HERPESVIRUS AND IMPACT ON RECOVERY IN SUDDEN SENSORINEURAL HEARING LOSS

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ABSTRACT

This study aims to investigate the presence of Herpesviridae and SARS-CoV-2 infections in patients with sudden sensorineural hearing loss (SSNHL) and their correlation with clinical and audiological outcomes.

A prospective cohort of 53 patients was evaluated between 2020 and 2024, including clinical assessment, pure-tone audiometry, MRI, and serologic/PCR testing for HSV-1/2, VZV, EBV, CMV and SARS-CoV-2. All patients received systemic corticosteroids; none underwent intratympanic therapy.

Viral markers were detected in 46.4%, mainly IgM for SARS-CoV-2 (26.4%), HSV-1/2 (22.6%), and CMV (5.7%). Coinfection (p= 0.0032), profound hearing loss (p=0.0173), and bilateral SSNHL (with 80% showing no recovery) were significantly associated with poorer outcomes. IgG positivity was high, suggesting prior exposure. Most patients were asymptomatic, supporting the hypothesis of viral reactivation.

These findings support the role of viral coinfections in worsening SSNHL outcomes. Early virologic testing and integrated diagnostic approaches may improve prognostic accuracy and guide individualized treatment strategies.

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INTRODUCTION

Sudden sensorineural hearing loss (SSNHL) is defined as a sensorineural hearing loss of at least 30 decibels, affecting three consecutive audiometric frequencies, that develops within a 72-hour period. Typically presents unilaterally and is often accompanied by tinnitus and/or vertigo.

The etiology of SSNHL remains idiopathic in approximately 70–90% of cases. However, members of the Herpesviridae family—including herpes simplex virus (HSV), varicella-zoster virus (VZV), epstein-Barr virus (EBV), and cytomegalovirus (CMV)—as well as SARS-CoV-2, have been proposed as potential viral triggers for cochlear injury.

Due to the limitations of cochlear biopsy, serologic and PCR tests serve as diagnostic alternatives.

This study investigates the presence of these viruses in SSNHL and their impact on hearing recovery

METHODS AND MATERIALS

A prospective cohort study was conducted from March 2020 to February 2024 at a tertiary outpatient clinic, involving patients aged 10 to 90 years diagnosed with SSNHL. Diagnosis was established based on the American Academy of Otolaryngology–Head and Neck Surgery (AAO-HNS) criteria, using pure-tone audiometry, speech audiometry, and tympanometry. Audiological assessments were performed at diagnosis and during follow-up visits. The four-frequency pure-tone average (4fPTA) was calculated from air conduction thresholds at 500, 1000, 2000, and 4000 Hz.

Virological evaluation included serologic and PCR testing for HSV-1/2, VZV, EBV, CMV, and SARS-CoV-2. Blood samples were collected in the acute phase (within 30 days of symptom onset) and again up to 60 days. Most patients (92.5%) started treatment within 15 days, and the remainder within 30 days.

For molecular analysis, DNA was extracted from peripheral blood mononuclear cell (PBMC) pellets and serologic testing was performed using quantitative ELISA assays to detect human IgM and IgG antibodies.

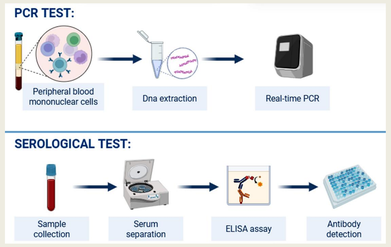

Figure 1– Workflow of virological analyses. (Top) Real-time PCR testing: DNA was extracted from PBMCs and used for amplification by real-time PCR. (Bottom) Serological testing: blood samples underwent serum separation and ELISA for antibody detection.

All patients underwent magnetic resonance imaging. Treatment consisted of oral prednisone at 1 mg/kg/day (maximum 60 mg/day) for 14 days, followed by tapering. Deflazacort was used in cases with comorbidities contraindicating prednisone. Intratympanic corticosteroids were not used.

Statistical analyses included the Cochran-Armitage trend test and Fisher's exact test to assess associations, and Poisson regression models with robust variance to identify factors associated with poor hearing recovery. A p-value <0.05 was considered statistically significant. Analyses were performed using SAS software, version 9.4.

The study was approved by the Institutional Research Ethics Committee (protocol #7.175.158), and written informed consent was obtained from all participants.

RESULTS

A total of 53 patients diagnosed with SSNHL were evaluated. Of these, 48 (90.57%) had unilateral involvement and 5 (9.43%) had bilateral involvement, totaling 58 ears. The sample was predominantly male (56.60%), with the highest incidence in the 40–49 age group (24.53%). Comorbidities were present in 35.85% of patients, with at least two associated conditions. Tinnitus was reported by 90.57%, and 52.83% experienced both tinnitus and vertigo.

At presentation, 30.2% of patients had severe hearing loss. Greater initial severity was significantly associated with poorer outcomes, with profound SSNHL showing the worst prognosis (p = 0.0173).

Virological analysis showed that 46.4% of patients tested positive for at least one virus, while 56.6% had no detectable viral infection.

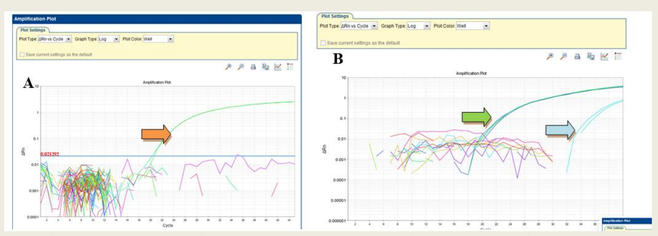

Figure 2 – (A) Real-time PCR run with primers targeting VZV. The nearly overlapping green lines indicate positive samples (orange arrow). Signals below the positivity threshold represent background noise and are considered negative samples. (B) Real-time PCR run with primers targeting HSV-1. Five positive samples can be observed. The lines with Ct values near 22 are HSV-1 controls (green arrow), and the light blue lines indicate positive controls for HSV-2 (blue arrow).

Viral coinfection was significantly associated with poor prognosis (p = 0.0032; Table 1). Notably, none of the coinfected patients showed clinical improvement, suggesting a potential link between coinfection and unfavorable SSNHL outcomes.

Table 1 – Distribution of patients according to viral overlap and clinical outcome

Viral Overlap*	1 – Recovery	2 – No Recovery/Worsening	Total	p-value#
None	23 (76.67)	7 (23.33)	30 (56.60)	0.0032
Single Virus Type	12 (70.59)	5 (29.41)	17 (32.07)	
Two Virus Types	0 (0.00)	6 (100.00)	6 (11.32)	

* values expressed as frequency (%)
# p-value obtained using the Cochran-Armitage trend test

As shown in Table 2, IgM positivity was observed for SARS-CoV-2 (26.4%), HSV-1/2 (22.6%), and CMV (5.7%). CMV DNA was detected by PCR in one patient (1.9%). No IgM or viral DNA was detected for EBV or VZV, indicating no evidence of acute or reactivated infection.

Table 2 – IgM Antibodies for Viral Infections

Category	HSV 1/2	EBV	CMV	VZV	SARS-CoV-2
Negative (ratio < 0.8)	35	53	50	49	34
Borderline (≥ 0.8 and < 1.1)	6	0	0	4	5
Positive (≥ 1.1)	12	0	3	0	14

As shown in Table 3, IgG serology indicated high prior exposure to HSV-1 (86.8%), EBV (98.1%), VZV (100%), and SARS-CoV-2 (52.8%). HSV-2 IgG was positive in 37.8% of patients. Elevated IgG titers (≥10× reference) were observed in most CMV-positive cases (94.1%), and in a substantial portion of VZV (52.3%) and EBV cases (20.8%), suggesting a robust immune response.

Table 3 –IgG Antibodies for Viral Infections

Category	HSV 1	HSV 2	EBV	VZV	CMV	SARS-CoV-2
Below reference value	7	33	1	0	0	25
Above reference value	46	20	52	53	51	28

Among the five patients with bilateral SSNHL, 80% experienced either worsening or no improvement. Three had no detectable viral infection, one had a single-virus infection, and one was coinfected.

Notably, most patients with positive viral serology reported no flu-like symptoms, supporting the hypothesis that viral reactivation—rather than recent symptomatic infection—may contribute to SSNHL pathophysiology.

DISCUSSION

Although SSNHL is traditionally considered idiopathic, increasing evidence suggests a viral contribution. This study investigates the role of herpesviruses and SARS-CoV-2 in acute SSNHL, correlating virological findings with clinical and audiological outcomes.

Virological analysis identified signs of active or recent infection in 46.4% of patients, based on IgM serology or PCR detection. SARS-CoV-2 (26.4%) and HSV-1/2 (22.6%) were the most frequently detected viruses. CMV reactivation, confirmed by both IgM and PCR in four patients, reinforces the hypothesis that asymptomatic viral reactivation may contribute to cochlear damage, even in immunocompetent individuals.

Viral coinfection was significantly associated with poorer prognosis (p = 0.0032), with no clinical improvement observed among coinfected patients, suggesting a possible synergistic effect on cochlear injury. In contrast, isolated HSV-1/2 or CMV infections were not independently linked to worse outcomes.

Additionally, bilateral SSNHL—80% of which showed no clinical improvement—and profound initial hearing loss were both associated with unfavorable recovery.

CONCLUSIONS

This study reinforces the role of viral reactivation in the pathogenesis of SSNHL, particularly during the acute phase and even in the absence of systemic symptoms. Viral coinfection, bilateral involvement, and profound hearing loss at onset were significantly associated with poorer outcomes, while isolated viral infections showed no significant impact on recovery. An integrated diagnostic approach—including serologic, molecular, and clinical evaluation—may enhance prognostic accuracy and support individualized treatment strategies.

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