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RESEARCH PAPER

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Clinical characteristics of sudden hearing loss during pregnancy

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Abstract

Objective: The objective of this study was to explore the clinical characteristics and management of sudden hearing loss (HL) during pregnancy, thus better guiding the clinical practice.

Methods: The clinical and follow-up data of 17 patients (17 ears) with sudden HL during pregnancy were analyzed retrospectively (the observe group). Twelve nonpregnant female patients (12 ears) with sudden HL of similar clinical characteristics were selected as the control group. The prognosis of the two groups was compared. All the patients were followed up after delivery, and two of them were readmitted to the hospital 1–2 months after delivery.

Results: The observe group had better improvement in hearing and a higher response rate compared to the control group. The pure tone hearing and speech recognition rate of patients could still be improved after the readmitted treatment, and the hearing could partially recover spontaneously during follow-up. The laboratory indicators that affect the inflammatory response and coagulation pathway were significantly different between the two groups.

Conclusions: The hearing condition of sudden HL during pregnancy is severe, and the prognosis of these patients is better than nonpregnant patients of similar clinical characteristics. Postpartum treatment is still effective, and some patients showed self-healing with time during follow-up. The inflammatory response and coagulation function may affect the hearing of patients through a metabolic pathway.

KEYWORDS

management, pregnancy, prognosis, sudden hearing loss

Key points

In this study, we analyzed the clinical characteristics of patients with sudden hearing loss during pregnancy, proposed an effective treatment strategy, and found some laboratory indicators that may affect the hearing of patients by a metabolic reaction.

INTRODUCTION

As a disease throughout the whole life cycle, sudden hearing loss (HL) is defined as a precipitous decline of hearing (>30 dB HL) in at least three continuous frequencies within 3 days, without an identifiable cause.[1] Sudden HL during pregnancy is a special condition with unknown etiology and is accompanied by tinnitus, vertigo, nausea, and vomiting.[2] Because of the special physiological state of pregnancy, the changes in estrogen and progesterone will have multiple effects. It is unclear whether these effects would interfere with the pathogenesis of sudden HL. In addition, how to guarantee medication safety and improve the hearing of the patients is a practical issue to be resolved urgently.

Dextran and steroids have been chosen to treat this disease.[3] Dextran, as a plasma dilator, can alleviate blood viscosity and improve microcirculation, but with allergic reactions, such as skin itching, urticaria, and asthma, in a small number of patients. The safety of steroids during pregnancy is not clear. It is necessary to find a safe and effective treatment strategy for pregnant patients with sudden HL. Our study summarized the clinical data of patients with sudden HL during pregnancy in our hospital, to find effective therapies, explore the possible causes, and better guide for clinical practice.

MATERIALS AND METHODS

The clinical data of 17 patients with sudden HL during pregnancy in our hospital from December 2013 to November 2022 were analyzed retrospectively (the observe group, OG). Twelve patients (12/17) received medicine treatment during pregnancy, three patients (3/17) received treatment immediately after delivery, and another two patients (2/17) refused treatment. Twelve female patients with sudden HL in the same age range but not in pregnancy were selected as the control group (CG). The details about the groups are shown in Figure 1. This study has passed the review of the hospital ethics committee (S2017-024-01).

Inclusion criteria: (1) Subjects meeting the diagnostic criteria of the guidelines for sudden HL[1]; (2) patients in OG were diagnosed as normal intrauterine pregnancy by obstetrics, with their fetus developing normally.

Exclusion criteria: HL caused by an acoustic neuroma, trauma, Meniere's disease, and ototoxic drugs was confirmed by a detailed inquiry of medical history and related imaging examination.

Assessment

All the patients provided a detailed history and underwent local inspections of the ear, nose, and throat, obstetric examination, physical examination, and otoscopy. They all underwent laboratory tests, pure tone audiometry, and test for speech recognition rate. Subsequently, some of them were followed up 1 month after discharge or 1 month after delivery. Postpartum newborns were followed up for health and hearing screening.

The efficacy was determined following the Chinese guidelines and was classified into four classes: cured (hearing returned to normal or to the predisease level), significantly effective (average hearing improvement of more than 30 dB HL in the impaired frequency), effective (average hearing improvement of 15–30 dB HL in the impaired frequency), and ineffective (average hearing improvement of less than 15 dB HL in the impaired frequency).[4]

The level of HL was classified into four tiers in terms of pure tone average (PTA, averaged over 0.5, 1.0, 2.0, and 4.0 kHz): mild (20–35 dB HL), moderate (35–50 dB HL), moderately severe

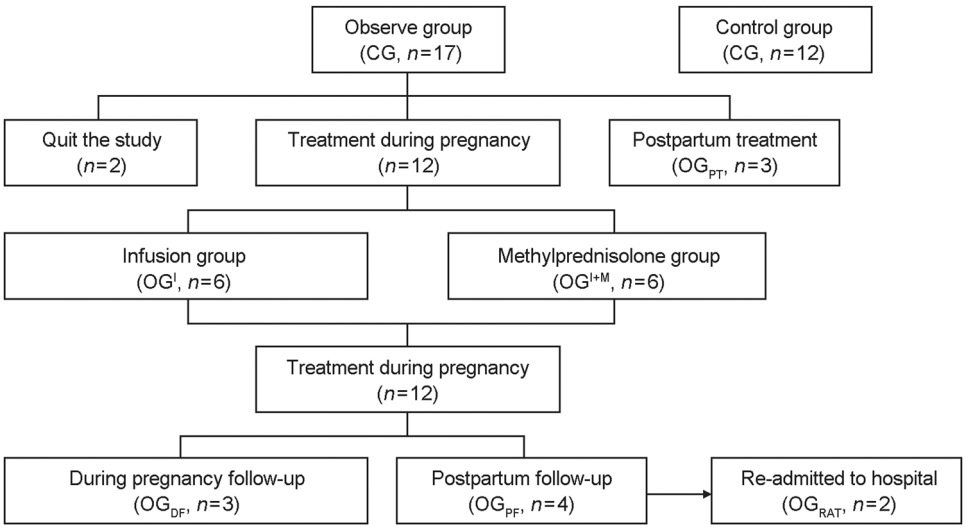

FIGURE 1 Details of the groups. CG, control group; OG, observe group; OG_{DF}, during pregnancy follow-up in OG; OG^{I}, infusion group in OG; OG^{I+M}, methylprednisolone group in OG; OG_{PF}, postpartum follow-up in OG; OG_{PT}, postpartum treatment in OG; OG_{RAT}, readmitted to hospital in OG.

(50–65 dB HL), severe (65–80 dB HL), profound (80–95 dB HL), and complete deafness (≥95 dB HL).[5]

Management

The treatment principles were as follows: First, the vital signs of the pregnant women were monitored and their general conditions were improved. Second, obstetrics consultation was arranged to assist in diagnosis and treatment. Finally, the treatments were glucose injection and mecobalamin, with or without postauricular injection of methylprednisolone. Patients who were not pregnant were given comprehensive treatments according to the Chinese guidelines for sudden HL.[4]

Treatment during pregnancy: Twelve pregnant patients in OG received treatment, with six patients (infusion group, OG^{I}) given 10% glucose (500 mL, intravenously, qd) and mecobalamin (Chinese Eisai, Chinese medicine H20174048) (0.5 mg, intravenously, qd) for a total of 7 days. The other six patients (methylprednisolone group, OG^{I+M}) received postauricular injections of methylprednisolone (Pfizer; approval number H20170197) (40 mg, qod) for a total of three times in addition to the above treatment.

Postpartum treatment (OG_{PT}): Another three patients in OG received treatment immediately after delivery, including *Ginkgo biloba* extract injection (Zhonghao International; approval number HC20140019) (87.5 mg, qd), dexamethasone sodium phosphate injection (10 mg, qd), and mecobalamin injection (0.5 mg, drip), all for 7 days.

According to the guidelines for sudden HL, patients in CG were given comprehensive treatments,[4] including *G. biloba* extract injection (87.5 mg, qd), alprostadil injection (Beijing Tade; national drug standard: H10980023) (10 μg, qd), and an injection of dexamethasone sodium phosphate (10 mg, qd) (the dose was halved after 3 days). Mecobalamin injection of 0.5 mg was dripped once a day. Batroxobin (Beijing Tuobi Western Pharmaceutical Co. Ltd.; H20030295) 10 BU was injected intravenously for the first time, followed by 5 BU once every other day, and changes in blood coagulation function were detected during the use. The total treatment course lasted for 14 days.

Statistical analyses

The clinical characteristics of patients in OG and CG were compared, including affected side, age, height, weight, onset days, pure tone hearing, tinnitus, vertigo concomitant rate, and type of audiogram. The therapeutic effects of the 12 patients in OG treated during pregnancy were compared with CG and that of OG^{I} with OG^{I+M}.

GraphPadPrism8.0 software was used for data analysis: the measurement data by normal distribution were described as mean ± standard deviation ($x \pm s$), and assessed using the independent-sample *t*-test. The nonparametric test was used for data inconsistent with normal distribution. The rate of counting data was assessed by χ^2 or Fisher's accurate test. To compare multiple groups of data, the analysis of variance or the nonparametric test was used. $P < 0.05$ was regarded as statistically significant.

RESULTS

Comparison of clinical characteristics of patients

There was no significant difference in clinical and audiological characteristics before treatment between OG and CG (Table 1). Among the 17 patients included, one (5.88%), nine (52.94%), and seven (41.18%) were in the first (begins from the first day of the pregnant woman's last menstrual period and lasts until the end of Week 12), second (begins at Week 13 and lasts until the end of Week 26), and third trimester of pregnancy (begins at Week 27 and lasts until the end of the pregnancy), respectively (the general condition of patients in OG was shown in Supporting Information: Table S1). For the hearing level, the number of patients in OG from normal, mild, moderate, moderately severe, severe, profound to complete deafness were 0, 3 (17.65%), 0, 1 (5.88%), 0, 3 (17.65%), and 10 (58.82%).

Comparison of prognosis between OG and CG

The prognosis of the 12 treated patients during pregnancy was compared with CG, including the improvement of hearing at each frequency, the recovery of speech recognition rate, and the judgment of curative effect stipulated in the guidelines.[4] The hearing condition of the two groups was shown in Figure 2A. In OG, all frequencies of hearing were improved significantly, while in CG, only 500, 1000, and 2000 frequencies were improved significantly. There were no significant improvements in the speech recognition rate before treatment and after treatment in OG ($P = 0.125$) and in CG ($P = 0.7188$).

The evaluation of response rate and PTA in the two groups was shown in Table 2. There was no significant difference in the PTA improvement between the two groups. The response rates for both groups of patients are 50%.

Comparison of prognosis between OG^{I} and OG^{I+M}

Of the patients in OG, six were treated with 10% glucose and mecobalamin (OG^{I}), and another six were treated by extra postauricular injection of methylprednisolone (OG^{I+M}). The prognosis of the two groups was compared and their hearing condition was shown in Figure 2B.

Before treatment, the hearing condition of patients in OG^{I} was slightly better than OG^{I+M} but without significant difference. The efficacy showed no significant improvement in OG^{I}, and the response rate was 33.33%. While there was significant improvement in 125,

TABLE 1 Comparison of clinical characteristics between observe and control groups.

Variables	OG (n = 12)	CG (n = 12)	P value
Left/right	6/6	6/6	>0.99
Age ($\bar{x} \pm s$, years)	30.50 ± 4.60	31.5 ± 2.81	0.53
Height ($\bar{x} \pm s$, cm)	162.0 ± 5.67	163.5 ± 5.05	0.50
Weight ($\bar{x} \pm s$, kg)	62.29 ± 11.22	57.87 ± 7.26	0.26
BMI ($\bar{x} \pm s$)	23.70 ± 3.80	21.71 ± 3.17	0.18
Onset days ($\bar{x} \pm s$)	9 ± 4.69	12.08 ± 7.67	0.25
Tinnitus	12 (100%)	12 (100%)	>0.99
Vertigo	6 (50%)	7 (58.33%)	>0.99
Pure tone hearing ($\bar{x} \pm s$, dB HL)			
125 Hz	70.00 ± 10.66	62.50 ± 12.88	0.13
250 Hz	83.33 ± 17.23	72.92 ± 16.58	0.15
500 Hz	99.58 ± 15.44	89.17 ± 20.21	0.17
1000 Hz	105.83 ± 18.93	93.33 ± 21.98	0.15
2000 Hz	103.33 ± 20.04	92.50 ± 22.81	0.23
4000 Hz	102.08 ± 23.59	93.33 ± 21.88	0.36
8000 Hz	91.25 ± 15.24	90.00 ± 13.65	0.83

Note: There was no significant difference in affected side, age, height, weight, BMI, onset days, tinnitus, vertigo concomitant rate, and pure tone hearing before treatment between OG and CG.

Abbreviations: BMI, body mass index; CG, control group; HL, hearing loss; OG, observe group.

250, 500, 4000, and 8000 Hz in OG^{I+M}, and the response rate was 66.67%.

Prognosis of three patients in OG_{PT}

In OG, three patients were treated immediately after delivery and were followed up 1 month after discharge. The hearing condition of these three patients was shown in Figure 2C. Statistical analysis indicated significant improvements in hearing between "before treatment" and "after treatment," and between "before treatment" and "follow-up" (Supporting Information: Table S2). The patients in this group showed no tendency of bleeding during the treatment, and their children were not breastfed.

Follow-up of patients in OG

All the patients were followed up after delivery, and the fetus had good health and normal hearing, with no side effects. Among the 12 patients who received treatment during pregnancy, three patients underwent audiological follow-up 1 month after discharge (during pregnancy follow-up group, OG_{DF}). Another four patients underwent postpartum follow-up (postpartum follow-up group, OG_{PF}), and two of them were readmitted to the hospital 1–2 months after delivery (readmitted treatment group, OG_{RAT}). The second course of the treatment was carried out according to the treatment plan of CG. The hearing condition of these patients was shown in Figure 2D. The details of the statistical analysis were showed in Supporting Information: Table S2.

The speech recognition rates of the two retreatment patients (OG_{RAT}) in "before treatment during pregnancy," "after treatment during pregnancy," "before treatment during postpartum," and "after treatment during postpartum" were $0 \rightarrow 8\% \rightarrow 12\% \rightarrow 36\%$ and $0 \rightarrow 0 \rightarrow 20\% \rightarrow 24\%$, respectively. It can be seen that postpartum retreatment can also improve the speech recognition rate of the patients.

Laboratory indicators

Some patients in this study received blood laboratory examination, including blood routine, biochemical tests, coagulation function, and immunological examination. We compared the laboratory indicators of individuals with sudden HL during pregnancy (OG, n = 17), individuals with normal sudden HL (CG, n = 12), and individuals with normal pregnancy and normal hearing (n = 14). Ten indexes of hemoglobin, red blood cell, white blood cell, neutrophil%, lymphocyte%, albumin, high-density lipoprotein, thrombin time, fibrinogen, and neutrophil-to-lymphocyte ratio, were statistically different among the groups (Table 3).

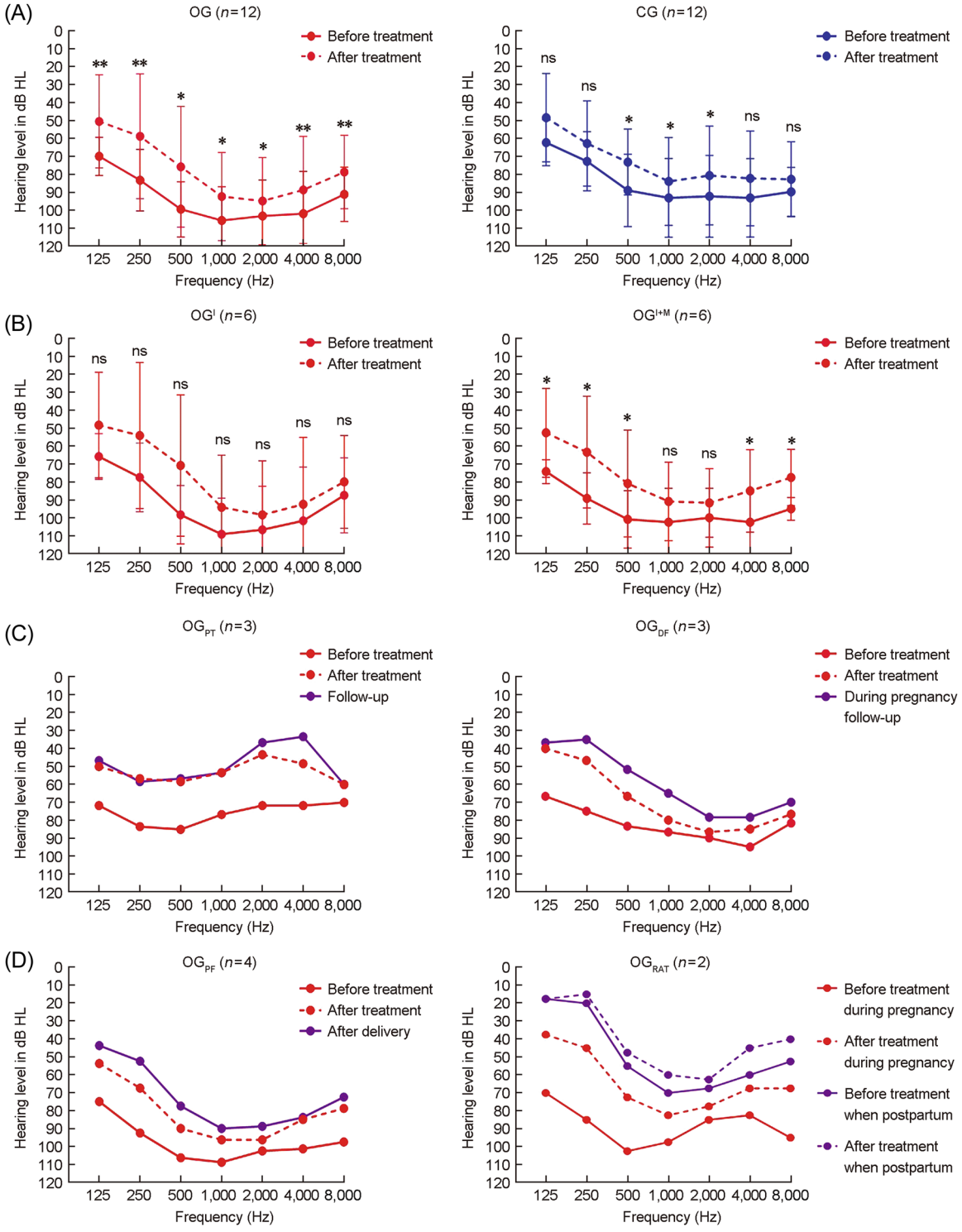

FIGURE 2 Hearing condition for different groups. (A) The hearing condition in the observe group and the control group. (B) The hearing condition in the infusion group and the methylprednisolone group. (C) The hearing condition of three patients treated immediately after delivery and the hearing condition of three patients followed up 1 month after discharge. (D) The hearing condition of four patients followed up after delivery and the hearing condition of two patients who received postpartum retreatment. CG, control group; OG, observe group; OG_{DF}, during pregnancy follow-up in OG; OG^{I}, infusion group in OG; OG^{I+M}, methylprednisolone group in OG; OG_{PF}, postpartum follow-up in OG; OG_{PT}, postpartum treatment in OG; OG_{RAT}, readmitted to hospital in OG. ns, $P \geq 0.05$; $^{*}P < 0.05$; $^{**}P < 0.01$; $^{***}P < 0.001$.

TABLE 2 Comparison of curative effect between observe and control groups.

Group	Cured	Significantly effective	Effective	Ineffective	Response rate	PTA before treatment ($\bar{x} \pm s$, dB HL)	PTA after treatment ($\bar{x} \pm s$, dB HL)	PTA improvement ($\bar{x} \pm s$, dB)
OG (n = 12)	0	2	4	6	50%	102.81 ± 17.46	88.02 ± 25.03	14.79 ± 14.42
CG (n = 12)	0	2	4	6	50%	97.08 ± 21.40	81.77 ± 24.90	15.31 ± 13.75
P value	>0.99	>0.99	>0.99	>0.99	>0.99	0.49	0.55	0.93

Note: There was no significant difference between the PTA improvement and the response rate between the two groups.
Abbreviations: CG, control group; HL, hearing loss; OG, observe group; PTA, pure tone average.

There were two patients who underwent sex hormone examination during pregnancy. The serum estradiol, serum prolactin, and serum progesterone were significantly increased. Nevertheless, they were all within the normal range in pregnancy. Another patient had a sex hormone examination after delivery, indicating all the indexes had returned to normal.

DISCUSSION

Sudden HL during pregnancy is a special disease.[2] The incidence of this disease in the Taiwan province of China in 2016 was 2.71/100,000, which was lower than that of normal patients in the same year (9.09/100,000).[6] According to the population census data for 2019 in South Korea, the incidence of sudden HL during pregnancy was 19.5/100,000, lower than that of nonpregnant women (60.7/100,000).[7] Both studies show that pregnant women have a lower probability of sudden HL relative to patients with normal physiological states, which may be explained by the protective effect of estrogen on hearing. On the one hand, some studies have found that estrogen receptor is expressed in the cochlea, which excites the auditory function and participates in the mechanism of hearing protection through interaction with the central nervous system.[8] Other studies have reported that testosterone can reduce the synchronization of entire neurons and affect the nerve conduction time, while estradiol can increase the synchronization of neurons and improve the coding ability of periodic components of speech signals.[9] Thus, it has a protective effect on hearing. On the other hand, the pathogenesis of this special disease can be the change of estrogen and progesterone content during pregnancy, which will have a series of effects on the body: (1) the blood fibrinogen of pregnant women is considerably higher than that of normal controls; the activation of coagulation and fibrinolysis system may lead to a hypercoagulable state[10]; (2) decreased erythrocyte deformability, increased aggregation, and increased plasma viscosity lead to a hypercoagulable state[7]; (3) the increase of blood volume and retention of water and sodium in the body easily affect low-frequency hearing[8]; (4) high concentration of estrogen leads to water–electrolyte imbalance and has an impact on the composition of endolymph[3]; and (5) changes in hormone levels may rapidly expand the acoustic neuroma.[11] Most of the above factors will lead to arterial stiffness and microvascular dysfunction, affecting the cochlear blood circulation.

Patients can be diagnosed with sudden HL during pregnancy if they meet the diagnostic criteria of the guidelines for sudden HL[1] and are diagnosed as normal intrauterine pregnancy by obstetrics. For the study of sudden HL during pregnancy, so far, a total of 13 retrospective studies have been found through database retrieval, as shown in Supporting Information: Table S3. Usually, the hearing condition for patients with sudden HL during pregnancy is from moderately severe to profound (from 63.4 to 83.1 dB HL).[3] In this study, a total of 17 patients with sudden HL during pregnancy were included, and most patients' hearing condition (76.47%) were from severe to complete deafness. It was speculated that most of the patients with mild HL or low-frequency decline type were diagnosed and treated in the outpatient clinic and were not admitted to the hospital, so they could not be included in the analysis.

For the treatment, our strategy is safer than previous studies. The intravenous infusion of glucose will not increase the volume load. The improvement in blood circulation by appropriate infusion can effectively ameliorate the state of hypercoagulability and high blood viscosity. Only the patients who were in the second or third trimester of pregnancy received postauricular methylprednisolone injection in our and previous study,[3] since the steroids could increase the risk of cleft lip and palate to the fetus in early pregnancy. According to the Food and Drug Administration reference classification of safe use during pregnancy, steroids were grade D in the first trimester and grade C in the second or third trimester of pregnancy, so steroids should be avoided in early pregnancy. In addition, compared with systemic administration, the postauricular injection adopted in this study can reduce the medicine volume entering the systemic blood circulation, and achieve satisfactory effect.[12,13]

The response rate in this study was 50%, which was the same as CG, and from other research about sudden HL during pregnancy, the response rate was from 40% to 88%,[14,15] which is also similar to our study.

The hearing condition can be self-healed with time from the date of follow-up. Patients who were untreated during the course of this disease from other studies, the self-healed condition was not obvious. So, medication or management is needed in sudden HL for antepartum or postpartum women rather than waiting for a natural course.[15]

As for the significant abnormal laboratory indicators, HDL and albumin are relatively higher due to a high intake of high-protein food. During pregnancy, women are in a state of physiological

TABLE 3 The obvious different laboratory indicators examination between observe and control groups.

Variables	Group	*P* value
Hb	OG versus CG	0.029
	OG versus N	0.982
	CG versus N	0.025
RBC	OG versus CG	0.004
	OG versus N	0.557
	CG versus N	0.056
WBC	OG versus CG	0.024
	OG versus N	0.955
	CG versus N	0.057
Neutrophil%	OG versus CG	<0.001
	OG versus N	0.942
	CG versus N	<0.001
Lymphocyte%	OG versus CG	<0.001
	OG versus N	0.984
	CG versus N	<0.001
Albumin	OG versus CG	0.0002
	OG versus N	0.265
	CG versus N	<0.001
HDL	OG versus CG	0.024
	OG versus N	0.723
	CG versus N	0.013
TT	OG versus CG	<0.001
	OG versus N	0.567
	CG versus N	0.003
FIB	OG versus CG	0.003
	OG versus N	0.644
	CG versus N	0.001
NLR	OG versus CG	0.021
	OG versus N	>0.999
	CG versus N	0.027

Abbreviations: CG, control group ($n = 12$); FIB, fibrinogen; Hb, hemoglobin; HDL, high-density lipoprotein; *N*, the group of individuals with normal pregnancy and normal hearing ($n = 14$); NLR, neutrophil-to-lymphocyte ratio; OG, observe group ($n = 17$); RBC, red blood cell; TT, thrombin time; WBC, white blood cell.

anemia owing to increased blood volume and blood dilution, so the red blood cells and hemoglobin will be abnormal. The WBC, neutrophil%, lymphocyte%, and NLR were inflammatory indicators, and thrombin time and fibrinogen were indicators of coagulation function. The above-mentioned laboratory indicators showed no differences between individuals with sudden HL during pregnancy and individuals with normal pregnancy and normal hearing. This suggests that these specific laboratory indicators are unique to the prenatal period, and may contribute to the occurrence of sudden HL. The pathogenesis of sudden HL during pregnancy may be related to inflammatory response and coagulation pathway. It may also explain the rationality of our management that the glucose infusion will ameliorate the state of hypercoagulability and high blood viscosity; the steroids will relieve the inflammatory response.

CONCLUSIONS

Most of the patients with sudden HL during pregnancy observed in this study occurred in the second and third trimester of pregnancy, and most of them were complete deafness. We proposed a new treatment strategy, which was effective and safer. During the follow-up, the hearing of patients can be self-healed with time, and the hearing can still be improved after the readmitted treatment. The pathogenesis of this disease may be related to inflammatory response and coagulation pathway.

AUTHOR CONTRIBUTIONS

Qiu-Ju Wang proposed the manuscript concept. Xiao-Nan Wu and Hong-Yang Wang analyzed the data and wrote the manuscript. Da-Yong Wang and Qiu-Ju Wang led the research and revised the manuscript. Xiao-Long Zhang collected the clinical data and did the statistical analysis. Guo-Hui Chen collected and organized the audiological data of the patients. Jing Guan and Yun Gao critically read and discussed the manuscript. All authors contributed to the study's conception and design, edited the manuscript, and approved the final version of the manuscript. We have no suggestions for Editorial Board Members and we have not had any prior discussions with any Scientific Editorial Board Member about the work described in the manuscript.

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CONFLICT OF INTEREST STATEMENT

Professor Qiu-Ju Wang is a member of World Journal of Oto-rhinolaryngology - Head & Neck Surgery (WJOHNS) editorial board and is not involved in the peer review process of this article.

DATA AVAILABILITY STATEMENT

The data analyzed during the current study are available from the corresponding author upon reasonable request.

ETHICS STATEMENT

This study is a retrospective study based on clinical data and has passed the review of the hospital ethics committee (S2017-024-01).

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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