RESEARCH

Long-term exposure to air pollution and the risk of developing sudden sensorineural hearing loss

Stella Chin-Shaw Tsai1,2†, Yi-Chao Hsu3†, Jung-Nien Lai4,5, Ruey-Hwang Chou6,7,8, Hueng-Chuen Fan1,9,10, Frank Cheau-Feng Lin11, Ruihong Zhang12, Cheng-Li Lin13 and Kuang-Hsi Chang1,6,14,15*•

Abstract

Background: The association between exposure to air pollution and sudden sensorineural hearing loss (SSNHL) has not been extensively discussed in the literature. Therefore, we conducted this nationwide study to evaluate the risk of SSNHL in Taiwanese residents with exposure to air pollution.

Methods: We enrolled subjects aged older than 20 years with no history of SSNHL from 1998 to 2010, and followed up until developing SSNHL, withdrawn from the National Health Insurance program, and the end of the database (2011/12/31). The air quality data are managed by Taiwan Environmental Protection Administration. The annual concentrations of PM2.5, SO2, CO, NO, and NO2 from 1998 to 2010 were classified into the three levels according to tertiles. We calculated the annual average of pollutants from baseline until the end of the study, and classified into tertiles. The adjusted hazard ratio (aHR) was estimated by using the multivariate Cox proportional hazard model.

Results: When considered continuous air pollutants concentration, subjects who exposed with higher concentration of CO (aHR = 2.16, 95% CI 1.50–3.11), NO (aHR = 1.02, 95% CI 1.01–1.03), and NO2 (aHR = 1.02, 95% CI 1.01–1.04) developing significant higher risk of SSNHL. When classified air pollutants concentration into low, moderate and high level by tertiles, and selected low level as reference, patients exposed with moderate (aHR = 1.56, 95% CI 1.20–2.04) or high level (aHR = 1.33, 95% CI 1.01–1.75) of PM2.5 showed significant higher risk of developing SSNHL.

Conclusion: This study indicated an increased risk of SSNHL in residents with long-term exposure to air pollution. Nevertheless, further experimental, and clinical studies are needed to validate the study findings.

Keywords: Air pollution, Sudden sensorineural hearing loss (SSNHL), Adjusted hazard ratio (aHR), National Health Insurance program

Introduction

Air pollution has become an important environmental issue in the last decade, especially in the developing and developed countries. The levels of air pollutants are highly and positively correlated with population density, vehicle emissions, agriculture, industrial emissions, power plants, and fossil fuel combustion [1, 2]. Exposure to air pollutants triggers systemic and tissue-specific inflammation [3, 4]. Previous studies have indicated that exposure to air pollution increases the risks of degeneration diseases, cerebrovascular and cardiovascular diseases, immunological diseases, malignant tumors, and ophthalmological diseases [5–12]. In addition, air pollution is the major environment-related risk factor for human mortality [13].
Although viral infection, environmental or occupational factors (such as loud noises, heavy metals, and organic solvents), autoimmune diseases, cardiovascular diseases, accidental events, endothelial dysfunction, metabolic diseases, and health habits (such as smoking and alcohol consumption) are risk factors for sudden deafness (sudden sensorineural hearing loss, SSNHL), the complex etiology of SSNHL remains unclear [14–23]. Exposure to air pollution increases oxidative stress, which can play an important role in endothelial dysfunction [24]. A previous study reports air pollution as a risk factor of developing sensorineural hearing loss [25]. However, the association between exposure to air pollution and SSNHL has not been extensively discussed in the literature. Therefore, we conducted this nationwide study to evaluate the risk of SSNHL in Taiwanese residents with exposure to air pollution.

Methods

Data source and study subjects
Taiwan government built a nationwide database, named National Health Insurance Database (NHIRD), since 1995 and included the medical record of health insurance single payer in Taiwan. The medical record included the history of outpatients, hospitalization, the prescriptions of medications and other medical services. As of today, more than 99% of Taiwan population were enrolled in the database. We conducted this study by Longitudinal Health Insurance Database (LHID 2000), which was randomly selected 1 million study subjects from NHIRD. All identification number were encrypted for the patients’ privacy. The history diagnoses are coded according to the International Classification of Disease, Ninth Revision, Clinical Modification (ICD-9-CM). The Research Ethics Committee of China Medical University and Hospital in Taiwan approved the study (CMUH-104-REC2-115-R4).

We enrolled subjects aged older than 20 years with no history of SSNHL from 1998 to 2010, and followed up until developing SSNHL, withdrawn from the NHI program, and the end of the database (2011/12/31).

Exposure measurement
The data regarding the air pollutants were collected from 74 ambient air quality monitoring stations across Taiwan. The air quality data are managed by Taiwan Environmental Protection Administration. The annual concentrations of PM$_{2.5}$, SO$_2$, CO, NO, and NO$_2$ from 1998 to 2010 were classified into the three levels according to tertiles: the PM$_{2.5}$ concentrations of the low-, mid-, and high-level groups were <30.29 (μg/m$^3$), 30.29–37.61 (μg/m$^3$) and >37.61 (μg/m$^3$), respectively. The SO$_2$ concentrations of the low-, mid-, and high-level groups were <3.57 (ppb), 3.57–5.51 (ppb) and >5.51 (ppb), respectively. The CO concentrations of the low-, mid-, and high-level groups were <0.61 (ppm), 0.61–0.76 (ppm) and >0.76 (ppm) respectively. The NO concentrations of the low-, mid-, and high-level groups were <5.04 (ppb), 5.04–8.90 (ppb) and >8.90 (ppb), respectively. The NO$_2$ concentrations of the low-, mid-, and high-level groups were <19.48 (ppb), 19.48–25.55 (ppb) and >25.55 (ppb), respectively.

Main outcome and covariates
The main outcome of this study was the SSNHL (ICD-9-CM: 3882; ICD-10-CM: H91.20, H91.21, H91.22, H91.23). SSNHL is most defined as sensorineural hearing loss of 30 dB or greater over at least three contiguous audiometric frequencies occurring within a 72-h period. This definition must be confirmed with pure tone audiometry and history taking before insurance could pay for the appropriate treatment. The demographic factors we considered included age, insurance fee, urbanization, and comorbidities. The common comorbidities including hypertension (HT, ICD-9-CM codes 401–405), diabetes mellitus (DM, ICD-9-CM code250), stroke, head injury (ICD-9-CM codes 850–854), chronic kidney disease (CKD, ICD-9-CM code 585), ischemic heart disease (IHD, ICD-9-CM codes 410–414), alcoholism (ICD-9-CM codes 305.0 and 303), asthma (ICD-9-CM code 493), Chronic obstructive pulmonary disease (COPD, ICD-9-CM codes 490–492, 494, and 496), impacted cerumen (IC, ICD-9-CM code 380.4), suppurrative and unspecified otitis media (SUOM, ICD-9-CM codes 382.0, 382.1, 382.2, 382.3, 382.4 and 382.9), chronic serous otitis media (CSOM, ICD-9-CM codes 381.10 and 381.19), otosclerosis (ICD-9-CM code 387.9) and rheumatoid arthritis (RA, ICD-9-CM code 714) were presented as confounding factors in this study.

Statistical analysis
We presented continuous variables by mean and standard deviation; categorical variables were shown by number and percentage. The difference between with and without SSNHL were tested by t-test and chi-square test for continuous and categorical variable, respectively. To analyze the exposures across the long-term period, we calculated the annual average of pollutants from baseline until the end of the study, and classified into tertiles: the low, moderate, and high-level groups. When compared mean and classified pollutants concentration in four level of urbanization (highly, moderately, boomtown and others), ANOVA test and chi-square test was applied, respectively.

The incidence rates of SSNHL were calculated, and the hazard ratio (HR) was estimated by using the multivariate Cox proportional hazard model, adjusting for age, sex, insurance fee, urbanization, and comorbidities.
Results

We totally enrolled 64,321 subjects in this study. 353 with SSNHL and the other 63,968 without SSNHL. Table 1 presented the distribution of demographics and comorbidities between two groups. The mean age of SSNHL and non-SSNHL were 45.58 and 39.12 years, and with 8.47 and 11.71 follow up years, respectively. Patients with SSNHL had significant higher percentage of HT (45.6%), DM (17.3%), IHD (27.5%), IC (12.5%), SUOM (11.6%) and COPD (29.5%) than non-SSNHL group. The distribution of the levels of insurance fee showed insignificant between two groups. Most study subjects lived in highly (34.3%) and moderately (32.6%) urbanized area. Table 2 showed the distribution of different pollutants concentration and SSNHL. SO₂ and NO₂ concentration showed insignificant difference between SSNHL and non-SSNHL group when calculated by mean or classified into levels. The mean of CO (0.76 vs 0.72) and NO (12.6 vs 11.0) concentration was significant higher in the group of SSNHL, respectively. Table 3 showed the association between pollutants concentration and urbanized level. The level of CO, NO and NO₂ showed the mean 0.81, 0.69, 0.70 and 0.59 (ppm); 14.14, 9.94, 10.73 and 6.80 (ppb); 24.58, 22.06, 23.39, and 18.63 (ppb) from highly urbanized, moderately, boomtown to others, respectively. The pollutants we mentioned above might highly associated with the level of urbanization. The risk of SSNHL and the level of air pollutants were calculated in Table 4. When considered continuous air pollutants concentration, subjects who exposed with higher concentration of CO (adjusted hazard ratio (aHR) = 2.16, 95% CI 1.50–3.11), NO (aHR = 1.02, 95% CI 1.01–1.03), and NO₂ (aHR = 1.02, 95% CI 1.01–1.04) developing significant higher risk of SSNHL.

Table 1 Distribution of the demographic data and comorbidities of the study participants

| Covariates       | SSNHL (n = 353) | Non-SSNHL (n = 63,968) | p       | Total (n = 64,321) |
|------------------|----------------|------------------------|---------|--------------------|
| Age Mean (SD)    | 45.58 (15.36)  | 39.12 (14.99)          | <0.001  | 39.16 (15.00)      |
| Follow years Mean (SD) | 8.47 (2.49)   | 11.71 (0.91)           | <0.001  | 11.69 (0.96)       |
| HT               | 161 (45.6%)    | 19,464 (30.4%)         | <0.001  | 19,625 (30.5)      |
| DM               | 61 (17.3%)     | 7023 (11.0%)           | <0.001  | 7084 (11.0)        |
| Stroke           | 19 (5.4%)      | 2586 (4.0%)            | 0.255   | 2605 (4.0)         |
| Head injury      | 27 (7.6%)      | 5237 (8.2%)            | 0.787   | 5264 (8.2)         |
| CKD              | 10 (2.8%)      | 1584 (2.5%)            | 0.796   | 1594 (2.5)         |
| IHD              | 97 (27.5%)     | 10,776 (16.8%)         | <0.001  | 10,873 (16.9)      |
| Alcoholism       | 7 (2.0%)       | 975 (1.5%)             | 0.629   | 982 (1.5)          |
| Nicotine         | 5 (1.4%)       | 1814 (2.8%)            | 0.149   | 1819 (2.8)         |
| Asthma           | 50 (14.2%)     | 7581 (11.9%)           | 0.208   | 7631 (11.9)        |
| COPD             | 104 (29.5%)    | 13,997 (21.9%)         | 0.001   | 14,101 (21.9)      |
| RA               | 1 (0.3%)       | 191 (0.3%)             | 1.000   | 192 (0.3)          |
| IC               | 44 (12.5%)     | 3466 (5.4%)            | <0.001  | 3510 (5.5%)        |
| SUOM             | 41 (11.6%)     | 3651 (5.7%)            | <0.001  | 3692 (5.7%)        |
| CSOM             | 2 (0.6%)       | 196 (0.3%)             | 0.296   | 198 (0.3%)         |
| Otosclerosis     | 0 (0)          | 14 (0.02%)             | 1.000   | 14 (0.02%)         |
| Insurance fee    | Lowest 59 (16.7%) | 10,633 (16.6%)  | 0.316   | 10,692 (16.6)      |
|                  | 2nd 102 (28.9%)| 20,987 (32.8%)         | 21,089 (32.8) |
|                  | 3rd 91 (25.8%) | 14,280 (22.3%)         | 14,371 (22.3) |
|                  | Highest 101 (28.6%) | 18,068 (28.2%)       | 18,169 (28.2) |
| Urbanization     | Highly 108 (30.6%) | 21,946 (34.3%)  | 0.002   | 22,054 (34.3)      |
|                  | Moderately 138 (39.1%) | 20,837 (32.6%)       | 20,975 (32.6) |
|                  | Boomtown 40 (11.3%) | 10,856 (17.0%)         | 10,896 (17.0) |
|                  | Others 67 (19.0%) | 10,329 (16.1%)         | 10,396 (16.2) |

HT: hypertension; DM: diabetes mellitus; CKD: chronic kidney disease; IHD: ischemic heart disease; Nicotine: nicotine dependence; COPD: chronic obstructive pulmonary disease; RA: rheumatoid arthritis; IC: impacted cerumen; SUOM: suppurative and unspecified otitis media; CSOM: chronic serous otitis media
### Table 2: Distribution of air pollutant exposure in study participants

| Pollutants | Levels | SSNHL \((n = 353)\) | Non-SSNHL \((n = 63,968)\) | \(p\) | Total \((n = 64,321)\) |
|------------|--------|---------------------|-----------------------------|------|---------------------|
| PM\(_{2.5}\) (μg/m\(^3\)) | Mean (SD) | 35.07 (8.74) | 34.79 (8.75) | 0.556 | 34.79 (8.75) |
|             | Low    | 92 (26.1%) | 21,393 | 33.4% | 21,485 | 33.4% |
|             | Moderate | 133 (37.7%) | 20,202 | 31.6% | 20,335 | 31.6% |
|             | High   | 128 (36.3%) | 22,373 | 35.0% | 22,501 | 35.0% |
| SO\(_2\) (ppb) | Mean (SD) | 4.91 (2.50) | 4.98 (2.41) | 0.557 | 4.98 (2.41) |
|             | Low    | 127 (36.0%) | 21,641 | 33.4% | 21,768 | 33.4% |
|             | Moderate | 111 (31.4%) | 19,691 | 30.8% | 19,802 | 30.8% |
|             | High   | 115 (32.6%) | 22,636 | 35.4% | 22,751 | 35.4% |
| CO (ppm) | Mean (SD) | 0.76 (0.33) | 0.72 (0.27) | 0.010 | 0.72 (0.27) |
|             | Low    | 124 (35.1%) | 22,582 | 35.3% | 22,706 | 35.3% |
|             | Moderate | 93 (26.3%) | 19,242 | 30.1% | 19,335 | 30.1% |
|             | High   | 136 (38.5%) | 22,144 | 34.6% | 22,280 | 34.6% |
| NO (ppb) | Mean (SD) | 12.60 (12.70) | 11.00 (10.13) | < 0.001 | 11.01 (10.15) |
|             | Low    | 119 (33.7%) | 21,754 | 34.0% | 21,873 | 34.0% |
|             | Moderate | 109 (30.9%) | 20,140 | 31.5% | 20,249 | 31.5% |
|             | High   | 125 (35.4%) | 22,074 | 34.5% | 22,199 | 34.5% |
| NO\(_2\) (ppb) | Mean (SD) | 22.99 (7.49) | 22.56 (6.55) | 0.216 | 22.56 (6.56) |
|             | Low    | 114 (32.3%) | 20,002 | 31.3% | 20,116 | 31.3% |
|             | Moderate | 101 (28.6%) | 21,284 | 33.3% | 21,385 | 33.3% |
|             | High   | 138 (39.1%) | 22,682 | 35.5% | 22,820 | 35.5% |

SD: standard deviation; ppb: parts per billion; ppm: parts per million

### Table 3: Distributions of air pollutants among urbanization zones

| Pollutants | Levels | Highly Urbanized \((n = 22,054)\) | Moderately Urbanized \((n = 22,975)\) | Boomtown \((n = 10,896)\) | Others \((n = 10,396)\) | \(p\) | Total \((n = 64,321)\) |
|------------|--------|-----------------------------------|-----------------------------------|---------------------|---------------------|------|---------------------|
| PM\(_{2.5}\) (μg/m\(^3\)) | Mean (SD) | 32.71 (7.85) | 35.68 (9.16) | 37.24 (8.44) | 34.86 (9.04) | < 0.001 | 34.79 (8.75) |
|             | Low    | 9906 (44.9) | 6335 (30.2) | 2651 (24.3) | 2593 (24.9) | < 0.001 | 21,485 (33.4) |
|             | Moderate | 7680 (34.8) | 6067 (28.9) | 3538 (32.5) | 3050 (29.3) | 0.936 | 20,335 (31.6) |
|             | High   | 4468 (20.3) | 8573 (40.9) | 4707 (43.2) | 4753 (45.7) | 20.249 | 22,501 (35.0) |
| SO\(_2\) (ppb) | Mean (SD) | 4.88 (2.09) | 5.23 (2.53) | 5.76 (2.74) | 3.86 (1.97) | < 0.001 | 4.98 (2.41) |
|             | Low    | 7275 (33.0) | 6100 (29.1) | 2700 (24.8) | 5693 (54.8) | 0.396 | 21,768 (33.8) |
|             | Moderate | 6833 (31.0) | 6737 (32.1) | 3233 (29.7) | 2999 (28.8) | 0.516 | 19,802 (30.8) |
|             | High   | 7946 (36.0) | 8138 (38.8) | 4963 (45.5) | 1704 (16.4) | 22,751 | 22,751 (35.4) |
| CO (ppm) | Mean (SD) | 0.81 (0.30) | 0.69 (0.24) | 0.70 (0.22) | 0.59 (0.21) | < 0.001 | 0.72 (0.27) |
|             | Low    | 5516 (25.0) | 7839 (37.4) | 3492 (32.0) | 5859 (56.4) | 0.204 | 22,706 (35.3) |
|             | Moderate | 4810 (21.8) | 6904 (32.9) | 4534 (41.6) | 3087 (29.7) | 20.249 | 22,280 (34.6) |
|             | High   | 11,728 (53.2) | 6232 (29.7) | 2870 (26.3) | 1450 (13.9) | 19,335 | 22,280 (34.6) |
| NO (ppb) | Mean (SD) | 14.14 (12.66) | 9.94 (8.21) | 10.73 (8.43) | 6.80 (6.75) | < 0.001 | 11.01 (10.15) |
|             | Low    | 4156 (18.8) | 7342 (35.0) | 3177 (29.2) | 7198 (69.2) | 0.156 | 21,768 (33.8) |
|             | Moderate | 6556 (29.7) | 7551 (36.0) | 4205 (38.6) | 1937 (18.6) | 20.249 | 22,280 (34.5) |
|             | High   | 11,342 (51.4) | 6082 (29.0) | 3514 (32.3) | 1261 (12.1) | 22,751 | 22,751 (35.4) |
| NO\(_2\) (ppb) | Mean (SD) | 24.58 (6.51) | 22.06 (6.30) | 23.39 (5.19) | 18.43 (6.41) | < 0.001 | 22.56 (6.56) |
|             | Low    | 4245 (19.2) | 7283 (34.7) | 2547 (23.4) | 6041 (58.1) | < 0.001 | 20,116 (31.3) |
|             | Moderate | 6127 (27.8) | 7354 (35.1) | 4930 (45.2) | 2974 (28.6) | 21,385 | 21,385 (33.2) |
|             | High   | 11,682 (53.0) | 6338 (30.2) | 3419 (31.4) | 1381 (13.3) | 22,820 | 22,820 (35.5) |

ppb: parts per billion; ppm: parts per million
When classified air pollutants concentration into low, moderate, and high level by tertiles, and selected low level as reference, patients exposed with moderate (aHR = 1.56, 95% CI 1.20–2.04) or high level (aHR = 1.33, 95% CI 1.01–1.75) of PM2.5 showed significant higher risk of developing SSNHL.

Discussion

This retrospective cohort study combined two large, longitudinal databases to evaluate the risk of SSNHL in Taiwanese residents with chronic exposure to air pollution. During the approximately 11-year follow-up, we enrolled 64,321 residents (353 in SSNHL; 63,968 in non-SSNHL) and found the participants who were exposed to PM2.5, CO, NO, and NO2 had a significantly higher risk of developing SSNHL. However, SO2 exposure was not similarly correlated.

According to Table 3, the distributions of PM2.5 and SO2 were not consistent with urbanization levels. This discrepancy may result from intensive agricultural activities in the less urbanized cities [28–30]. Fossil fuel combustion in industrial facilities or power plants is the major source of SO2 emissions [31]. Because of the high land value and appropriate land and emission standards, industrial factories or power plants are not preferably setup in areas with a high population density.

This nationwide study with minimized selection bias has several limitations. First, we considered the medical convenience; thus, the definition of residential address was based on the location of medical institutions where participants most frequently received therapy for acute respiratory infections. According to this definition, there was a potential bias of excluding subjects without related medical records. However, evidence indicates that these people most likely had less air pollutant exposure [32–34]. This may result in an underestimation of SSNHL cases. Second, SSNHL is an emergency otologic condition. There were more frequent hospital visits by residents in highly urbanized cities with high levels of air pollutants than other areas. Although this may result in surveillance bias and an overestimation of the risk of SSNHL, previous evidence indicates the obvious narrowing of health disparities between urban and non-urban areas.

Table 4 Adjusted HR of SSNHL in the moderate and high concentration groups compared to the values in the low concentration group

| Pollutants | Levels | n of SSNHL | Person-Years | IR | aHR | 95%CI | p     |
|------------|--------|------------|--------------|----|-----|-------|-------|
| PM2.5 (μg/m^3) | Continuous | 1.01 | 0.99 | 1.02 | 0.311 |       |
| Low        | 92     | 251,573    | 0.37         | Reference |
| Moderate   | 133    | 238,157    | 0.56         | 1.56 | 1.20 | 2.04 | 0.001 |
| High       | 128    | 262,340    | 0.49         | 1.33 | 1.01 | 1.75 | 0.043 |
| SO2 (ppb)  | Continuous | 1.01 | 0.96 | 1.05 | 0.811 |       |
| Low        | 127    | 253,994    | 0.50         | Reference |
| Moderate   | 111    | 231,810    | 0.48         | 1.01 | 0.78 | 1.31 | 0.927 |
| High       | 115    | 266,267    | 0.43         | 0.96 | 0.74 | 1.24 | 0.754 |
| CO (ppm)   | Continuous | 2.16 | 1.50 | 3.11 | <0.001 |       |
| Low        | 124    | 265,999    | 0.47         | Reference |
| Moderate   | 93     | 226,689    | 0.41         | 0.96 | 0.73 | 1.26 | 0.754 |
| High       | 136    | 259,382    | 0.52         | 1.27 | 0.99 | 1.65 | 0.065 |
| NO (ppb)   | Continuous | 1.02 | 1.01 | 1.03 | <0.001 |       |
| Low        | 119    | 255,830    | 0.47         | Reference |
| Moderate   | 109    | 237,175    | 0.46         | 1.14 | 0.86 | 1.49 | 0.363 |
| High       | 125    | 259,066    | 0.48         | 1.22 | 0.93 | 1.61 | 0.151 |
| NO2 (ppb)  | Continuous | 1.02 | 1.01 | 1.04 | 0.012 |       |
| Low        | 114    | 235,391    | 0.48         | Reference |
| Moderate   | 101    | 250,758    | 0.40         | 0.93 | 0.71 | 1.23 | 0.625 |
| High       | 138    | 265,922    | 0.52         | 1.25 | 0.96 | 1.63 | 0.105 |

n of SSNHL: number of patients with hearing loss; IR: incidence rate (per 1000 person-years); IR: incidence rate; aHR: adjusted hazard ratio in the multivariate analysis after adjusting for age, insurance fee, urbanization, HT, DM, stroke, head injury, CKD, IHD, alcoholism, nicotine dependence, COPD, asthma, RA, impacted cerumen, suppurative and unspecified otitis media, chronic serous otitis media, and otosclerosis.
urban and rural areas because of the NHI program removing some barriers and providing free health care in the less urbanized areas [35, 36]. Third, although the records of SSNHL were acquired according to the claim data from the NHIRD instead of by physical examination, the SSNHL diagnosis was validated by audiology examinations and neurological findings to avoid strict fines from Taiwan Bureau of National Health Insurance. Fourth, patients’ occupation and health behaviors, such as smoking and alcohol consumption, which are considered risk factors of SSNHL, were not available from the NHIRD. Hence, we considered insurance fees, COPD, asthma, nicotine dependence, and alcoholism in the multivariate analysis. Smoking behavior was highly correlated with the development of COPD and asthma [37–40]. The diagnosis of alcoholism was according to patients’ attitudes and drinking behaviors [41]. In several previous NHIRD-related studies, COPD, asthma, nicotine dependence, and alcoholism were considered risk factors instead of smoking and drinking [42–44]. Fifth, traffic-related air pollutants co-occur with noise. It is not feasible to clarify the contributions of air pollution and noise individually due to the lack of noise data in the two large databases. Therefore, the application of the present study is limited. Despite these limitations, the present nationwide study with a long follow-up period might reduce the impacts of biases. We divided the five pollutants into high and low by median, and combined PM$_{2.5}$ with any of other four pollutants to evaluate the risk of SSNHL (Additional file 1). However, it seems the synergistic effects are not obvious.

**Conclusion**

In conclusion, we redefined the residential area by the location of hospital or clinics rather than the addresses of group insurance applicants and considered the proxy covariates of health behaviors to overcome the inherent limitation of the NHIRD. This study indicated an increased risk of SSNHL in residents with exposure to air pollution. Nevertheless, further experimental, and clinical studies are needed to validate the study findings.

**Supplementary Information**

The online version contains supplementary material available at https://doi.org/10.1186/s12967-021-03095-8.

**Additional file 1.** Combined PM$_{2.5}$ with any of other four pollutants to evaluate the risk of SSNHL.

**Acknowledgements**

We thank the grant supports from the following sources: Tungs’ Taichung MetroHarbor Hospital research grant (TTMHH-R1 10012), Taiwan Ministry of Health and Welfare Clinical Trial and Research Center of Excellence (MOHW104-TDU-B-212-113002), China Medical University Hospital, Academia Sinica Taiwan Biobank, Stroke Biosignature Project (BN104010092), NRPB Stroke Clinical Trial Consortium (MOST 103-2325-B-039-006), Tseng-Lien Lin Foundation, Taichung, Taiwan, Taiwan Brain Disease Foundation, Taipei, Taiwan, Katsuzo and Kiyo Aoshima Memorial Funds, Japan, and CMU under the Aim for Top University Plan of the Ministry of Education, Taiwan.

We thank the staff of the Management Office for Health Data of China Medical University Hospital for their contributions to this study.

**Disclosure statement**

All authors declare that there is no conflicts of interest. This study was approved in part by Taiwan Ministry of Health and Welfare Clinical Trial and Research Center of Excellence (MOHW104-TDU-B-212-113019). The committee agree to waive the requirement for consent.

**Authors’ contributions**

Conceptualization: K-HC; methodology: K-HC, C-LL; formal analysis: K-HC and C-LL; investigation: all authors; writing (original draft preparation): K-HC; writing (review and editing): all authors; visualization: all authors; supervision: K-HC; project administration: K-HC. All authors read and approved the final manuscript.

**Funding**

This study is supported in part by Taiwan Ministry of Health and Welfare Clinical Trial Center (MOHW109- TDU-B-212-114004), MOST Clinical Trial Consortium for Stroke (MOST 108-2321-B-039-003), Tseng-Lien Lin Foundation, and Tungs’TaiChung MetroHarbor Hospital (TTMHH-R1 10012).

**Availability of data and materials**

Data are available from the NHIRD published by Taiwan National Health Insurance Bureau. Due to the ‘Personal Information Protection Act’, data cannot be made publicly available (http://nhird.nhri.org.tw/en/index.html).

**Declarations**

**Ethics approval and consent to participate**

This study was approved by the Ethics Review Board of China Medical University and Hospital, Taiwan (CMUH-104-REC2-115). The IRB waived the consent requirement.

**Consent for publication**

Not applicable.

**Competing interests**

The authors declare that they have no competing interests.

**Author details**

1Department of Medical Research, Tungs’ Taichung Metroharbor Hospital, Taichung 43503, Taiwan. 2Department of Otolaryngology, Tungs’Taichung Metroharbor Hospital, Taichung 43503, Taiwan. 3Institute of Biomedical Sciences, Mackay Medical College, New Taipei City 252, Taiwan. 4Graduate Institute of Biomedical Sciences, China Medical University Hospital, Taichung 40402, Taiwan. 5Department of Chinese Medicine, China Medical University Hospital, Taichung 40402, Taiwan. 6Department of Chinese Medicine, China Medical University Hospital, Taichung 40447, Taiwan. 7Graduate Institute of Biomedical Sciences, China Medical University, Taichung 40402, Taiwan. 8Center for Molecular Medicine, China Medical University Hospital, Taichung 40402, Taiwan. 9Department of Biotechnology, Asia University, Taichung 41354, Taiwan. 10Department of Pediatrics, Department of Medical Research, Tungs’Taichung Metroharbor Hospital, Taichung 43503, Taiwan. 11Department of Rehabilitation, Jen-Teh Junior College of Medicine, Nursing and Management, Miaoli 35664, Taiwan. 12Department of Thoracic Surgery, Chung Shan Medical University Hospital, Taichung 40201, Taiwan. 13Department of Science and Teaching, The Fourth Central Hospital of Baoding City, Baoding, Hebei, China. 14Management Office for Health Data, China Medical University Hospital, Taichung 40402, Taiwan. 15General Education Center, Jen-Teh Junior College of Medicine, Nursing and Management, Miaoli 35664, Taiwan. 16Center for General Education, China Medical University, Taichung 404, Taiwan.

Received: 15 September 2020 Accepted: 27 September 2021

**Published online:** 12 October 2021

**References**

1. Forberg B, Stjernberg N, Wall S. People can detect poor air quality well below guideline concentrations: a prevalence study of annoyance reactions and air pollution from traffic. Occup Environ Med. 1997;54(1):44–8.
2. Liu J, Wexzler DL, Chen Q, Zhang Q, Song Y, Peng W, et al. Air pollutant emissions from Chinese households: a major and underappreciated ambient pollution source. Proc Natl Acad Sci USA. 2016;113(28):7756–61.

3. Block ML, Calderon-Cardona L. Air pollution mechanisms of neuroinflammation and CNS disease. Trends Neurosci. 2009;32(9):506–16.

4. Kundnali M, Jemett M, Garcia-Estevez R, Basagnano X, Beckerman R, Gilliland F, et al. Ambient air pollution and the progression of atherosclerosis in adults. PLoS ONE. 2010;5(2):e9996.

5. Ritz B, Lee PC, Hansen J, Lassen CF, Ketzel M, Sorensen M, et al. Traffic-related air pollution and Parkinson's Disease in Denmark: a case-control study. Environ Health Perspect. 2016;124(3):351–6.

6. Lisabeth LD, Escobar JD, Dvoroch JT, Sanchez BN, Majerlik J, Brown DL, et al. Ambient air pollution and risk for ischemic stroke and transient ischemic attack. Ann Neurol. 2008;64(1):53–9.

7. Chang KH, Hsu HC, Mau CH, Hu CY, Lu HC, Kao CH, et al. Air pollution exposure increases the risk of rheumatoid arthritis: a longitudinal and nationwide study. Environ Int. 2016;94:95–9.

8. Chang MY, Chang MY, Muo CH, Wu TN, Chen CY, Kao CH. Increased risk of dementia in patients exposed to nitrogen dioxide and carbon monoxide: a population-based retrospective cohort study. PLoS ONE. 2014;9(8):e103708.

9. Chang KH, Hsu PY, Lin CL, Lin CL, Joo SH, Liang CL. Traffic-related air pollutants increase the risk for age-related macular degeneration. J Intern Med. 2019;67(7):1076–81.

10. Fan HC, Chen CY, Hsu YC, Chou RH, Teng CL, Chiu CH, et al. Increased risk of nasopharyngeal carcinoma with exposure to air pollution. PLoS ONE. 2018;13(9):e0204568.

11. Chang KH, Chang MV, Mau CH, Wu TN, Hwang BF, Chen CY, et al. Exposure to air pollution increases the risk of osteoporosis: a nationwide longitudinal study. Medicine. 2015;94(47):e733.

12. Xiong DF, Xu CD, Liao KY, Ying TY, Cheng SP, Hu MG, et al. Spatial association between outdoor air pollution and lung cancer incidence in China. BMC Public Health. 2019;19(1):1377.

13. Gordon SE, Bruce NG, Gregg L, Hlabib PL, Kurni OP, Lamm KB, et al. Respiratory risks from household air pollution in low and middle-income countries. Lancet Respir Med. 2014;2(10):823–30.

14. Amonni A, Banchini C, Bonin M, Corbella A, Fellin R, Martini A, et al. Diabetes, cardiovascular risk factors and idiopathic sudden sensorineural hearing loss: a case-control study. Audiol Neurootol. 2010;15(2):111–5.

15. Chen X, Fu YY, Zhang TY. Role of viral infection in sudden hearing loss. J Int Med Res. 2019;47(7):2865–72.

16. Jeong J, Lim H, Lee K, Hong CE, Choi HS. High risk of sudden sensorineural hearing loss in severe alcoholic liver disease according to a population-based national sample cohort study. Audiol Neurootol. 2019;24(5):224–30.

17. Levy JM, Amedee RG. In reference to Systematic review of the evidence for the etiology of adult sudden sensorineural hearing loss. Laryngoscope. 2010;120(11):2347.

18. Chau JK, Lin JR, Rashbash J, Irvine RA, Westerberg BD. Systematic review of the evidence for the etiology of adult sudden sensorineural hearing loss. Laryngoscope. 2010;120(3):101–21.

19. Ostrea A, Box RC, Gaston A, Prostad LA, Martin A, Sudden bilateral sensorineural hearing loss as an unusual consequence of accidental ingestion of potassium hydroxide. Med Princ Pract. 2010;19(5):406–8.

20. Capaccio P, Pignataro L, Ianni LM, Sigurdsson PE, Novembre V, De Giuseppe R, et al. Unbalanced oxidative status in idiopathic sudden sensorineural hearing loss. Eur Arch Otorhinolaryngol. 2012;269(2):449–53.

21. Umesawa M, Kobashi K, Kitch R, Nitoh SY, Ogawa K, Hato N, et al. Relationships among drinking and smoking habits, history of diseases, body mass index and idiopathic sudden sensorineural hearing loss in Japanese patients: Acta Otolaryngol. 2017;137(sup655):s1–s23.

22. Quanoia A, DeCeglie V, Debuy J, Endothelial dysfunction in idiopathic sudden sensorineural hearing loss: a review. Audiol Res. 2016;6(1):151.

23. Choi YH, Kim K. Noise-induced hearing loss in Korean workers: co-exposure to organic solvents and heavy metals in nationwide industries. PLoS ONE. 2014;9(5):e97538.

24. Migliore L, Coppede F. Environmental-induced oxidative stress in neurodegenerative disorders and aging. Mutat Res. 2009;674(1–2):273–84.

25. Chang KH, Tsai SC, Lee CY, Chou RH, Fan HC, Lin FC, et al. Increased risk of sensorineural hearing loss as a result of exposure to air pollution. Int J Environ Res Public Health. 2020;17(6):1969.

26. Choi HG, Min C, Kim SY. Air pollution increases the risk of SNHL: a nested case-control study using meteorological data and national sample cohort data. Sci Rep. 2019;9(1):8270.

27. Lee HM, Kim MJ, Kim DJ, Uhm TW, Yi SB, Han JH, et al. Effects of meteorological factor and air pollution on sudden sensorineural hearing loss using the health claims data in Busan, Republic of Korea. Am J Otolaryngol. 2019;40(3):389–93.

28. Telkati C, Chica RA, Lees M, Vaccaro C. Fungal spores and pollen in particulate matter collected during agricultural activities in the Po Valley (Italy). J Environ Sci. 2016;46:229–40.

29. Lelièvre J, Evans JS, Frais M, Giannadaki D, Posser A. The contribution of outdoor air pollution sources to premature mortality on a global scale: Nature. 2015;523(7559):367–71.

30. Pholthuang W, Suwatthiga P, Chhetryamuklul T, Hongsteab S, Limpaseni W, Ikemori F, et al. The influence of the open burning of agricultural biomass and forest fires in Thailand on the carbonaceous components in particle-sized fractionated particulate. Environ Pollut. 2019;247:238–47.

31. Luoto M, Imhoff RE, Valente RL, Parklund WJ, Tanner RL. Rates of conversion of sulfur dioxide to a scrubbed power plant flue gas. J Air Waste Manag Assoc. 2001;51(10):1408–13.

32. Zheng PW, Wang J, Zhang ZY, Shen P, Chai PF, Li D, et al. Air pollution and hospital visits for acute upper and lower respiratory infections among children in Ningbo, China: a time-series analysis. Environ Sci Pollut Res Int. 2017;24(23):18860–9.

33. Shamsiarov NN, Galeev KA, Khamkova PF, Dautov FF, Lusipova NZ. Evaluation of ambient air pollution on children’s morbidity with acute respiratory infections of the upper airway. Gig Sant. 2002;44:1–3.

34. Khinnane GC, Twairi P. Air pollution in India and related adverse respiratory health effects: past, present, and future directions. Curr Opin Pulm Med. 2018;24(2):108–16.

35. Shou-Hia C, Tung-Liang C. The effect of universal health insurance on health care utilization in Taiwan results from a natural experiment. JAMA. 1997;278(2):89–93.

36. Huang NY, Yip W, Chang HJ, Chou YJ. Trends in rural and urban differentials in incidence rates for ruptured appendectomies under the National Health Insurance in Taiwan. Public Health. 2006;120(11):1055–63.

37. Siroen V, Pin I, Orvuzcyn MP, Le Moul N, Kaufmann F. Relationships of active smoking to asthma and asthma severity in the EGSEA study. Epidemiological study on the Genetics and Environment of Asthma. Eur Respir J. 2000;15(3):470–7.

38. Gilliland FD, Islam T, Berhanie K, Gauderman WJ, McConnell R, Avol E, et al. Regular smoking and asthma incidence in adolescents. Am J Respir Crit Care Med. 2006;174(10):1094–100.

39. Foisy BA, Thornton A, Lee PN. Systematic review with meta-analysis of the epide⁃miological evidence relating smoking to COPD, chronic bronchitis and emphysema. BMC Pulm Med. 2011;11:36.

40. Pauwels RA, Bousquet J. Burden and clinical features of chronic obstructive pulmonary disease (COPD). Lancet. 2002;360(9344):1223–33.

41. Enoch MA, Goldman D. Problem drinking and alcoholism: diagnosis and treatment. Am Fam Phys. 2002;65(3):441–8.

Publisher’s Note
Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.