Ann Med Res

Current issue list available at AnnMedRes

Annals of Medical Research

journal page: www.annalsmedres.org

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

Elif Sari[a,*], Taskin Tokat[b], Aynur Aliyeva[c], Mehmet Karadag[d], Fatma Eren[e], Tolgahan Catli[f], Levent Olgun[g]

[a]*Istanbul Aydın University, VM Medikal Park Florya Hospital, Department of Otorhinolaryngology-Head and Neck Surgery, Istanbul, Türkiye*
[b]*Sakarya University Education and Research Hospital, Department of Otorhinolaryngology-Head and Neck Surgery, Sakarya, Türkiye*
[c]*The Catholic University of Korea Seoul St. Mary Hospital, Department of Otorhinolaryngology-Head and Neck Surgery, Seoul, South Korea*
[d]*Hatay Mustafa Kemal University, Faculty of Medicine, Department of Biostatistics, Hatay, Türkiye*
[e]*Istanbul University, Cerrahpasa Faculty of Medicine, Department of Public Health, Istanbul, Türkiye*
[f]*Istinye University, Faculty of Medicine, Department of Otorhinolaryngology-Head and Neck Surgery, Istanbul, Türkiye*
[g]*Baskent University, Zubeyde Hanim Research Center, Department of Otorhinolaryngology-Head and Neck Surgery, Izmir, Türkiye*

ARTICLE INFO

Keywords:
Sensorineural hearing loss
Vitamin D
Audiometry

Received: Jul 06, 2022
Accepted: May 03, 2023
Available Online: 26.05.2023

DOI:
10.5455/annalsmedres.2022.07.206

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.

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, ıt has a potent immunomodulator activity through cytokine and immunoglobulin synthe-

*Corresponding author:
Email address: ctf_elif@hotmail.com (Elif Sari)

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. İn this respect, we aimed to evaluate the possible correlation between vitamin D deficiency and ISSHL and the importance as a risk factor of vitamin D deficiency in the etiology of ISSHL.

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 İmaging (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., Meniere'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 SSHL 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 basedon 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 ISSHL 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).

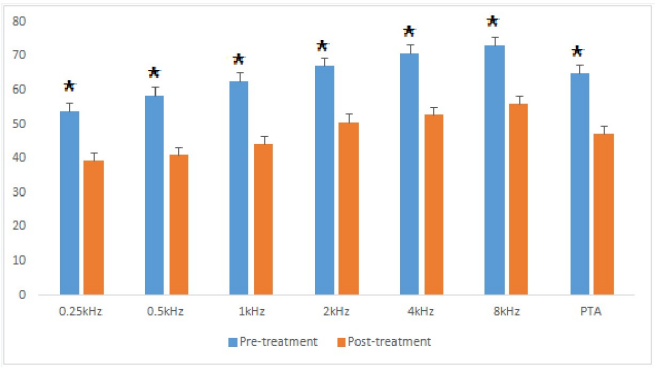

Figure 1. Comparison of hearing results before and after treatment.

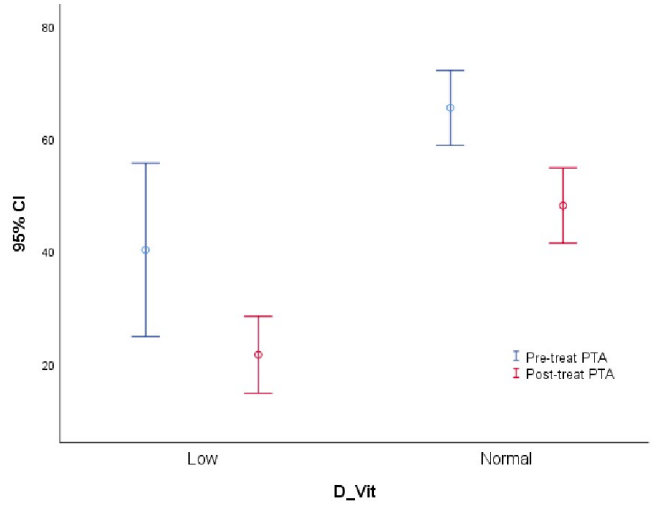

Figure 2. Comparison of initial hearing levels and post-treatment hearing outcomes between vitamin D groups.

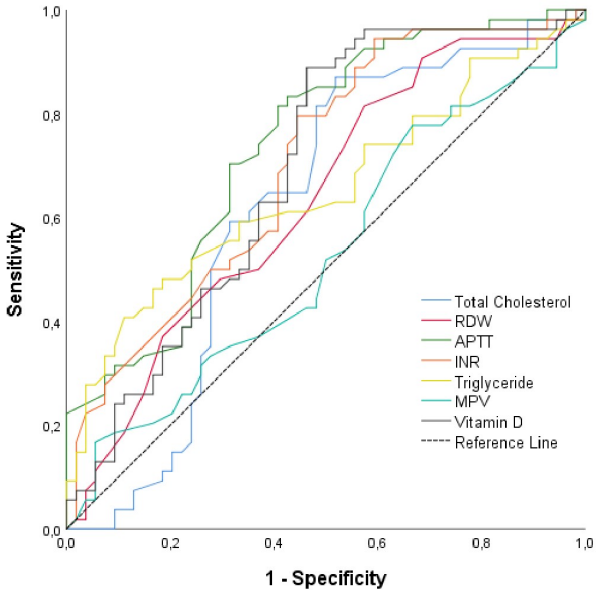

Figure 3. Roc analys for sudden hearing loss.

Table 1. Demographic and clinical characteristics of the study population.

	Study Group	Control Group	Total	
	Mean±sd	Mean±sd	Mean±sd	p
Age	50.75±13.29	49.67±14.61	50.21±13.91	0.688
Female /Male	22/33	31/24	55/55	0.056
Total Cholesterol	209.04±40.93	193.15±59.7	201.09±51.57	**0.022**
Tryglyceride	117.64±88.47	142.05±69.05	129.85±79.94	**0.004**
HDL	59.98±17.68	65.49±23.35	62.74±20.8	0.383
LDL	142.65±39.63	158.22±42.61	150.44±41.7	**0.048**
Hg	13.66±1.63	13.12±1.53	13.39±1.59	0.076
Neu %	74.52±10.99	68.61±13.01	71.54±12.36	**0.013**
PLT/lym	203.81±117.1	168.65±114.53	186.23±116.63	0.114
Lym	1.58±0.7	1.86±0.67	1.72±0.69	**0.037**
MCH	28.72±2.19	30.45±2	29.6±2.26	**0.001**
MCHC	32.5±1.08	32.38±1.38	32.44±1.23	0.632
PLT	260.22±53.96	257±63.35	258.61±58.59	0.775
RDW	15.73±2.1	15.73±0.6	15.73±1.53	**0.015**
MPV	11.2±1.3	11.35±1.23	11.27±1.26	0.548
Glucose	128.73±44.19	108.78±25.02	118.75±37.12	**0.004**
aPTT	31.44±2.91	28.05±4.24	29.75±4.00	**0.001**
INR	2.67±11.72	3.07±13.18	2.87±12.41	0.869
Pre-treat PTA	62.74±23.66		62.74±23.66	---
Post-treat PTA	45.24±23.47		45.24±23.47	---
Vit D	17.27±15.73	31.31±27.21	24.29±23.22	**0.001**

p value was obtained from Student t or Mann Whitney U test sd:standard deviation, Hg: hemoglobin; Neu: neutrophil; PLT/lym: platelet/lymphocyte; PLT: platelet; Lym: lymphocyte; MCH: mean corpuscular hemoglobin; MCHC: mean corpuscular hemoglobin concentration; RDW: red cell distribution width; MPV: mean platelet volume; aPTT: activated partial thromboplastin time; INR: international normalized ratio; Pre-treat PTA: pretreatment pure tone audiometry, Post-treat PTA: posttreatment pure tone audiometry.

However, there was a trend towards a difference in gender distribution between the two groups, with a higher propor-

Table 2. Comparison of vitamin D levels.

	Low vitamin D	Normal vitamin D		
	Mean±sd	Mean±sd	P[1]	P[2]
Pre-treat PTA	40.28±14.66	65.49±23.16	0.010	0.703
Post-treat PTA	21.67±6.50	48.13±23.18	0.002	
P[3]	0.028	<0.001		

Comparison of mean PTA before and after treatment between vitamin D groups P[1](Mann Whitney U). Comparison of the recovery rates in the post treatment mean PTA between vitamin D groups. P[2](Mann Whitney U). Comparison of mean PTA before and after treatment in vitamin D groups P[3](wilxocon test).

tion of females in the control group (22/33 vs 31/24, p=0.056).

Several laboratory parameters were significantly different between the two groups. Total cholesterol was higher in the study group (209.04±40.93 vs 193.15±59.7, p=0.022), while triglycerides were lower (117.64±88.47 vs 142.05±69.05, p=0.004). LDL cholesterol was also lower in the control group (142.65±39.63 vs 158.22±42.61, p=0.048). There was no significant difference in HDL cholesterol between the two groups.

Other laboratory parameters that were significantly different between the study and control groups included neutrophil percentage (74.52±10.99 vs 68.61±13.01, p=0.013), lymphocytes (1.58±0.7 vs 1.86±0.67, p=0.037), mean corpuscular hemoglobin (MCH) (28.72±2.19 vs 30.45±2, p=0.001), glucose (128.73±44.19 vs 108.78±25.02, p=0.004), aPTT (31.44±2.91 vs 28.05±4.24, p=0.001), and vitamin D (17.27±15.73 vs 31.31±27.21, p=0.001). There was no significant difference in platelet count, red cell distribution width (RDW), or mean platelet volume (MPV) between the two groups.

Of the patients in group 1, 44 were determined to have tinnitus (80 %), and 27 patients had vertigo (49.1 %). There was no statistically significant difference between the groups regarding age, gender, smoking status, and alcohol intake rate.

In a comparison of the groups regarding commonly presenting additional symptoms was found a significant difference in total cholesterol, triglycerides, LDL, RDW, and aPTT (p=0.022, p=0.004, p=0.048, p¬=0.015, and p=0.001 respectively). Still, no significant difference was found in upper airway infection history, hypertension, diabetes mellitus, hemoglobin, and HDL (p=0.824, p=0.807, p=0.200, p=0.076, and p=0.383, respectively) (Table 1). The mean vitamin D level was 17.27±15.73 ng/ml in group 1 and 31.31±27.21 ng/ml in group 2. They analyzed vitamin D levels between groups 1 and 2, a statistically significant difference (p 0.001) (Table 1). Vitamin D levels were found to be lower in patients with SSHL compared to the control grup. In study group, mean PTA before treatment was 62.74±23.66 dB HL (range 28-117 dB), after treatment was 45.24±23.47 dB HL (range 6-101 dB HL). In the study group posttreatment to Siegel's criteria, there was complete healing in 21.8 % (n=12) of the patients, partial improvement in 16.3 % (n=9), slight improvement in 18.1 % (n=10), and no response in 43.6 % (n=24). A statistically significant difference had found in mean PTA and all audiometric frequencies before and after treatment (Figure 1). Group 1 was divided into 2 groups as patients with normal and low Vitamin D values. There was a statistically significant difference between the group with low vitamin D value and the group with normal vitamin D value in terms of mean PTA before and after treatment. (p=0.010 and p=0.002, respectively). Pretreatment and posttreatment hearing levels were higher in the group with normal vitamin D (Table 2) (Figure 2).

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 posttreatment pure tone audiometry (PTA). The mean PTA before treatment was significantly lower in the low vitamin D group (40.28 ± 14.66) compared to the normal vitamin D group (65.49 ± 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 ± 6.50) compared to the normal vitamin D group (48.13 ± 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 analys for sudden hearing loss.

Test Result Variable(s)	Cut-off	AUC (95%CI)	SE	Sensitivity	Specificity	p
Total Cholesterol	>174	0.623 (0.513 0.734)	0.056	0.870	0.481	**0.027**
RDW	>15.65	0.635 (0.530 0.740)	0.054	0.815	0.426	**0.015**
aPTT	>29.25	0.739 (0.645 0.832)	0.048	0.833	0.574	**0.001**
INR	<1.19	0.702 (0.604 0.800)	0.050	0.796	0.556	**0.001**
Tryglyceride	>91.50	0.651 (0.547 0.756)	0.053	0.481	0.815	**0.007**
MPV	>9.75	0.528 (0.418 0.637)	0.056	0.167	0.944	0.621
Vitamin D	<22.16	0.691 (0.590 0.793)	0.052	0.889	0.537	**0.001**

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 mechanism(s) 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 protocols based on evidence. In recent studies, many theories and novel risk factors have been investigated to elucidate the pathogenesis of the SSHL. Although the role of pathophysiological achievement underlying SSHL remains unclear, vitamin D affecting these mechanisms seems to be an important prognostic factor.

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

1. Pecorari G, Riva G, Naqe N, Bruno G, Nardo M. & Albera R. (2019). Long-term Audiometric Outcomes in Unilateral Sudden Sensorineural Hearing Loss without Recurrence. The Journal of international advanced otology, 15(1), 56–61. https://doi.org/10.5152/iao.2019.6670.
2. Hıra İ, Yaşar M, Kaya A, Bayram A, Özcan İ. (2021). Prognostic Value of Fibrinogen/HDL Ratio in Idiopathic Sudden Sensorineural Hearing Loss. J Int Adv Otol. Mar;17(2):91-95. DOI: 10.5152/iao.2020.7438.
3. Durakovic N, Valente M, Goebel JA, Wick CC. (2019). What defines asymmetric sensorineural hearing loss? Laryngoscope. May;129(5):1023-1024. DOI: 10.1002/lary.27504.
4. Lawrence R, Thevasagayam R. (2015). Controversies in the management of sudden sensorineural hearing loss: an evidence-based review. Clin Otolaryngol. Jun;40(3):176-82. DOI: 10.1111/coa.12363.
5. Paprocki J, Sutkowy P, Piechocki J, Woźniak A. (2021). Association between Vitamin D Supplements, Oxidative Stress Biomarkers, and Hyperbaric Therapy in Patients with Sudden Sensorineural Hearing Loss. Oxidative Medicine and Cellular Longevity, Article ID 8895323, 10 pages. https://doi.org/10.1155/2021/8895323.
6. Roth DE, Abrams SA, Aloia J, et al. (2018). Global prevalence and disease burden of vitamin D deficiency: a roadmap for action in low- and middle-income countries. Ann N Y Acad Sci. Oct;1430(1):44-79. doi: 10.1111/nyas.13968.
7. Pludowski P, Holick M.F, Grant W.B, Konstantynowicz J et al. (2018). Vitamin D supplementation guidelines. J. Steroid Biochem. Mol. Biol. Jan;175:125-135. doi: 10.1016/j.jsbmb.2017.01.021.
8. Chirumbolo S, Bjørklund G, Sboarina A, Vella A. (2017). The Role of Vitamin D in the Immune System as a Pro-survival Molecule. Clin Ther. May;39(5):894-916. DOI: 10.1016/j.clinthera.2017.03.021.
9. Wang TJ, Pencina MJ, Booth, SL, Jacques PF, Ingelsson E., Lanier K, Benjamin EJ, D'Agostino RB, Wolf M. & Vasan RS. (2008). Vitamin D deficiency and risk of cardiovascular disease. Circulation, 117(4), 503–511. https://doi.org/10.1161/CIRCULATIONAHA.107.706127.
10. Holick MF 2004 Vitamin D: importance in the prevention of cancers, type 1 diabetes, heart disease, and osteoporosis. Robert H. Herman Memorial Award in Clinical Nutrition Lecture. Am J Clin Nutr. 2003; 79:362–371.
11. Berridge MJ. Vitamin D deficiency and diabetes. Biochem J.2017;474(8):1321-1332.
12. Welsh J. (2017). Function of the vitamin D endocrine system in mammary gland and breast cancer. Mol Cell Endocrinol. Sep 15;453:88-95. DOI: 10.1016/j.mce.2017.04.026.
13. Talebi, H., Moallemi, M., & Ghorbani, M. (2019). Evaluation of Saccule Function in Patients with Vitamin D Deficiency. Journal of audiology & otology, 23(1), 49–52. https://doi.org/10.7874/jao.2018.00304.
14. Taneja MK, Taneja V. (2012). The role of vitamin D in the prevention of deafness. Indian J Otol April 1;18(2):55.
15. Carpinelli MR, Wise AK, Burt RA. (2011). Vitamin D-deficient diet rescues hearing loss in Klotho mice. Hear Res. May;275(1-2):105-9. doi: 10.1016/j.heares.2010.12.009.
16. Rubin R. (2013) Calcium and the secretory process. Springer Science & Business Media; June 29, 2013, Boston.
17. Stachler RJ, Chandrasekhar SS, Archer SM, et al. (2012). Clinical practice guideline: sudden hearing loss. Otolaryngol Head Neck Surg. Mar;146(3 Suppl): S1-35. DOI: 10.1177/0194599812436449.
18. Zou J, Minasyan A, Keisala T, Zhang Y, Wang JH, Lou YR, Kalueff A, Pyykkö I, Tuohimaa P. (2008). Progressive hearing loss in mice with a mutated vitamin D receptor gene. Audiol Neurootol. 2008;13(4):219-30. DOI: 10.1159/000115431.
19. Kwon HJ. (2016). Vitamin D receptor deficiency impairs inner ear development in zebrafish. Biochem Biophys Res Commun. 2016 Sep 16;478(2):994-8. DOI: 10.1016/j.bbrc.2016.08.070.
20. Minasyan A, Keisala T, Zou J, Zhang Y, Toppila E, Syvälä H, Lou YR, Kalueff AV, Pyykkö I, Tuohimaa P. (2009). Vestibular dysfunction in vitamin D receptor mutant mice. J Steroid Biochem Mol Biol. Apr;114(3-5):161-6. DOI: 10.1016/j.jsbmb.2009.01.020.
21. Brookes GB. (1983). Vitamin D deficiency--a new cause of cochlear deafness. J Laryngol Otol. May;97(5):405-20. DOI: 10.1017/s0022215100094330.
22. Ghazavi H, Kargoshaie AA, Jamshidi-Koohsari M. (2020). Investigation of vitamin D levels in patients with Sudden Sensory-Neural Hearing Loss and its effect on treatment. Am J Otolaryngol. 2020 Mar-Apr;41(2):102327. DOI: 10.1016/j.amjoto.2019.102327.
23. Chen X, Fu, Y. Y., & Zhang TY. (2019). Role of viral infection in sudden hearing loss. The Journal of international medical research, 47(7), 2865–2872. https://DOI.org/10.1177/0300060519847860.
24. Wilson WR, Veltri RW, Laird N, Sprinkle PM. (1983). Viral and epidemiologic studies of idiopathic sudden hearing loss. Otolaryngol Head Neck Surg. Dec;91(6):653-8. DOI: 10.1177/019459988309100612.
25. Suda T, Abe E, Miyaura C, et al. (1982). Induction of differentiation of human myeloid leukemia cells by 1α,25-dihydroxy vitamin D. In Norman AW, 3 Schaefer K, Herrath DV, Grigdeit HG, eds. Vitamin D, Chemical, Biochemical, and Clinical Endocrinology of Calcium Metabolism: Proceedings of the Fifth Workshop on Vitamin D, Williamsburg, VA, USA. Berlin, Germany: Walter de Gruyter; 1982:59–64.
26. Dietrich T, Joshipura KJ, Dawson-Hughes B, Bischoff-Ferrari HA. (2004). Association between serum concentrations of 25-hydroxyvitamin D3 and periodontal disease in the US population. Am J Clin Nutr. Jul;80(1):108-13. DOI: 10.1093/ajcn/80.1.108.

27. Bikle DD. Vitamin D regulation of immune function. (2011). Vitam Horm. 86:1-21. DOI: 10.1016/B978-0-12-386960-9.00001-0.
28. Nagpal S, Na S, Rathnachalam R. (2005). Noncalcemic actions of vitamin D receptor ligands. Endocr Rev. Aug;26(5):662-87. DOI: 10.1210/er.2004-0002.
29. Mathieu C, Adorini L. (2002). The coming of age of 1,25-dihydroxy vitamin D(3) analogs as immunomodulatory agents. Trends Mol Med. Apr;8(4):174-9. DOI: 10.1016/s1471-4914(02)02294-3.
30. Cantorna MT, Zhu Y, Froicu M, Wittke A. (2004). Vitamin D status, 1,25-dihydroxyvitamin D3, and the immune system. Am J Clin Nutr. Dec;80(6 Suppl):1717S-20S. DOI: 10.1093/ajcn/80.6.1717S.
31. Chung JH, Lee SH, Park CW, Kim C, Park JK, Shin JH. (2016). Clinical significance of arterial stiffness in idiopathic sudden sensorineural hearing loss. Laryngoscope. Aug;126(8):1918-22. DOI: 10.1002/lary.25853.
32. Gaddipati VC, Kuriacose R, Copeland R, Bailey BA, Peiris AN. (2010). Vitamin D deficiency: an increasing concern in peripheral arterial disease. J Am Med Dir Assoc. Jun;11(5):308-11. DOI: 10.1016/j.jamda.2010.02.002.
33. Holick MF. (2006). High prevalence of vitamin D inadequacy and implications for health. Mayo Clin Proc. Mar;81(3):353-73. DOI: 10.4065/81.3.353.
34. Zhao L, Li J, Liang H, Li L. & Yang J. (2021). Association between serum lipid levels and idiopathic sudden sensorineural hearing loss. BMC Otolaryngology, 21(1), 125. doi: 10.1186/s12887-021-02644-6.
35. Bae SC, Shin YH, Lee JH, Kim YH. & Lim HW. (2019). Inflammatory markers in idiopathic sudden sensorineural hearing loss: A propensity score matching analysis. Clinical and Experimental Otorhinolaryngology, 12(1), 37-42. doi: 10.21053/ceo.2018.00560.
36. Han JJ, Lee SH, Shin SO, Yoo HS. & Park HJ. (2018). Characteristics of tinnitus and vertigo in Meniere's disease. Auris Nasus Larynx, 45(1), 56-62. doi: 10.1016/j.anl.2017.03.011.
37. Gao M, Singh S, Ng S. & Yap M. (2016). Association between serum vitamin D insufficiency and hearing loss: A systematic review and meta-analysis. Nutrition Reviews, 74(5), 293-307.
38. Hossein-Abadi, R., Atri, M., Mahmoudi-Gharaei, J., & Ashrafi, M. R. (2017). Association of serum vitamin D deficiency with hearing impairment in Iranian children. International Journal of Pediatric Otorhinolaryngology, 98, 1-5.