Evaluation of Role of Prognostic Factors on Hearing Outcome in Unilateral Idiopathic Sudden Onset Sensorineural Hearing Loss

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ABSTRACT

Introduction
Owing to its uncertain and possible etiologies, the use of multiple empirical treatment regimens, and the possibility of spontaneous recovery, it becomes important to look for the possible prognostic factors affecting the outcome of sudden sensorineural hearing loss (SSNHL).

Materials and Methods
This prospective observational study was conducted with the primary aim of analyzing the role of various possible prognostic factors on the outcome of idiopathic SSNHL including demographic (age, gender), audio-vestibular (pre-treatment hearing loss in the affected ear, hearing in the contralateral ear, the time elapsed between onset of hearing loss and start of treatment, type of hearing loss in terms of frequencies affected), presence of tinnitus/vertigo and comorbidities (diabetes, hypothyroidism & deranged lipid profile/dyslipidemia).

Results
The absence of vertigo and tinnitus led to better hearing outcomes while raised HbA1c levels, deranged lipids, and thyroid profiles adversely affected the outcome.

Conclusion
Vertigo, tinnitus, raised HbA1c levels, deranged lipids, and thyroid profiles are possible negative prognostic factors. Better pretreatment hearing levels in the affected and unaffected ears prompted improved recovery.

Keywords
Tinnitus; Glycated Hemoglobin; Prognosis; Hearing Loss; Sudden; Vertigo; Hypothyroidism; Dyslipidemias; Demography; Lipids

Among the leading causes of disability worldwide, hearing loss also holds a significant position. Patients who suffer from hearing loss are unable to localize sounds and find difficulty in understanding speech and are thus bound to face social isolation to a variable extent. This also puts them at an increased risk of developing depression and anxiety disorders. Idiopathic sudden sensorineural hearing loss (ISSNHL), can be defined as hearing loss of ≥30dB in 3 consecutive frequencies of pure tone average (PTA) within 3 days/72 hours. The estimated worldwide annual incidence of the disease is 5-20 per 100,000 population. Although all ages and both sex are affected by this disease, the peak age ranges from 30-60 years. When SSNHL develops most of the cases are unilateral and the bilateral disease is seen only in 0.44 – 3.4 % of patients. Owing to the uncertain
etiology of the disease, various hypotheses have been proposed and are considered to understand the disease. These include but are not limited to viral infection, vascular ischemia affecting the inner ear, autoimmune pathologies, metabolic derangements, etc. \(^9, 10\)

Formulating a standard treatment plan is difficult for clinicians due to uncertain etiology and this is further complicated by the fact that a significant proportion of the patients (30-65%) recover spontaneously within 15 days of disease onset.\(^11, 12\) Considering the uncertain and varied etiology, various empirically used therapeutic options include corticosteroids, anti-viral agents, anti-inflammatory agents, vasodilators, diuretics, rheological substances, and hyperbaric oxygen therapy.\(^4, 11, 13-15\) Amongst all available options steroids in oral or systemic form have been considered most effective and are used frequently.\(^10\)

Despite spontaneous recovery and treatment with various available not all patients gain complete functional recovery.\(^16, 17\) This mandates a probe into the various prognostic factors affecting disease outcomes. The available literature suggests that the prognosis of SSNHL is dependent on several factors, including patient age, presence of vertigo at onset, degree of hearing loss, audiometric configuration, and time between the onset of hearing loss and treatment. Available studies (those mentioned in the discussion section) regarding the role of prognostic factors suggested variable results. Thus we conducted this prospective observational study to analyze the role of various prognostic factors on the recovery of idiopathic sudden onset unilateral sensorineural hearing loss.

**Materials and Methods**

This prospective observational study carried out in the department of otorhinolaryngology at a tertiary care center, which included 70 patients as subjects.

We conducted this study with the primary aim of analyzing the role of various prognostic factors on the outcome of idiopathic sudden onset unilateral sensorineural hearing loss including demographic (age, gender), audio-vestibular (pre-treatment hearing loss in the affected ear, hearing in the contralateral ear, the time elapsed between onset of hearing loss and the start of treatment, type of hearing loss in terms of frequencies affected), presence of tinnitus/vertigo and comorbidities (diabetes, hypothyroidism & deranged lipid profile/ dyslipidemia). This study also had the objective to assess the simultaneous occurrence of vestibular symptoms like tinnitus and vertigo in patients suffering from SSNHL.

All the patients visiting the hospital over a defined period of 18 months with complaints of sudden onset unilateral hearing loss and volunteered to participate in the study were included after excluding the patients with the following congenital middle ear and inner ear malformations, middle ear diseases, conductive or mixed hearing loss, bilateral sudden hearing loss, inner ear diseases with a defined etiology (such as trauma, perilymph fistula, multiple sclerosis, Meniere’s disease, retro-cochlear disease, having ototoxic drug intake and history of mumps infection).

On the very first visit, every patient who met the inclusion criteria, was explained the study protocol, and if they volunteered to participate, written informed consent was obtained from every individual. A detailed history was obtained from everyone based on a pre-formed format giving special emphasis on the onset, duration, and anything attributable to the causation of hearing loss. An otoscopic examination was done to assess the tympanic membrane. Patients were subjected to pure tone audiometry on the day of presentation and the average hearing level at 500 Hz, 1000 Hz, 2000 Hz, and 4000 Hz was calculated. Investigations including complete blood count, ESR, VDRL, random blood sugar and serum thyroid profile, and Magnetic Resonance Imaging of the brain (to rule out intracranial causes) were done for all. The aforementioned potential prognostic factors were recorded for everyone. All the patients received similar treatment. Patients were re-subjected to audiometry 30 days after completion of treatment and the following parameters were calculated:

1. Hearing gain \{pre-treatment hearing level (affected ear) - post-treatment hearing level (affected ear)\}
2. Relative hearing gain \(\frac{\text{hearing gain}}{\text{initial hearing level in the affected Ear}}\)
3. Recovery Rate \( \{ \text{pretreatment hearing level (affected ear)} - \text{post-treatment hearing level (affected ear)} / \text{difference in initial hearing level between affected and unaffected ear} \) 

For statistical analysis, categorical variables were presented in number and percentage (%), and continuous variables were presented as mean ± SD and median. The normality of data was tested by the Kolmogorov-Smirnov test. Quantitative variables were compared using unpaired t-test/Mann-Whitney test between two groups and ANOVA/Kruskal Wallis test was used for comparison between more than two groups. Pearson correlation coefficient/Spearman rank correlation was used to assess the association of outcome with various parameters. A p-value of <0.05 was considered statistically significant.

Results

We used Seven-Pattern classification of the initial hearing loss pattern in SSNHL (as mentioned below) proposed by Chang N-C et al.\(^{18}\)

- Low tone > 30 dB loss at 250 Hz, and > 30 dB loss at 1000 and 4000 Hz in comparison with the other ear
- Mid tone > 30 dB loss at 1000 Hz, and > 30 dB loss at 250 and 4000 Hz in comparison with the other ear
- High tone > 30 dB loss at 4000 Hz, and > 30 dB loss at 250 and 1000 Hz in comparison with the other ear
- Low-to-mid tone > 30 dB loss at 250 and 1000 Hz, and > 30 dB loss at 4000 Hz in comparison with the other ear
- Mid-high tone > 30 dB loss at 1000 and 4000 Hz, and > 30 dB loss at 250 Hz in comparison with the other ear
- Flat loss > 30 dB loss at 250, 1000, and 4000 Hz in comparison with the other ear, but the average hearing loss was not exceed 90 dB
- Total loss > 30 dB loss at 250, 1000, and 4000 Hz in comparison with the other ear, and the average hearing loss exceed 90 dB

Out of 70 patients included in the study, PTA showed the following types of audiograms:

- 2 patients (2.85%) showed low tone loss
- 1 patient (1.42%) had high tone loss
- 3 patients (4.28%) were seen having low to midline loss
- Maximum patients 56 (80%) were having flat loss
- 8 patients (11.42%) had total loss

Final computation of data denoting hearing recovery is as follow (Table I).

<table>
<thead>
<tr>
<th>RECOVERY TYPE</th>
<th>FINAL HEARING</th>
<th>NUMBER OF PATIENT</th>
<th>% DISTRIBUTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete</td>
<td>Better than 25 dB</td>
<td>08</td>
<td>11.43%</td>
</tr>
<tr>
<td>Partial</td>
<td>between 25 - 45 dB</td>
<td>36</td>
<td>51.43%</td>
</tr>
<tr>
<td>Slight</td>
<td>Poorer than 45 dB</td>
<td>18</td>
<td>25.71%</td>
</tr>
<tr>
<td>No</td>
<td>Poorer than 75 dB</td>
<td>08</td>
<td>11.43%</td>
</tr>
</tbody>
</table>

The detailed analysis of hearing outcome results in terms of defined parameters (Hearing gain, relative hearing gain, recovery rate) with respect to various prognostic parameters is as follow.

Out of 70 participants 21 (30%) were females and 49 (70%) were males, the recovery parameters (Mean ± Standard deviation) were found as shown in table below (Table II). There was no statistically significant difference noted in the hearing improvement between males and females.

70 participants in the study were distributed in four age groups comprising d” 30 year, 31-40 years, 41-50
years and > 50 year. Relation between frequency distribution of various age groups and recovery parameters (Mean ± Standard deviation) are shown in table below (Table III). There was no statistical significant difference in the hearing gain, recovery rate and relative hearing gain over the various age groups. However, an inverse relationship was noted between the age and the relative hearing gain i.e. as the age increases, relative hearing gain decreases as compared to younger age group in the study population. The co-relation between age and relative hearing gain is as shown in Figure 1.

Co-relation between pre-treatment hearing levels of affected and unaffected ear and various parameters is as follow (Table IV). The results suggested that the pretreatment hearing level in the affected ear has a significant role in the hearing outcome. While, the hearing level in the unaffected ear had a significant role in relative hearing gain.

The frequency distribution of patients presenting in varying time frame and correlation with hearing outcome parameters is as follow (Table V). There was no statistically significant difference in the hearing gain, recovery rate and relative hearing gain in the patients presenting after 1 week, 2 weeks, 3 weeks and 4 weeks of onset of hearing loss.

The interpretation of data with respect to type of hearing loss, suggested that the mean hearing gain, mean recovery rate and mean relative hearing gain was less in low to mid tone hearing loss but there was no statistical significant difference between the three parameters when compared to other types of audiograms.

Out of 70 patients 16 (22.85%) patients presented with associated complain of tinnitus. The hearing gain (Mean ± standard deviation) for the patient with and without were 22.08 ± 7.69, 24.75 ± 8.59 respectively. The recovery rates (Mean ± standard deviation) were 0.47 ± 0.16, 0.63 ± 0.2 for patients with and without tinnitus. The relative hearing gain for tinnitus patients was 0.33 ± 0.12 while for patients without it was 0.41 ± 0.13. There was a statistically significant difference in recovery rate and relative hearing gain between the two groups positively favoring the group who did not complain of tinnitus.
Fig. 1. Correlation between Age and Relative hearing gain

Table IV: Correlation between pre-treatment hearing levels of affected and unaffected ear and outcome parameters

<table>
<thead>
<tr>
<th>HEARING LEVEL</th>
<th>STATISTICAL PARAMETER</th>
<th>HEARING GAIN</th>
<th>RECOVERY RATE</th>
<th>RELATIVE HEARING GAIN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Affected ear (pre-treatment)</td>
<td>Correlation Coefficient</td>
<td>0.229</td>
<td>-0.331</td>
<td>-0.367</td>
</tr>
<tr>
<td></td>
<td>P value</td>
<td>0.056</td>
<td>0.0051</td>
<td>0.0018</td>
</tr>
<tr>
<td>Unaffected ear (pre-treatment)</td>
<td>Correlation Coefficient</td>
<td>0.002</td>
<td>0.087</td>
<td>-0.304</td>
</tr>
<tr>
<td></td>
<td>P value</td>
<td>0.9868</td>
<td>0.4735</td>
<td>0.0106</td>
</tr>
</tbody>
</table>

Table V: Frequency distribution of patients presenting in varying time frame and correlation with hearing outcome parameters

<table>
<thead>
<tr>
<th></th>
<th>1 WEEK</th>
<th>2 WEEK</th>
<th>3 WEEK</th>
<th>4 WEEK</th>
<th>P-VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>24</td>
<td>12</td>
<td>20</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>Hearing Gain</td>
<td>25.42 ± 8.2</td>
<td>23.33 ± 8.62</td>
<td>23.58 ± 9.66</td>
<td>23.45 ± 7.29</td>
<td>0.845</td>
</tr>
<tr>
<td>Recovery Rate</td>
<td>0.62 ± 0.18</td>
<td>0.61 ± 0.25</td>
<td>0.58 ± 0.19</td>
<td>0.55 ± 0.22</td>
<td>0.673</td>
</tr>
<tr>
<td>Relative Hearing Gain</td>
<td>0.42 ± 0.12</td>
<td>0.4 ± 0.15</td>
<td>0.37 ± 0.13</td>
<td>0.37 ± 0.14</td>
<td>0.561</td>
</tr>
</tbody>
</table>
Majority of the patients, 62 (88.57%) out of 70 reported no vertigo. The outcome parameters were compared between the two groups with and without vertigo as an associated symptom for SSNHL. Hearing gain (Mean ± standard deviation) for the two groups were 22.71 ± 7.4, 24.33 ± 8.58 respectively. Recovery rates were 0.47 ± 0.2, 0.61 ± 0.2 & relative hearing gain parameters were 0.35 ± 0.14, 0.4 ± 0.13 respectively for the groups with and without vertigo. Statistical analysis showed that the recovery rate was significantly more in patients not having vertigo as an associated symptom.

The patients included in this study were categorized in three groups having HbA1c in the range of 4-6, 6-8 and more than 8. The three groups had 52, 16 and 2 patients respectively. Various outcome parameters in terms of Mean ± standard deviation for the respective groups are as follows; Hearing gain (24.94 ± 8.38, 22.71 ± 8.25 & 15 ± 7.07 ), Recovery rate (0.62 ± 0.2, 0.53 ± 0.17 & 0.29 ± 0.11) and Relative hearing gain (0.41 ± 0.13, 0.36 ± 0.12 & 0.21 ± 0.09). The data analysis demonstrated a higher recovery rate and relative hearing gain in the group having HbA1c in the range of 4-6% as compared to those in the range of 6-8% and > 8.

Only 6 out of total 70 patient had abnormal thyroid profile. When compared with patient having normal thyroid profile the recovery parameters (Mean± standard deviation) were as follow; 1. Hearing gain (14.72 ± 4.27 & 25.03 ± 8.18), recovery rate (0.35 ± 0.18 & 0.62 ± 0.19) and relative hearing gain (0.23 ± 0.1 & 0.41 ± 0.13). The data interpretation showed that all three parameters were had improved outcomes in patient with normal thyroid profile in comparison to those with abnormal thyroid profile.

The various hearing outcome parameters were also assessed concerning serum levels of triglyceride (63 had levels d”150 mg/dl and 7 had >150 mg/dl), serum HDL levels (17 had <40 mg/dl & 53 had 40-60 mg/dl) and serum LDL levels (52 had <100 mg/dl & 18 >/=100 mg/dl). The analysis of results showed that the recovery rate was significantly better in the cases having serum triglyceride levels d”150 mg/dL. There was a significant improvement of all three parameters of hearing outcome in the cases having HDL in the range of 40-60 mg/dL& cases having LDL<100 mg/dL.

After adjusting the confounding factors for every outcome parameter Multivariate linear regression with every outcome parameter as dependent suggested HbA1C as an independent prognostic factor affecting the relative hearing gain and recovery rate, while the pre-treatment hearing level in the affected ear was found to independently affect the recovery rate.

**Discussion**

Owing to its uncertain and multiple possible etiologies, use of multiple empirical treatment regimens, and the possibility of spontaneous recovery, it becomes important to look for the possible prognostic factors affecting the outcome. Multiple studies have been done so far to ascertain these but consensus about these is lacking. We conducted this study to contribute and help build literature into this still debatable area.

Our results concerning sex/ gender as a prognostic factor suggested no significant difference between the two categories which is comparable to other studies. While there have been studies showing favorable hearing outcomes in males. A possible attribute of this can be the small sample size of our study population.

Evaluation of age as a prognostic factor in our study suggested no statistically significant difference in the hearing outcome parameters over the various age groups. However, an inverse relationship was noted between age and relative hearing gain. Various studies have suggested age as a negative prognostic factor. In other studies, there has been no significant correlation between age with hearing outcome as a prognostic factor. The recovery rate in children with SSNHL is considered comparable to that in adults, but children have a higher complete recovery rate when compared to adults.

Pretreatment hearing levels showed a positive correlation with hearing outcomes in our study. There was no statistically significant difference in the hearing outcome parameters in this study concerning time elapse/onset of hearing loss, similar results are there in the
Studies have reported significant improvement in hearing outcomes in patients presenting within the first seven days of onset of idiopathic sudden sensorineural hearing loss.\textsuperscript{20, 22, 26} There was no statistically significant difference in the hearing outcomes among the various audiometric configurations found in our study, the reason being the majority of the cases had similar audiometric configurations. Various studies have shown the significant impact of the audiogram shape on hearing recovery, with higher rates of recovery found for low-frequency or mid-frequency hearing loss compared with flat or down sloping.\textsuperscript{18, 22, 27, 28, 29} The reason for this is cochlear basal turn hair cells representing the higher frequencies are more prone to damage. Atay et al have suggested that patients with a flat audiogram had better relative hearing gain.\textsuperscript{24}

In our study, we found tinnitus as a negative prognostic factor. There are very few studies supporting this.\textsuperscript{30} While, studies are reporting better outcomes in hearing improvement in patients presenting with tinnitus, attributing this to the possible presence of functioning hair cells.\textsuperscript{23, 31} Vertigo also has been shown to have a negative prognostic impact in our study. The recovery rate was more in cases without vertigo in our study. Other studies have also reported associated vertigo to be a poor prognostic factor.\textsuperscript{20, 21, 23, 32}

In our study, we found better recovery rate and relative hearing gain in patients with HbA1c in the range of 4-6% as compared to those in the range of 6-8% and >8% implying diabetes as an adverse prognostic factor. Hyperglycemia causes a change in plasma osmolarity impacting the hair cell mobility and function which could manifest sudden sensorineural hearing loss as reported in a study done by Wag et al in which, 44.8% showed profound hearing loss with incomplete recovery.\textsuperscript{33}

Nakashima et al reported that abnormal thyroid levels are a risk factor for sudden deafness.\textsuperscript{34} We found a significant difference in the hearing outcome in cases with abnormal thyroid profiles as compared to those who had normal thyroid profiles.

Studying the lipid profile as a prognostic marker, we report a significantly better recovery in the cases having serum triglycerides in the range of 70-110 mg/dL as compared to others. Suggesting that vascular occlusion (due to thromboembolic events) is the possible mechanism contributing to an increased risk of sudden hearing loss, studies conducted by Mosnier et al, Cadon et al, and Ciccone et al reported high levels of total cholesterol and LDL is significantly associated with sudden sensorineural hearing loss.\textsuperscript{35, 36, 37}

In the multivariate linear regression analysis, HbA1c and pretreatment hearing level in the affected ear were found to be the independent prognostic factors for relative hearing gain and recovery rate.

We consider the non-homogenous distribution of study subjects in the various subgroups as a possible limitation of this study. A larger study group would help overcome this limitation and would probably yield more robust results.

**Conclusion**

From our study, we conclude that the factors such as age, gender, time of onset of treatment, and audiometric configuration do not influence the recovery of hearing in cases of sudden sensorineural hearing loss. The absence of vertigo and tinnitus led to better hearing outcomes, while raised HbA1c levels, deranged lipids, and thyroid profiles adversely affected the outcome. Hearing recovery was significantly affected by the pretreatment hearing levels in the affected and unaffected ears. Among the above factors, HbA1c affects the relative hearing gain and the recovery rate, and the pretreatment hearing level in the affected ear independently influenced the recovery rate. However, a study with a larger sample size is needed to arrive at more robust results.

**References**

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