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Clinical significance of evaluation of some metabolic and hematological parameters in patients with sudden sensorineural hearing loss

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Abstract

Background

Sudden sens orineural hearing loss (SSNHL) is a medical emergency, being mostly an idiopathic disease. Understanding the pathogenesis of SSNHL may help physicians for diagnosis and intervention.

Objective

The aim of the present study was to investigate some metabolic and hematological parameters in patients with SSNHL and related them to their clinical condition.

Patients and methods

The study was conducted on 50 patients with SSNHL and 20 age-matched and sex-matched controls. Both groups were subjected to audiological and laboratory evaluation of their fasting blood sugar (FBS), lipid profile, thyroid function test, neutrophil–lymphocyte ratio, and platelet–lymphocyte ratio. Moreover, the relation between these laboratory parameters and the severity of hearing loss was studied.

Results

By comparing patients with parameters in both groups, FBS, triglycerides (TG), neutrophil–lymphocyte ratio, and platelet–lymphocyte ratio were found to be significantly increased in the patient group. Moreover, increased FBS, TG, and free thyroxine appeared to be related to the severity of the hearing loss.

Conclusion

Hyperglycemia, hypertriglyceridemia, and hyper-inflammatory state can be considered as risk factors in the pathogenesis of SSNHL. Moreover, increased serum levels of FBS, TG, and free thyroxine are closely associated with the severity of the disease.

Keywords: Hematological parameters, metabolic parameters, sudden sensorineural hearing loss

Introduction

Sudden sensorineural hearing loss (SSNHL) is defined as SNHL of at least 30 dB over three successive pure-tone frequencies in less than 3 days. The reported incidence is rare ranging from 5 to 20 per 100 000 individuals [1]. SNHL is usually idiopathic in up to 90% of cases; it is presented unilaterally in 95% of patients. SSNHL was rarely presented bilaterally in 5% of cases [2].

Although several etiologies, including infection, otologic disease, trauma, and prothrombotic susceptibility have been confirmed, but most cases are idiopathic. Prothrombotic susceptibility has been demonstrated to be one of the causes for ischemic changes in the inner ear. Microcirculatory failure and inflammatory state were mostly hypothesized for idiopathic sudden sensorineural hearing loss (ISSHL) [3].

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The inner ear can be directly affected by alteration in serum insulin as well as by variation in plasma glucose levels. Hearing impairment was more prevalent among adults with diabetes than among those without [4]. Moreover, previous studies have shown that hearing acuity can be affected by lipid metabolism, and serum cholesterol levels have been considered as a significant risk factor in SSNHL [5]. Quaranta *et al.* [6] reported that high cholesterol level in peripheral blood correlates with poorer hearing recovery in ISSHL. Serum thyroid hormone levels have also been correlated with human auditory function; hearing acuity changes have been attributed due to hyperfunction or hypofunction of the thyroid gland [7].

Chronic inflammation has been considered as one of the most important causes of ISSHL. Zhang *et al.* [1] reported that neutrophil–lymphocyte ratio (NLR) and platelet–lymphocyte ratio (PLR) predict the state of chronic inflammation in patients with SSNHL. Chen *et al.* [8] suggested that NLR might be a useful biomarker to determine the onset of ISSHL and its prognosis.

Aim

The aim of this study was to investigate selected metabolic and hematological parameters in patients with SSNHL and to analyze the relationship between each parameter and the clinical condition of the patients.

Patients and methods

This study was conducted on 50 patients with SSNHL selected from Audiology Unit of Hearing and Speech Institute. The control group consists of 20 healthy, age-matched and sex-matched individuals. An informed consent was obtained from all participants participating in the study. All participants were subjected to a collection of demographic data (sex and age). Basic audiological evaluation was done for all participants using Two Channel Audiometer (model AC40; Interacoustic, Denmark) in the form of the following:

(1) Pure-tone audiometry
   (a) Air conduction thresholds were tested at the following frequencies: 0.25, 0.5, 1, 2, 4, and 8 kHz.
   (b) Bone conduction thresholds at the following frequencies: 0.5, 1, 2, and 4 kHz.
(2) Speech reception threshold: using Arabic spondee words.
(3) Word discrimination score: using Arabic Phonetically Balanced words [9].
(4) Acoustic Immittancemetry Testing was done using middle ear analyzer (model Az26; Interacoustics) in the form of tympanometry and acoustic reflex threshold measurements.

The inclusion criterion in SSNHL was a loss of at least 30 dB in three or more successive frequencies that occurred with sudden onset over a 72-h period.

Venous blood samples were collected from all participants in plain tubes and tubes that contained EDTA following 12-h fast. Complete blood cell counts were performed from the EDTA tubes with an automated blood cell counter (Phoenix NCC-3300, Neomedica, Ireland). NLR and PLR were calculated. In healthy adult people, NLR ranges between 0.78 and 3.53 [10] and PLR ranges between 61 and 239 [11].

Blood samples in the plain tubes were centrifuged at 3000 rpm and sera were separated for fasting blood glucose, total cholesterol (TC), triglycerides (TGs), and high-density lipoprotein (HDL)-cholesterol estimation using a semi-automated chemistry analyzer (Prestige Diagnostics, Ballymena, Northern Ireland, UK). Low-density lipoprotein (LDL)-cholesterol was calculated by Friedewald formula. The remaining sera were collected in aliquots and stored at − 20 until used for thyroid function test evaluation. Free T4 and thyroid-stimulating hormone (TSH) were assayed by chemiluminescent assay using an automated immunoassay analyzer (centaur XPT; Siemens, Germany).

The following reference ranges were considered: fasting blood sugar (FBS) 70–110 mg/dl, TC up to 200 mg/dl, LDL up to 160 mg/dl, HDL 40–60 mg/dl, TG up to 150 mg/dl, free thyroxine (FT4) 0.6–1.54 mg/dl, and TSH 0.5–4.2 μU/ml [12].

Statistical analysis

Data analysis was performed using the Statistical Package for the Social Sciences (SPSS) of the International Business Machines Corporation (IBM Corp., Chicago, Illinois, USA), version 22, 2013.

Data were expressed as mean ± SD for quantitative parametric measures in addition to both number and percentage for categorized data.

The following tests will be done:

(1) Comparison between two independent mean groups for parametric data using Student *t* test.
(2) Comparisons between the three groups with respect to normally distributed numeric variables were done using one-way analysis of variance followed by Bonferroni post-hoc test. *P* value more than 0.05 is nonsignificant and *P* value less than or equal to 0.05 is significant.

Results

All participants underwent pure-tone audiometry. Table 1 shows that there was a statistically significant difference between pure-tone thresholds in the control group and the patient group.

Both patient and control group were subjected to laboratory investigations, and the results were compared between the two groups as mean and SD using Student *t* test. There was a statistically significant increase in FBS, TG, NLR, and PLR levels in the patient group when compared with the control group. Otherwise, no statistically significant differences were found in TC, LDL, HDL, FT4, and TSH levels between the two groups (Table 2).

The patient group was categorized according to the severity of hearing loss (HL) into three subgroups: moderate HL (41–55 dB), moderately severe HL (56–70 dB), and severe HL (71–90 dB). Table 3 shows that there is a statistically significant difference between pure-tone thresholds in moderate, moderately severe, and severe HL subgroups within the patient group.

A comparison among the three subgroups was done for each laboratory parameter, and there was no statistically significant difference when analysis of variance test was applied among the three subgroups (Table 4).

Bonferroni post-hoc test revealed a statistically significant increase in FBS levels when we compared moderately severe HL subgroup with moderate HL subgroup, severe HL subgroup with moderately severe subgroup, and severe HL subgroup with moderate HL subgroup. Moreover, there was a statistically significant increase of TG levels of severe HL subgroup when we compared them with moderately severe HL subgroup. Moreover, there was a statistically significant increase of FT4 levels of moderately severe HL subgroup when we compared them with moderate HL subgroup and severe HL subgroup when we compared them with moderate HL subgroup (Table 5).

Table 1: Comparison between pure-tone thresholds in control group and patient group

Frequencies (kHz)	Patient group	Control group	*P*
0.25	58.00±8.02	14.25±2.93	0.000*
0.5	61.30±7.81	15.00±2.81	0.000*
1	65.20±9.84	15.50±4.26	0.000*
2	70.30±11.71	16.00±4.17	0.000*
4	74.70±12.67	17.25±3.80	0.000*
8	76.60±14.86	19.00±4.47	0.000*

*: Significant. Data are presented as mean±SD. *P* value more than 0.05 (nonsignificant) and *P* value less than or equal to 0.05 (significant).

Table 2: Comparison between laboratory results in patient group and normal group

Parameters	Patient group (*n*=50)	Control group (*n*=20)	*t*	*P*
FBS	145.06±72.64	82.3±10.16	2.86	0.01*
TC	186.42±50.52	158.25±38.18	1.76	0.095
TG	179±105.3	124.1±38.68	3.15	0.01*
LDL	139.5±50.89	132.12±37.64	0.22	0.83
HDL	46.76±13.29	48.05±9.06	−0.35	0.73
FT4	1.79±1.48	1.26±0.39	1.42	0.17
TSH	2.84±1.62	2.63±0.95	−0.2	0.98
NLR	4.01±0.97	2.00±0.9	8.15	0.00*
PLR	192.7±21.24	123.35±21.96	10.13	0.00*

*: Significant. Data are presented as mean±SD. FBS, fasting blood sugar; FT4, free thyroxine; HDL, high-density lipoprotein; LDL, low-density lipoprotein; NLR, neutrophil–lymphocyte ratio; PLR, platelet–lymphocyte ratio; TC, total cholesterol; TG, triglyceride; TSH, thyroid-stimulating hormone. *P* value more than 0.05 (nonsignificant) and *P* value less than or equal to 0.05 (significant).

Table 3: Comparison between pure-tone thresholds in moderate, moderately severe, and severe hearing loss within patient group

Frequencies (kHz)	Moderate SNHL	Moderately severe SNNHL	Severe SNHL	*P*
0.25	47.22±2.64	53.33±3.09	64.42±4.55	0.000*
0.5	50.56±3.91	56.67±3.91	67.69±3.53	0.000*
1	52.78±2.64	59.67±4.42	72.69±6.67	0.000*
2	56.11±4.17	61.67±4.88	80.19±5.56	0.000*
4	58.89±4.86	65.33±4.99	85.58±5.71	0.000*
8	59.33±6.21	69.33±1.76	88.85±4.08	0.000*

*: Significant. Data are presented as mean±SD. SNHL, sensorineural hearing loss. *P* value more than 0.05 (nonsignificant) and *P* value less than or equal to 0.05 (significant).

Discussion

SSNHL is an emergency disease requiring immediate diagnosis and treatment. The pathogenesis of SSNHL remains controversial, which delays the preventive and therapeutic strategy making. Some pathophysiological mechanisms, including vascular disease, viral infection, metabolic disease, autoimmunity, trauma, and other factors, are supposed to be the causes of SSNHL [13].

Metabolic parameters

Microcirculatory disturbance may be the main cause of SSNHL. The blood supply for cochlea is cochlear artery which is a terminal artery without any collateral vessels for compensation of any occlusion of cochlear artery [14]. Therefore, any disease affecting the cochlear perfusion may lead to reduction of oxygen supply to cochlea causing SSNHL [15]. Cardiovascular and metabolic diseases such as hypertension, diabetes mellitus, hyperlipidaemia, and hormonal disturbances may reduce the elasticity of blood vessels and accelerate the formation of atherosclerosis. So, this interferes with cochlear perfusion [16]. Several studies have related the microangiopathy induced by these comorbidities to the association with SSNHL [17].

Hyperglycemia

In this study, among patients with SSNHL, there was a statistically significant increase in FBS compared with the control group. There is a statistically significant increase in FBS levels in patients with moderately severe HL in comparison with patients with moderate HL. Moreover, there is a statistically significant increase in FBS levels in patients with severe HL in comparison with patients with moderately severe HL and between patients with severe HL in comparison with patients with moderate HL. These data are in agreement with previous results showing a higher frequency of glucose disorders in patients with dizziness and/or HL than in the normal population [18]. Fukui *et al.* [19] found a high frequency of hyperglycemia within the SSNHL population. Later, Oiticica and Bittar [20] observed a significantly higher frequency of hyperglycemia more than twice that expected for the population.

Table 4: Statistical comparison between mean values of laboratory parameters regarding the severity of hearing loss (analysis of variance test)

Parameters	Moderate HL ($n=9$)	Moderately severe HL ($n=15$)	Severe HL ($n=26$)	*F*	*P*
FBS	103.11±24.67	143.2±67.7	181.81±105.77	3.03	0.06
TC	188.67±38.76	207.87±28.25	226.12±9.19	2.22	0.12
TG	143.78±72.45	150.6±63.26	207.73±126.59	2.11	0.13
LDL	109.44±38.68	127.33±43.97	142.73±56.56	1.56	0.22
HDL	49.57±12.3	50.13±11.4	43.85±14.37	1.32	0.28
FT4	2.57±2.49	1.35±0.68	1.72±1.17	2.2	0.12
TSH	2.65±1.3	2.98±1.92	3.1±1.52	0.31	0.74
NLR	3.34±1.22	3.26±0.89	4.09±0.86	2.89	0.07
PLR	194.67±19.26	194.53±20.42	191.85±21.81	0.11	0.9

Data are presented as mean±SD. FBS, fasting blood sugar; FT4, free thyroxine; HDL, high-density lipoprotein; HL, hearing loss; LDL, low-density lipoprotein; NLR, neutrophil–lymphocyte ratio; PLR, platelet–lymphocyte ratio; TC, total cholesterol; TG, triglyceride; TSH, thyroid-stimulating hormone. *P* value more than 0.05 (nonsignificant) and *P* value less than or equal to 0.05 (significant).

Table 5: Post-hoc test between the three groups for each parameter

	LSD (*P*)		
Parameters	Moderate HL vs. moderately severe HL	Moderately severe HL vs. severe HL	Severe HL vs. moderate HL
FBS	0.016*	0.01*	0.00*
TC	0.79	0.17	0.2
TG	0.41	0.05*	0.26
LDL	0.58	0.42	0.26
HDL	0.79	0.17	0.39
FT4	0.001*	0.1	0.006*
TSH	0.27	0.41	0.53
NLR	0.97	0.99	0.34
PLR	0.44	0.71	0.78

*: Significant. FBS, fasting blood sugar; FT4, free thyroxine; HDL, high-density lipoprotein; HL, hearing loss; LDL, low-density lipoprotein; LSD, least significant difference; NLR, neutrophil–lymphocyte ratio; PLR, platelet–lymphocyte ratio; TC, total cholesterol; TG, triglyceride; TSH, thyroid-stimulating hormone. *P* value more than 0.05 (nonsignificant) and *P* value less than or equal to 0.05 (significant).

The mechanism by which hyperglycemia leads to sudden deafness is not so clear. Experimental studies showed that fluctuations in serum glucose lead to changes in serum osmolarity, which affect outer hair cell motility, function, and impair cochlear microphonics [21]. Lisowska *et al.* [22] suggested that changes in cochlear micromechanics and in the retro cochlear auditory pathway may cause subclinical hearing impairment in diabetic patients. The loss of hair cells occurs during conditions of glucose deprivation, with inner hair cells being more liable than outer hair cells [23].

The American National Health Survey also supported our data by showing that hearing impairment is more prevalent among adults with diabetes (21.3%) compared with those without diabetes (9.4%) [4]. Teranishi *et al.* [24] reported that patients with SSNHL showed diabetes mellitus more frequently than normal persons.

Dyslipidemia

Previous studies have shown that auditory function can be affected by lipid metabolism. Metabolic syndrome, like dyslipidemia, hypertension, and diabetes, was highly related to microangiopathy. Dyslipidemia is associated with low HDL, high LDL, hypercholesterolemia, and/or triglyceridemia. It can interfere with blood supply by plaque formation, endothelial dysfunction, vascular remodeling, vascular inflammation, and vessel obstruction. These mechanisms make the cochlea vulnerable to microvascular ischemia as it is supplied by the labyrinthine artery which is a terminal artery without collateral arterial blood flow [13].

On the contrary, experimental chronic hypercholesterolemia metabolically stresses inner ear tissue, inducing cochlear glycogen accumulation and edema in both the stria vascularis and outer hair cells [25].

Our data showed a statistically significant increase in TG levels in patient group when compared with the control group. Otherwise, no statistically significant differences were found in TC, LDL, and HDL levels between the two groups. Moreover, there was a statistically significant increase of TG levels of severe HL subgroup when we compared them with moderately severe HL subgroup. Similarly, Evans *et al.* [26] suggested that chronic dyslipidemia associated with elevated TGs might decrease auditory function. Moreover, the studies by Mohammed[27] and Li *et al.* [28] showed that there was significant difference in the means of lipid profile, especially TG, between patient and control groups. They suggested that lipid profile was associated with the incidence and prognosis of SSNHL.

In previous studies, serum cholesterol levels have been considered as an acquired risk factor in the SSNHL population. Zhang *et al.*[1] found that patients with higher LDL and lower HDL values were more reliable for successive bilateral SSNHL. They also concluded that correction of dyslipidemia in patients with SSNHL leads to hearing improvement. This confirms that dyslipidemia was associated with the onset of HL and its prognosis. Moreover, Oiticica and Bittar [20] observed

a significantly higher frequency of hypercholesterolemia among patients with SSNHL. Regarding TG levels, the differences observed in both previous studies were not significant.

All studies are in agreement that hyperlipidemia seems to be significantly associated with the incidence of SSNHL with some differences in lipid profile parameters may be owing to differences in the sample size.

Thyroid dysfunction

In this study, there was a statistically significant increase of FT4 levels of moderately severe HL subgroup in comparison with moderate HL subgroup. Moreover, on comparing FT4 levels in severe HL subgroup with moderate HL subgroup, the results suggest an association between elevated FT4 and the severity of HL. In agreement with our study, Oiticica and Bittar [20] reported that thyroid diseases were more frequent in patients with SSNHL than in the general population. Tsai *et al.* [7] found an association between hyperthyroidism and SSNHL and that association of hyperthyroidism with patients with high-risk SSNHL might help physicians for proper diagnosis and intervention.

Oiticica and Bittar [20] conducted a study on patients with SSNHL and noticed that thyroid dysfunction was more common among these patients than among the normal population. Nakashima *et al.* [29] studied SSNHL risk factors, reporting that patients with thyroid disease had a higher ratio for SSNHL than those without such history.

Other studies have related the thyroid dysfunction to hypercoagulability and venous thrombosis, which may affect blood supply of the cochlea, thus causing SSNHL [30]. Impaired auditory function particularly at high frequencies has been reported in patients with hyperthyroidism due to autoimmune disease [31]. Both subclinical and clinical hyperthyroidism affect the coagulation-fibrinolytic balance and promote a prothrombotic state, which may increase the risk of SSNHL [32].

The reason for these associations might be due to thyroid autoantibodies, which mediate peripheral or central hearing organ dysfunction, increasing susceptibility to SSNHL [33]. The previously mentioned results suggested that preexisting thyroid diseases are involved in SSNHL pathogenesis.

Hematological parameters

In this study, there was a statistically significant increase in NLR and PLR levels in the patient group when compared with the control group, and no relation was found between these parameters and the severity of HL.

Similarly, Kum *et al.* [34] and Chen *et al.* [8] found that patients with SSNHL had significantly higher NLR than controls. Moreover, NLR was significantly higher in patients who did not recover than those who did. These findings indicate that NLR might be an important biomarker for prognosis of SSNHL. Moreover, Qiao *et al.* [35] found that the average NLRs and PLRs of patients with SSNHL before treatment were both significantly higher than in controls.

Previous studies have revealed an association of SSNHL with chronic inflammation [2,36]. A strong relationship between cochlear damage and inflammatory markers has been shown [37]. Steroid treatment helps to treat SSNHL by reducing inflammation in the inner ear. Chronic inflammation is a common causative factor of SSNHL, which increases the risk of microvascular damage and ischemia leading to atherogenesis [38]. Thus, the pathophysiology of SSNHL is associated with affection of cochlear blood supply. Simultaneously, circulating inflammatory molecules lead to harmful effects on the cochlear vasculature [39].

Doo *et al.* [39] concluded that markers associated with inflammation in patients with SSNHL include higher WBC, neutrophil, monocyte, and lymphocyte counts, and composite markers associated with inflammation in these patients include higher NLR and PLR.

Conclusion

This study concluded that some metabolic parameters (hyperglycemia and hypertriglyceridemia) are considered significant risk factors for SSNHL. These metabolic parameters may be related to the vascular damage occurs in SSNHL. Moreover, some inflammatory markers (NLR and PLR) can be used as reliable and cost-effective indicators for the inflammatory pathogenesis of SSNHL. Our data reinforce the vascular hypothesis and the inflammatory mechanism for pathogenesis of SSNHL. Moreover; hyperglycemia, hypertriglyceridemia, and hyperthyroidism appear to be closely associated with the severity of SSNHL.

Recommendations

Further studies may be needed on a larger sample size and with following up the patients for NLR and PLR as prognostic biomarkers.

Ethical Clearance

This study followed local laws and the Declaration of Helsinki. The study was approved by the institute ethics committee.

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Conflicts of interest

There are no conflicts of interest.

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