Assessment of vitamin D levels in patients with sudden sensorineural hearing loss

Elif Sari, Taskin Tokat, Aynur Aliyeva, Mehmet Karadag, Fatma Eren, Tolghahan Catli, Levent Olgun

Istanbul Aydin University, VM Medikal Park Florya Hospital, Department of Otorhinolaryngology-Head and Neck Surgery, Istanbul, Türkiye
Sakarya University Education and Research Hospital, Department of Otorhinolaryngology-Head and Neck Surgery, Sakarya, Türkiye
The Catholic University of Korea Seoul St. Mary Hospital, Department of Otorhinolaryngology-Head and Neck Surgery, Seoul, South Korea
Hatay Mustafa Kemal University, Faculty of Medicine, Department of Biostatistics, Hatay, Türkiye
Istanbul University, Cerrahpasa Faculty of Medicine, Department of Public Health, Istanbul, Türkiye
Istinye University, Faculty of Medicine, Department of Otorhinolaryngology-Head and Neck Surgery, Istanbul, Türkiye
Baskent University, Zubeyde Hanım Research Center, Department of Otorhinolaryngology-Head and Neck Surgery, Izmir, Türkiye

ARTICLE INFO

Keywords:
Sensorineural hearing loss
Vitamin D
Audiometry

Abstract

Aim: Vitamin D is important in antiproliferative, immunomodulatory, prodifferentiative effects, metabolic functions, and neuromuscular activity. We try to evaluate the relation between vitamin D deficiency and Idiopathic Sudden Sensorineural Hearing Loss (ISSHL) and its impact on response to treatment.

Materials and Methods: This study was performed prospectively in 2 groups, 55 participants with SSHL and 55 with normal hearing without middle ear pathology. All patient information such as age, gender, lipid values, coagulation parameters, audiometry results, and vitamin D level was recorded at baseline. Patients with SSHL received steroid therapy at a decreasing dose of 1 mg/kg/day, and their response to treatment had evaluated according to posttreatment audiometry tests.

Results: Vitamin D level in the SSHL group with a mean of 17.27 ± 15.73 ng/ml was significantly less than the control group (31.31 ± 27.21 ng/ml; p-value =0.001). The mean pure-tone audiometry (PTA) before treatment was 62.74 ± 23.66 dB HL (range 28-117 dB) and 45.24 ± 23.47 dB HL after treatment (range 6-101 dB HL). The patient group with less vitamin D values was statistically significant than the group with normal vitamin D values in terms of mean PTA before and after treatment (respectively: p=0.010; p=0.002). Pretreatment and posttreatment hearing levels were statistically higher in the group with normal vitamin D. Vitamin D values below 22.16 were a risk factor for sudden hearing loss (p=0.001).

Conclusion: In our study, participials with SSHL found a higher vitamin D deficiency level. The role of pathophysiological mechanisms underlying SSHL remains uncertain; vitamin D affecting these mechanisms seems to be an important prognostic factor.

Copyright © 2023 The author(s) - Available online at www.annalsmedres.org. This is an Open Access article distributed under the terms of Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License.

Introduction

Sudden Sensorineural Hearing Loss (SSHL) is a hearing loss of at least 30 dB at three consecutive frequencies within 72 hours [1]. SSHL was observed in 5 to 20 per 100,000 people per year [2]. A unilateral hearing loss associated with tinnitus, vertigo, and aural fullness, while bilateral involvement is rare, is the most common form in ENT practice [3]. The etiology of SSHL is still unclear, and there are many theories about the origin of this disease, including infectious, vascular, autoimmune, neoplastic, neurologic, metabolic, and conditions [4]. Recently, novel markers and risk factors have been proposed to elucidate diagnosis and prognosis in patients with SSHL. One of these parameters is vitamin D, which profoundly affects optimal health [5].

Vitamin D is a fat-soluble hormone obtained through exposure to sunlight, fortified foods, and multivitamins [6]. Vitamin D is essential for bone health, antiproliferative, proliferative effects, metabolic functions, and neuromuscular activity [7]. Moreover, it has a potent immunomodulatory activity through cytokine and immunoglobulin synthe-
sis of B and T lymphocytes [8]. Vitamin D’s importance in treating type 1 diabetes mellitus, rheumatoid arthritis, multiple sclerosis, hypertension, cardiovascular diseases, cancer, and autoimmune diseases is still under investigation [9-12].

Due to the presence of vitamin D receptors in the inner ear, vitamin D deficiency may cause problems in the inner ear [13-15]. According to these studies, the deficiency of vitamin D may cause disturbing the metabolism of calcium in the cochlea resulting in a metabolic type of sensorineural hearing loss. Additionally, calcium metabolism may cause disturbances in the physiology of the cochlear neurons [16]. Related to the mentioned theories may be considered that vitamin D deficiency is associated with hearing loss directly or indirectly. In this respect, we aimed to evaluate the possible correlation between vitamin D deficiency and ISSNHL and the importance as a risk factor of vitamin D deficiency in the etiology of ISSNHL.

**Materials and Methods**

This study was designed in the University of Health Sciences Izmir Bozyaka Education and Research Hospital between Nov 1, 2016, and Sep 31, 2018. The ethics committee of the University of Health Sciences Izmir Bozyaka Education and Research Hospital approved this study (approval number: 03 and date 25/10/2016). All the participants provided written informed consent to participate in the study. The patients in the study were designed as a study group formed of subjects with hearing loss and a control group including the issues with normal hearing.

Inclusion criteria of the study group were as follows:

1. About a 72-h, 30 dB decrease in three frequencies SSHL.
2. With no other hearing problems, ear manipulation, or surgery on the affected side.
3. No Magnetic Resonance Imaging (MRI) pathological signs
4. Hearing loss, unknown cause
5. Applying to the hospital in the first seven days.

The control group consisted of patients with a normal hearing range without any ear pathology (<25 dB). Patients with otitis media, a defined cause of acute hearing loss (e.g., Menière’s disease, retrocochlear disease, acute trauma), ototoxic drugs, radiotherapy or chemotherapy, liver or renal dysfunction, neurologic disease, and later coming than 14 days from the onset had excluded. Temporal MRI with gadolinium contrast was performed to evaluate ear pathologies in the leading group of patients. Each of the subjects in the study group had matched with the issues having identical features in the control group.

**Audiologic evaluation and treatment**

All patients analyzed blood samples, and biochemical markers had determined in terms of Hg, coagulometric tests, serologic tests, serum electrolyte, and vitamin D levels.

All patients underwent a standard otolaryngological examination. 0.25, 0.5, 1, 2, 3, 4, and 8 kHz thresholds were used for calculated air-bone conduction in pure-tone audiometry (PTA), and speech discrimination scores (SDS) were also noted. PTA had obtained before and during the first, second, and fourth weeks after the first treatment.

All participants with ISSNHL were treated according to the guidelines with descending doses of prednisolone steroids (at 1 mg/kg per day) [17]. Patients with comorbidities (DM, HT, and others.) were treated in association with the standard treatment.

Treatment results were evaluated by PT audiometry, using the average hearing levels at 0.25, 0.5, 1, 2, 3, 4, and 8 Hz. The mean PTA at the second and fourth weeks after treatment was used for statistical data analysis. Siegel criteria were used to evaluate the effect of treatment and were categorized as follows:

1. Final threshold ≤25 dB - Healing
2. Gain ≤15 dB, final threshold 25 - 45 dB- Partial improvement
3. Gain ≤15 dB, final threshold ≤45 dB- Slight improvement
4. Gain ≥15 dB and absolute hearing ≤75 dB- No response

**Statistical analysis**

The data relating to patients’ blood values and audiology variables were analyzed with Statistical Package for the Social Sciences (IBM SPSS Statistics, version 24.0 for Windows, Armonk, NY, USA) for medical statistics. Student T-tests for normally distributed indices and Mann-Whitney for un normally distributed indices were performed to compare independent groups. The Pearson and Exact Chi-square tests were used to analyze the categorized parameters, while the Shapiro Wilk test was used to evaluate the continuous baseline variables. The cut-off value was determined by ROC analysis of the disease using the variables of vitamin D, triglyceride, total cholesterol, red blood cell distribution width (RDW), mean platelet volume (MPV), and activated partial thromboplastin time (aPTT), international normalized ratio (INR). A p-value of less than 0.05 was considered statistically significant for all statistical analyses. Descriptive statistics (percentages, frequencies, means, and standard deviations) had used to present all variables.

The receiver operating characteristic (ROC) curve analysis using disease status as a classification variable was performed for determining an optimal vitamin D, triglyceride, total cholesterol, red blood cell distribution width (RDW), mean platelet volume (MPV), and activated partial thromboplastin time (aPTT), international normalized ratio (INR). Cut-off values for disease based on the Youden index (sensitivity + specificity – 1). The maximum value of the Youden index was considered as the optimal cutoff point.

The sample size was estimated using a power calculation based on 0.54 unit reduction in the Vitamin-D level in the Sudden Sensorineural Hearing Loss (SSHL) group compared to the Control group. At least 55 patients and 55 control would be needed to detect a significant difference between the Control and obese groups at an 80% power level and an a error of 5%. In this study, the sample size
was calculated based on the effect size calculated over the distances of the vitamin D parameter values in two independent groups with a plot study.

**Results**

According to the inclusion criteria described in this section, this study included 55 patients who underwent IS-SHL between Nov 1, 2016, and Sep 31, 2018. The mean age of patients (22 female, 33 male) was 50.7 ± 13.2 (range 19-78). The control group comprised 55 patients with a standard hearing reference without middle ear pathology (<25 dB). The mean age of the patients (24 female, 31 male) was 49.67 ± 14.61 (range 20-88) years (Table 1). In this study patient group and control group were designated as group 1 and group 2, respectively.

The Table 1 provides demographic and clinical characteristics of the study population, including means and standard deviations for various parameters in both the study and control groups. The results of statistical tests comparing the two groups are also presented, with p-values indicating the level of significance. In terms of age, there was no significant difference between the study and control groups (mean ± sd: 50.75 ± 13.29 vs 49.67 ± 14.61, p=0.688).

**Figure 1.** Comparison of hearing results before and after treatment.

**Figure 2.** Comparison of initial hearing levels and post-treatment hearing outcomes between vitamin D groups.

However, there was a trend towards a difference in gender distribution between the two groups, with a higher propor-
Comparison of mean PTA before and after treatment in vitamin D groups \(^{2}\) (Mann-Whitney U). Comparison of the recovery rates in the post-treatment mean PTA between vitamin D groups. \(^{2}\) (Mann-Whitney U).

<table>
<thead>
<tr>
<th></th>
<th>Low vitamin D</th>
<th>Normal vitamin D</th>
<th>(p^{1})</th>
<th>(p^{2})</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-treat PTA</td>
<td>40.28(\pm)14.66</td>
<td>65.49(\pm)23.16</td>
<td>0.010</td>
<td>0.703</td>
</tr>
<tr>
<td>Post-treat PTA</td>
<td>21.67(\pm)6.50</td>
<td>48.13(\pm)23.18</td>
<td>0.002</td>
<td></td>
</tr>
<tr>
<td>(p^{3})</td>
<td>0.028</td>
<td>-0.001</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 2 presents a comparison of vitamin D levels between two groups, those with low vitamin D and those with normal vitamin D levels, and their effect on pre- and post-treatment pure tone audiometry (PTA). The mean PTA before treatment was significantly lower in the low vitamin D group (40.28 \(\pm\)14.66) compared to the normal vitamin D group (65.49 \(\pm\)23.16) with a \(p\)-value of 0.010 (Mann-Whitney U test). After treatment, the mean PTA was significantly lower in the low vitamin D group (21.67 \(\pm\)6.50) compared to the normal vitamin D group (48.13 \(\pm\)23.18) with a \(p\)-value of 0.002 (Mann-Whitney U test). The recovery rate in the post-treatment mean PTA was significantly different between the low and normal vitamin D groups with a \(p\)-value of 0.028 (Mann-Whitney U test) and <0.001 (Wilcoxon test), respectively.

Vitamin D levels had a significant relationship with response to treatment. In patients showing complete recovery (<25 dB), vitamin D levels were higher compared to the rest of the subjects (\(p=0.001\)). Vitamin D levels showed a trend towards lower values in the patients with no healing (>75 dB), according to the patients showing recovery.

Table 3 reports the results of the ROC analysis for sudden hearing loss using various test results as potential predictive variables. The table shows the cut-off values, AUC (95% CI), standard error (SE), sensitivity, specificity, and \(p\)-values for each of the variables tested. The results show that five out of the seven variables tested have a statistically significant predictive value for sudden hearing loss. These variables include aPTT, INR, vitamin D, total cholesterol, and RDW. The cut-off values for these variables are >29.25, <1.19, <22.16, >174, and >15.65, respectively. The AUC values range from 0.528 to 0.739, with aPTT having the highest AUC value (0.739) and MPV having the lowest (0.528). The sensitivity values range from 0.167 to 0.889, with vitamin D having the highest sensitivity value (0.889) and MPV having the lowest (0.167). The specificity values range from 0.426 to 0.944, with MPV having the highest specificity value (0.944) and total cholesterol having the lowest (0.481).

As a result of ROC analysis, it was found that a vitamin D value below 22.16 was a risk factor for sudden hearing loss (\(p=0.001\)). AUC (Area Under Curve) value was 0.691 (0.590-0.793), sensitivity value was 0.889, and specificity value was 0.537. In addition, it had seen that total cholesterol value is 174, triglyceride value is 91.5, RDW value is 15.65, aPTT value is 29.25, MPV value is above 9.75, and INR value is below 1.19 are risk factors for sudden hearing loss (Table 3) (Figure 3).
Table 3. ROC analysis for sudden hearing loss.

<table>
<thead>
<tr>
<th>Test Result Variable(s)</th>
<th>Cut-off</th>
<th>AUC (95%CI)</th>
<th>SE</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Cholesterol</td>
<td>≥174</td>
<td>0.623 (0.513 0.734)</td>
<td>0.056</td>
<td>0.870</td>
<td>0.481</td>
<td>0.027</td>
</tr>
<tr>
<td>RDW</td>
<td>≥15.65</td>
<td>0.635 (0.530 0.740)</td>
<td>0.054</td>
<td>0.815</td>
<td>0.426</td>
<td>0.015</td>
</tr>
<tr>
<td>aPTT</td>
<td>≥29.25</td>
<td>0.739 (0.645 0.832)</td>
<td>0.048</td>
<td>0.833</td>
<td>0.574</td>
<td>0.001</td>
</tr>
<tr>
<td>INR</td>
<td>&lt;1.19</td>
<td>0.702 (0.604 0.800)</td>
<td>0.050</td>
<td>0.796</td>
<td>0.556</td>
<td>0.001</td>
</tr>
<tr>
<td>Tryglyceride</td>
<td>≥9.150</td>
<td>0.651 (0.547 0.756)</td>
<td>0.053</td>
<td>0.481</td>
<td>0.815</td>
<td>0.007</td>
</tr>
<tr>
<td>MPV</td>
<td>&gt;9.75</td>
<td>0.528 (0.418 0.637)</td>
<td>0.056</td>
<td>0.167</td>
<td>0.944</td>
<td>0.621</td>
</tr>
<tr>
<td>Vitamin D</td>
<td>&gt;22.16</td>
<td>0.691 (0.590 0.793)</td>
<td>0.052</td>
<td>0.889</td>
<td>0.537</td>
<td>0.001</td>
</tr>
</tbody>
</table>

RDW: red cell distribution width; aPTT: activated partial thromboplastin time; INR: international normalized ratio; MPV: mean platelet volume.

**Discussion**

Given the relation between hearing loss and cognitive decline, it is reasonable that sudden hearing loss may lead to a wide range of social, psychological, and physical troubles. Therefore, many researchers have focused on restoring hearing ability and defining prognostic factors for SSHL. The precise cause of SSHL has not been identified, but various pathophysiological mechanisms have been proposed to clarify the etiology. Previous studies reported that patients with hearing disorders had a high level of vitamin D deficiency [18-20]. A study performed on patients with bilateral hearing loss reported that the most likely cause for the situation is the demineralization of the cochlea, which may associate with vitamin D deficiency [21]. Additionally, animal studies reported that hearing loss and vestibular disorders associated with vitamin D receptor dysfunction [20]. In a recent survey, Ghazavi et al. stated that the prevalence of vitamin D deficiency in patients with SSHL was more than in healthy people [22].

Viral, vascular, and autoimmune factors are famous theories that may also be related to vitamin D deficiency. A viral infection is a popular but confusing cause of SSHL [23]. Wilson et al. investigated the relationship between viral seroconversions and ISSHL [24]. The ability of vitamin D to induce monocyte autophagy and the primary role of autophagy in the immune system has been demonstrated in previous studies [25,26]. Vitamin D modulates and controls the adaptive immune response, and its deficiency affects the immune system, primarily to respond to viral infections [27]. Immune signaling systems have directed vitamin D research into immunology, cancer, autoimmune, and cardiovascular diseases [28-30]. Impairment of cochlear microcirculation is another frequently theorized cause of SSHL. The cochlear vascular tree, feeding the cochlea, is of a terminal type, with no collateral vessels. Additionally, cochlear hair cells are susceptible to ischemic damage because of their hypermetabolic activity. Thus, impaired poor cochlear perfusion with microvascular damage are significant causes of SSHL.

Choung et al. investigated that arterial stiffness is strongly associated with developing SSHL and that increased arterial stiffness may influence its severity [31]. Gaddipati et al. examined the relation between vitamin D deficiency and peripheral arterial disease. They reported that vitamin D deficiency had been inversely correlated with cardiomyocyte and vascular smooth muscle cell proliferation, coronary calcification, and increased carotid intima-media thickness. Also vitamin D deficit can cause vascular calcification and stiffness [32].

Multiple sclerosis is the first autoimmune disorder investigated about vitamin D’s role in chronic illnesses. Subsequently, many studies have reported that vitamin D can prevent the onset of multiple sclerosis, autoimmune diseases, and rheumatoid arthritis. Recently, many tissues and organ systems have their D receptors, and synthetic analogs such as VDR 2 ligands can cause antiproliferation or immunomodulatory activities [33].

The findings of this study suggest that there may be significant differences in laboratory parameters between patients with idiopathic sudden sensorineural hearing loss (ISSHL) and those with normal hearing. These differences include elevated total cholesterol, decreased triglycerides and LDL cholesterol, increased neutrophil percentage, decreased lymphocytes, decreased MCH, increased glucose, prolonged aPTT, and decreased vitamin D levels in the patient group compared to the control group.

These results are consistent with previous studies that have shown an association between hearing loss and various metabolic and inflammatory factors. For example, a study by Zhao et al. found that patients with ISSHL had higher levels of total cholesterol, LDL cholesterol, and triglycerides compared to controls. In addition, the study by Bae et al. reported that patients with ISSHL had higher levels of inflammatory markers such as CRP and neutrophil-to-lymphocyte ratio (NLR) compared to controls [34-36].

Another interesting finding in this study was the high incidence of tinnitus and vertigo in patients with ISSHL, with 80% of patients experiencing tinnitus and 49.1% experiencing vertigo. This is consistent with previous studies that have reported a high prevalence of tinnitus and vertigo in patients with hearing loss [36].

The results presented in Table 2 indicate a significant relationship between vitamin D levels and response to treatment in patients with sudden hearing loss. The study found that patients with low vitamin D levels had significantly lower pre- and post-treatment pure tone audiometry (PTA) scores compared to those with normal vitamin D levels. Moreover, the recovery rate in the post-treatment mean PTA was significantly different between the low and normal vitamin D groups.

These findings are consistent with previous research that has shown a correlation between vitamin D deficiency and
hearing loss. A study by Gao et al. found that low serum vitamin D levels were significantly associated with an increased risk of hearing loss in older adults. Similarly, a study by Hossein-Abadi et al. reported that patients with hearing loss had significantly lower levels of serum vitamin D compared to healthy controls [37,38].

The findings have directed vitamin D research into the diseases associated with low serum vitamin D levels. Given that many etiological theories interacted with specific mechanisms initiated by vitamin D deficiency, SSHL may be considered one of the mentioned diseases. Although our results were significantly associated between vitamin D concentrations and SSHL, the study has several limitations. Firstly, SSHL is a disease presenting etiology widely and has not been identified as a precise cause.

This study provides further evidence for the association between metabolic and inflammatory factors and idiopathic sudden sensorineural hearing loss. The high incidence of tinnitus and vertigo in patients with ISSHL highlights the importance of addressing these symptoms in the management of hearing loss.

Conclusion

Much needs to be learned about pathogenesis for satisfaction with audiological rehabilitation and better management of patients with sudden SSHL. More studies are required to create more valuable and standardized treatment options. Firstly, SSHL is a disease presenting etiology widely and has not been identified as a precise cause.

Much needs to be learned about pathogenesis for satisfaction with audiological rehabilitation and better management of patients with sudden SSHL. More studies are required to create more valuable and standardized treatment options. Firstly, SSHL is a disease presenting etiology widely and has not been identified as a precise cause.

Ethical approval

The ethics committee of the University of Health Sciences Izmir Bozyaka Education and Research Hospital approved this study (approval number=03 and date 25/10/2016). References


