

Clinical management and progress in sudden sensorineural hearing loss during pregnancy

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Abstract

Sudden sensorineural hearing loss (SSNHL) is a relatively rare, but distressing, disease in pregnant women. Little is known about the causes, clinical manifestations, treatments, and prognosis of SSNHL. Some hypotheses have been proposed to explain the pathophysiological mechanism of SSNHL, but most of them have not been identified. This article reviews the existing literature to present a summary of this clinical problem. Most patients suffer from SSNHL in the second or third trimester, and show moderate to profound hearing loss. The interval between the initial treatment and onset of hearing loss is less than 10 days in most patients. Some patients with SSNHL show tinnitus, vertigo, or dizziness, and fullness of the ear. Although some patients have a tendency for self-cure, treatment with intravenous dextran 40 combined with intratympanic corticosteroids is probably a safe and effective therapeutic strategy for pregnant patients with SSNHL. Further clinical research is necessary to identify the best therapeutic strategy for these patients.

Keywords

Sudden sensorineural hearing loss, pregnancy, dextran, intratympanic steroid, tinnitus, vertigo, acoustic neuroma

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Introduction

Sudden sensorineural hearing loss (SSNHL) is an emergency medical condition, which is defined as hearing loss of at least 30 dB in three contiguous frequencies within 3 days. As a symptom of acute impairment of the inner ear, the etiology ¹Department of Otolaryngology Head and Neck Surgery, Xiangya Hospital of Central South University, Changsha, Hunan, PR China

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of SSNHL has been proposed by some hypotheses, but most of these etiologies have not been identified. With an increase in the incidence of SSNHL, it is no longer considered as a rare disease. An American survey estimated the annual incidence of SSNHL at 27 per 100,000 people,¹ and a study in Germany showed a prevalence as high as 160 cases per 100,000 per year.² However, this clinical disorder may occur at a low incidence rate in pregnant women. A population-based study from Taiwan showed an incidence of SSNHL at 2.71 per 100,000 pregnant women.³

series of obvious physiological A changes occur during pregnancy, which lead to considerable challenges on the hormonal system, cardiovascular system. others.4,5 hematological system, and Although these changes are proposed to cause occurrence and development of SSNHL in pregnant women, all of them have not been confirmed.⁶ A retrospective study in Taiwan showed that SSNHL was attributed to 21% of inner ear disorders in pregnant women.⁷ There have been few reports involving SSNHL in pregnant women because of its rare occurrence. Therefore, little is known of the causes, clinical manifestations, treatments, and prognosis of SSNHL. This review focuses on the possible etiologies, clinical manifestations, treatments and prognosis of SSNHL in pregnant women to present a summary of this clinical problem.

Literature search

We searched the China National Knowledge Infrastructure (CNKI), Wanfang Database, VIP Database, Chinese Biomedical Literature (CMB), PubMed, Embase PubMed, and EMBASE databases using the keywords "pregnancy" OR "gestation" AND "sudden sensorineural hearing loss" OR "sudden hearing loss" OR "sudden deafness", and limited the results to l March 2019. All search results were merged, and duplicate articles and reviews were removed. We also searched key article reference lists to find additional related publications. We identified 10 articles related to our research topic.

Possible etiologies

Hormonal changes

exact etiology of **SSNHL** The in pregnant women has not been identified. Nonetheless, the relationship between hormonal changes and hearing loss was frequently discussed in previously published articles. Production and excretion rates of sex steroid hormones (estrogen and progesterone) are significantly increased when a woman is pregnant. These female hormonal changes can cause an electrolyte imbalance (excessive salt and water retention), which leads to an apparent increase in the volume of extracellular fluid.⁸⁻¹⁰ Previous studies have shown widespread expression of estrogen receptors in humans and rodent cochleae.^{11,12} When hormonal fluctuations occur in the cochleae, the chemical compositions (e.g., concentrations of sodium) of endolymph and perilymph may also be disturbed. If water-sodium retention occurs in the endolymph, endolymphatic hydrops may occur in the cochlea and then SSHNL may occur when the vestibular membrane ruptures, which is similar to the pathological process of Ménière's disease.^{6,9} On the basis of this hypothesis, Hou and Wang⁵ defined this clinical problem as a new disease related to pregnancy called pregnancyinduced SSNHL, which is different from non-pregnant SSNHL. Although many studies have suggested that sex steroid hormones may interrupt cochlear microcirculation and cause sudden hearing loss, correlation analysis between the level of sex hormones and hearing loss still remains uncertain.³

Cardiovascular and hematological changes

Anatomically, the cochlea is supplied by the labyrinth artery. As a terminal artery, the labyrinth artery is vulnerable to vascular occlusion. Accordingly, most changes in the cardiovascular system and hematological system occur in the second month of pregnancy, and plateau in the second or third trimester.¹³ There is usually a rise in some coagulation factors (VII, VIII, IX, X, XII) and fibrinogen, and a fall occurs in factor XI in pregnancy.⁵ Therefore, a hypercoagulable state with increased activation of blood coagulation and the fibrinolysis system appears during normal pregnancy. However, these changes in the hypercoagulable state could increase plasma viscosity and erythrocyte aggregation, and decrease erythrocyte deformability in pregnant women. This may lead to an increase in the risk of thromboembolism in the labyrinth artery and vascular occlusion in the cochlear microcirculation,^{5,13,14} and may further evoke SSNHL.

Immune-mediated disorders

According to previous reports, SSNHL is sometimes associated with acquired autoimmune system disorder.^{15–17} Wiles et al.¹⁷ reported two cases of SSNHL with antiphospholipid (AP) antibodies and discussed the probable causative association. As an autoimmune disease, AP syndrome is defined by the presence of AP antibodies or anticardiolipin antibody in association with vascular thrombosis and/or pregnancy-related complications. AP syndrome can cause thrombosis in the cochlea, placenta, and vessels, and this subsequently leads to SSHNL and abortion.^{16,17}

Other etiologies

Acoustic neuroma is reported in up to 15% of patients with SSNHL and thus might be

an etiology of SSNHL during pregnancy.6,18,19 During the last 3 or 4 months of gestation, hormonal changes may rapidly enlarge acoustic neuroma. A gradual increase in volume of the acoustic neuroma and vascularity of the vestibular nerve myelin sheath can then commence or worsen the symptoms of acoustic neuroma, and even evoke SSNHL.²⁰ Moreover, undesirable lifestyle habits and stress during pregnancy might increase the risk of SSNHL.3,5 Hou and Wang⁵ also found that a pregnant patient suffered from SSNHL after emotional excitation. In 2008, Pawlak-Osinska et al.²¹ presented a case of repeatable SSNHL in a woman during her first and second pregnancies. These authors speculated that suffering sudden deafness in the first pregnancy is a risk factor of another occurrence during following pregnancies.

Clinical manifestations and examinations

A few case series studies involving pregnant SSNHL have been published, and the total number of patients was less than 150 (Table 1). A study in Taiwan showed that most cases of SSNHL during pregnancy occurred in the last trimester, and younger pregnant women had a relatively lower occurrence of SSNHL than did older pregnant women.³ In a retrospective analysis of pregnant SSNHL from the south of China,¹⁸ clinical manifestations of pregnant patients with SSNHL showed that 57% had moderate hearing loss and 38% reached severe or profound deafness. Additionally, all of the pregnant patients in this study were in the last two trimesters. According to previous studies with detailed information of clinical manifestations (Table 1), more than 80% of pregnant patients with SSNHL suffered from this problem in the second or third trimester. Moreover, most pregnant patients were primiparas without systemic disease or precipitating factors.^{3,6,18} Hearing loss in most pregnant

References	Patients Age (n) (year	Age (years)	Trimester during pregnancy	Affected ear side, left, n (%)	Onset of hearing loss	Initial hearing threshold (dB)	Characteristics of hearing loss	Co-existing symptoms	Oral steroids	Intratympanic steroids (times)	Dextran 40 iv	Other treatment	Final hearing threshold (dB)	Outcome (Siegel's criteria)	Notes
	œ	30.3±4.5 (26–37)	2 in the second and 4 in the third	5 (83.3)	5.3±5.0 (1-14) days	90.5±18.8	Severe to profound (n = 5) Moderately severe (n = 1)	Tinnitus (n = 6) Fullness (n = 3) Dizziness (n = 3)	1	All patients received intratympanic dexamethasone (3–14)	1	1	425±145 (23-59)	Overall recovery rate was 33.3%, including 16.7% complete recovery and 16.7%	
2 ²²	30	27.7±3.3 (21–35)	6 in the first. 17 (56.7) 4.8±3.7 14 in the (1–14 second. days and 10 in the third	17 (56.7)	4.8±3.7 (1–14) days	63.4±25.1	Ascending $(n = 3)$ (n = 3) Descending $(n = 3)$ Flat $(n = 12)$ Profound $(n = 12)$	Tinnitus $(n = 21)$ Vertigo $(n = 7)$	1	 16 patients received intratympanic dexamethasone (3) 	All patients received 500 mL dextran-40 per day for 10 days	I	43.7±25.5 (10-90)	recovery Overall racevery rate was 60.0%, includ- ing 33.3% complete recovery and 26.7% partial	
3 ²⁴	24	28.1±3.3 (21–35)	4 in the first, 14 (58.3) 4.8±3.8 9 in the (1–14 second, days and 11 in the third	14 (58.3)	4.8±3.8 (1-14) days	71.8±21.1	Ascending $(n = 2)$ (n = 2) Descending $(n = 2)$ (n = 2) Flat $(n = 6)$ Profound $(n = 14)$	$\begin{array}{l} Tinnitus \\ (n=17) \\ Vertigo \\ (n=6) \\ Fullness \\ (n=5) \end{array}$	I	 13 patients received intratympanic dexamethasone (3) 	All patients received 500 mL dextran 40 per day for 10 days	I	No data	recovery recovery recovery recovery 50.0%, includ- ing 33.3% complete recovery and 16.7%	

Table 1. General information of pregnant patients with SSNHL from previous studies.

(continued)

References	Patients Age (n) (year	Age (years)	Trimester during pregnancy	Affected ear side, left, n (%)	Onset of hearing loss	Initial hearing threshold (dB)	Characteristics of hearing loss	Co-existing Oral symptoms stero	sp	Intratympanic steroids (times)	Dextran 40 iv	Other treatment	Final hearing threshold (dB)	Outcome (Siegel's criteria)	Notes
419	~	27.4±3.5 (22-32)	6 in the second and 1 in the third	No data	5 (6 hours to 12 days)	70.3±22.2	No data	No data +			All patients received 500 mL dextran 40 per day for 14 days	Low flow oxygen	42.3±30.0	Overall recovery rate was 71.4%, includ- ing 14.3% complete recovery and 57.1% partial	l patient had acoustic neuroma
2 B	5	26.2±3.3 (22–35)	19 in the second and 1 in the third	No data	5 (8 hours to 15 days)	No data	Ascending (n = 6) (n = 7) Profound (n = 5) Irregular (n = 3)	No data +			17 patients received 500 mL dextran 40 per day for 10 days	2 patients received puerarin injection 250 mL	No data	recovery Overall recovery rate was 76.2%, includ- ing 61.9% complete recovery and 14.3%	I patient had acoustic neuroma, and 2 were self-cured
¢5	2	30, 31	2 in the first 1 (50)	I (50)	7, 10 days	26.3, 96.3	Ascending $(n = 1)$ Profound $(n = 1)$	Tinnitus – (n = 2) Fullness (n = 2)		1	I	One patient received HBO and acupuncture therapies	12.5, 73.8	partial recovery Overall recovery rate was 50%	l was self-cured
79	-	42	Third	(0) 0	No data	27.5	Ascending	1		1	I	I	21	50% com- plete recovery Complete recovery	

Table I. Continued.

(continued)

Pati References (n)	Patients Age (n) (years)	Trimester during pregnancy	Affected ear side, left, n (%)	Onset of hearing loss	Initial hearing threshold (dB)	Characteristics of hearing loss	Co-existing symptoms	Oral steroids	Intratympanic steroids (times)	Dextran 40 iv	Other treatment	Final hearing threshold (dB)	Outcome (Siegel's criteria)	Notes
8 ²¹ I	25 (first time)	Second (first time)	(0) 0	2 days	38.8	Irregular (fluted)	Tinnitus	+	I	I	B vitamins and vasodilators	11.3	Complete recovery	The patient was self-cured
	27 (second time)	ίĒ	(001) 1	No data	42.5	Irregular (fluted)	I	I	I	I	I	8.8	Complete recovery	at the second time
9 ²⁵ 6	30.5 (25–35)	2 ir	2 (33.3)	No data	55.5 ±19.8	Ascending (n = 1) Descending (n = 1)	Tinnitus $(n=6)$ Dizziness $(n=4)$	I	All patients received intratympanic dexamerhasone	2 patients	4 patients received carbogen	23.7±18.7	Overall recovery rate was 66.7% includ-	
		third				Flat 3 Basin (n = 1)							ing 50% complete recovery and 16.7% partial	
10 ⁶ 12	: 28.9±3.6 (24–37)	 4 in the first, 3 in the second, and 5 in the third 	8 (66.7)	3 (1–9) days	83.1±22.1 No data	No data	Vertigo $(n = 4)$	1	1	6 patients	1	58.8±29.2	recovery In the treated group, the overall recovery rate was 33.3%, includ-	l patient had acoustic neuroma; l was self-cured
													ing 16.7% complete recovery and 16.7% partial recovery	

begets cherta. Complete recovery is a mid meaning reverbent unit 20 do, partial recovery is more than a realing gain and a mid meaning reverbered to any 50 db, sught recovery is a mid hearing level >45 dB with a hearing level >45 dB with a hearing gain of ≤15 dB. HBO: hyperbaric oxygen; iv: intravenously; Sudden sensorineural hearing loss, SSNHL

patients is unilateral and some of them may also have tinnitus, vertigo, or dizziness, and fullness of the ear.^{5,6,22–25} However, the irregularity and diversity of these accompanied symptoms appear to be related to a lack of detailed descriptions in other studies.^{18,19}

Studies have reported that audiological changes are found during pregnancy because of high levels of sex hormones, and these changes return to normal once pregnancy is finished.^{8,26} Patients routinely receive audiometry tests, acoustic immittance, distortion product otoacoustic emissions, auditory brainstem response, and other audiological examinations for diagnosis of SSNHL. Tympanograms are normal in cases of SSNHL. Zeng et al.¹⁸ analyzed the audiometric curves of 21 pregnant patients and found that 57% (12/21) of patients showed moderate hearing loss. Furthermore, 38% (8/21) of patients reached severe or profound deafness, and most of them were in a low-mid frequency falling curve (n = 6) and flat curve (n = 7). However, in some recent studies, such as those by Xu et al²², Fu et al.²³, and Shi et al.²⁴, most pregnant patients suffered from severe or profound deafness.

Treatments

The equivocal etiologies of SSNHL lead to many empirical treatment protocols for these patients. However, the most frequently recommended therapy for SSNHL is systemic or topical administration of steroids and hyperbaric oxygen (HBO) therapy.²⁷ Prescriptions of other medicines (e.g., antivirals, thrombolytics, vasodilators, vasoactive substances, and antioxidants) to patients are not recommended. However, the therapeutic strategy for pregnant patients with SSNHL is particularly challenging because of the limited clinical experience. Otolaryngologists should consider whether there are sufficient benefits to pregnant patients with SSNHL when they attempt to save their hearing by taking the risk of exposing the fetuses to side effects.³ Previous studies have reported that hearing of a few pregnant patients returned to normal levels several days later or after delivery without any treatment.^{5,6,18,21} Because of the fear of maternal complexity and side effects on the fetuses, as well as the self-cure tendency in some cases of SSNHL, some pregnant otolaryngologists prefer patients and no medication and choose conservative treatment, including bed rest and carbogen therapy.²⁸ However, even though some cases may spontaneously recover after delivery occurs, emergency treatment is mandatory for ethical reasons. Therefore, many other otolaryngologists advocate positive treatment.^{22,23} The interval between the initial treatment and onset of hearing loss is less than 10 days in many pregnant patients (Table 1). Although SSNHL has the tendency of spontaneous self-cure in adult men and non-pregnant women, the natural course of SSNHL during pregnancy has not been established.¹⁰ Optimum management of this clinical problem is controversial. The following empirical therapies can be considered on the basis of previous studies.

Dextran 40

In the clinic, dextran 40 is widely and successfully used as a plasma expander for thrombotic diseases and flap transplantation. Dextran 40 decreases blood viscosity and enhances the microcirculation in guinea pigs, and then reduces cochlear hypoxia,²⁹ Accordingly, patients with SSNHL who were treated with intravenous dextran 40 showed marked hearing improvement.^{6,30} In Wang and Young's study,⁶ intravenous dextran 40 treatment led to remarkable improvement in the hearing of six pregnant patients with SSNHL These authors also

found a significant difference in hearing improvement between the dextran 40 group and control group. Unfortunately, some adverse effects (e.g., coagulopathy, acute renal failure, or non-cardiogenic pulmonary edema) have been reported when dextran 40 was used as a therapy of SSNHL.³¹ However, there is no apparent adverse effect of dextran 40 when used as a therapy for pregnant SSNHL.^{6,18,19,22,24} Therefore, the therapeutic benefits probably outweigh the potential risk of dextran 40 in pregnant patients and their fetuses.

Corticosteroid therapy

Another alternative treatment for SSNHL is corticosteroid therapy, including systemic corticosteroids and topical corticosteroids.^{15,27,32} Corticosteroids work via reduction of inflammation and the immune response, a change in the mircrovascular circulation, and a direct effect on sensory epithelium of the cochleae.^{15,32} Despite promising therapeutic effects, this therapy has rarely been tested on pregnant woman because of detrimental fetal effects. Corticosteroids affect the metabolic and endocrine balance of various fetal organs after excessive prenatal exposure of corticosteroids.³³ Therefore, systemic corticosteroids are not recommended in pregnant women at the first trimester when the human embryo is most insults.³⁴ vulnerable to teratogenic However, corticosteroid therapy is thought to be safe when corticosteroids are used in the third trimester according to Ambro et al.'s prescribing guidelines.³⁵ Zeng et al.¹⁸ and Zhang¹⁹ also showed that oral prednisone use in pregnant women with SSNHL achieved a satisfactory recovery. There were also no apparent harmful side effects found in the mothers and infants who were followed up for several years.

Intratympanic corticosteroids are increasingly used in patients with SSNHL as a topical corticosteroid therapeutic option,

especially in patients in whom systemic corticosteroids are contraindicated or declined^{32,36} This therapy is also recommended as initial therapy for severe and profound SSNHL by some otologists.^{37,38} Treatment of topical intratympanic corticosteroid injection provides a high dose of corticosteroids in the perilymph through the intact round membrance.^{37,38} The cochlear pharmacokinetics of intratympanic corticosteroids have been confirmed in animal models.³⁹ This therapeutic method is relatively easy to carry out under local anesthesia in an outpatient clinic or ward, and it is well tolerated by the patients. Most patients can understand the concept of intratympanic corticosteroid treatment and readily accept this therapeutic method.³⁶ Intratympanic corticosteroid injection is superior to systemic administration of corticosteroids because it not only provides topical high-dose therapeutic effects in the affected ear, but it also avoids the harmful side effects of systemic concentrations of corticosteroids.^{32,36,37,39} Traditionally, dexamethasone and methylprednisolone have been used in intratympanic injection, but methylprednisolone (US FDA category B) may be more suitable than dexamethasone (US FDA category C) for pregnant patients. Previous studies have shown that pregnant patients with SSNHL can achieve complete or partial recovery without any side effects after intratympanic corticosteroid injection.^{22–24,40} Fu et al.²³ showed that all of their six patients showed relatively satisfactory improvement in hearing after intratympanic corticosteroid injection, and the mean improvement in hearing was 48 ± 7.33 dB. Therefore, intratympanic corticosteroid therapy should be recommended to pregnant patients with SSNHL.

Chinese herbal medicine

Chinese herbal medicine is popular with patients with sudden deafness in China and other East Asian countries.⁴¹ Chinese

herb extracts, especially puerarin and ginkgo biloba extract, are most frequently used in clinical practice.^{18,41} Unfortunately, most of these herb extracts cannot be used in pregnant patients, and only puerarin has been proven to be safe.^{18,42} Zeng et al.¹⁸ showed a satisfactory improvement in hearing in two pregnant patients with SSNHL after a course of intravenous puerarin (14 days).

HBO therapy

HBO therapy is recommended to use as an adjuvant treatment for SSNHL in nonpregnant patients.43,44 However, HBO therapy during pregnancy is controversial in the clinic because of the potential adverse effects of hyperoxic exposure, such as retinopathy of prematurity, teratogenicity, and cardiovascular adverse effects, which may occur in the fetus.⁴⁵ However, careful review of clinical studies has suggested that a short duration of hyperoxic exposure during HBO therapy can be well tolerated by the fetus in all stages of pregnancy.⁴⁵ There is no evidence of harmful human neonatal outcomes with HBO therapy at 2 atmospheres for 2 hours' duration.⁴⁶ Xiao et al.47 subjected pregnant rabbits to lipid peroxidation during late pregnancy and treated them with HBO therapy. No deleterious effects of this treatment on the fetuses were observed. In the clinic, a pregnant patient with SSNHL received HBO therapy in the first trimester.⁵ There was no improvement in hearing at the time of hospitalization, and no adverse effects to the newborn were observed after cesarean delivery.

Other therapies

Traditional Chinese approaches, including acupuncture and ocular needling, are thought to be beneficial in patients with SSNHL.^{48,49} In Hou and Wang's⁵ study, the symptoms of tinnitus and aural fullness disappeared in a pregnant patient with SSNHL after treatment with HBO and acupuncture for 7 days. However, there was no improvement in the hearing threshold. When a pregnant patient with SSNHL was diagnosed with acoustic neuroma via magnetic resonance imaging, multidisciplinary therapy was required involving otologists, neurosurgeons, obstetricians, and anesthetists.⁶ Additionally, management depended on the trimester of pregnancy and neurological status.

Prognosis

Various prognostic factors have been assessed to predict recovery from SSNHL, including age, onset of hearing loss, initial hearing loss, types of audiogram, accompanying symptoms, therapeutic method, and systemic diseases, such as diabetes mellitus and hypertension.^{22,24,43} However, there is no relevant case series research on the prog-SSNHL during nosis of pregnancy. According to previous studies (Table 1), most pregnant patients with SSNHL achieved complete or partial recovery after treatment according to Siegel's criteria.⁵⁰ The short interval between initial treatment and onset of hearing loss may be associated with favorable recovery of hearing in pregnant patients. However, further studies need to be performed to determine this issue.

Summary

SSNHL is a relatively rare disease during pregnancy with different inconclusive etiologies, irregular clinical features, and equivocal audiological findings. A thorough medical history, detailed ear, nose, and throat examination, and appropriate audiological evaluation are mandatory for SSNHL. In addition to an ear, nose, and throat examination, an examination by an obstetrician is also important. Blood tests should be performed, including a routine blood test, biochemical blood test, clotting factors, erythrocyte sedimentation rate, sex hormone analysis, and antiphospholipid antibodies. Imaging examinations of the brain and inner ears should be carried out to rule out an acoustic neuroma when acute hearing loss occurs or within 3 months after delivery. Most patients suffer from SSNHL in the second or third trimester, and show moderate to profound hearing loss. The interval between the initial treatment and onset of hearing loss is less than 10 days in most patients. Some patients exhibit tinnitus, vertigo, or dizziness, and fullness of the ear.

For medical treatment of SSNHL, intravenous dextran 40 can be used after carefully weighing the therapeutic benefits versus side effects. Intratympanic corticosteroid injection, as a safe and topical therapeutic option, also should be recommended to pregnant patients with SSNHL. Systematic corticosteroid therapy can be used at the third trimester. Intravenous puerarin is another alternative treatment for SSNHL during pregnancy. The safety and effectiveness of HBO therapy for pregnant SSNHL needs to be further confirmed. Overall, treatment of intravenous dextran 40 combined with intratympanic corticosteroid is probably a safe and effective therapeutic strategy for pregnant patients with SSNHL at the present stage. Much more knowledge is required about the etiology and clinical manifestations of SSNHL. Additionally, further clinical research is necessary to identify the best therapeutic strategy for this clinical problem.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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