

## Comparative Study for Use of Steroids in Treatment of Sudden Sensorineural Hearing Loss in COVID19 Patients

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### ABSTRACT

**Introduction:** Viruses are identified to lead to neurological manifestation, like anosmia, facial paralysis and sudden sensorineural hearing loss (SSNHL). Throughout the preceding SARS epidemic, corona-viruses were stated be accompanied with losses of smell and taste senses because of neural injuries.

**Aim:** This research aims to study the existence of (SARS-CoV-2) in cases with only SSHNL throughout the COVID19 pandemic and effectiveness on intratympanic steroid injections on development of cases.

**Methods:** This work involved 20-cases with the single complaint of unilateral SSNHL to the otolaryngology out-patient clinics. The cases were directed to be assessed for SARS-CoV-2 by real time polymerase chain reactions (RT-PCR) test. Cases received systemic steroids, intratympanic steroids or combined and were then audiological assessed.

**Results:** RT-PCR test for SARS-CoV-2 was positive in 13 cases. A positive responding to COVID19-definite therapy in the SARS-CoV-2 positive SSNHL cases has been observed. Most of cases received intratympanic steroids showed significant improvement than non-received ( $p=0.005$ ). Also, cases received combined intratympanic and systemic steroids showed significant improvement than non-received ( $p=0.021$ ), while improvement in cases received systemic steroids or vasodilators showed no statistical significant difference than non-received ( $p=0.306$  and  $0.595$ , respectively).

**Conclusion:** It must be recalled that nonspecific signs like SSNHL can be the only symptom with which to know a COVID19 case. Recognition of such nonspecific presentations of COVID19 cases is crucial throughout this pandemic time for avoiding infectious spreading via isolations and early initiations of COVID19 targeted therapy.

**Keywords:** COVID19, Sudden sensorineural hearing loss, Pandemic, SARS-CoV-2, Intratympanic steroids.

### INTRODUCTION

Sudden sensorineural hearing losing (SSNHL) is defined as sensorineural hearing losing  $\geq 30$  dB at 3 consecutive audiometric frequencies among over 3 days. SSNHL is considered one of the commonest complaints in otologic and audiology routines (1.5-1.7/100 new cases presented in our work). In only 7 to 45% of cases, a definite cause may be recognized and definite treatment regimen can be utilized for therapy. Most of cases with SSNHL has no recognizable reason for hear losing and is considered as "idiopathic" <sup>(1)</sup>.

An acute respiratory disorder, produced by a new corona-virus (SARSCoV-2, formerly identified as 2019-nCoV), the corona-virus disorder-2019 (COVID19) has spread through China and received universal consideration. WHO declared the COVID19 epidemic as an emergency to the public health with worldwide. The majority cases infected with the COVID19 suffered from mild to moderate respirational sickness and recovered without aggressive therapy <sup>(2)</sup>.

COVID19 signs appear in 2 to 14 days following to exposures (built on the incubating interval of COVID19). The signs of COVID19 can be fatigue, cough, fever, and a small number of cases presented with stomach infections signs. The aging and comorbidities can be accompanied with acute

respirational distress syndrome (ARDS) and cytokine storm <sup>(3)</sup>.

Numerous infections with viruses could lead to hearing loss. These cases made by viruses could be acquired or congenital, unilateral or bilateral. Specific viral infection can directly harm inner ear, others could persuade inflammatory responding which then lead to this injury, while others may cause superadded bacterial or fungal infections, causing hearing losses. Characteristically, virus-made hearing losses are sensorineural, while conductive and mixed hearing losses can occur with bacterial rather than viral infections. Infrequently, hearing recovery afterward the infections could happen spontaneously <sup>(4)</sup>.

Hearing losses caused by virus may be mild or severe to deep, unilateral or bilateral. Mechanisms of incidence of hearing losses caused by various viruses differ significantly, ranged between direct injury to inner ear structure, inner ear hair cells and organs of Corti, reaching to inductions of host immune-intermediated injury <sup>(5)</sup>.

Viruses were recognized to lead to neurological manifestation, like facial paralysis, anosmia, and SSNHL <sup>(6)</sup>. Throughout SARS epidemic, corona-viruses have been stated to be accompanied with losses of taste and

smell because of neural injuries<sup>(7)</sup>. Few studies of SSNHL have found in the literature accompanied with the COVID19. Identifications of cases presenting with nonspecific signs throughout the pandemic can have a significant function in breaking the infecting chains and decreasing transmissions. So, this research aims to study the existence of SARS-CoV-2 in cases presenting with only SSNHL throughout the pandemic of COVID19.

## PATIENTS AND METHOD

### Ethical approval

**The current study protocol was obtained from Ain Shams University Faculty of Medicine Research Ethics Committee (REC) FWA 00017585 with reference number FMASU P46a/2020. Ethics guidelines for human experimentation by the World Medical Association's Helsinki Declaration were adhered to. Informed consent was taken from each patient.**

Twenty cases were eligible for the research if they were existing with the single complaint of unilateral unexpected hearing losing to the otolaryngology outpatient clinic from 1 May 2021 and 30 November 2021. SSNHL was recognized as hearing losses of >30 dB at 3 successive frequencies at minimum over an interval of less than 3 days<sup>(8)</sup>. Audio-logical testing established SSNHL in all the cases. The cases were then directed to the infectious disorders clinic to be evaluated for SARS-CoV-2. Taking strict protections – in a security cabinet with disposable isolating dresses, gloves, N95 masks, and shields – pharyngeal secretions specimens were gathered from the oropharynx and then the nasopharynx through straight contacts with swabs. The specimens were sent to the lab for RT-PCR test.

Cases then were subjected to committee to discuss the options of therapy which were: 1) Three settings of intratympanic injections of dexamethasone 8 mg per set using 22G spinal needle in anterosuperior quadrant of tympanic membrane on the affected side. 2) Systemic steroids according to body weight in the form of prednisone 20 mg tablet. 3) Vasoactive drug to enhance cochlear microcirculation using pentoxifylline 400 mg twice daily. Duration of therapy was 10 days for systemic drugs.

Cases then accepted the full protocol of therapy or chose one modality according to health status and considering flare up of virus infection with systemic steroids a possibility.

Post therapy audiological assessment was done for all cases.

### Case 1

Female case 55 years old with no past medical disorder presented to the clinic after 3 days of newly

developed tinnitus and aural fullness in the right ear with no other symptoms either otological or related to COVID symptoms. Examination was unremarkable. Audiological evaluation revealed right profound SSNHL for all frequencies with type (A) tympanogram. She was advised about PCR for COVID 19, which later on confirmed positive infection; Magnetic resonance imaging on cerebellopontine angle (MRI- CPA) was done and it was free, she accepted the full protocol of management.

10 days post therapy revealed improvement in the symptoms and audiological showed mild low frequency SNHL at 45 db HL.

### Case 2

Female case 42 years old with past medical history of hypertension on angiotensin converting enzyme inhibitor( ACEI) twice daily presented after 7 days of newly developed aural fullness and hearing impairment in the right side with no other symptoms of COVID infection, nothing was specific in examination. Audiological evaluation showed right severe to profound mid and high frequencies SNHL with type (A) tympanogram. She was tested positive for COVID 19 infection. MRI was done with no abnormality detected.

She accepted only intratympanic injection with pentoxifylline 400 mg, 10 days after therapy Audiological evaluation showed no remarkable changes.

### Case 3

Female case 37 years old with no past medical history presented with left sudden hearing impairment associated with aural fullness, vertigo and headache, and nothing in clinical examination.

Audiological evaluation showed mid frequency sensorineural hearing loss, with no MRI signs.

She received systemic steroid and ITS improved-on 4<sup>th</sup> day with complete recovery after one week.

### Case 4

13 years old male adolescent presented with right side sudden fullness and impaired hearing 3 days after onset of pharyngitis. Audiogram showed moderate to severe high frequency SNHL. The parents of the case refused the therapy with steroid either systemic or local, no improvement.

### Case 5

40 years male case presented with left sided fullness, with anosmia and loss of taste sensation of 3 days duration, audiogram showed bi-lateral high frequency SNHL, mild on right (Rt) side and moderate on left (Lt) side,

Case refused intratympanic injection and systemic steroid with no apparent improvement.

**Statistical methods**

Data were analyzed using IBM® SPSS® Statistics version 26 (IBM® Corp., Armonk, NY). Categorical variables are presented as numbers and percentages, and inter-group differences are compared using the Pearson chi-squared test or Fisher’s exact test. Time to event analysis is done using the Kaplan-Meier method. Multivariable binary logistic regression analysis was used to identify predictors of occurrence or recovery of smell/taste loss in COVID-19 patients. Factors associated with the outcome of interest at the P < 0.2 level by bivariate analysis are selected for entry in multivariable logistic regression to identify independent predictors. P-values < 0.05 are considered statistically significant.

**RESULTS**

This study included twenty cases; their demographic data are shown in table 1.

**Table 1: Demographic data of cases**

Variables	N=20
<b>Age (years)</b>	
mean±SD	42.7±18.8
Range	5-72
<b>Gender (n,%)</b>	
Male	8(40%)
Female	12(60%)
<b>Onset of symptoms (days)</b>	
mean±SD	11.7±8.2
Range	3-30
<b>Comorbidities (n,%)</b>	
HTN*	10(50%)
DM**	8(40%)

\*HTN:hypertension.

\*\*DM:diabetes mellitus.

In table 2, 70% presented with vertigo, and 70% had anosmia. Left ear was more affected (75%) than right ear (25%).

**Table 2: Clinical presentations data of cases**

Variables	N=20
Tinnitus	7(35%)
Vertigo	14(70%)
<b>Affected side</b>	
✚ Rt side	5(25%)
✚ Lt side	15(75%)
Fever	8(40%)
Anosmia	14(70%)
Chest symptoms	5(25%)

Cases PCR results were positive in 65% of cases and audiogram results showed moderate affection in 50% of patients as shown in table 3.

**Table 3: Investigation results of cases**

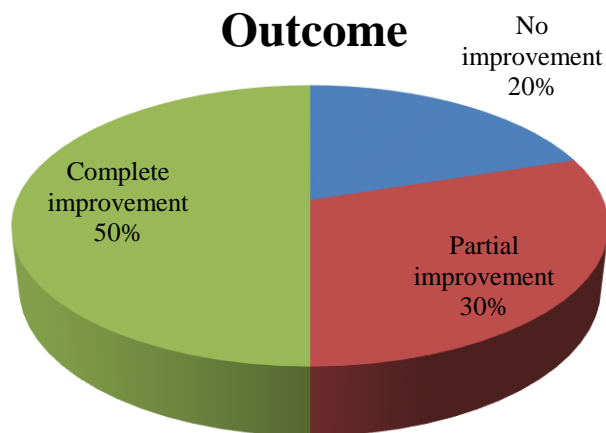
Investigation results	N=20
<b>Audiogram</b>	
✚ Mild	5(25%)
✚ Moderate	10(50%)
✚ Severe/profound	5(25%)
<b>PCR</b>	
✚ Positive	13(65%)
✚ Negative	7(35%)

Table 4 illustrates methods of intervention utilized as 80% received intratympanic steroids.

**Table 4: Method of intervention distribution of cases**

Intervention	N=20
✚ Systemic steroids	11(55%)
✚ IT steroids	16(80%)
✚ Vasodilators	9(45%)
✚ Systemic +IT steroids	9(45%)

As in figure 1, 10 cases (50%) showed complete improvement.



**Figure 1: Distribution of outcome among cases**

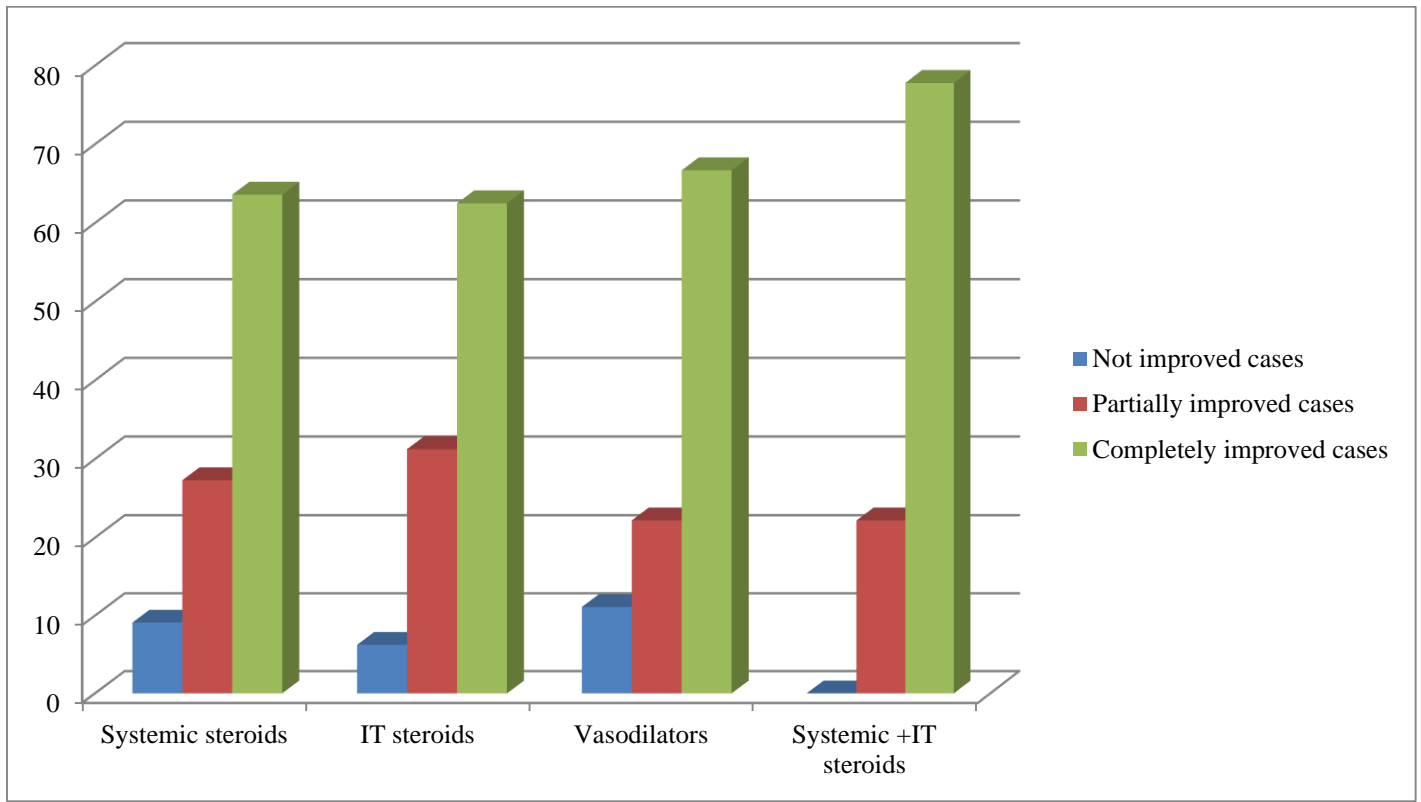
In table 5, Most of cases received intratympanic steroids showed significant improvement than non-received. Also, cases received combined intratympanic and systemic steroids showed significant improvement than non-received, while improvement in cases received systemic steroids or vasodilators showed no statistical significant difference than non-received.

**Table 5: Clinical outcomes of different methods of intervention among cases**

Intervention	Not improved cases	Partially improved cases	Completely improved cases	P value
<b>Systemic steroids</b>				
Yes	1(9.1%)	3(27.3%)	7(63.6%)	0.692
No	2(22.1%)	1(11.1%)	1(11.1%)	
<b>IT steroids</b>				
Yes	1(6.25%)	5(31.25%)	10(62.5%)	0.319
No	2(22.1%)	1(11.1%)	1(11.1%)	
<b>Vasodilators</b>				
Yes	1(11.1%)	2(22.2%)	6(66.7%)	0.714
No	4(36.1%)	3(27.1%)	4(36.1%)	
<b>Systemic +IT steroids</b>				
Yes	0(0%)	2(22.2%)	7(77.8%)	0.069
No	4(36.4%)	4(36.4%)	3(27.3%)	

*Fisher exact test used*

Figure 2 presented distribution of clinical outcome (improvement) in each group of interventions. Cases received systemic and intratympanic steroids shows the elevated proportion of cases revealed complete improvement, while cases received intratympanic steroids showed the highest proportion of patients showed partial and complete improvement.



**Figure 2: Distribution of clinical outcomes of different methods of intervention among cases.**

## DISCUSSION

The SSNHL pathogenesis is still not clear, even if virus infections and vascular disorders are the more shared mechanism supported. Other suggested pathogenetic concepts comprise auto-immune or immunologic disorder, and ototoxic injuries<sup>(9)</sup>.

The definite pathogenic function of virus infections in inner ear structural injury wasn't ultimately established<sup>(10)</sup>. Among the possible causes of SSNHL, vascular contribution has raised much consideration, even if not various researches in the literature have studied the correlation between SSNHL and vascular disorder to date. The cochlea has high sensitivity to disruptions of blood flowing. In animal models it was found that occlusion of labyrinthine vessels causes non-reversible hearing losses; cochlear hair cells have elevated metabolic activities and are mainly vulnerable to hypoxic or ischemic damages. Cochlear micro-vascular disorders may be related to elevated plasma viscosities, to micro embolic and/or thrombotic conditions<sup>(11)</sup>. Association between cochlear blood flow and hearing affection is essential to improve the therapy and diagnosing of deafness that possibly rises from circulatory irregularities. But, accomplishing such considerate was a challenge owing to the experimental complications involving monitoring cochlear blood flowing, as the investigation of cochlear circulations must include in vivo scans of blood flowing with micro scale resolution, and owing to the deep locations of the cochlea within the temporal bone<sup>(12)</sup>. We found only a few new retrospective researches in literature of small groups of cases impacted by clinical vascular disorder and SSNHL. **Lee et al.** concluded that 4 out of 12 cases in his work have SSNHL previous the onset of an anteroinferior cerebellar artery stroke<sup>(13)</sup>.

Disagreement is still surrounding the requirement and treatment options of idiopathic SSNHL. One of the origins of this current argument is the fact that idiopathic SSNHL impulsively resolved in 45 to 65% of cases. Several agents were studied for the therapy of idiopathic SSNHL counting anti-inflammatory agents, antimicrobials, vitamins, calcium antagonists, vital minerals, volume expanders, vasodilators, defibrinogenators, hyperbaric-oxygen, diuretics, and bed rest. The number and variety of therapies resulted from the current argument over the etiology of idiopathic SSNHL, the comparative infrequency of the disorder, and the lack of a clearly superior treatment<sup>(13)</sup>.

Commonly, primarily hopeful outcomes are revealed in patients series and small trials, but larger researches are either non-conclusive or show non-significant development in hearing results by treatment<sup>(12)</sup>. U.S. physicians in a survey, 100% of the

otolaryngologists concluded that treatment of idiopathic SSNHL, while 97% of generalists either directed to an otolaryngologist for more therapy (71%) or treated the hearing losses themselves (26%)<sup>(14)</sup>. When surveyed, 98% of U.S. otolaryngologists stated treatment of idiopathic SSNHL with oral steroids; moreover, 8% of otolaryngologists described the usage of intratympanic steroids<sup>(15)</sup>. Corticoids are believed to progress idiopathic SSNHL via dropping inflammations and edema in the inner ear<sup>(16)</sup>. An early report mixed the data from 2 distinctly administered double-blinded RCTs of a number of 67 cases using various corticosteroid régimes, revealed a better hearing recovery in cases using steroids (78%) in comparison with placebo (38%)<sup>(17)</sup>. Succeeding tries to duplicate this research reveal conflicting results regarding the benefits of corticosteroids in idiopathic SSNHL, and there are problems in terms of methodologies with a lot of these trials<sup>(18)</sup>.

Intratympanic (IT) corticosteroids are being progressively utilized in the managing idiopathic SSNHL. IT-steroid application causes higher perilymph levels of steroids than systemic administrations, at minimum in guinea pigs; but IT steroids aren't absorbed into the systemic circulations. Primarily, they have been utilized mostly in the context of cases with contraindication to systemic steroid treatment and cases who have unsuccessful systemic steroid administrations<sup>(19)</sup>.

In the present work, most of cases received intratympanic steroids showed significant improvement than non-received. Also, cases received combined intratympanic and systemic steroids showed significant improvement than non-received, while improvement in cases received systemic steroids or vasodilators showed no statistical significant difference than non-received.

**Halpin and Rauch** have lately revealed that IT usage of corticosteroids isn't inferior to systemic steroids for idiopathic SSNHL with threshold <70 dB HL<sup>(20)</sup>.

Cases in this study received systemic and intratympanic steroids showed the highest percentage of cases revealed complete improvement, while cases received intratympanic steroids showed the highest percentage of cases revealed partial and complete improvement.

In a review of 104 involved otolaryngologists, 50% of accused stated utilizing anti-herpetic treatment (acyclovir, famciclovir, etc.) in combinations with corticosteroids for the therapy of idiopathic SSNHL in spite of absence of indication of effectiveness<sup>(14)</sup>. Other therapeutic modalities, counting "shotgun" methods joining multi-modalities of therapy, are as well commonly achieved with no good clinical indication of their efficacy for idiopathic SSNHL.

The COVID 19 pandemic has affected people universally. Numerous cities were principally hard-hit in the USA. Autopsies have been achieved on 4 decedents from New Orleans, LA. Each confirmed positive for SARS-CoV-2 by RT-PCR and had lab results notable for raised fibrinogen, ferritin, PT and D dimer level at the period of hospital stay<sup>(14)</sup>.

## CONCLUSION

It must be recalled that nonspecific signs like SSNHL can be the only symptom with which to know a COVID19 case. Recognition of such nonspecific presentations of COVID19 cases is crucial throughout this pandemic time for avoiding infectious spreading via isolations and early initiations of COVID19 targeted therapy and avoiding potentially damaging standard SSNHL treatment that comprises intratympanic and systemic steroids.

## Conflict of Interest and financial sponsorship:

The authors have no conflict of interest to disclose.

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