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Original Research Article

Low serum prestin level as a potential biomarker for sudden sensorineural hearing loss: a cross-sectional study

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ABSTRACT

Background: Prestin (SLC26A5) is a membrane motor protein that has a role in amplification and electromotility of the outer hair cells of the cochlea. Sudden sensorineural hearing loss (SSNHL) is a rapidly emerging hearing impairment caused by damage to the cochlear hair cells. Therefore, this study aims to analyse the potential of prestin serum as a biomarker in establishing the diagnosis of SSNHL.
Methods: This study is a cross-sectional analytical observational study conducted at Prof I.G.N.G. Ngoerah general hospital, a tertiary hospital in Bali involving 13 SSNHL patients who had not yet received therapy, as well as 12 healthy control subjects. Serum prestin levels were assessed using enzyme-linked immunosorbent assay (ELISA), and audiometric examinations were performed to assess the degree of hearing loss. Data were analyzed using IBM SPSS statistics version 30.0 computer program. The normal serum prestin level was identified through receiver operating characteristic (ROC) curve analysis. The analysis was further performed with Chi-square or Fisher's exact as alternative tests and logistic regression by controlling the confounding variables to determine the risk factors of SSNHL. Statistically significant result defined as p value <0.05.
Results: According to the ROC curve analysis, the normal serum prestin threshold was 450.7 pg/ml. Serum prestin levels <450.7 pg/ml were categorized as low, and ≥450.7 pg /ml as high. Based on the Fisher exact test, low serum prestin levels were significantly associated to SSNHL with the OR 7.7 (95% CI 1.159-11.171, p=0.041). Logistic regression analysis was further performed by controlling the confounding variables and showed that low serum prestin level was significantly an independent predictor of SSNHL with an Adjusted OR 15.4 (95% CI 1.028-230.9, p=0.0048).
Conclusions: Low prestin serum levels are significantly promising potential biomarkers in the diagnosis of SSNHL.

Keywords: Prestin, Sudden sensorineural hearing loss, Biomarker

INTRODUCTION

Hearing loss refers to a reduction in auditory function, ranging from mild impairment to complete deafness, arising from disrupted transmission of sound stimuli from the ear to the central nervous system.[1] It has been reported as the fourth leading cause of disability worldwide.[2] More than 90% of hearing loss cases are sensorineural in nature. Sensorineural hearing loss may be congenital (present at birth) or acquired (developing

later in life). Sudden sensorineural hearing loss (SSNHL) is defined as a rapid decline in sensorineural hearing exceeding 30 dB across at least three consecutive frequencies within a period of less than 72 hours.[3,4] SSNHL is considered a neurotological emergency and is associated with damage to cochlear hair cells, vestibulocochlear nerve dysfunction, and abnormalities within the central auditory processing pathways.[5,6] The etiology of SSNHL is mostly idiopathic, with other causes including vascular disorders, viral infections, endolymphatic hydrops, cochlear membrane rupture, and autoimmune diseases.[7] In certain cases, vascular abnormalities, infections, or autoimmune diseases in SSNHL may indirectly damage hair cells, which ultimately affects the metabolic activity of the inner ear.[7]

The current standard diagnostic approach for hearing loss, particularly sensorineural hearing loss (SNHL), involves pure tone audiometry testing along with the patient's clinical history.[8] Nevertheless, advances in neurotology and molecular biology have increased interest in the application of molecular biomarkers as adjunctive diagnostic tools, especially for the early detection of SNHL. Biomarkers are defined as objectively measurable biological parameters that reflect cellular physiological states, disease-related pathophysiological changes, or biological responses to therapeutic interventions.[9] In sensorineural hearing loss, biomarkers have the potential to identify early-stage hearing loss, potentially before the abnormalities detectable by conventional audiometric assessments.[9]

The specific biomarker most commonly associated with damage to the outer hair cells of the cochlea is prestin. Prestin constitutes the fifth member of the SLC26A superfamily of eleven membrane transporter proteins.[10] Localized within the lateral membrane of cochlear outer hair cells, prestin is responsible for cochlear sensitivity and frequency selectivity. It regulates outer hair cell electromotility by mediating rapid length changes through hyperpolarization and depolarization in response to sound-induced alterations in membrane potential. These processes occur on a microsecond timescale in a cycle-by-cycle manner at frequencies up to 20 kHz, thereby contributing to cochlear amplification. Prestin also facilitates the bidirectional conversion of electrical and mechanical energy.[11] All of the above findings highlight the advantages of prestin as a molecular motor, differentiating it from other known molecular motors.[11]

Damage to or loss of prestin has a substantial impact on auditory function, resulting in the loss of electromotility, shortening of outer hair cells, and reduced hearing sensitivity. Several studies have also reported that prestin mutations in humans are associated with sensorineural hearing loss.[11] Prestin (SLC26A5) is exclusively expressed in outer hair cells of the cochlea, therefore apoptosis of these cells results in macrophage-mediated phagocytosis followed by release of prestin into the bloodstream. Prestin is therefore considered a promising biological marker of outer hair cell damage in sensorineural hearing loss and represents a valuable research target for supporting the diagnosis and management of sensorineural hearing loss, particularly SSNHL. Accordingly, this study aims to evaluate the role of serum prestin as a biomarker in SSNHL.

METHODS

This study received ethical approval from the Research Ethics Committee of the Faculty of Medicine, Udayana (Approval No. 0248/UN/14.2.2.VII.14/LT/2025). A total of 25 participants were enrolled, consisting of 16 men and 9 women, aged 24 to 71 years. The case group comprised 13 patients presenting with SSNHL who were treated at a Prof I.G.N.G. Ngoerah general hospital, tertiary hospital in Bali between April and September 2025, whereas the control group consisted of 12 individuals with normal hearing. Inclusion criteria for the case group were patients diagnosed with SSNHL who had not yet received treatment. Exclusion criteria included middle ear infection or tympanic membrane perforation, a history of ear surgery, use of ototoxic medications, and exposure to excessive noise. All subjects underwent a structured medical interview, otoscopic examination, audiometric evaluation, venous blood sampling, and filled out written informed consent prior to participation.

Otoscopic examination was conducted to confirm that the external auditory canal and tympanic membrane were intact and free of infectious pathology. Hearing thresholds were subsequently assessed using an audiometer (GSI Audiostar Pro).

A total of 5 ml of the subject's venous blood was placed in a tube and stored at room temperature until complete coagulation occurred. Samples were then centrifuged at 3000 rpm for 15 minutes, and the serum was stored at −20°C until prestin measurement. Serum prestin concentrations were quantified using the human prestin (SLC26A5) ELISA Kit (Cat. No. E4170Hu, BT LAB, China; range 10-3000 pg/ml; sensitivity 4.87 pg/ml) following the manufacturer’s instructions.

Statistical analysis

Statistical analyses were conducted using IBM SPSS Statistics version 30. Serum prestin concentrations were evaluated using a Receiver operating characteristic (ROC) curve to determine the optimal cut-off value for distinguishing study groups. Comparisons of serum prestin levels between the case and control groups were performed using the Chi-square test or Fisher’s exact test when Chi-square assumptions were not met. Logistic regression analysis was subsequently performed to identify significant risk factors for SSNHL after adjustment for potential confounding variables. Statistically significant results were considered if p value was <0.05.

RESULTS

Serum prestin was detected in all participants across both study groups. The demographic characteristics of the subject are summarized in Table 1. A total of 9 (69.2%) of the 13 subjects with SSNHL were male, with the largest age group being 41-60 years (38.5%). The characteristics of SSNHL subjects are presented in Table 2. The onset of deafness was reported to be mostly within 3 days (76.9%), with bilateral deafness being the most common (53.8%). The most common degree of deafness was profound deafness (61.5%), and the majority of subjects had no associated comorbid conditions (69.2%).

Table 1: Demographic characteristics of subjects.

Variables	Case group N (%)	Control group N (%)
Age (years)	47 (24-71)	34 (30-52)
<20	1 (7.7)	0 (0)
21-40	4 (30.8)	11 (91.7)
41-60	5 (38.5)	1 (8.3)
>60	3 (23.1)	0 (0.0)
Gender		
Male	9 (69.2)	7 (58.3)
Female	4 (30.8)	5 (41.7)

Table 2: Characteristics of sudden SNHL subjects.

Variables	N	%
Onset (days)		
≤3	10	76.9
4-7	1	7.7
>7	2	15.4
Site of ear		
Unilateral	6	46.2
Bilateral	7	53.8
Degree of deafness		
Mild	1	7.7
Moderate	1	7.7
Moderate severe	2	15.4
Severe	1	7.7
Profound	8	61.5
Comorbid disease		
Yes	4	30.8
No	9	69.2

ROC curve analysis identified a serum prestin cut-off value of 450.7 pg/ml. Serum prestin concentrations below this threshold were classified as low, and is associated with a risk of SSNHL. Whereas, concentrations equal to or above 450.7 pg/ml were classified as high.

In the SSNHL group, 84.6% of subjects exhibited low serum prestin levels (<450.7 pg/ml). In contrast, 58.3% of individuals in the control group demonstrated high serum prestin concentrations. Fisher's exact test revealed a statistically significant difference in serum prestin levels between the two groups, with an odds ratio (OR) of 7.7 (95% confidence interval (CI): 1.159-11.171; p=0.041).

Table 3: Distribution of serum prestin based on case and control groups.

Prestin serum	Groups		OR	95% CI	P value
	Case (n=13)	Control (n=12)			
<450.7 pg/ml	11 (84.6)	5 (41.7)	7.7	1.159-11.171	0.041
≥450.7 pg/ml	2 (15.4)	7 (58.3)	Ref		

Table 4: Logistic regression analysis of the effect of low prestin serum levels on the occurrence of sudden sensorineural hearing loss.

Variables	AOR	95% CI	P value
Prestin serum <450.7 pg/ml	15.4	1.028-230.9	0.048
Age	0.9	0.796-1021	0.102
Gender	5.5	0.384-78.0	0.210

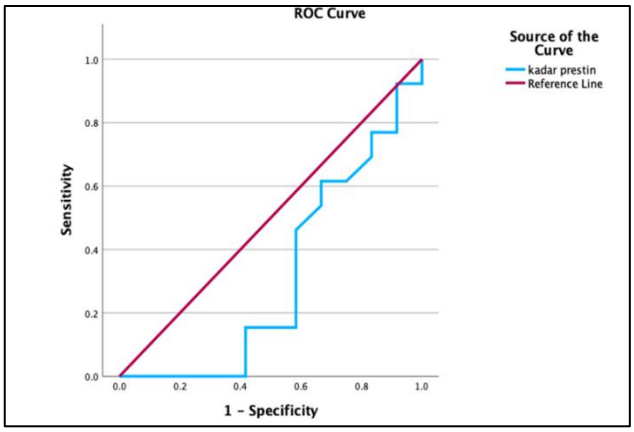

Figure 1: ROC curve of prestin serum in both groups.

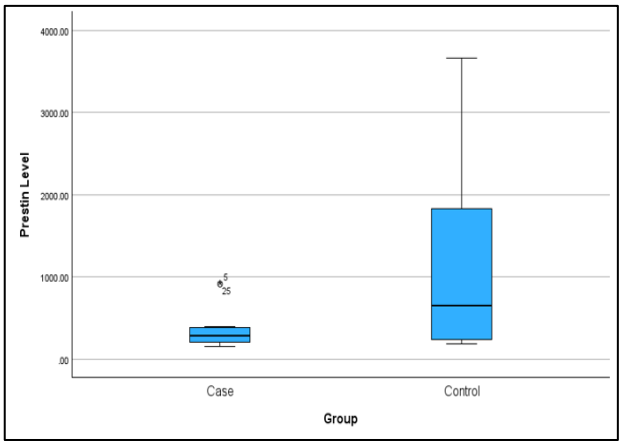

Figure 2: Distribution of prestin serum in patients with sudden sensorineural hearing loss and the control group.

The analysis was then continued with logistic regression, controlling for the confounding variables of age and gender, to determine the risk factors that significantly contribute to SSNHL The results showed that low serum prestin concentration was also a significant risk factor for SSNHL, with an adjusted odds ratio (AOR) of 15.4 (95% CI: 1.028-230.9; p=0.048).

DISCUSSION

SSNHL is classified as a neurotological emergency and is commonly associated with injury to cochlear hair cells, dysfunction of the vestibulocochlear nerve, and abnormalities within central auditory processing pathways.[5,6] Among the biomarkers linked to cochlear outer hair cell damage, prestin has gained considerable attention. Prestin is the fifth member of the 11-protein SLC26A superfamily of membrane transporters.[10] It exclusively expressed in the lateral membrane of outer hair cells and plays a critical role in cochlear sound amplification signal dependent on electromotility. Prestin is known to rapidly alter the conformation of outer hair cells in the cochlea using transmembrane potential and kinetic energy, which distinguishes it from other molecular motors.[12,13]

Outer hair cell death may result from acoustic trauma, exposure to ototoxic agents, or age-related degenerative processes. Outer hair cell death can occur via apoptosis, necrosis, or necroptosis.[14] Apoptotic outer hair cells are subsequently phagocytosed by macrophages, along with intracellular components including prestin. Prestin has been detected within the phagosomes of supporting cells before ultimately being released into the systemic circulation.[15] Given its molecular weight of approximately 80 kDa, prestin is presumed to be capable of crossing the blood-labyrinth barrier, and enter the circulation.[15] This suggests that serum prestin concentration is associated with cochlear damage and hearing function.[9,15]

In this study, serum prestin concentrations among 13 patients with SSNHL (age range 27-71 years; mean 48.08±4.12 years) ranged from 157.89 to 928.30 pg/ml, with a mean value of 375.96±70.90 pg/ml. In contrast, the control group (age range 30-52 years; mean 35.67±1.67 years) exhibited serum prestin levels ranging from 181.58 to 3662.60 pg/ml, with a mean concentration of 1215.13±352.61 pg/ml.

The precise mechanisms underlying prestin release into the systemic circulation remain incompletely understood. In individuals with normal hearing, prestin can be detected in the blood, indicating normal prestin circulation in the outer hair cells of the cochlea. However, baseline prestin levels vary widely across species and are influenced by factors such as cochlear length and the number of outer hair cells.[16] Sun et al, reported on 14 patients with idiopathic SSNHL (aged 31-72 years, mean 57.9±15.4 years) found serum prestin concentrations ranging from 295.25 to 9648. 80 pg/ml with an average of 1955.98±2501.48 pg/ml, while in the control group, serum prestin levels ranged from 85.4 to 1628.25 pg/ml with an average of 840.24±496.22 pg/ml.[17]

The serum prestin levels in our study were lower in the SSNHL group compared with the control group. The concentration of prestin in the bloodstream is related to the natural circulation of prestin in the outer hair cells and damage to the cochlea.[15] Sensorineural hearing loss is closely associated with outer hair cell dysfunction.[18] Structural alterations or loss of outer hair cells may reduce cellular texture of prestin and decrease the density of the cochlea, thereby leading to reduced prestin levels in the circulation.[16]

To date, no studies have established serum prestin threshold values associated with the risk of SSNHL or sensorineural hearing loss. Accordingly, ROC curve analysis was performed in this study to identify an optimal prestin cut-off value. The best cut-off point was determined to be 450.7 pg/ml. Serum prestin concentrations below this threshold were categorized as low and considered to be associated with an increased risk of SSNHL.

The analysis in this study was then continued with a Fisher's exact test, with the results showing that low serum prestin levels significantly increased the risk of SSNHL by 7.7 times compared to subjects with high serum prestin levels (p=0.041). Furthermore, to determine the risk factors that significantly contribute to SSNHL, a logistic regression analysis was performed by controlling the confounding variables of age and gender, resulting in an adjusted OR value of 15.4. This finding indicates that low serum prestin levels significantly increase the risk of SSNHL after controlling for these variables.

A decline in circulating prestin levels may occur following the clearance of damaged outer hair cells from the cochlea.[19,20] The hypothesis proposed by Parham and Dyhrfjeld-Johnsen. 2016 states that when outer hair cells undergo apoptosis, prestin concentration is expected to increase immediately after damage, and when the apoptosis mechanism stops, prestin concentration is expected to decrease back to baseline values, then eventually fall below baseline values, reflecting a reduction in the number of outer hair cells remaining/surviving.[21]

Reduced prestin levels following cochlear injury may also result from disturbances in cochlear homeostasis leading to outer hair cell loss or damage. In such conditions, the remaining outer hair cells release smaller amounts of prestin into the circulation, contributing to decreased serum concentrations.[1,2] Decreased prestin levels may also be caused by an imbalance in the production of free radicals and cochlear antioxidants.

Damage and apoptosis of outer hair cells may occur as a result of ROS (reactive oxygen species)-mediated injury.[22] Additionally, the timing of serum prestin measurement relative to symptom onset or cellular injury may influence detected prestin levels.[23]

Based on the findings of this study, low serum prestin concentrations demonstrate promising potential as a biomarker for SSNHL. This study successfully analyzed the serum prestin threshold associated with SSNHL risk and controlled for confounding variables such as age and gender, revealing that low serum prestin levels significantly increase the risk of SSNHL.

Despite these findings, this study has several limitations that should be acknowledged. Specifically, the causes of sensorineural hearing loss in this study sample were relatively heterogeneous and did not focus on cases of idiopathic SSNHL, and the sample size was limited. Moreover, age distribution differed between groups, with the control group predominantly consisting of individuals aged 21-40 years, while the case group was evenly distributed across each age group. Therefore, further research should be conducted on a larger sample size focusing on idiopathic SSNHL, with a similar age distribution in the control and case groups, is warranted to clarify the diagnostic and prognostic value of serum prestin. This work was supported by the Institute for research and community service (LPPM), Udayana University, Indonesia (Grant No. B/229.412/UN14.4.A/PT.01.03/2005).

CONCLUSION

Low serum prestin concentrations demonstrate a promising potential as a biomarker for diagnosis of SSNHL.

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