$), better initial contralateral hearing ($p<0.001$), and the absence of dizziness ($p=0.015$).

Conclusion

In conclusion, the present study demonstrated that combined oral zinc and coenzyme Q10 treatment was both safe and effective in addressing sudden sensorineural hearing loss. This therapeutic approach was linked to a high recovery rate and substantial improvements in pure tone audiometry. Additionally, it was observed that older age, the presence of diabetes mellitus (DM), longer symptom duration, and advanced hearing loss stage- were identified as risk factors associated with poorer outcomes in ISSNHL patients undergoing combined oral zinc and coenzyme Q10 therapy.

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Author contribution

Authors contributed equally in the study**.**

Conflicts of interest

No conflicts of interest

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