

Original Research

The Relationship between Sudden Sensorineural Hearing Loss and Serum Sex Hormone Levels in Perimenopausal Women

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Abstract

Background: The purpose of the study was to explore the relationship between sudden sensorineural hearing loss (SSNHL) and serum sex hormone levels in perimenopausal women, as well as to further investigate the influence of these indicators for SSNHL in perimenopausal women. **Methods:** A total of 156 patients with SSNHL and 149 healthy individuals during perimenopause who received treatment or underwent physical examination in the Fourth Hospital of Shijiazhuang from August 2023 to December 2023 were selected to participate in this retrospective cohort study. The variances in fundamental patient data were analyzed using the Mann-Whitney U test and Chi-square test. We employed multivariate logistic regression to examine the association between serum levels of follicle stimulating hormone (FSH), luteinizing hormone (LH), estradiol (E2), progesterone (P), testosterone (T), prolactin (PRL) levels and the occurrence of SSNHL in perimenopausal women. Spearman analysis was used to analyze the correlation between perimenopausal women serum sex hormone levels and SSNHL. **Results:** Compared to the non SSNHL group, the SSNHL group women had lower serum levels of E2 and P (35.08 ± 12.49 pmol/L and 0.63 ± 0.24 nmol/L) vs. (43.46 ± 10.17 pmol/L and 0.84 ± 0.13 nmol/L) ($p < 0.05$). Multiple logistic regression analysis demonstrated that E2 and P were both at higher risk with the development of SSNHL. Spearman correlation analysis found that E2 and P are negatively correlated with pure tone hearing threshold in perimenopausal women. **Conclusions:** SSNHL in perimenopausal women may be related to their serum levels of sex hormones.

Keywords: sudden sensorineural hearing loss; perimenopausal; sex hormones

1. Introduction

Sudden sensorineural hearing loss (SSNHL) is a common clinical disease, defined as sudden and unexplained sensorineural hearing loss that occurs within 72 hours and affects at least two adjacent frequencies with a hearing loss of ≥ 20 dB HL (hearing level) [1]. The mechanism by which it occurs is controversial, although the dysfunction of local microcirculation leading to structural changes and dysfunction in the cochlea is a well-recognized theory [2,3]. In perimenopausal women, ovarian function begins to decline and hormone levels decrease, causing a series of changes in the activity of the hypothalamic-pituitary-ovarian axis [4–6]. It has been reported that sex hormone levels are not only significantly correlated with menopausal syndromes, but also closely related to various clinical symptoms during menopause [7,8].

The relationship between hormonal changes and hearing loss has been reported in previous studies [9,10]. For example, when a woman is pregnant, the secretion of estrogen and progesterone in the body will significantly increase. These changes in female hormones will cause excessive retention of salt and water, which will lead to a significant increase in extracellular fluid volume, thus increasing the probability of hearing loss [11]. When hormonal fluctuations occur in the cochlea, the chemical components of en-

dolymphatic and periauricular fluid can also be disturbed. Although many studies have suggested that sex hormones may interfere with cochlear microcirculation and contribute to sudden hearing loss, the correlation analysis between sex hormone levels and hearing loss is still uncertain [12]. This study explored the relationship between SSNHL and serum sex hormone (follicle stimulating hormone (FSH), luteinizing hormone (LH), estradiol (E2), progesterone (P), testosterone (T), prolactin (PRL)) levels in perimenopausal women, which can be used to guide the diagnosis and treatment of female SSNHL patients.

2. Materials and Method

2.1 Study Participants

A total of 156 patients with SSNHL and 149 healthy individuals during perimenopause who received treatment or underwent physical examination in the Fourth Hospital of Shijiazhuang from August 2023 to December 2023 were selected to participate in this retrospective cohort study. The average age of patients in the SSNHL study group was 51.62 ± 5.49 years, while the average age of the control group was 52.77 ± 6.83 years. There was no statistical difference in age between the two groups. The research received approval from the Ethics Committee at The Fourth Hospital of Shijiazhuang and all the researchers col-



Table 1. Basic characteristics of SSNHL patients and the control group.

Variables	Control (n = 149)	SSNHL (n = 156)	p-value
BMI (kg/m ²)			
<24 kg/m ²	51 (34.2)	57 (36.5)	0.673 ^b
≥24 kg/m ²	98 (65.8)	99 (63.5)	
Years of education (n%)			
<16 years	85 (57.0)	87 (55.8)	0.822 ^b
≥16 years	64 (43.0)	69 (44.2)	
Family yearly income (n%)			
<100,000 CNY (About US\$14,300)	71 (47.7)	79 (50.6)	0.602 ^b
≥100,000 CNY (About US\$14,300)	78 (52.3)	77 (49.3)	
Drinking			
Yes	23 (15.4)	36 (23.1)	0.091 ^b
No	126 (84.6)	120 (76.9)	
Migraine			
Yes	8 (5.4)	22 (14.1)	0.010 ^b
No	141 (94.6)	134 (85.9)	
Family history of diabetes			
Yes	12 (8.1)	16 (10.3)	0.505 ^b
No	137 (91.9)	140 (89.7)	
Smoking			
Yes	5 (3.4)	11 (7.1)	0.148 ^b
No	144 (96.6)	145 (92.9)	
Calcium (mmol/L)	2.15 (2.10–2.21)	2.12 (2.08–2.16)	0.037 ^a
Iron (μmol/L)	11.52 (7.45–16.18)	11.39 (7.15–15.84)	0.514 ^a
Zinc (μmol/L)	6.13 (5.04–7.82)	6.29 (5.37–7.46)	0.153 ^a
Copper (μmol/L)	29.04 (25.36–34.17)	27.98 (23.14–35.71)	0.278 ^a
CRP (mg/L)	54.38 (24.73–77.19)	59.76 (28.19–80.49)	0.026 ^a

BMI, body mass index; CNY, Chinese Yuan; CRP, C-reactive protein; SSNHL, sudden sensorineural hearing loss.

The differences between the SSNHL and Control groups were obtained using the Mann-Whitney U test (^a) and the Chi-square test (^b), $p < 0.05$ was considered to be significant.

lected data in strict accordance with the ethical requirements throughout the study. Exclusion criteria included participants with vertigo, hypertension, myocardial infarction, history of acute cerebrovascular attack, liver and kidney diseases, diabetes, and recent use of steroids or hormone drugs. The basic characteristics of SSNHL patients and the control group are shown in the Table 1.

2.2 Diagnosis of SSNHL

The definition of SSNHL utilized in this study is a sensorineural hearing loss of ≥30 dB at three consecutive frequencies as stated by “Clinical Practice Guideline: Sudden Hearing Loss (Update) Executive Summary” [13].

The selection criteria for the perimenopausal period were adult women aged 40 to 60 years old, and the menstrual changes complied with the following conditions: ≥2 menstrual cycles have changed and the time is >7 days, and the menopause time is <12 months.

2.3 Data Collection

5 mL of venous blood was collected from all patients fasting in the early morning, and the serum was collected

after centrifugation. Electrochemiluminescence method (Chemiluminescence instrument, Hormone detection kits, Roche Diagnostics GmbH, Mannheim, Germany) was used to detect FSH, LH, E2, P, T, and PRL levels. The range and intra and inter-assay coefficients of variability for the test indicators used in the study are shown in the Table 2.

2.4 Statistical Analysis

We utilized SPSS 22.0 (IBM-SPSS Statistics, Chicago, IL, USA) for conducting statistical analysis on the data. The median (range) and frequencies (percentage) were used to describe continuous and categorical variables, respectively. The Mann-Whitney U test was employed to assess the significant variance among non-normally distributed continuous variables, while Chi-square test was utilized for comparing categorical variables. Multivariate logistic regression analysis was conducted to examine the association between SSNHL and FSH, LH, E2, P, T, and PRL respectively. The Pearson analysis method was used for correlation analysis. All statistical analyses with significant differences were considered to be $p < 0.05$.

Table 2. Range and intra and inter-assay coefficients of variability.

	FSH (IU/L)	LH (IU/L)	E2 (pmol/L)	P (nmol/L)	T (nmol/L)	PRL (nmol/L)
Range	0.3–200	0.1–200	0.2–200	0.02–20	0.01–20	0.002–21.4
Intra-assay	1.3–1.9	0.6–1.2	1.4–2.3	1.2–1.9	0.8–1.7	1.3–3.0
Inter-assay	3.2–4.1	1.6–2.2	2.1–4.6	2.3–5.1	1.5–3.3	1.9–5.2

FSH, follicle stimulating hormone; LH, luteinizing hormone; E2, estradiol; P, progesterone; T, testosterone; PRL, prolactin.

3. Results

According to the inclusion and exclusion criteria, 305 participants were analyzed finally. Flow chart of participants participation in the study was showed in Fig. 1.

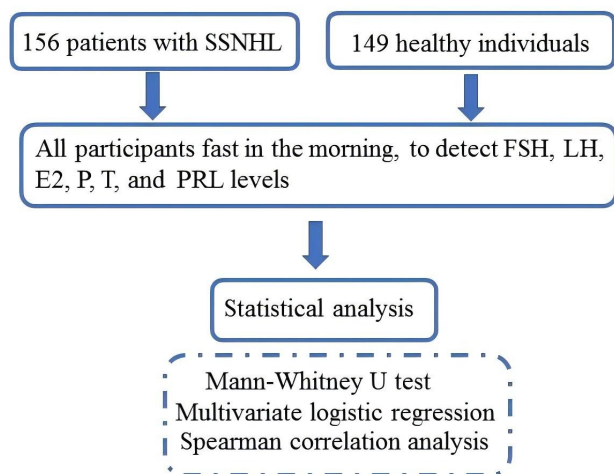


Fig. 1. Flow chart of participants participation in the study. SSNHL, sudden sensorineural hearing loss; FSH, follicle stimulating hormone; LH, luteinizing hormone; E2, estradiol; P, progesterone; T, testosterone; PRL, prolactin.

3.1 Comparison of Sex Hormone Levels in SSNHL and Normal Controls

We compared the sex hormone levels between SSNHL and normal controls in Table 3. We found that the E2 and P levels in the SSNHL group were significantly lower than those in the control group ($p < 0.05$). However, there was no significant difference in FSH, LH, T, and PRL between the two groups ($p > 0.05$).

3.2 Correlation Analysis between Sex Hormones and Pure Tone Hearing Threshold

The average pure tone hearing threshold of 156 patients in the perimenopausal group was 56.74 ± 8.39 dB. We applied Spearman correlation analysis between sex hormones and pure tone hearing threshold in perimenopausal women. Perimenopausal women P and E2 levels were negatively associated with pure tone hearing threshold values, while there was no significant correlation between FSH, LH, T, PRL and pure tone hearing threshold values

Table 3. Sex hormone levels between SSNHL and normal group.

Variables	Control (n = 149)	SSNHL (n = 156)	<i>p</i> -value
FSH (IU/L)	57.63 (42.37–70.56)	57.12 (40.68–72.45)	0.468
LH (IU/L)	36.55 (28.17–45.72)	36.71 (26.51–45.98)	0.377
E2 (pmol/L)	43.46 (38.49–60.71)	35.08 (32.26–59.14)	0.002
P (nmol/L)	0.84 (0.54–1.18)	0.63 (0.31–0.97)	<0.001
T (nmol/L)	0.62 (0.26–1.11)	0.59 (0.24–0.93)	0.073
PRL (nmol/L)	0.45 (0.27–0.73)	0.44 (0.15–0.76)	0.249

FSH, follicle stimulating hormone; LH, luteinizing hormone; E2, estradiol; P, progesterone; T, testosterone; PRL, prolactin.

($p > 0.05$). In this regard, multivariate logistic regression analysis was used to further confirm whether serum E2 and P were significantly and independently correlated with SSNHL. The spearman correlation analysis between sex hormones and pure tone hearing threshold are shown in the Table 4.

Table 4. Spearman correlation analysis between sex hormones and pure tone hearing threshold.

Variables	<i>r</i>	<i>p</i> -value
FSH (U/L)	−0.016	0.563
LH (U/L)	0.029	0.495
E2 (pmol/L)	−0.277	<0.001
P (nmol/L)	−0.312	<0.001
T (nmol/L)	−0.046	0.423
PRL (nmol/L)	−0.021	0.529

FSH, follicle stimulating hormone; LH, luteinizing hormone; E2, estradiol; P, progesterone; T, testosterone; PRL, prolactin; *r*, correlation coefficient.

3.3 Associations between Sex Hormone Levels and SSNHL

We further performed a logistic regression analysis of the associations between E2, P and the risk of SSNHL. Based on the mean concentration of all 305 subjects, E2 and P were categorized into high-value and low-value groups, respectively, and these groups were subsequently incorporated into the regression analysis as categorical variables. The results revealed that E2 and P were associated with the risk of SSNHL in either Model 1 (univariate regres-

Table 5. Associations between E2, P and SSNHL.

Variables	Model 1		Model 2	
	OR (95% CI)	<i>p</i> -value	OR (95% CI)	<i>p</i> -value
E2 <39.51 pmol/L	1.058 (1.026–1.091)	<0.001	1.043 (1.012–1.059)	<0.001
P <0.71 nmol/L	1.035 (1.021–1.059)	<0.001	1.030 (1.010–1.048)	<0.001

E2, Estradiol; P, progesterone; OR, odds ratio; CI, confidence interval.

sion analysis) and Model 2 (adjusted for maternal gestational age, body mass index (BMI), reproductive history, FSH, LH) ($p < 0.05$). The associations between E2, P and SSNHL are shown in the Table 5. Based on these results, our study indicated that perimenopausal women serum E2 and P were independent risk factors for SSNHL.

4. Discussion

SSNHL affects a wide range of people and is common in middle-aged and elderly individuals. Internal ear circulation disorders, microvascular dysfunction and metabolic disorders are widely recognized as pathological mechanisms [14,15]. Moreover, SSNHL is associated with platelet aggregation, activation, and abnormal lipid metabolism, and abnormal hormonal regulation may be the underlying cause of such metabolic abnormalities [16]. Perimenopause is a special stage for women, as their ovarian endocrine function begins to decline and sex hormone indicators begins to change, leading to a series of pathologies in various tissues and systems of the body [17,18]. Therefore, it is imperative to study the correlation between hormone levels and sudden deafness in perimenopausal women.

In this study, we found that E2 and P levels were significantly decreased in perimenopausal women with SSNHL. It has been reported that estrogen receptors are widely expressed in the human inner ear in cochlear hair cells, spiral ganglia, vascular cords, spiral arteries, outer hair cells and inner hair cells [19]. This implies that women's auditory function is related to fluctuations in estrogen. It is through these receptors that estrogen regulates the blood supply to the inner ear. When estrogen levels suddenly decrease, these receptors increase the blood viscosity in the inner ear, which not only affects the microcirculation of the inner ear, but also increases the risk of thrombosis [20,21]. Yadav *et al.* [22] studied the relationship between menstrual cycle and female hearing, and found that female hearing was affected by the changes of estrogen and progesterone levels during the menstrual cycle. Kim *et al.* [23] conducted a study on perimenopausal women and found that these patients faced greater risk of hearing loss as the levels of E2 decreased in the body. The aforementioned reports bear similarities to the present study. Some researchers suggest that estrogen exerts a protective effect on nerve cells. As estrogen levels decline, this protective effect diminishes, and the vasomotor function becomes less stable, as a result, it may adversely affect hearing [24].

The study applied Spearman correlation analysis between sex hormones and pure tone hearing threshold in perimenopausal women. We found that perimenopausal women P and E2 levels were negatively associated with pure tone hearing threshold values. Logistic regression analysis showed that E2 (odds ratio (OR) = 1.043, $p < 0.001$) and P (OR = 1.030, $p < 0.001$) were associated with the risk of SSNHL. Although the OR value is small, this association is not very obvious, we believe that these indicators are still worthy of attention. No significant changes were found in the levels of FSH, LH, P, and PRL in the SSNHL group and control group, which may be related to the small number of cases in this study. Further research is needed on a larger sample of this population. Based on these findings, steroid replacement therapy may be used as an adjunctive therapy for the prevention, diagnosis, and treatment of sudden deafness during perimenopause. A recent study has found the effectiveness of steroid therapy in patients with SSNHL, Jakov group conducted a single-center retrospective longitudinal cohort study on 55 patients in a tertiary referral otology center. It found that 30 patients (55%) that showed significant improvement in their pure tone audiogram (PTA) hearing threshold average (≥ 15 dB) after steroid treatment [25]. However, the number of participants in this study is small, so it can not fully explain the problem.

By monitoring sex hormone indicators, it is helpful for clinicians to analyze the pathogenesis, therapeutic measures, and prognosis of perimenopausal patients with SSNHL. However, the effects of estrogen changes on the body are multifaceted, and the etiology and pathogenesis of perimenopausal SSNHL still need to be further investigated.

5. Conclusions

In conclusion, we demonstrate that E2 and P levels in the SSNHL patients were significantly lower than those in the normal perimenopausal women. No significant difference in FSH, LH, T, and PRL between the two groups. P and E2 levels in perimenopausal women were negatively associated with pure tone hearing threshold values. Perimenopausal women serum E2 and P were independent risk factors for SSNHL. Of course, our research also has certain shortcomings, such as the absence of data pertaining to the treatment process of SSNHL and the influence of hormone therapy on SSNHL. However, our research to some extent demonstrates the relationship between SSNHL and serum

sex hormone levels in permanent women, which plays a significant role in guiding the diagnosis and treatment of female patients with SSNHL.

Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Author Contributions

SXW designed the research study. SXW and KW performed the research. DLS and JZ analyzed the data. SXW and DLS wrote the manuscript. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of the fourth Hospital of Shijiazhuang (20200133). The manuscript was a retrospective case review, and consent to participate was not applicable.

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Conflict of Interest

The authors declare no conflict of interest.

References

- [1] Härkönen K, Kivekäs I, Rautiainen M, Kotti V, Vasama JP. Quality of Life and Hearing Eight Years After Sudden Sensorineural Hearing Loss. *The Laryngoscope*. 2017; 127: 927–931.
- [2] Ciorba A, Corazzi V, Bianchini C, Aimoni C, Skarzynski H, Skarzynski PH, *et al*. Sudden sensorineural hearing loss: Is there a connection with inner ear electrolytic disorders? A literature review. *International Journal of Immunopathology and Pharmacology*. 2016; 29: 595–602.
- [3] Young YH. Contemporary review of the causes and differential diagnosis of sudden sensorineural hearing loss. *International Journal of Audiology*. 2020; 59: 243–253.
- [4] Burger HG, Hale GE, Dennerstein L, Robertson DM. Cycle and hormone changes during perimenopause: the key role of ovarian function. *Menopause (New York, N.Y.)*. 2008; 15: 603–612.
- [5] Hale GE, Robertson DM, Burger HG. The perimenopausal woman: endocrinology and management. *The Journal of Steroid Biochemistry and Molecular Biology*. 2014; 142: 121–131.
- [6] Uehara M, Wada-Hiraike O, Hirano M, Koga K, Yoshimura N, Tanaka S, *et al*. Relationship between bone mineral density and ovarian function and thyroid function in perimenopausal women with endometriosis: a prospective study. *BMC Women's Health*. 2022; 22: 134.
- [7] Ko SH, Kim HS. Menopause-Associated Lipid Metabolic Disorders and Foods Beneficial for Postmenopausal Women. *Nutrients*. 2020; 12: 202.
- [8] Faubion SS, King A, Kattah AG, Kuhle CL, Sood R, Kling JM, *et al*. Hypertensive disorders of pregnancy and menopausal symptoms: a cross-sectional study from the data registry on experiences of aging, menopause, and sexuality. *Menopause (New York, N.Y.)*. 2020; 28: 25–31.
- [9] Frisina RD, Bazard P, Bauer M, Pineros J, Zhu X, Ding B. Translational implications of the interactions between hormones and age-related hearing loss. *Hearing Research*. 2021; 402: 108093.
- [10] Armstrong NM, Espeland MA, Chen JC, Masaki K, Wactawski-Wende J, Li W, *et al*. Associations of Hearing Loss and Menopausal Hormone Therapy With Change in Global Cognition and Incident Cognitive Impairment Among Postmenopausal Women. *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences*. 2020; 75: 537–544.
- [11] Xu M, Jiang Q, Tang H. Sudden sensorineural hearing loss during pregnancy: clinical characteristics, management and outcome. *Acta Oto-laryngologica*. 2019; 139: 38–41.
- [12] Xie S, Wu X. Clinical management and progress in sudden sensorineural hearing loss during pregnancy. *The Journal of International Medical Research*. 2020; 48: 300060519870718.
- [13] Chandrasekhar SS, Tsai Do BS, Schwartz SR, Bontempo LJ, Faucett EA, Finestone SA, *et al*. Clinical Practice Guideline: Sudden Hearing Loss (Update). *Otolaryngology–head and Neck Surgery: Official Journal of American Academy of Otolaryngology–Head and Neck Surgery*. 2019; 161: S1–S45.
- [14] Zand V, Dadgarnia M, Baradaranfar M, Meybodian M, Vaziri-bozorg S, Fazilati M. The association between metabolic syndrome and the prognosis of idiopathic sudden sensorineural hearing loss. *European Archives of Oto-rhino-laryngology: Official Journal of the European Federation of Oto-Rhino-Laryngological Societies (EUFOS): Affiliated with the German Society for Oto-Rhino-Laryngology - Head and Neck Surgery*. 2023; 280: 1411–1415.
- [15] Cavallaro G, Pantaleo A, Pontillo V, Barbara F, Murri A, Quaranta N. Endothelial Dysfunction and Metabolic Disorders in Patients with Sudden Sensorineural Hearing Loss. *Medicina (Kaunas, Lithuania)*. 2023; 59: 1718.
- [16] Sun H, Jiang W, Wang J. The prognostic value of peripheral blood parameters on all-frequency sudden sensorineural hearing loss. *Brazilian Journal of Otorhinolaryngology*. 2023; 89: 101302.
- [17] Larroy C, Marin Martin C, Lopez-Picado A, Fernández Arias I. The impact of perimenopausal symptomatology, sociodemographic status and knowledge of menopause on women's quality of life. *Archives of Gynecology and Obstetrics*. 2020; 301: 1061–1068.
- [18] Huang C, Luo B, Wang J, Ao Y, Xiong W, Liao S. Depressive symptoms and physical activity among community-dwelling perimenopausal women: a prospective longitudinal study. *BMC Psychiatry*. 2023; 23: 93.
- [19] Lipford E. Elucidating the Localization of Estrogen and Estrogen-Related Receptors in the Inner Ear [master's thesis]. University of Maryland: Baltimore. 2020.
- [20] Jian H, Yu G, Chen G, Lin N, Wang H. Correlation between auditory-vestibular functions and estrogen levels in postmenopausal patients with Meniere's disease. *Journal of Clinical Laboratory Analysis*. 2019; 33: e22626.

- [21] Guerra J, Devesa J. Hormone therapy: challenges for treating hearing impairments. *SN Comprehensive Clinical Medicine*. 2019; 1: 603–615.
- [22] Yadav A, Tandon OP, Vaney N. Auditory evoked responses during different phases of menstrual cycle. *Indian Journal of Physiology and Pharmacology*. 2002; 46: 449–456.
- [23] Kim SH, Kang BM, Chae HD, Kim CH. The association between serum estradiol level and hearing sensitivity in postmenopausal women. *Obstetrics and Gynecology*. 2002; 99: 726–730.
- [24] Liu Z, Mu S, Wang X. Effect of estrogen on recovering the injured nervous system. *Pakistan Journal of Pharmaceutical Sciences*. 2015; 28: 1471–1476.
- [25] Ajduk J, Košec A, Kelava I, Ries M, Gregurić T, Kalogjera L. Recovery From Sudden Sensorineural Hearing Loss May Be Linked to Chronic Stress Levels and Steroid Treatment Resistance. *American Journal of Audiology*. 2019; 28: 315–321.