Prevalence of Subjective Olfactory Dysfunction and Its Risk Factors: Korean National Health and Nutrition Examination Survey

Woo Hyun Lee¹, Jee Hye Wee¹, Dong-Kyu Kim¹, Chae-Seo Rhee¹, Chul Hee Lee¹, Soyeon Ahn², Ju Hyun Lee², Yang-Sun Cho³, Kun Hee Lee⁴, Kyung Soo Kim⁵, Si Whan Kim⁶, Ari Lee⁷, Jeong-Whun Kim¹*

¹ Department of Otorhinolaryngology, Seoul National University Bundang Hospital, Seongnam; Seoul National University College of Medicine, Seoul, South Korea, 2 Medical Research Collaborating Center, Seoul National University Bundang Hospital, Seongnam, South Korea, 3 Department of Otorhinolaryngology-Head and Neck Surgery, Sungkyunkwan University School of Medicine, Seoul, South Korea, 4 Department of Otorhinolaryngology-Head and Neck Surgery, Kyung Hee University School of Medicine, Seoul, South Korea, 5 Department of Otorhinolaryngology-Head and Neck Surgery, Yonsei University College of Medicine, Seoul, South Korea, 6 Department of Otorhinolaryngology-Head and Neck Surgery, Hallym University College of Medicine, Anyang, South Korea, 7 Division of Chronic Disease Surveillance, Korea Centers for Disease Control & Prevention, Seoul, South Korea

Abstract

Background: Population-based studies for olfactory dysfunction are lacking. The aim of this study is to evaluate the prevalence of subjective olfactory dysfunction and its risk factors in the Korean general population.

Methods: The data were obtained from the 2009 Korea National Health and Nutrition Examination Survey (KNHANES), which was a cross-sectional survey of non-institutionalized population all around the country (n = 10,533). All interviewees underwent medical interviews, physical examinations, endoscopic examination and blood/urine tests. Whether sense of smell has been normal or abnormal during the last 3 months was asked. Complete olfaction data were obtained from 7,306 participants and the participants were divided into normosmic and hyposmic group. Multivariate logistic regression analyses were performed to identify its risk factors.

Results: The weighted prevalence of subjective olfactory dysfunction was 4.5%. Its increased prevalence was significantly associated with the increasing age for both men and women. In the multivariate analyses, low income (adjusted odds ratio [OR] = 1.43, 95% Confidence Interval [CI] = 1.01–2.03), habitual exposure to air pollutants (adjusted OR = 2.18, CI = 1.33–3.55), a history of hepatitis B (adjusted OR = 3.10, CI = 1.25–7.68), rhinitis (adjusted OR = 1.78, CI = 1.26–2.51) and chronic sinusitis (adjusted OR = 14.55, CI = 10.06–21.05) were risk factors of olfactory dysfunction.

Conclusion: Our population-based study showed that olfactory dysfunction was quite prevalent and several risk factors were associated with impaired sense of smell. Given its prevalence, further researches for its prevention and management are required.

Introduction

The loss of sense of smell decreases quality of life and may contribute to the failure in recognizing hazardous substances or unpleasant odors. [1] This problem can develop changes in appetite and this may make a nutritional problem especially in the elderly. Persons who have olfactory dysfunction are at an increased risk of danger from leaking gas, smoke, food spoilage, and pollution. [2] Although it is usually not a life-threatening or highly morbid condition, [3] it is important to recognize undiagnosed olfactory dysfunction and its etiology in order to prevent these possible complications. So far, population-based studies for olfactory dysfunction are lacking. The National Health Interview Survey (NHIS) of the United States including about 42,000 households showed that the prevalence of self-reported olfactory problems was 1.4%. [1] There were another two population-based studies in the Western countries, which were based on psychophysical tests. In the Epidemiology of Hearing Loss Study (EHLS) of individuals aged 53 to 97 years in Beaver Dam, 24.5% were found to have impaired sense of smell, [4] and the Skovde population-based study of the general Swedish adult population aged ≥20 years, 19.1% were found to have olfactory dysfunction. [5] However, there has been no large group study for olfactory impairment in the Asian population.

Although olfactory dysfunction needs to be objectively diagnosed and managed by clinicians, it is also important to know the prevalence of self-reported olfactory dysfunction which may determine whether they are likely to seek medical attention. [6]
The current investigation was conducted to determine the prevalence of self-reported olfactory dysfunction in the large Korean population who were randomly selected. This study is also aimed to identify the risk factors of olfactory dysfunction through analyses of systematic medical questionnaires, endoscopic examinations and blood/urine tests.

Materials and Methods

Population

The Korea Centers for Disease Control and Prevention and the Korean Society of Otorhinolaryngology-Head and Neck Surgery have collaboratively collected medical history and clinical measurement data from a representative sample of the Korean population in the Korean National Health and Nutrition Examination Survey (KNHANES). The KNHANES 2009 data set was used, which included information on the presence of subjective olfactory dysfunction and endoscopic findings of the ear, nose and throat (ENT). A total of 12,722 individuals of 4,000 households were invited to participate in the KNHANES 2009. These participants were randomly selected from a panel to represent the population of South Korea. The panel was extracted by using a multistage clustered and stratified random sampling method that was based on the National Census Data. Among 12,722 selected individuals, 10,533 (82.8%) agreed to participate in the clinical examination. Analyses were conducted for the data from 7,306 participants who answered to the questionnaire for the presence of olfactory dysfunction. However, the other general characteristics of the subjects included were comparable with those of the subjects excluded. The average age of the 7,306 participants was 49.3±16.5 years (range, 20–95 years) and the ratio of male to female was 1:1.32. Written informed consents were obtained from all the participants prior to the survey and approval for this research was obtained from the Institutional Review Board of the Seoul National University Bundang Hospital.

ENT Evaluation, Medical History and Clinical Examination

The endoscopic ENT examinations and interview for otolaryngologic medical history were performed by trained ENT residents according to the standardized protocols. A total of 108 surveys were conducted by four survey teams during a time span of 27 weeks all over the country. Each survey team consisted of one ENT resident, three nurses, two interviewers, and one coordinator. Each survey was performed in a mobile examination unit vehicle at the pre-assigned places. A single visit was required for each participant to the examination unit vehicle. All the questionnaires, ENT examinations and blood/urine samplings were performed during the single visit. A total of 87 ENT residents from 43 teaching hospitals were recruited for performing ENT examinations. The Epidemiology Committee of the Korean Society of Otorhinolaryngology-Head and Neck Surgery verified the quality control of the survey.

The olfactory questionnaire was asked about whether the participants have had problems with the sense of smell during the past three months. The participants with a positive response were considered hyposmic and those with a negative response normosmic. Chronic rhinosinusitis was ascertained when nasal polyps were observed or more than one of the symptoms such as anterior/posterior nasal drip, nasal obstruction, facial pain/pressure, and olfactory dysfunction were present for more than 3 months (anterior/posterior nasal drip or nasal obstruction should be included as a presenting symptom). Otitis media was defined when there was a perforation in the tympanic membrane, cholesteatoma including a retraction pocket, or inflammation in the tympanic membrane with effusion. The diagnosis of rhinitis was made when they have had a history of rhinorrhea, sneezing, itching, and nasal obstruction for the last one year without cold symptoms. The deviation of the nasal septum was defined when an asymmetric displacement to one or both sides of the nasal cavities was observed after vasoconstriction of the nasal cavities.

Other medical histories were obtained by trained interviewers of the Korea Center of Disease Control and Prevention. A set of structured questionnaires were asked. The socioeconomic status (income, education, residency and occupation), smoking, drinking, a history of habitual exposure to air pollutants or chemical substances were asked and the participants were categorized. The study population was split into 6 subgroups by age. Body mass index was categorized into normal (<25 Kg/m²) and obese (≥25 Kg/m²). Residency was categorized into urban and rural areas according to the official address of the subjects. Home income was calculated by equivalized gross household income per month in each year and grouped into 4 quartiles. In the analysis, the subjects were divided into low (1st and 2nd quartiles) and high (3rd and 4th quartiles) groups. Subjects who graduated from middle or elementary school were considered to have a low level of education, and those from high school or college were considered to have a high level of education. Occupation was categorized by following the Korean Standard Classification of Occupations. The occupational categories were as follows: white collar (included managers, professionals, clerks, service/sales workers, unemployed, retired, students, and housewives) and blue collar (agriculture, forestry, fishery workers, craft and related trade workers, plant and machine operators and assemblers, and simple labor). Smoking status was classified into two categories: non-smoker (a person who has smoked below 5 pack smoking) and smoker (a person who has smoked more than 5 pack smoking). Alcohol consumption was assessed by asking the participants about their average frequency of alcoholic beverage consumption during the month prior to the interview.

Blood and urine samples were also tested. All the collected blood and urine samples were transported to a single designated laboratory (Neodin Medical Institute, Seoul, Korea) and analyzed according to their qualified standard protocols and equipments.

Statistical Analyses

The data were analyzed with SPSS (version 18.0, SPSS Inc, Chicago, IL, USA), which is a software package that incorporates
Table 1. Prevalence of olfactory dysfunction according to the general characteristics of KNHNES participants according to the presence of olfactory dysfunction (weighted for the multistage sampling design of KNHANES 2009).

| Characteristics       | Unweighted total number | Olfactory dysfunction Weighted, % (SE) | P value |
|-----------------------|-------------------------|----------------------------------------|---------|
|                       | No                      | Yes                                    |         |
| Overall               | 7306                    | 95.5 (0.4) 4.5 (0.4)                    |         |
| Age                   |                         |                                        | <0.001  |
| 20–29                 | 936                     | 97.4 (0.5) 2.6 (0.5)                    |         |
| 30–39                 | 1407                    | 96.5 (0.6) 3.5 (0.6)                    |         |
| 40–49                 | 1473                    | 96.7 (0.6) 3.3 (0.6)                    |         |
| 50–59                 | 1233                    | 94.7 (0.8) 5.3 (0.8)                    |         |
| 60–69                 | 1203                    | 92.6 (1.0) 7.4 (1.0)                    |         |
| ≥70                   | 1054                    | 91.4 (1.0) 8.6 (1.0)                    |         |
| Sex                   |                         |                                        | 0.302   |
| Male                  | 3149                    | 95.3 (0.5) 4.7 (0.5)                    |         |
| Female                | 4157                    | 95.8 (0.4) 4.2 (0.4)                    |         |
| Education             |                         |                                        | <0.001  |
| ≤Middle school        | 2867                    | 93.7 (0.7) 6.3 (0.7)                    |         |
| ≥High school          | 4380                    | 96.3 (0.4) 3.7 (0.4)                    |         |
| Missing               | 59                      |                                        |         |
| Income                |                         |                                        | <0.001  |
| ≤50 percent           | 3240                    | 94.2 (0.6) 5.8 (0.6)                    |         |
| >50 percent           | 3983                    | 96.4 (0.4) 3.6 (0.4)                    |         |
| Missing               | 83                      |                                        |         |
| Occupation            |                         |                                        | 0.022   |
| White collar          | 5287                    | 95.9 (0.4) 4.1 (0.4)                    |         |
| Blue collar           | 1937                    | 94.5 (0.6) 5.5 (0.6)                    |         |
| Missing               | 82                      |                                        |         |
| Residence             |                         |                                        | 0.469   |
| Rural                 | 5408                    | 95.4 (0.5) 4.6 (0.5)                    |         |
| Urban                 | 1898                    | 96.0 (0.6) 4.0 (0.6)                    |         |
| Body mass index       |                         |                                        | 0.601   |
| ≤25 kg/m²             | 4926                    | 95.4 (0.5) 4.6 (0.5)                    |         |
| ≥25 kg/m²             | 2331                    | 95.7 (0.5) 4.3 (0.5)                    |         |
| Air Pollutants        |                         |                                        | 0.001   |
| Exposure              | 399                     | 92.0 (1.6) 8.0 (1.6)                    |         |
| No exposure           | 6884                    | 95.7 (0.4) 4.3 (0.4)                    |         |
| Missing               | 23                      |                                        |         |
| Chemical substance    |                         |                                        | 0.399   |
| Exposure              | 230                     | 94.2 (1.9) 5.8 (1.9)                    |         |
| No exposure           | 7053                    | 95.6 (0.4) 4.4 (0.4)                    |         |
| Missing               | 23                      |                                        |         |
| Smoking               |                         |                                        | 0.709   |
| <5 packs              | 4382                    | 95.6 (0.4) 4.4 (0.4)                    |         |
| ≥5 packs              | 2864                    | 95.4 (0.5) 4.6 (0.5)                    |         |
| Missing               | 60                      |                                        |         |
| Alcohol drinking      |                         |                                        | 0.519   |
| ≤4times/month         | 5746                    | 95.6 (0.4) 4.4 (0.4)                    |         |
| ≥2times/week          | 1573                    | 95.2 (0.7) 4.8 (0.7)                    |         |
| Missing               | 23                      |                                        |         |

SE, standard error; Air pollutants, habitual exposure to air pollutants in workplace; Chemical substance, habitual exposure to chemical substances in workplace. doi:10.1371/journal.pone.0062725.t001
Table 2. Prevalence of olfactory dysfunction according to the medical conditions of KNHANES participants.

| Characteristic | Unweighted total number | Olfactory dysfunction Weighted, % (SE) |
|---------------|-------------------------|----------------------------------------|
|               | No                      | Yes                                    | P value     |
| ENT diseases  |                         |                                        |             |
| Chronic rhinosinusitis | 402 | 68.8 (3.3) | 31.2 (3.3) | <0.001 |
| Rhinitis       | 1669                    | 91.6 (0.9) | 8.4 (0.9)  | <0.001 |
| Chronic otitis media | 261 | 90.5 (2.4) | 9.5 (2.4)  | 0.001  |
| Septal deviation | 3090  | 95.2 (0.5) | 4.8 (0.5)  | 0.405  |
| Cardiovascular disease |                        |                                        |             |
| Hypertension   | 1513                    | 93.8 (0.7) | 6.2 (0.7)  | 0.001  |
| Stroke         | 143                     | 93.7 (1.8) | 6.3 (1.8)  | 0.236  |
| Angina         | 137                     | 94.1 (2.0) | 5.9 (2.0)  | 0.398  |
| Arrhythmia     | 292                     | 95.5 (1.1) | 4.5 (1.1)  | 0.963  |
| Metabolic disease |                         |                                        |             |
| Diabetes mellitus | 573                  | 95.7 (0.8) | 4.3 (0.8)  | 0.850  |
| Thyroid disease | 254                     | 89.9 (2.7) | 10.1 (2.7) | 0.001  |
| Hyperlipidemia | 574                     | 94.4 (1.1) | 5.6 (1.1)  | 0.205  |
| Low-HDL cholesterolemia | 1802  | 94.0 (0.9) | 6.0 (0.9)  | 0.014  |
| Pulmonary disease |                         |                                        |             |
| Tuberculosis   | 400                     | 95.5 (0.4) | 4.5 (0.4)  | 0.833  |
| Asthma         | 224                     | 87.9 (3.7) | 12.1 (3.7) | 0.001  |
| COPD           | 43                      | 94.7 (2.7) | 5.3 (2.7)  | 0.749  |
| Bronchiectasis | 25                      | 90.0 (7.5) | 10.0 (7.5) | 0.296  |
| Gastro-intestinal disease |              |                                        |             |
| Gastric ulcer  | 452                     | 95.3 (1.1) | 4.7 (1.1)  | 0.800  |
| Hepatitis B    | 86                      | 86.4 (4.6) | 13.6 (4.6) | 0.001  |
| Neuromuscular disease |            |                                        |             |
| Rheumatoid arthritis | 148                  | 93.6 (2.3) | 6.4 (2.3)  | 0.336  |
| Arthritis      | 967                     | 92.4 (1.1) | 7.6 (1.1)  | <0.001 |
| Osteoporosis   | 539                     | 90.6 (1.5) | 9.4 (1.5)  | <0.001 |
| Neoplastic disease |                         |                                        |             |
| Gastric cancer | 49                      | 86.3 (6.2) | 13.7 (6.2) | 0.016  |
| Hepatic cancer | 11                      | 94.7 (10)  | 5.3 (5.3)  | 0.870  |
| Colon cancer   | 17                      | 89.4 (8.3) | 10.6 (8.3) | 0.260  |
| Others         |                         |                                        |             |
| Depression     | 277                     | 93.8 (1.6) | 6.2 (1.6)  | 0.195  |
| Anemia         | 473                     | 95.2 (1.0) | 4.8 (1.0)  | 0.751  |
| Atopic dermatitis | 161                   | 93.0 (2.1) | 7.0 (2.1)  | 0.121  |
| Cataract       | 660                     | 92.5 (1.1) | 7.5 (1.1)  | <0.001 |

HDL, high density lipoprotein; COPD, chronic obstructive pulmonary disease; ENT, ear-nose-throat.

All ENT diseases were diagnosed by ENT residents.
doi:10.1371/journal.pone.0062725.t002

sample weights and adjusts analysis for the complex sample design of the survey. We used the KNHANES sampling weight variables, along with masked variance primary sampling unit and stratum variables. This adjustment allowed the estimation of the entire non-institutionalized Korean population from the sample. Survey sample weights were used in all the analyses. The chi-square test was used to compare the characteristics between normosmic and hyposmic participants. The independent t-test was used to analyze blood and urine test results. After performing univariate analyses of variables, the multiple logistic regression analysis was performed including variables with values of p<0.20 in the univariate analyses to calculate adjusted odds ratios (OR) and their 95% confidence interval (CI). After conversion of continuous variables to dichotomous variables (normal vs. abnormal) according to their normal laboratory range, blood and urine test results were also included in the multivariate logistic model. A p-value <0.05 was considered significant. Missing data were considered to be missing completely at random.
Results

Prevalence of Olfactory Dysfunction

Of 7,306 participants, 360 (4.9%) had olfactory dysfunction and its weighted prevalence was 4.5%. The prevalence of olfactory dysfunction according to the general characteristics of the participants is shown in Table 1. The chi-square analyses showed that sex, occupation, residence, body mass index, habitual exposure to chemical substances, smoking and drinking did not affect the prevalence of olfactory dysfunction. A logistic regression analysis using olfactory dysfunction as the outcome variable and their age as a continuous variable after adjustment for sex showed a significant increasing trend of the prevalence with age (adjusted OR, 1.026; CI, 1.019–1.033; P value, 0.001). There was no significant difference was found between two genders in each age subgroup, except 30–39 years when the participants were categorized by a decade of age (Figure 1). The increased prevalence was significantly associated with lower education level (p < 0.001), lower income (p < 0.001) and habitual exposure to air pollutants (p = 0.001).

The chi-square analyses from the medical history data set demonstrated that several medical conditions were associated with olfactory dysfunction (Table 2). Among ENT diseases, chronic sinusitis, rhinitis and chronic otitis media were associated with olfactory dysfunction. In the univariate analyses, hypertension, thyroid disease, low HDL (high density lipoprotein) cholesterolemia, asthma, hepatitis B, arthritis, osteoporosis, gastric cancer and cataract were also associated with olfactory dysfunction. In the independent t-test analyses of blood and urine test results, olfactory dysfunction was associated with decreased levels of blood HDL cholesterol and urine creatinine and increased levels of blood GOT (glutamic oxaloacetic transaminase), BUN (blood urea nitrogen) and lead (Table 3).

Multivariate Analyses of Risk Factors

In multivariate logistic regression analyses, the effect of each variable was adjusted for all the other variables (Table 4). In reference to the youngest subgroup aged 20–29 years, the odds of having olfactory dysfunction were significantly higher in the older subgroups aged 50–59 years (adjusted OR, 2.09; 95% CI, 1.16–3.77), 60–69 years (adjusted OR, 2.58; 95% CI, 1.31–5.08) and 70 years or older (adjusted OR, 3.17; 95% CI, 1.93–7.14). Lower income (adjusted OR, 1.43; 95% CI, 1.01–2.03), habitual exposure to air pollutants (adjusted OR, 2.18; 95% CI, 1.33–3.55), a history of hepatitis B (adjusted OR, 3.10; 95% CI, 1.25–7.68), rhinitis (adjusted OR, 1.78; 95% CI, 1.26–2.51) and chronic sinusitis (adjusted OR, 14.5; 95% CI, 10.06–21.05) were significantly associated with self-reported olfactory dysfunction. However, all of the blood and urine test results were not associated with the olfactory dysfunction.

Discussion

This is the first large population-based study reporting the prevalence of subjective olfactory dysfunction in Asia. The weighted prevalence of subjective olfactory dysfunction in the Korean population was 4.5%. In other words, it is equivalent approximately to 1.7 million (according to the current census population of South Korea) Korean adults. The prevalence was 4.5%.

Table 3. Comparison of blood/urine tests between normosmic and hyposmic participants.

| Variable                          | Olfactory dysfunction weighted (SE) | P value |
|-----------------------------------|------------------------------------|---------|
|                                   | No (N=7306)                        | Yes (N=360) |
| Blood test                        |                                    |          |
| Fasting glucose (mg/dL)           | 96.90 (1.30)                       | 97.39 (1.24) | 0.705 |
| HbA1c (%)                         | 7.30 (0.23)                        | 7.37 (0.21) | 0.761 |
| Insulin (µIU/mL)                  | 9.89 (0.32)                        | 9.56 (0.31) | 0.300 |
| Total cholesterol (mg/dL)         | 186.14 (2.20)                      | 186.60 (2.17) | 0.835 |
| HDL cholesterol (mg/dL)           | 52.28 (0.88)                       | 50.03 (0.88) | 0.010 |
| Triglyceride (mg/dL)              | 135.70 (7.80)                      | 143.98 (7.76) | 0.289 |
| LDL cholesterol (mg/dL)           | 110.96 (4.79)                      | 106.35 (4.71) | 0.337 |
| GOT (IU/L)                        | 22.41 (0.88)                       | 24.35 (0.85) | 0.037 |
| GPT (IU/L)                        | 22.49 (1.73)                       | 23.80 (1.71) | 0.451 |
| BUN (mg/dL)                       | 14.17 (0.25)                       | 14.81 (0.25) | 0.013 |
| Vitamin D (ng/mL)                 | 17.74 (0.40)                       | 17.76 (0.43) | 0.953 |
| Alkaline phosphatase (IU/L)       | 221.99 (3.43)                      | 222.19 (3.32) | 0.954 |
| Lead (µg/dL)                      | 2.49 (0.14)                        | 2.89 (0.14) | 0.006 |
| Mercury (µg/L)                    | 5.10 (0.41)                        | 5.80 (0.41) | 0.094 |
| Cadmium (µg/L)                    | 1.08 (0.07)                        | 1.09 (0.07) | 0.936 |
| Urine test                        |                                    |          |
| Creatinine (mg/L)                 | 158.54 (6.03)                      | 143.99 (5.86) | 0.017 |
| Sodium (g/day)                    | 131.69 (4.00)                      | 134.51 (3.94) | 0.482 |
| Cotinine (ng/mL)                  | 445.86 (64.07)                     | 393.55 (63.01) | 0.415 |

HbA1c, hemoglobin A1c; HDL, high density lipoprotein; LDL, low density lipoprotein; GOT, glutamic oxaloacetic transaminase; GPT, glutamic pyruvic transaminase; BUN, blood urea nitrogen.

doi:10.1371/journal.pone.0062725.t003
Table 4. Adjusted odds ratio for the association between olfactory dysfunction and risk factors.

| Exposure                  | Adjusted OR | CI          | P value |
|---------------------------|-------------|-------------|---------|
| Age group                 |             |             |         |
| 20–29                     | 1.00        |             |         |
| 30–39                     | 1.08        | 0.60–1.95   | 0.792   |
| 40–49                     | 1.31        | 0.73–2.37   | 0.360   |
| 50–59                     | 2.09        | 1.16–3.77   | 0.014   |
| 60–69                     | 2.58        | 1.31–5.08   | 0.006   |
| ≥70                       | 3.71        | 1.93–7.14   | <0.001  |
| Income (≤50 percent)      | 1.43        | 1.01–2.03   | 0.042   |
| Education (Middle school) | 0.67        | 0.43–1.04   | 0.075   |
| Occupation (Blue collar)  | 1.21        | 0.86–1.69   | 0.256   |
| Air pollutants            | 2.18        | 1.33–3.55   | 0.002   |
| Hypertension              | 0.94        | 0.63–1.41   | 0.796   |
| Arthritis                 | 0.99        | 0.62–1.58   | 0.968   |
| Osteoporosis              | 1.32        | 0.81–2.13   | 0.259   |
| Asthma                    | 1.84        | 0.81–4.20   | 0.143   |
| Depression                | 0.85        | 0.38–1.87   | 0.688   |
| Atopic dermatitis         | 1.16        | 0.50–2.69   | 0.713   |
| Thyroid disease           | 1.71        | 0.83–3.50   | 0.142   |
| Cataract                  | 1.06        | 0.69–1.63   | 0.784   |
| Gastric cancer            | 1.44        | 0.64–6.08   | 0.612   |
| Hepatitis B               | 3.10        | 1.25–7.68   | 0.014   |
| Low HDL cholesterolemia   | 1.41        | 0.97–2.05   | 0.067   |
| Rhinitis                  | 1.78        | 1.26–2.51   | 0.001   |
| Chronic otitis media      | 1.34        | 0.74–2.43   | 0.328   |
| Chronic sinusitis         | 14.55       | 10.06–21.05 | <0.001  |
| HDL (<40 mg/dL)           | 0.82        | 0.62–1.10   | 0.192   |
| GOT (>40 IU/L)            | 1.82        | 0.86–3.81   | 0.113   |
| BUN (>24 mg/dL)           | 1.90        | 0.92–3.93   | 0.080   |
| Lead (>10 μg/dL)          | 1.07        | 0.38–3.04   | 0.888   |
| Mercury (>15 μg/dL)       | 1.20        | 0.42–3.34   | 0.730   |

OR, odds ratio; CI, confidence interval; HDL, high density lipoprotein; GOT, glutamic oxaloacetic transaminase; BUN, blood urea nitrogen; each exposure variable is adjusted for all other variables in the table; After conversion of continuous variables to dichotomous variables (normal vs. abnormal) according to their normal laboratory range, blood and urine test results were included in the multivariate logistic model.

doi:10.1371/journal.pone.0062725.t004

obtained from a national survey, KNHANES 2009, which randomly recruited participants.

Prevalence studies based on psychophysical or semi-objective tests can provide more objective information. The prevalence evaluated by psychophysical tests in the Epidemiologic Hearing Loss Study was much higher than that obtained by questionnaires. The gap between the prevalence of self-reported olfactory dysfunction and that of semi-objective olfactory dysfunction increased with age. [4] This suggests that elderly persons would be likely to be unaware of their impaired sense of smell. The sensitivity of subjective olfactory dysfunction was low (20%) but the specificity was very high (94%). Furthermore, the sensitivity of subjective olfactory dysfunction decreased with age. [4] Another study also showed that self-reported olfactory dysfunction had low sensitivity (43.9%) and high specificity (85.4%). [5] These findings suggest that many people with an impaired sense of smell may be unaware of their olfactory problem. Given the low sensitivity of self-reported questionnaire, the present study shows that olfactory dysfunction is not a negligible disease because the self-reported prevalence was as high as 4.5% in our study. Therefore, it is important to identify the prevalence of self-reported olfactory dysfunction to make the patients seek medical attention, initiate medical care and prevent possible complications.

The present study also identified several risk factors associated with olfactory dysfunction. Age, socioeconomic status, environment and some medical conditions were likely to affect the impaired sense of smell. The odds of having olfactory dysfunction increased with age in both men and women in the present study. A previous large population study in the U.S. [1] showed similar results in that the prevalence of self-reported olfactory dysfunction was 1.99%, 2.56%, and 4.6% for subgroups aged 55–64 years, 65–74 years, and 75 years or older, respectively. Several mechanisms may be involved in age-related olfactory dysfunction. Long-lasting injuries to the olfactory mucosa such as various co-morbidities or exposure to environmental olfactory toxicants have been speculated to lead to the replacement of olfactory mucosa with respiratory epithelium. [7] Atrophy of the olfactory bulb and tract occurs in elderly people as the number of glomeruli and mitral cells decreases with age. [8–10] Structural magnetic resonance imaging showed an age-associated volume loss in the mesial temporal lobe which is important for olfactory processing. [11].

With regard to gender, some studies performed in the Western countries showed that olfactory dysfunction was more prevalent in men than in women. [12,13] However, our nationwide study demonstrated that its prevalence was not statistically different between men and women. The different result may be caused by differences in the study design and population. Given that our study samples were selected in a random fashion to represent the whole national population and asked by ENT residents who have been trained for olfactory disorders, there is unlikely to be sexual differences in olfactory dysfunction in Koreans.

As previously reported, [4] lower income was also found to be associated with olfactory dysfunction in our study. People with higher income may have better access to health care or have healthier lifestyles than people with lower incomes. [14] Environmental factors such as an exposure to chemicals or air pollution can also be factors associated with olfactory dysfunction. KNHANES showed that the habitual exposure to air pollutants in their workplaces was significantly associated with the higher prevalence of olfactory dysfunction. This finding suggests that we should also involve olfactory toxicity when the effects of air pollution in the workplaces on our health and quality of life are evaluated. On the other hand, a questionnaire about the habitual exposure to chemicals in their workplaces could not show its detrimental effects on olfaction in our study even if there were some reports for olfactory impairment caused by an occupational exposure to airborne industrial chemicals. [15–18] Tobacco smoking might also be a factor affecting the sense of smell. However, its harmful effects on olfaction are under controversy [5] and we could not observe its significant effects. Some studies have reported adverse effects of smoking on olfactory function, [19,20] whereas other studies reported no effect on olfaction. [21,22] Even if our cross-sectional study failed in identifying the olfactory toxicity of chemicals and smoking, further studies are required after several related factors such as exposure amount and duration are more strictly controlled.
Airway diseases can also affect the sense of smell. Although upper airway diseases such as chronic sinusitis and rhinitis were significantly associated with olfactory dysfunction, lower airway diseases such as bronchial asthma and chronic pulmonary airway disease showed no association. It is well known that hyposmia, dysosmia and dysgeusia are common symptoms in hepatitis. Improvement in olfactory acuity was inversely related to the plasma-bilirubin level and directly related to the plasma-retinol-binding-protein level in acute hepatitis.

To our knowledge, this is the first large population-based study showing that a history of hepatitis B is associated with olfactory dysfunction although its mechanism is unclear. The present study also has some limitations. First, olfactory function was evaluated by questionnaires instead of psychophysical tests. However, as ENT questionnaires were asked by trained ENT residents, the decision of olfactory dysfunction may be clinically quite relevant. Secondly, as this is neither a longitudinal study nor a strictly controlled experimental study, the causal relationship of the risk factors with olfactory dysfunction may be inconclusive. Nevertheless, the results may be reliable because this is a nationwide population-based study all around the country. Thirdly, the control of the diseases which may relate to olfactory dysfunction may be quite relevant. Secondly, as this is neither a longitudinal study nor a strictly controlled experimental study, the causal relationship of the risk factors with olfactory dysfunction may be inconclusive. Nevertheless, the results may be reliable because this is a nationwide population-based study all around the country. Thirdly, the control of the diseases which may relate to olfactory dysfunction may pose influences on results. However, whether those diseases have been well controlled or not could not be evaluated in this study.

In conclusion, our population-based study showed that 4.5% of Korean population suffered from olfactory dysfunction. In addition to ENT diseases and medical conditions, old age, low income and habitual exposure to air pollutants were associated with an increased risk of impaired sense of smell. Given the quite high prevalence of olfactory dysfunction in Korea, further researches for its prevention and management are required.

Acknowledgments
We would like to express our sincerest gratitude and appreciation to 87 residents of the Department of Otorhinolaryngology-Head and Neck Surgery from 45 training hospitals in South Korea and the members of the Korea Centers for Disease Control & Prevention who participated in this survey.

Author Contributions
Study supervision: CSR CHL JWK. Critical revision of the manuscript for important intellectual content: CSR CHL JWK. Conceived and designed the experiments: WHL JWK. Performed the experiments: WHL JHW DKK JWK. Analyzed the data: WHL JHW SA JHL JWK. Contributed reagents/materials/analysis tools: YSC KHL KSK SWK CSR CHL AL. Wrote the paper: WHL JWK.

References

1. Hoffman HJ, Ishii EK, MacTurk RH (1998) Age-related changes in the prevalence of smell/taste problems among the United States adult population. Results of the 1994 disability supplement to the National Health Interview Survey (NHIS). Am N Acad Sci 855: 716–722.

2. Denis L, Norman M (2009) Anosmia: Loss of smell in the elderly. Otalaryngol Clin N Am 42: 123–131.

3. Toller SV (1999) Assessing the impact of anosmia: review of a questionnaire’s findings. Chem Senses 24: 705–712.

4. Murphy C, Schubert CR, Cruickshanks KJ, Klein BE, Klein R, et al. (2002) Prevalence of olfactory impairment in older adults. JAMA 288: 2307–2312.

5. Bramerson A, Johansson L, Ek L, Nordin S, Bende M (2004) Prevalence of olfactory dysfunction: the Skövde population-based study. Laryngoscope 114: 733–737.

6. Nordin S, Bramerson A, Bende M (2004) Prevalence of self-reported poor odor detection sensitivity: the Skövde population-based study. Acta Otolaryngol 124: 1171–1173.

7. Nakashima T, Kimmelman CP, Snoke JF Jr (1984) Structure of human fetal and adult olfactory neuroepithelium. Arch Otolaryngol 110: 641–646.

8. Bhatnagar KP, Kennedy RC, Baron G, Greenberg RA (1987) Number of mitral cells and the bulb volume in the aging human olfactory bulb: a quantitative morphological study. Anat Rec 218: 73–87.

9. Jones N, Ros D (1998) Olfaction: a review. J Laryngol Otol 112: 11–24.

10. Meisami E, Mikhail I, Bain D, Bhatnagar KP (1998) Human olfactory bulb: aging of glomeruli and mitral cells and a search for the accessory olfactory bulb. Ann N Y Acad Sci 855: 708–713.

11. Jernigan TL, Archibald SL, Fennema-Notestine C, Gamst AC, Stout JC, et al. (2001) Effects of age on tissues and regions of the cerebrum and cerebellum. Neurobiol Aging 22: 581–594.

12. Ship JA, Pearson JD, Cruise LJ, et al. (1996) Longitudinal changes in smell identification. The journals of gerontology Series A, Biological sciences and medical sciences; 51: M68–91.

13. Ship JA, Weiffenbach JM (1993) Age, gender, medical treatment, and medication effects on smell identification. Journal of gerontology 1993; 48: M36–32.

14. Schubert CR, Cruickshanks KJ, Fischer ME, Huang GH, Klein BE, et al. (2012) Olfactory impairment in an adult population: the Beaver Dam Offspring Study. Chem Senses 37: 325–334.

15. Gobba F (2006) Olfactory toxicity: long-term effects of occupational exposures. Int Arch Occup Environ Health 79: 322–331.

16. Amoore JE (1986) Effects of chemical exposure on olfaction in humans. In: Barrow CS (ed) Toxicology of the nasal passages. Hemisphere Publishing, Washington, DC, 155–190.

17. Doty RL (ed) (2003) Handbook of olfaction and gustation. Marcel Dekker, New York.

18. Doty RL, Mc Keown DA, Lee WW, Shaman P (1995) A study of the test-retest reliability of ten olfactory tests. Chem Senses 20: 455–456.

19. Weinstock RS, Wright HN, Smith DU (1993) Olfactory dysfunction in diabetes mellitus. Physiol Behav 53: 17–21.

20. Joyner RE (1964) Effect of cigarette smoking on olfactory acuity. Arch Otolaryngol 80: 576–579.

21. Hubert HB, Fabsitz RR, Feinleib M, Brown KS (1980) Olfactory sensitivity in human: genetic versus environmental control. Science;9: 607–609.

22. Venstrom D, Amoore JE (1968) Olfactory threshold in relation to age, sex or smoking. J Food Sci;33: 264–265.

23. Temmel AF, Pahlinger S, Quin C, Munda P, Ferraci P, et al. (2005) Dysfunction of the liver affects the sense of smell. Wien Klin Wochenschr;117: 26–30.

24. Landis BN, Konnerth CG, Hummel T (2004) A study on the frequency of olfactory dysfunction. Laryngoscope 114: 1764–9.

25. Henkin RI, Smith FR (1971) Hyposmia in acute viral hepatitis. Lancet 1: 823–826.