# Original Research Paper

## Otorhinolaryngology

## PROSPECTIVE STUDY ON PROGNOSTIC FACTORS OF SUDDEN SENSORINEURAL HEARING LOSS USING MULTIVARIATE LOGISTIC REGRESSION ANALYSIS IN A TERTIARY CARE CENTRE IN KOLKATA

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| Dr. Sohini Chakrabarti* | Senior Resident, NRS Medical College and Hospital, Kolkata. *Corresponding Author |
| Dr. Monoj Mukherjee | Associate Professor, NRS Medical College and Hospital, Kolkata. |
| Dr. Biswajit Sikder | Professor, NRS Medical College and Hospital, Kolkata. |

**ABSTRACT** Sudden sensorineural hearing loss (SSNHL) is a rare disease of the inner ear (5 to 20 cases per 100,000 persons per year) of unknown cause and unexpected clinical course that leads to hearing disability.

Sudden sensorineural hearing loss (SSNHL) is a symptom of cochlear injury. It is characterized by sudden onset and, within a few hours, reaches its maximum peak. It may be accompanied by vertigo and tinnitus. Many hypotheses have been put forward to explain its etiology: vascular diseases, viral inflammation, trauma, or other lesions. In most cases, the cause of SSNHL cannot be identified. Because of the problematic identification of the cause, many regimens have been used to treat SSNHL. There is probably no other disease for which such a large number of different treatment regimens have been proposed. The prognosis of SSNHL is variously reported as ranging from cured to no change. Thus, determining the prognosis for Sudden Sensorineural Hearing Loss is difficult. In previous reports, the prognosis of SSNHL was affected by various factors, such as age, the number of days from onset until presentation, initial hearing level, and the presence of vestibular symptoms , the method used for treatment etc.

When more than one factor may affect outcome, multivariate analyses, which can adjust for the effects of other factors, are necessary. Logistic regression analysis provides a model for multivariate analyses that can examine at regular intervals the relation between several factors and disease (or all events) after adjusting for the influence of other factors. We used multiple logistic regression analysis to determine which factors are most strongly related to outcome in patients with SSNHL.

## INTRODUCTION

Sudden sensorineural hearing loss (SSNHL) is a rare disease of the inner ear (5 to 20 cases per 100,000 persons per year) of unknown cause and unexpected clinical course that leads to hearing disability [1, 2].

Sudden sensorineural hearing loss (SSNHL) is a symptom of cochlear injury. It is characterized by sudden onset and, within a few hours, reaches its maximum peak. It may be accompanied by vertigo and tinnitus [1]. Many hypotheses have been advanced to explain its etiology: vascular diseases, viral inflammation, trauma, or other lesions. In most cases, the cause of SSNHL cannot be identified.

Because of the problematic identification of the cause, many regimens have been used to treat SSNHL. There is probably no other disease for which such a number of different treatment regimens have been proposed, and today many different regimens, some more invasive than others, are advocated. Vasodilators, vitamins, steroids, anticoagulants, histamine, tranquilizers, diuretics, prostacyclin, hypervolemic hemodilution, carbogen, hyperbaric oxygen, and stellate ganglion block have all been reported to be effective in some cases, applied separately or together [17, 18].

The prognosis of SSNHL is variously reported as ranging from cured to no change. Thus, determining the prognosis for Sudden Sensorineural Hearing Loss is difficult. In previous reports, the prognosis of SSNHL was affected by various factors, such as age, the number of days from onset until presentation, initial hearing level, and the presence of vestibular symptoms, the method used for treatment etc [1-3].

When more than one factor may affect outcome, multivariate analyses, which can adjust for the effects of other factors, are necessary. Logistic regression analysis provides a model for multivariate analyses that can examine at regular intervals the relation between several factors and disease (or all events) after adjusting for the influence of other factors [4]. We used multiple logistic regression analysis to determine which factors are most strongly related to outcome in patients with SSNHL.

## MATERIALS AND METHODS

This **prospective study** was done in the **department of ENT, NRS medical college, Kolkata,** over a period of two years **from January 2018 to December 2019**. The patients presenting with chief complaint of single sided sudden hearing loss in our OPD were thoroughly examined to select the candidate for this study.

## AIMS AND OBJECTIVES

1. To determine the prognostic factors in patients with single sided sudden sensorineural hearing loss by using multivariate logistic regression analysis for adjusting influence of multiple factors together.
2. Identification of these indicators can help in counseling patients and in assessment of treatment efficacy.

## INCLUSION CRITERIA

1. The patients presenting with single sided 30 dB or more hearing loss on three or more contiguous frequencies developed within 72 hours were included in this study.
2. The patients presenting within three month of initiation of Symptoms were included.

## EXCLUSION CRITERIA

1. Infective changes in ear
2. Any identifiable aetiology post trauma, cerebello pontine angle tumors or other retrocochlear lesions
3. Unwilling for injection in ear
4. The cases with delayed presentation i.e. after 3 month of initiation of symptoms were not included

Total **90 patients** of SSNHL were selected for the study. Patients have given written consent for injection in ear and were followed up to 6 months. Thorough clinical history was taken. Patient was thoroughly examined before each injection. Special query done regarding presence of associated symptoms i.e. tinnitus, vertigo, associated factors. History of smoking, diabetes, family history of SSNHL was also taken. Associated comorbidities like CML and MUMPS and SLE were found in a total of 6 patients. One patient with diagnosed CML, one with SLE. And 4 patients came with post mumps SSNHL.

Thorough examination, otoscopy and pure tone audiometry was done for all the cases before initiation of therapy. Four contiguous frequency average hearing threshold was noted on 500Hz, 1000Hz, 2000Hz and 4000Hz. All patients were tested audiologically to identify if retrocochlear lesions were present like Tone decay test, speech discrimination score. All patients underwent MRI bain to rule out cerebello pontine angle tumors.

Initially, intratympanic dexamethasone injection was started on 1st visit. Dexamethasone injection preparation with 2mg/ml was taken. 0.5ml of this preparation was loaded in a 2.5ml injection syringe. 24gm intravenous Cannula' with '24G intravenous Cannula needle was fitted with the syringe. Ear canal was thoroughly cleaned and 10% xylocaine sprayed on tympanic membrane for local anaesthesia. The tympanic membrane was visualised by zero degree 2.7 mm Hopkin's rod telescope and camera system. Under direct vision, the needle was inserted in the middle ear through postero-inferior quadrant and dexamethasone injection given to fill the middle ear. Head was tilted to the ipsilateral side immediately and the position was maintained for 30 minutes. Patient was asked not to swallow for that time. It helps for longer duration stay of injected steroids in the middle ear.

The intratympanic injection was repeated every 7th day and four injections given in this way for 4 weeks. Repeat pure tone audiometry was done after 4th injection at 6 weeks after presentation.

Then repeated at 3 months and 6 months again. We have not prescribed antivirals to any patient.

We evaluated the prognostic factors for hearing recovery. The following factors studied:
• Age
• Sex
• Number of days until presentation
• Vestibular symptom (vertigo, tinnitus)
• Initial mean hearing level at 0.5 kHz, 1 kHz, 2 kHz and 4 kHz
• Association with smoking, diabetes
• Association with other comorbidities like post mumps, SLE or CML

We had grouped our patients into 3 classes - Cured ©, Not Cured (NC) and Partially Cured (PC). Complete recovery or Cured is defined as pure tone average of 25-35 dB or better in the affected ear. Not Cured means the same as the initial degree of hearing loss even after receiving treatment. Partially Cured is improvement in hearing but not complete recovery. We performed **multivariate logistic regression** analyses on the above. We tested the statistical significance of the independent variables with the chi-square test (two-sided), and we estimated odds ratio and 95% confidence interval. The regression coefficients represent the change in odds ratio for the unit change in the corresponding independent variable.

We performed two independent logistic regression analyses with outcome (Cured / Partially Cured and Not Cured) as the dependent variable, assigning scores of 0 to Not Cured and 1 for Cured / Partially Cured. We first performed analyses for those in the Not Cured and Cured groups alone. Second analysis was performed for those in the Not Cured and Partially Cured groups alone.

Age, number of days until presentation, and initial mean hearing level were handled as continuous variables. We statistically analyzed the data with **R-version-3.6.2.**

## RESULTS
A total of 48 men and 42 women were taken in our study , ranging in age from 14 to 69 years. A total of 46% patients presented with tinnitus initially. As for the medical history, diabetes mellitus was noted in 24 (26%) and none of our patients had family history of SSNHL.

The hearing outcome of SSNHL was cured in 30 patients (33%), partially cured in 33 (37%), and not cured in 27 (30%).

We performed the first analysis for those in the **Not Cured and Cured groups (Table 1)**. The factors most strongly related to outcome were the number of days until presentation (p = 0.0008) and presence of tinnitus (p = 0.0074) and age (p = 0.0125) and initial mean level of hearing (p = 0.0324) . A longer period until presentation, presence of tinnitus and advanced age and poor initial hearing level were associated with lower rates of recovery. We found no significant relation to outcome for other factors like sex, presence of diabetes, history of smoking and presence of vertigo.

We performed the second analysis for those in the **Not Cured and Partially Cured group (Table 2)**. The number of days until presentation (p = 0.001), presence tinnitus (p = 0.0047), and initial mean hearing level (p = 0.05), were most strongly related to outcome.

**A longer period until presentation, subjective tinnitus and severe to profound initial hearing loss were associated with lower rates of cure**. No other factor was significantly related to the outcome. Hence sex, advanced age, history of smoking, family history, diabetes mellitus did not affect the outcome in this group. It was noted that in all six patients with comorbidities like CML, SLE and post measles the outcomes were Not Cured.

**Table 1: Data - Not Cured vs Cured**

| Independent variable | Regression Coefficient | Std. Error | p-value | Odds Ratio (95% CI) |
|---|---|---|---|---|
| Initial mean Hearing | -0.0900 | 0.0421 | 0.0324 | 0.914 (0.830 - 0.985) |
| No of days until presentation | -0.1210 | 0.0359 | 0.0008 | 0.886 (0.813 - 0.940) |
| Age | -0.0756 | 0.0303 | 0.0125 | 0.927 (0.869 - 0.981) |
| Sex | -1.8900 | 1.1823 | 0.1099 | 0.151 0.010 - 1.229) |
| Tinnitus | -4.0019 | 1.4947 | 0.0074 | 0.018 (0.000 - 0.211) |

**Method:** Multivariate Logistic Regression

**Continuous Variables:** Age, Initial Level of Hearing, Onset of Therapy

**Factor Variables:** Sex (M=1, F=0), Tinnitus (Y=1, N=0)

**Dependent Variable:** Not Cured = 0 / Cured = 1

**Table 2: Data - Not Cured vs Partially Cured**

| Independent variable | Regression Coefficient | Std. Error | p-value | Odds Ratio (95% CI) |
|---|---|---|---|---|
| Initial mean Hearing | -0.0580 | 0.0297 | 0.0512 | 0.944 (0.882 - 0.995) |
| No of days until presentation | -0.1006 | 0.0306 | 0.001 | 0.904 (0.843 - 0.952) |
| Age | -0.0042 | 0.0344 | 0.9027 | 0.996 (0.930 - 1.068) |
| Sex | -0.9602 | 1.0191 | 0.3461 | 0.383 (0.044 - 2.663) |
| Tinnitus | -3.4925 | 1.2352 | 0.0047 | 0.030 (0.001 - 0.227) |

**Method:** Multivariate Logistic Regression

**Continuous Variables:** Age, Initial Level of Hearing, Onset of Therapy

**Factor Variables:** Sex (M=1, F=0), Tinnitus (Y=1, N=0)

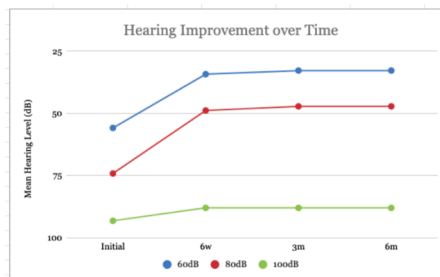**Dependent Variable:** Not Cured = 0 / Partially Cured = 1



**Figure I:** Hearing improvement over 6months. Maximum improvement occurred in the first 6 weeks after presentation and very minimal thereafter till 3 months. Beyond 3 months up to 6 months there was no further improve men

## DISCUSSION
Prognostic factors in SSNHL are important because identification of these indicators can help in counseling patients and in assessment of treatment efficacy.

Many studies have described predictive indicators to identify patients with a good prognosis needing no or minimal treatment. Only a few of

these studies have included a model for calculating the probability for patient recovery, which may be important for clinical work. The first serious attempt at staging sudden hearing loss was proposed by Mattox and Simmons [1] . Prognostic scales have also been described by Byl [2] and Laird and Wilson [3].

Most physicians who treat SSNHL are particularly interested in searching for prognostic factors. The most often reported factors include, age and gender of the patients, the type of audio gram and level of hypoacusis, methods of treatment, the coexistence of other otologic symptoms such as tinnitus and vertigo, duration of hearing loss, dynamics of hearing recovery, and time of treatment initiation.

Although previous investigations have assessed the relation of individual factors to outcome, to our knowledge, few studies have used multivariate analysis to evaluate the contributions of multiple factors. We used multiple logistic regression analysis to determine which factors are most strongly related to outcome in patients with SSNHL.

Logistic regression analysis provides a model for multivariate analyses that can examine at regular intervals the relation between several factors and disease (or all events) after adjusting for the influence of other factors. When more than one factor might affect outcome, multivariate analyses, which can adjust for the effects of other factors, are necessary [4].

### Prognostic Factors
The following prognostic factors were studied.

### AGE
For instance, age is frequently mentioned as a prognostic factor, and older patients tend to have worse hearing recovery [5-7]

In our study too advanced age is a poor prognostic factor for outcome in the group cured and not cured.

Others have found no correlation between age and outcome [8].

### SEX
Male sex is considered to be related to have a better hearing outcome [9].

But our study found that sex is not significant prognostic factor.

### VERTIGO
It is another well-recognized prognostic indicator and correlates with poor hearing recovery [10-11].

We have not found vertigo to be an important prognostic factor.

### TINNITUS
The initial symptoms of SSNHL may be predictors of the prognosis. In our study, 46% of affected ears had tinnitus, and this correlated with worse recovery rates.

Opinions on the value of tinnitus as a prognostic factor in SSNHL are inconsistent [12].

### ONSET OF THERAPY
Better hearing improvement is noted for subjects with less elapsed time from the onset to the start of treatment [13-14]

Several studies have concluded that the earlier the patient receives treatment, the better the outcome. Shaia and Sheehy [15] reported better prognosis when the patient received treatment within 1 month. Byl [2] reported a complete recovery rate of 56% when the patients were observed within 7 days, but only 27% of those observed 30 days or later had similar results.

In our study in both groups time elapsed before onset of therapy or days until presentation has been found as an important significant factor. . In our study, 71% of the patients who received treatment within 7 days from onset of symptoms had a complete recovery,however, beyond 2weeks upto 1month 88% patients had partial but not complete recovery.
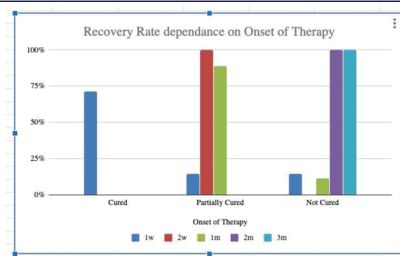


**Figure II:** Maximum patients who presented within 7days of onset of symptoms were cured (71%), patients who presented at 2 weeks were mostly partially cured and ones who presented late (one or two months late) were mostly not cured.

### INITIAL HEARING LEVEL
subjects with mild hearing loss have a propensity to recover more frequently than those with severe hearing loss (Byl [2]), Initial mean level of hearing is an important prognostic factor in our study too.
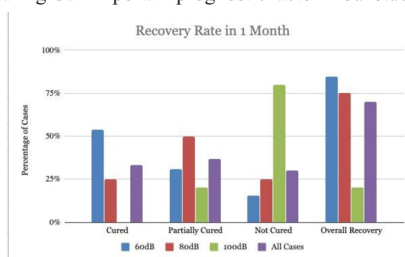


**Figure III:** 54% patients who presented with upto 60dB loss were totally cured, whereas cure rate dropped to 25% when initial mean hearing level was 80dB, and none of the patients who presented with profound hearing loss (90-100dB) recovered.

### COMORBIDITIES
Medical illness like diabetes mellitus and hypertension is thought to be unrelated to clinical outcome [16].

In our study history of diabetes, smoking, family history has not been found to affect the outcome significantly.

### Strength of the Study
The strength of this study was its use of detailed diagnostic procedures, reasonable case representation, and the large number of consecutive patients (suggesting that the reported associations might not be chance findings).

### Limitations of the Study
1. Lack of any control group, we did not assess the influence of treatment on recovery.
2. Because of the uncertainties regarding cause and pathogenesis, the treatment of SSNHL remains highly empirical. At this time, no single study has demonstrated clearly the beneficial effect of a given therapy that would unquestionably surpass the spontaneous recovery rate.
3. It is likely that multifactorial etiopathologies underlie the disease, having led to many different regimens of therapy, including vasodilators, anticoagulants, corticosteroids, vitamins, plasma expanders, histamines, antiviral agents, contrast media, hyperbaric oxygen, and carbogen inhalations. Currently, the most commonly agreed upon treatment for this condition is corticosteroids intratympanic or oral or intravenous. The lack of a universally accepted definition for SSNHL and for its recovery limits the ability to compare and evaluate the treatment protocol
4. To prove a treatment is effective, a statistical analysis in a randomized double-blind study must be used. However, such a study is not possible in our community.

### CONCLUSION
First, immediately after onset of disease, the patient should consult a physician as soon as possible for diagnosis and treatment. Then, predicting good prognosis in younger patients with mild hearing loss, earlier onset of therapy and no tinnitus is possible . Thus, our results will increase the ability to predict the outcome for SSNHL which is beneficial for information, education and communication at the community level **(IEC).** However, physicians must discuss with their patients the etiology and treatment options and jointly determine a

treatment plan.

## REFERENCES

[1] Mattox DE, Simmons FB. Natural history of sudden sensorineural hearing loss.Ann Otol Rhinol Laryngol 1977;86:463Y80.
[2] Byl FM Jr. Sudden hearing loss: eight years_ experience and suggested prognostic table. Laryngoscope 1984;94:647Y61.
[3] Laird N, Wilson WR. Predicting recovery from idiopathic sudden hearing loss. Am J Otol 1983;4:161Y4.
[4] Kleinbaum DG, Kupper LL, Morgenstern H. Epidemiologic Research, Principles and Quantitative Methods. New York: Van Nostrand Reinhold Company, 1982:27-29.
[5] Chang, N. C., Ho, K. Y., & Kuo, W. R. (2005). Audiometric patterns and prognosis in sudden sensorineural hearing loss in southern Taiwan. Otolaryngol Head Neck Surg, 133, 916 –922.
[6] Zadeh, et al.,2003 Zadeh, M. H., Storper, I. S., & Spitzer, J. B. (2003). Diagnosis and treatment of sudden-onset sensorineural hearing loss: a study of 51 patients. Otolaryngol Head Neck Surg, 128, 92–98.
[7] Fetterman, et al., 1996; Fetterman, B. L., Saunders, J. E., & Luxford, W. M. (1996). Prognosis and treatment of sudden sensorineural hearing loss. Am J Otol, 17, 529 –536.
[8] Wilson WR, Gulya AJ. Sudden sensorineural hearing loss. In: Cummings CW, Fredrickson JM, Harker LA, Krause CJ, Schuller DE, eds. OtolaryngologyYHead and Neck Surgery. St. Louis, MO:Mosby, 1993:3103Y12.)
[9] Xenellis, J., Karapatsas, I., Papadimitriou, N., et al. (2006). Idiopathic sudden sensorineural hearing loss: prognostic factors. J Laryngol Otol, 120, 718 –724.
[10] Kiris, M., Cankaya, H., Icli, M., et al. (2003). Retrospective analysis of our cases with sudden hearing loss. J Otolaryngol, 32, 384 –387.
[11] Park, H. M., Jung, S. W., & Rhee, C. K. (2001). Vestibular diagnosis as prognostic indicator in sudden hearing loss with vertigo. Acta Otolaryngol Suppl, 545, 80 – 83.).
[12] Ben David J, Luntz M, Magamsa I, Fradis M, Sabo E, Podoshin L. Tinnitus as a prognostic sign in idiopathic sudden sensorineural hearing loss. Int Tinnitus J 2001;7:62Y4.
[13] Mattox & Lyles, 1989 Mattox, D. E., & Lyles, C. A. (1989). Idiopathic sudden sensorineural hearing loss. Am J Otol, 10, 242–247.
[14] Narozny, W., Kuczkowski, J., Kot, J., et al. (2006). Prognostic factors in sudden sensorineural hearing loss: our experience and a review of the literature. Ann Otol Rhinol Laryngol, 115, 553–558.
[15] Shaia FT, Sheehy JL. Sudden sensori-neural hearing impairment: a report of 1,220 cases. Laryngoscope 1976;86:389Y98.)
[16] Ceylan, A., Celenk, F., Kemaloglu, Y. K., et al. (2007). Impact of prognostic factors on recovery from sudden hearing loss. J LaryngolOtol, 121, 1035–1040.
[17] Suckfull M, Wimmer C, Jager B, Schorn K, Thiery J.Heparin-induced extracorporallow-density-Iipoprotein precipitation (H.E.L.P.) to improve the recovery of hearing in patients with sudden idiopathic hearing loss. Eur Arch Otorhinolaryngol 2000;257:59-61.
[18] Mattox DE, Lyles CA. Idiopathic sudden sensorineural hearing loss. Am J Otol 1989;I0:242-7