

# Sudden sensorineural hearing loss is associated with chronic rhinosinusitis: population-based study

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## Abstract

**Background:** This study aimed to evaluate the association of chronic rhinosinusitis with sudden sensorineural hearing loss using a population-based database.

**Methods:** Sampled subject data were obtained from the Taiwan Longitudinal Health Insurance Database 2000. A total of 3325 patients with sudden sensorineural hearing loss were identified and 9975 controls were randomly selected. A conditional logistic regression was used to calculate the odds ratio for having been previously diagnosed with chronic rhinosinusitis, for cases and controls.

**Results and conclusion:** The adjusted odds ratio of having prior chronic rhinosinusitis among cases compared to controls was 1.36 (95 per cent confidence interval = 1.16–1.60). The significant relationship between sudden sensorineural hearing loss and chronic rhinosinusitis was most pronounced among those patients aged 44 years or less (compared to controls) (odds ratio = 2.18; 95 per cent confidence interval = 1.63–2.92). However, the significant relationship between sudden sensorineural hearing loss and prior chronic rhinosinusitis was not sustained for patients older than 60 years compared to controls.

**Key words:** Sudden Deafness; Hearing Loss, Sudden; Sensorineural Hearing Loss; Rhinitis; Sinusitis

## Introduction

Sudden sensorineural hearing loss (SNHL) is an acute insult of the cochlea and/or retrocochlear structures. The annual incidence of sudden SNHL ranges from 5 to 20 per 100 000 people worldwide.<sup>1</sup> Most cases of sudden sensory hearing loss are idiopathic; however, many theories have been proposed to explain the condition.<sup>2</sup> Currently, there are four major theories to explain the cause of sudden SNHL: viral infection, vascular compromise, intracochlear membrane rupture and auto-immune inner-ear disease.<sup>3,4</sup>

In addition to systemic factors, it has been reported that local inflammation or an infection adjacent to the hearing systems can contribute to the pathogenesis of sudden SNHL. Park *et al.* reported that sudden SNHL might be associated with acute otitis media.<sup>5</sup> Despite the close anatomical and physiological relationships between the nose and ears, chronic rhinosinusitis, a relatively common disease, is seldom regarded as a significant risk factor for sudden SNHL.

Chronic rhinosinusitis is a prevalent chronic illness, affecting at least 14 per cent of adults in the US

population.<sup>6</sup> Preseptal cellulitis, orbital cellulitis, subperiosteal abscess, orbital abscess and cavernous sinus thrombophlebitis have previously been reported to be common local complications of rhinosinusitis.<sup>7</sup> Chronic rhinosinusitis has also been associated with the development of nasopharyngeal cancer, implying that chronic rhinosinusitis might do more harm to adjacent structures than expected.<sup>8</sup>

Although it is possible that inflammatory processes or specific viral infections may elevate the risk of sudden SNHL, there is no evidence that inflammation or infection of the nasal cavity or sinuses could damage the inner ear. Thus, to date, the association between sudden SNHL and chronic rhinosinusitis remains unclear. This study aimed to investigate the association between chronic rhinosinusitis and sudden SNHL by evaluating a population-based database.

## Materials and methods

### Database

The data for the subjects sampled in this case-control study were obtained from the Longitudinal Health

Insurance Database ('LHID 2000'). Taiwan began implementing its National Health Insurance programme in 1995. The Longitudinal Health Insurance Database 2000 consists of all the original medical claims and registration files for 1 000 000 enrollees under the National Health Insurance programme. These selected 1 000 000 enrollees were randomly retrieved from all enrollees listed in the 2000 Registry of Beneficiaries ( $n = 23.72$  million). Therefore, the Longitudinal Health Insurance Database 2000 enables researchers to follow up all medical care utilisations for these 1 000 000 enrollees since the initiation of the National Health Insurance programme. Several researchers have demonstrated the high validity of the data from the National Health Insurance programme. In addition, hundreds of papers employing the Longitudinal Health Insurance Database 2000 have been published in internationally peer-reviewed journals.<sup>9</sup>

This study was exempt from full review by the Institutional Review Board of the National Defense Medical Center because the Longitudinal Health Insurance Database 2000 consists of de-identified secondary data released to the public for research purposes.

#### Study sample

We selected cases by first including 3420 patients aged 18 years or older who had received a first-time diagnosis of sudden SNHL (International Classification of Diseases, Ninth Revision, Clinical Modification ('ICD-9-CM') code 388.2) in an ambulatory care visit (including out-patient departments of hospitals and clinics) or during hospitalisation between 1 January 2002 and 31 December 2011, and we only included sudden SNHL cases diagnosed by a certified otorhinolaryngologist. Furthermore, this study only included patients who had at least two sudden SNHL diagnoses in ambulatory care settings or one sudden SNHL diagnosis while hospitalised ( $n = 3325$ ), in order to increase the diagnostic validity of sudden SNHL. We only included those patients who had at least two sudden SNHL diagnoses in ambulatory care settings because the diagnosis of sudden SNHL was always confirmed on subsequent follow-up visits within the same 'episode' of sudden SNHL in Taiwan. We defined the first ambulatory care visit or hospitalisation for treatment of sudden SNHL as the index date for cases.

We likewise retrieved control data from the remaining enrollees of the Longitudinal Health Insurance Database 2000. We randomly selected 9975 controls (3 controls per case) to match the cases in terms of sex, age group (less than 40, 40–44, 45–49, 50–54, 55–59, 60–64, 65–69 and over 69 years) and index year. For cases, the year of the index date was the year in which patients had received their first diagnosis of sudden SNHL. For controls, the year of the index date was simply a matched year in which the controls utilised medical care. Thereafter, we further designated the first utilisation of medical care occurring in the index year as the index date for controls. We also

ensured that no controls had a history of sudden SNHL before their index date.

#### Chronic rhinosinusitis diagnosis

This study identified subjects with a principal diagnosis of chronic rhinosinusitis (International Classification of Diseases, Ninth Revision, Clinical Modification code 473). As administrative datasets are criticised for poor diagnostic validity, we only included subjects diagnosed with chronic rhinosinusitis by a certified otorhinolaryngologist, in order to increase the diagnostic validity. In addition, we only selected subjects who had received a chronic rhinosinusitis diagnosis before the index date.

#### Statistical analysis

We utilised SAS software (SAS, Cary, North Carolina, USA) to perform all statistical analyses in this study. Chi-square tests were used to explore statistical differences between cases and controls in terms of geographical location (northern, central, eastern and southern Taiwan) and selected medical co-morbidities (diabetes, hypertension, coronary heart disease, hyperlipidaemia, renal disease, bacterial or cryptococcal meningitis, otitis media, rheumatoid arthritis, mumps, systemic lupus erythematosus, human immunodeficiency virus or acquired immunodeficiency syndrome, and syphilis). We also performed conditional logistic regression analyses (conditioned on sex, age group and index year) to calculate the odds ratio and the corresponding 95 per cent confidence interval (CI) for having previously been diagnosed with chronic rhinosinusitis, for cases and controls.

#### Results

The mean age of the total study sample was  $51.3 \pm 17.0$  years; respective ages for cases and controls were 52 and 51.5 years ( $p = 0.242$ ). Table I shows the distributions of demographic characteristics of sudden SNHL patients and controls, after matching for sex, age group and index year. In order to counteract the problem of multiple comparisons, we applied the Bonferroni correction to test each individual hypothesis at a significance level of 0.003 (i.e.  $0.05 / 16$ ).

We found that cases had consistently higher prevalence rates of various selected co-morbidities than controls; these included diabetes (24.9 vs 18.9 per cent,  $p < 0.001$ ), hypertension (41.0 vs 35.8 per cent,  $p < 0.001$ ), coronary heart disease (24.0 vs 19.6 per cent,  $p < 0.001$ ), hyperlipidaemia (33.3 vs 29.4 per cent,  $p < 0.001$ ), renal disease (9.6 vs 7.2 per cent,  $p < 0.001$ ) and otitis media (11.3 vs 5.3 per cent,  $p < 0.001$ ).

Table II presents the prevalence of prior chronic rhinosinusitis in cases and controls. In total, 742 of the sampled subjects (5.58 per cent) had a history of chronic rhinosinusitis prior to the index date; 236 (7.10 per cent) were cases and 506 (5.07 per cent) were controls. A chi-square test indicated that there was a significant difference in the prevalence of prior chronic rhinosinusitis between cases and controls ( $p < 0.001$ ).

**TABLE I**  
CHARACTERISTICS OF SUDDEN SNHL PATIENTS AND CONTROLS\*

Characteristic	Sudden SNHL patients <sup>†</sup>	Controls <sup>‡</sup>	<i>p</i>
Sex (male)	1738 (52.3)	5214 (52.3)	>0.999
Age (years)			>0.999
– < 40	875 (26.3)	2625 (26.3)	
– 40–44	276 (8.3)	828 (8.3)	
– 45–49	295 (8.9)	885 (8.9)	
– 50–54	367 (11.0)	1101 (11.0)	
– 55–59	379 (11.4)	1137 (11.4)	
– 60–64	326 (9.8)	978 (9.8)	
– 65–69	311 (9.4)	933 (9.4)	
– ≥70	496 (14.9)	1488 (14.9)	
Geographical region of Taiwan			0.028
– Northern	1607 (48.3)	4784 (48.0)	
– Central	827 (24.9)	2294 (23.0)	
– Eastern	832 (25.0)	2678 (26.9)	
– Southern	59 (1.8)	219 (2.2)	
Diabetes	829 (24.9)	1872 (18.9)	<0.001
Hypertension	1363 (41.0)	3568 (35.8)	<0.001
Coronary heart disease	797 (24.0)	1952 (19.6)	<0.001
Hyperlipidaemia	1106 (33.3)	2930 (29.4)	<0.001
Renal disease	319 (9.6)	718 (7.2)	<0.001
Bacterial or cryptococcal meningitis	6 (0.2)	9 (0.1)	0.180
Rheumatoid arthritis	75 (2.3)	208 (2.1)	0.555
Otitis media	377 (11.3)	532 (5.3)	<0.001
Syphilis	25 (0.8)	36 (0.4)	0.004
Mumps	5 (0.2)	18 (0.2)	0.718
HIV or AIDS	3 (0.1)	2 (0.0)	0.071
Systemic lupus erythematosus	5 (0.2)	6 (0.1)	0.117

Data represent numbers (and percentages) of subjects, unless indicated otherwise. \*Total *n* = 14 088; <sup>†</sup>*n* = 3325; <sup>‡</sup>*n* = 9975. SNHL = sensorineural hearing loss; HIV = human immunodeficiency virus; AIDS = acquired immunodeficiency syndrome

Table II also shows the odds ratios and corresponding 95 per cent CIs for prior chronic rhinosinusitis for cases and controls. The conditional logistic regression (conditioned on sex, age group and index year) showed that the crude odds ratio of prior chronic rhinosinusitis for cases compared to controls was 1.43 (95 per cent CI = 1.22–1.68, *p* < 0.001). After adjusting for geographical region, hypertension, diabetes, hyperlipidaemia, renal disease, coronary heart disease, otitis media and syphilis, the odds ratio of having prior chronic rhinosinusitis among cases compared to controls was 1.36 (95 per cent CI = 1.16–1.60, *p* < 0.001).

We further performed analyses of the odds ratio for prior chronic rhinosinusitis by age group. Table III shows that the significant relationship between sudden SNHL and prior chronic rhinosinusitis was most pronounced among those aged 44 years or less, with an adjusted odds ratio of 2.18 (95 per cent CI = 1.63–2.92, *p* < 0.001) for cases compared to controls. However, it is noteworthy that for those aged 60 years or older, the significant relationship between sudden SNHL and prior chronic rhinosinusitis was not sustained (odds ratio = 1.00; 95 per cent CI = 0.74–1.36), after adjusting for geographical region, hypertension, diabetes, hyperlipidaemia, renal disease, coronary heart disease, otitis media and syphilis.

**Discussion**

In this study, we demonstrated that sudden SNHL was associated with chronic rhinosinusitis in patients of a younger age (less than 60 years). Most cases of sudden SNHL remain idiopathic; however, many theories have been proposed to explain the development of sudden SNHL.<sup>2</sup> Aetiological theories of idiopathic sudden SNHL include viral infection, autoimmune disease, vascular insult and labyrinthine membrane rupture.<sup>3,4</sup> There is considerable evidence implicating viral infections as a cause of sudden SNHL. A non-controlled study reported that 17–33 per cent of patients recalled a predisposing viral illness event after they were diagnosed with sudden SNHL.<sup>10</sup> Another study found that rates of seroconversion for the herpesvirus family were significantly higher in the sudden hearing loss population, indicating a viral element for this disease.<sup>11</sup> Furthermore, temporal bone histopathological studies have shown damage to the cochlea consistent with viral injuries in patients with sudden SNHL.<sup>10</sup> While it appears that infections were responsible for the inner-ear damage in some sudden SNHL patients, the route of infection and explanation as to how they affected the inner ear remain unknown. Being a neighbouring structure, it is possible that infections in the sinuses could contribute to the pathogenesis of sudden SNHL.

However, currently, there are no reports of possible relations between chronic rhinosinusitis and sudden SNHL. In our previous study, we found that the chronic rhinosinusitis might contribute to the development of nasopharyngeal carcinoma.<sup>8</sup> This association may be mediated by many local inflammatory

**TABLE II**  
PREVALENCE AND ODDS RATIOS FOR PRIOR CHRONIC RHINOSINUSITIS

Prior chronic rhinosinusitis?	Sudden SNHL patients* ( <i>n</i> (%))	Controls <sup>†</sup> ( <i>n</i> (%))	Crude OR (95% CI) <sup>‡</sup>	Adjusted OR** (95% CI) <sup>‡</sup>
Yes	236 (7.1)	506 (5.1)	1.43 <sup>§</sup> (1.22–1.68) 1.00	1.36 <sup>§</sup> (1.16–1.60) 1.00

Odds ratios calculated using a conditional logistic regression which was conditioned on sex, age group and year of the index date. \**n* = 3325; <sup>†</sup>*n* = 9975. <sup>‡</sup>For sudden sensorineural hearing loss. \*\*Adjusted for geographical region, hypertension, diabetes, hyperlipidaemia, renal disease, coronary heart disease, otitis media and syphilis. <sup>§</sup>Indicates *p* < 0.001. SNHL = sensorineural hearing loss; OR = odds ratio; CI = confidence interval

TABLE III  
PREVALENCE AND ODDS RATIOS FOR PRIOR CHRONIC RHINOSINUSITIS BY AGE GROUP

Prior chronic rhinosinusitis?	Sudden SNHL patients (n (%))	Controls (n (%))	Crude OR (95% CI)*	Adjusted OR <sup>†</sup> (95% CI)*
In 18–44 year olds				
– Yes	86 (7.5)	119 (3.5)	2.24 <sup>‡</sup> (1.68–2.98) 1.00	2.18 <sup>‡</sup> (1.63–2.92) 1.00
In 45–59 year olds				
– Yes	89 (8.6)	211 (6.6)	1.32 <sup>§</sup> (1.02–1.71) 1.00	1.28 <sup>§</sup> (1.01–1.68) 1.00
In 60 year olds or older				
– Yes	41 (6.4)	104 (5.5)	1.18 (0.81–1.71) 1.00	1.00 (0.74–1.36) 1.00

Odds ratios calculated using a conditional logistic regression which was conditioned on sex, age group and year of the index date. \*For sudden sensorineural hearing loss. <sup>†</sup>Adjusted for geographical region, hypertension, diabetes, hyperlipidaemia, renal disease, coronary heart disease, otitis media and syphilis. <sup>‡</sup>Indicates  $p < 0.001$ ; <sup>§</sup>indicates  $p < 0.05$ . SNHL = sensorineural hearing loss; OR = odds ratio; CI = confidence interval

factors, including tumour necrosis factor (TNF)- $\alpha$ , an important proinflammatory cytokine expressed during the sinusitis process.<sup>12</sup> In a recent study, Demirhan *et al.* found evidence that supports the role of TNF- $\alpha$  in the pathophysiology of sudden SNHL.<sup>13</sup> It is possible that inflammatory mediators induced by the rhinosinusitis process can spread locally to adjacent auditory structures and affect the inner ear.

The increased oxidative stress that occurs during sinusitis attacks might also be responsible for ‘pararhinosinusitis’ involvement.<sup>14</sup> Researchers have found that genes involved in nitric oxide and reactive oxygen species regulation in patients with chronic rhinosinusitis were altered.<sup>15</sup> Noise-induced hearing loss is known to be highly associated with oxidative stress.<sup>16</sup> Capaccio *et al.* reported that oxidative stress can be a risk factor for developing sudden SNHL.<sup>17</sup> Findings of these studies provide some evidence to support the possible association between chronic rhinosinusitis and sudden SNHL found in our study.

It is interesting that this association seems to be found only in chronic rhinosinusitis patients aged less than 60 years. This finding is difficult to explain. However, if one considers the above-mentioned immune-mediated mechanisms linking chronic rhinosinusitis to sudden SNHL, our finding may be reasonable. Indeed, it has been proven that human immune responses are attenuated by ageing, and many inflammatory cytokines are expected to be less activated in older compared to younger chronic rhinosinusitis patients.<sup>18</sup>

The major limitation of this study is the potential surveillance bias. It is possible that patients with rhinosinusitis visited doctors more often, and thus their disease was more easily detected once the sudden SNHL event had occurred. Chronic rhinosinusitis patients were more likely to have aural symptoms due to eustachian tube dysfunction, and thus may have received hearing tests more frequently. However, it is also possible that the diagnosis of sudden SNHL was underestimated, as patients with chronic rhinosinusitis may have considered their hearing-related symptoms to be common eustachian tube dysfunction events and hence did not aggressively seek immediate evaluation.

Another limitation is the lack of information on treatment for the rhinosinusitis group. In this database study, it is difficult to evaluate how these subjects were treated, and therefore there might be some subjects who had been adequately treated for their rhinosinusitis, but were still included in the rhinosinusitis group. This could potentially affect the accuracy of our data interpretation. Moreover, limited by our insurance-based database, the information regarding the use and the dosages of the potentially ototoxic medications was not complete. This results in a confounding covariate which is difficult to adjust for. Some antibiotics that may have been used in the treatment of chronic rhinosinusitis, including the macrolide family and even penicillin, are known for their potential ototoxicity.<sup>19,20</sup> Although the results of our study reached statistical significance, we remind readers to keep in mind these limitations in the interpretation of our results.

Finally, the determination of the time period between the diagnosis of rhinosinusitis and sudden SNHL is especially difficult and controversial. The time it takes for nasal infection or inflammation to reasonably result in an inflammatory or immunogenic insult to the inner ear is unknown. The cause and effect relationship between chronic rhinosinusitis and the development of sudden SNHL remains difficult to establish. Nevertheless, the results of our study are statistically significant, and we believe this limitation would have little impact on interpretations of the data.

- **Inflammatory processes may elevate the risk of sensorineural hearing loss (SNHL)**
- **An infection adjacent to hearing systems can contribute to SNHL pathogenesis**
- **There was an association between SNHL and chronic rhinosinusitis**
- **This association was most pronounced in those younger than 44 years**

This study can enhance our understanding of rhinosinusitis co-morbidities. It should be emphasised that

the 'association' between chronic rhinosinusitis and sudden SNHL presented in this study should not be interpreted as a 'cause and effect' relationship, as both conditions might be the result of a common causative factor. More research including epidemiological studies in other regions or countries is encouraged to confirm the findings of the present study. We suggest that physicians be aware of the possible association between chronic rhinosinusitis and sudden SNHL when dealing with rhinosinusitis cases.

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Dr S-D Chung takes responsibility for the integrity of the content of the paper

Competing interests: None declared

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