

Original Article

The association between allergic rhinitis and triple H (hyperlipidemia, hypertension, hyperglycemia): a population-based case control study

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Background & objectives: To investigate the association between allergic rhinitis (AR) and triple H (hyperlipidemia (HPL), hypertension (HTN), and hyperglycemia) in Taiwan.

Methods: This population-based case control study was based on data obtained from Taiwan's National Health Insurance Research Database (NHIRD) for the period 2002-2010.

Results: After logistic regression, the results indicated that among AR HPL patients, those aged 35-49 have a higher risk of HTN (aOR 1.158, 95%CI: 1.079-1.244). There was also a risk of HPL in all age groups, with the highest risk among those aged <35 years (aOR 1.609, 95%CI: 1.412-1.833). Males with AR had a higher risk of HTN in all age groups, with the highest risk among those aged 35-49 (aOR 1.222, 95%CI: 1.141-1.308). There was also a higher risk of HPL in all age groups, with the highest risk among those aged <35 (aOR 1.441, 95%CI: 1.288-1.612). There was no association with hyperglycemia.

Interpretation & conclusions: The results of the present study demonstrated that AR is associated with HTN and HPL, but not hyperglycemia.

Keywords: Allergic rhinitis, Hyperlipidemia, Hypertension, Hyperglycemia, Population-Based Case Control Study

INTRODUCTION

Allergic rhinitis (AR) is not only the most widespread disease among adults, but is also one of the most common chronic diseases in the US

[1], with an estimated prevalence as high as 20-40%. Moreover, this prevalence is increasing yearly [2,3]. The Association of Asthma Education of Taiwan indicated that 30-50% of people in Taiwan suffer from AR. AR is a hypersensitivity reaction mediated by immunoglobulin E (IgE) due to exposure to natural allergen [2,4]. The typical symptoms of AR include itchy nose, sneezing, pruritus, nasal obstruction, rhinorrhea, and eye redness [2]. Moreover, coughing, runny nose, ear fullness, sadness, and difficulty falling asleep may

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impact on the quality of life of affected persons. The estimated public health expenditures for AR are as high as 0.2 to 5 billion US dollars [1].

Hypertension (HTN) is one of the most important public health issues in middle- and low-income countries. In many high-income countries, interventions by public health departments have reduced the prevalence of HTN. The World Health Organization estimated the prevalence of HTN worldwide at 29.2% in males and 24.8% in females in 2012, which is equivalent to approximately one billion people in total. HTN is the leading global risk factor with a mortality rate of 13.5% [5] and is a critical factor for many other diseases such as stroke, coronary heart disease, cancers, cardiovascular disease, hyperlipidemia (HPL), and hyperglycemia [6,7,8,9].

HPL is an important public health problem with high incidence and prevalence. The highest prevalence of HPL is in Europe at 54%, followed by the US at 48%. The prevalence of HPL increases significantly with increasing income level of a country. There are 25% and over 50% of adults with HPL in low-income and high-income countries, respectively [10]. The Ministry of Health and Welfare in Taiwan has reported that the prevalence of HPL has increased yearly from 13.8% in 1996 to 16.2% to in 2007 [11], as have associated medical costs. HPL is an important risk factor in various diseases including stroke, coronary heart disease, cardiovascular disease, hyperglycemia, and HTN [8,12,13].

Hyperglycemia is not only one of the top ten causes of death, but is also one of the most important challenges for public health globally [14]. In 2013, global statistics demonstrated that approximately 0.382 billion people suffer from and about 15,000 to 51,000 people die due to hyperglycemia every year [14]. In China, hyperglycemia has become a serious public health issue since 1970 and the overall prevalence and morbidity rates increase with age [15]. Hyperglycemia is also associated with a huge medical cost burden in the US [16,17,18]. Furthermore, hyperglycemia is the principal risk factor for several diseases including coronary heart disease, cardiovascular disease, HTN, and HPL [19,20].

There are several risk factors for HTN including

age, sex, central obesity, alcohol consumption, and family history of HTN or hyperglycemia [21]. The risk factors for HPL are age, hyperglycemia, BMI, HTN, and gender [22,23]. To date, the influence of AR on HTN, HPL, and hyperglycemia remains unclear. The aim of this study was to explore the associations among AR and HTN, HPL, and hyperglycemia in Taiwan using the National Health Insurance Research Database (NHIRD).

Methods

Documalets obtained from the NHIRD for collecting secondhand information for public research purposes were used and this study was approved by the Institutional Review Board of Chung Shan Medical University Hospital (CS2-15106). Participants' information was gathered from 2002 to 2010 using the Longitudinal Health Insurance Database. The subjects were Taiwanese nationals who were alive before 2010. The basic characteristics included age (divided into groups of <35, 35-49, 50-64, and ≥65 years), gender, occupation (classified by insurance category of ID as soldiers and civil servants, general occupation, agriculture and fisheries, low income households, other occupation, and dependent population), level of urbanization, and comorbidities. Comorbidities included cardiovascular disease (430-438), congestive heart failure (428), peripheral vascular disease (433.9), chronic obstructive pulmonary disease (COPD, 490-496), osteoarthritis (715), and triple H (HPL, HTN, and hyperglycemia). Diagnoses of individual diseases, based on diagnostic codes, were classified by ICD-9-CM into HTN (401, 402, 403, 404, 405, 437.2), HPL (272, A189), hyperglycemia (250, A181), and AR (477). Triple H patients with at least two outpatient visits and AR patients with at least 10 outpatient visits were selected.

SAS 9.4 EG (SAS Institute Inc., Cary, NC, USA) was used to analyze the data. The Chi-square test was utilized to compare the basic demographic characteristics between AR and non-AR patients. Multivariate logistic regression was used to examine the associations among AR and HTN, HPL, and hyperglycemia. AR during the period 2001–2010 was regarded as the independent

Table 1. Demographic characteristics of allergic rhinitis-exposed and non-exposed individuals in 2010.

	(n= 807470)	(n= 106080)	Chi-square	P
	No AR	AR		
Gender				
Female	423264 (52.42%)	44128 (48.85%)	414.0704	<0.001
Male	384206 (47.58%)	46202 (51.15%)		
Age				
<35	356242 (44.12%)	36698 (57.64%)	6122.1364	<.0001
35-49	196334 (24.32%)	20647 (17.81%)		
50-64	158049 (19.57%)	20332 (14.26%)		
>= 65	96845 (11.99%)	10232 (10.29%)		
Occupational castegory				
Soldiers and civil servants	40165 (4.97%)	4533 (5.02%)	9631.513	<.0001
General occupation	343464 (42.54%)	29426 (32.58%)		
Agriculture and fisheries	70752 (8.76%)	5254 (5.82%)		
Low income households	19715 (2.44%)	3081 (3.41%)		
Other occupation	74804 (9.26%)	5402 (5.98%)		
Dependent population	258570 (32.02%)	42634 (47.20%)		
Urbanization level				
Highly urbanized	246452 (30.52%)	28445 (31.49%)	222.2527	<.0001
Moderate urbanization	243390 (30.14%)	28132 (31.14%)		
Emerging town	145612 (18.03%)	15668 (17.35%)		
General town	104566 (12.95%)	11571 (12.81%)		
Aged township	13686 (1.69%)	1279 (1.42%)		
Agricultural town	26759 (3.31%)	2509 (2.78%)		
Remote township	24766 (3.07%)	2554 (2.83%)		
Kimen and Lienchiang	2239 (0.28%)	172 (0.19%)		

variable while HTN, HPL, and hyperglycemia were regarded as dependent variables. Adjustmalets were constructed for age, gender, income, and residential area [24]. A P-value of less than 0.05 was considered statistically significant.

Results

Records from 897,800 subjects who were alive before 2010 were analyzed. Table 1 shows the

demographics and characteristics of patients. The percentage of males (48.85%) with AR was greater than the percentage of females with AR (51.15%). Moreover, the majority of patients with AR were less than 35 years old (57.64%, $p < 0.0001$). In terms of occupation, the majority fell into the category of dependent population (47.20%), followed by general occupation (32.58%). As to urbanization level, the majority lived in highly urbanized cities (31.49%,

Table 2. Logistic regression analysis of factors associated with triple H disease. Abbreviation: aOR, adjusted odds ratio; CI, confidence interval. Adjusted for age, gender, occupational category, urbanization level, and comorbidities.

	Logistic regression model					
	Hypertension		Hyperlipidemia		Hyperglycemia	
	aOR	95% CI	aOR	95% CI	aOR	95% CI
Allergic rhinitis (Reference: non-allergic rhinitis)						
Allergic rhinitis exposed	1.086	(1.057-1.116)***	1.296	(1.265-1.329)***	0.826	(0.801-0.852)***
Age in 2010						
	1.081	(1.080-1.082)***	1.037	(1.036-1.037)***	1.039	(1.038-1.039)***
Gender (Reference: female)						
Male	1.318	(1.299-1.338)***	1.042	(1.027-1.057)***	1.172	(1.152-1.192)***
Occupational category (Reference: general occupation)						
Soldiers and civil servants	0.936	(0.907-0.965)***	1.072	(1.040-1.105)***	0.932	(0.896-0.969)***
Agriculture and fisheries	0.845	(0.822-0.868)***	0.574	(0.558-0.590)***	0.874	(0.847-0.901)***
Low income households	0.917	(0.878-0.957)***	0.382	(0.367-0.398)***	0.834	(0.799-0.870)***
Other occupation	0.929	(0.906-0.953)***	0.757	(0.739-0.777)***	1.012	(0.983-1.043)
Dependent population	0.867	(0.850-0.884)***	0.573	(0.562-0.584)***	0.918	(0.897-0.938)***
Urbanization level (Reference: moderate urbanization)						
Highly urbanized	0.965	(0.947-0.983)***	1.093	(1.074-1.113)***	0.924	(0.904-0.944)***
Emerging town	1.045	(1.022-1.068)***	0.903	(0.883-0.923)***	1.004	(0.978-1.030)
General town	1.112	(1.085-1.140)***	0.877	(0.856-0.899)***	0.979	(0.952-1.007)
Aged township	1.139	(1.077-1.204)***	0.868	(0.821-0.918)***	1.002	(0.943-1.064)
Agricultural town	1.253	(1.201-1.306)***	0.851	(0.816-0.888)***	0.990	(0.945-1.038)
Remote township	1.184	(1.133-1.237)***	0.908	(0.869-0.948)***	1.026	(0.977-1.077)
Kimen and Lienchiang	0.883	(0.769-1.014)	1.174	(1.031-1.338)*	0.878	(0.752-1.025)
Comorbidity (Reference: without)						
Hypertension	-	-	4.171	(4.102-4.241)***	2.902	(2.844-2.961)***
Hyperlipidemia	4.157	(4.089-4.225)***	-	-	6.728	(6.610-6.848)***
Diabetes	2.657	(2.604-2.710)***	6.328	(6.216-6.442)***	-	-
Cardiovascular disease	2.865	(2.785-2.947)***	0.905	(0.884-0.927)***	1.207	(1.178-1.236)***
Congestive heart failure	2.699	(2.570-2.834)***	0.658	(0.634-0.682)***	1.175	(1.133-1.219)***
Peripheral vascular disease	1.580	(1.483-1.683)***	1.411	(1.337-1.488)***	1.300	(1.233-1.371)***
COPD	1.196	(1.174-1.218)***	1.026	(1.008-1.045)***	1.014	(0.993-1.035)
Osteoarthritis	1.281	(1.258-1.304)***	1.550	(1.523-1.577)***	0.999	(0.980-1.019)

Abbreviation: aOR, adjusted odds ratio; CI, confidence interval.

Adjusted for age, gender, occupational category, urbanization level, and comorbidities.

Table 3. Logistic regression analysis of factors associated with triple H disease by gender.

	Hypertension		Hyperlipidemia		Hyperglycemia	
	Female aOR (95%CI)	Male aOR (95%CI)	Female aOR (95%CI)	Male aOR (95%CI)	Female aOR (95%CI)	Male aOR (95%CI)
Allergic rhinitis (Reference: non-allergic rhinitis)						
Allergic rhinitis exposed	1.072 (1.031-1.114)	1.114 (1.073-1.156)	1.396 (1.348-1.446)	1.234 (1.192-1.278)	0.896 (0.858-0.936)	0.770 (0.737-0.804)
Age in 2010	1.091 (1.090-1.092)	1.074 (1.073-1.075)	1.045 (1.044-1.046)	1.029 (1.028-1.030)	1.037 (1.036-1.038)	1.041 (1.040-1.042)
Occupational category (Reference: general occupation)						
Soldiers and civil servants	0.806 (0.768-0.847)	1.040 (0.999-1.082)	0.994 (0.949-1.042)	1.138 (1.093-1.185)	0.885 (0.831-0.942)	0.963 (0.915-1.013)
Agriculture and fisheries	0.907 (0.871-0.943)	0.783 (0.754-0.812)	0.595 (0.572-0.619)	0.563 (0.542-0.585)	0.909 (0.870-0.950)	0.835 (0.799-0.871)
Low income households	1.122 (1.044-1.206)	0.873 (0.828-0.922)	0.637 (0.596-0.681)	0.335 (0.318-0.352)	1.094 (1.020-1.173)	0.738 (0.699-0.779)
Other occupation	0.873 (0.84-0.908)	0.970 (0.938-1.002)	0.837 (0.806-0.869)	0.700 (0.677-0.724)	0.956 (0.913-1.001)	1.053 (1.013-1.095)
Dependent population	0.925 (0.900-0.950)	0.771 (0.748-0.794)	0.683 (0.666-0.701)	0.443 (0.431-0.456)	0.950 (0.922-0.980)	0.875 (0.846-0.905)
Urbanization level (Reference: moderate urbanization)						
Highly urbanized	0.927 (0.902-0.952)	1.009 (0.984-1.035)	1.088 (1.060-1.116)	1.107 (1.080-1.136)	0.926 (0.898-0.955)	0.925 (0.897-0.953)
Emerging town	1.046 (1.013-1.081)	1.036 (1.006-1.067)	0.883 (0.855-0.911)	0.913 (0.886-0.941)	1.064 (1.025-1.105)	0.950 (0.916-0.984)
General town	1.159 (1.118-1.201)	1.073 (1.038-1.11)	0.859 (0.830-0.890)	0.896 (0.866-0.927)	1.001 (0.961-1.043)	1.019 (0.935-1.111)
Aged township	1.118 (1.030-1.213)	1.154 (1.068-1.247)	0.831 (0.768-0.898)	0.901 (0.833-0.975)	0.989 (0.908-1.076)	1.019 (0.935-1.111)
Agricultural town	1.362 (1.281-1.448)	1.168 (1.102-1.237)	0.814 (0.767-0.864)	0.891 (0.839-0.945)	0.976 (0.913-1.044)	1.002 (0.939-1.070)
Remote township	1.234 (1.158-1.315)	1.138 (1.072-1.208)	0.896 (0.842-0.954)	0.918 (0.863-0.976)	1.036 (0.966-1.110)	1.014 (0.947-1.087)
Kimen and Lienchiang	0.750 (0.610-0.921)	1.006 (0.833-1.213)	1.169 (0.966-1.413)	1.172 (0.979-1.403)	0.938 (0.752-1.170)	0.829 (0.668-1.030)
Comorbidity (Reference: without)						
Hypertension	-	-	3.587 (3.501-3.674)	4.642 (4.536-4.750)	3.153 (3.062-3.248)	2.678 (2.606-2.753)
Hyperlipidemia	3.586 (3.502-3.672)	4.616 (4.512-4.723)	-	-	6.649 (6.481-6.822)	6.726 (6.563-6.893)
Diabetes	2.927 (2.842-3.014)	2.433 (2.367-2.501)	6.301 (6.140-6.466)	0.955 (0.924-0.987)	-	-
Cardiovascular disease	2.475 (2.374-2.581)	3.269 (3.147-3.396)	0.890 (0.859-0.921)	0.955 (0.924-0.987)	1.271 (1.228-1.316)	1.160 (1.121-1.200)
Congestive heart failure	2.716 (2.529-2.917)	2.608 (2.438-2.79)	2.716 (2.529-2.917)	2.608 (2.438-2.79)	2.716 (2.529-2.917)	2.608 (2.438-2.79)
Peripheral vascular disease	1.620 (1.487-1.764)	1.542 (1.404-1.694)	1.620 (1.487-1.764)	1.542 (1.404-1.694)	1.620 (1.487-1.764)	1.542 (1.404-1.694)
COPD	1.283 (1.249-1.318)	1.151 (1.121-1.181)	1.283 (1.249-1.318)	1.151 (1.121-1.181)	1.283 (1.249-1.318)	1.151 (1.121-1.181)
Osteoarthritis	1.218 (1.189-1.248)	1.282 (1.249-1.317)	1.218 (1.189-1.248)	1.282 (1.249-1.317)	1.218 (1.189-1.248)	1.282 (1.249-1.317)

Abbreviation: aOR, adjusted odds ratio; CI, confidence interval. Adjusted for age, gender, occupational category, urbanization level, and comorbidities.

$p < 0.0001$).

After adjusting for age, gender, occupational category, urbanization level, and comorbidities, the results of logistic regression showed that the probabilities of HTN and HPL increase and are associated with AR, while the probability of hyperglycemia is not associated with AR. The adjusted OR (aOR) of HTN was 1.086 (95%CI: 1.057-1.116), that of HPL was 1.296 (95%CI: 1.265-1.329), and that of hyperglycemia was 0.826 (95%CI: 0.801-0.852). This shows that AR is a risk factor for HTN and HPL, but not for hyperglycemia (Table 2).

Males and females were grouped together and analyzed, adjusting for age, occupational category,

urbanization level, and comorbidities, as shown in Table 3. The results indicated that HPL with AR is associated with higher risks of HTN (aOR 1.072, 95%CI: 1.031-1.114) and HPL (aOR 1.396, 95%CI 1.348-1.446), but not hyperglycemia. Males with AR have higher risks of HTN (aOR 1.114, 95%CI 1.073-1.156) and HPL (aOR 1.234, 95%CI: 1.192-1.278), but not hyperglycemia.

Low income households were associated with higher risks of HTN (aOR 1.122, 95%CI 1.044-1.206) and hyperglycemia (aOR 1.094, 95%CI 1.020-1.173) among HPL patients with AR. Male soldiers and civil servants with AR had higher risks of HTN (aOR 1.040, 95%CI: 0.999-1.082) and HPL (aOR 1.138, 95%CI: 1.093-1.185). Moreover,

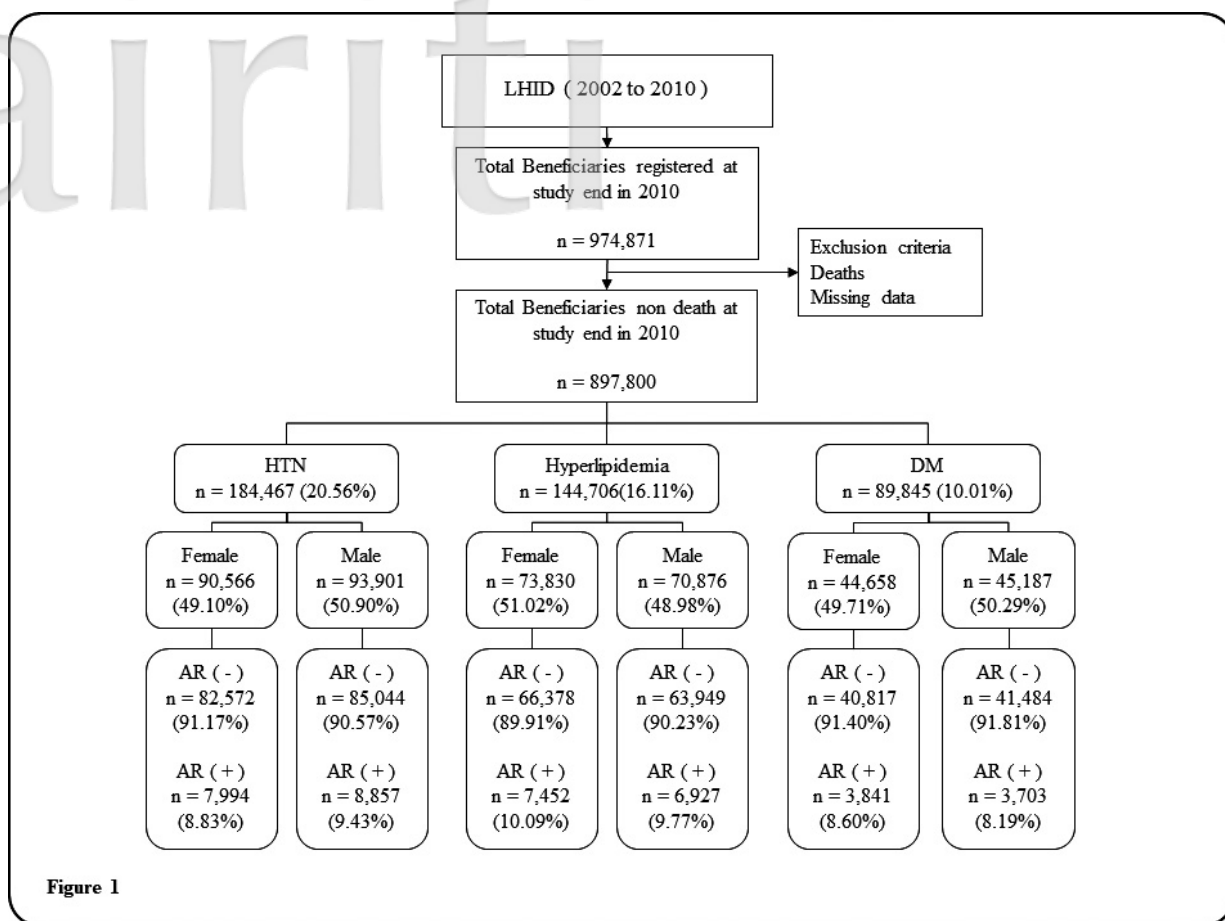


Figure 1. Flow chart of allergic rhinitis and triple H disease (2002–2010).

in terms of urbanization level, agricultural town was associated with a higher risk of HTN (aOR 1.362, 95%CI: 1.281-1.448), whereas highly urbanized area was associated with a higher risk of HPL (aOR 1.088, CI 1.060-1.116) among females with AR. Among males with AR, those living in an agricultural town had a higher risk of HTN (aOR 1.168, 95%CI: 1.102-1.237), whereas those living in a highly urbanized area had a higher risk of HPL (aOR 1.107, 95%CI: 1.080-1.136).

Further analyses were conducted to assess the risks of diseases after logistic regression, adjusting for age, gender, occupational category, urbanization level, and comorbidities. The results indicated that HPL with AR is associated with higher risks of HTN in the 35-49 age group (aOR 1.158, 95%CI: 1.079-1.244), HPL in the <35 age group (aOR

1.609, 95%CI: 1.412-1.833), HPL in the 35-49 age group (aOR 1.340, 95%CI: 1.247-1.441), HPL in the 50-64 age group (aOR 1.371, 95%CI: 1.295-1.452), and HPL in the ≥ 65 age group (aOR 1.272, 95%CI: 1.185-1.366). There was no association with hyperglycemia. Males with AR had higher risks of HTN in the <35 age group (aOR 1.154, 95%CI: 1.020-1.306), the 35-49 age group (aOR 1.222, 95%CI: 1.141-1.308), the 50-64 age group (aOR 1.102, 95%CI: 1.035-1.172), and the ≥ 65 age group (aOR 1.146 95%CI: 1.062-1.236). Risk of HPL was also higher in the <35 age group (aOR 1.441, 95%CI: 1.288-1.612), the 35-49 age group (aOR 1.356, 95%CI: 1.265-1.039), the 50-64 age group (aOR 1.358, 95%CI: 1.275-1.477), and the ≥ 65 age group (aOR 1.204, 95%CI: 1.128-1.285). There was no association with hyperglycemia. These results

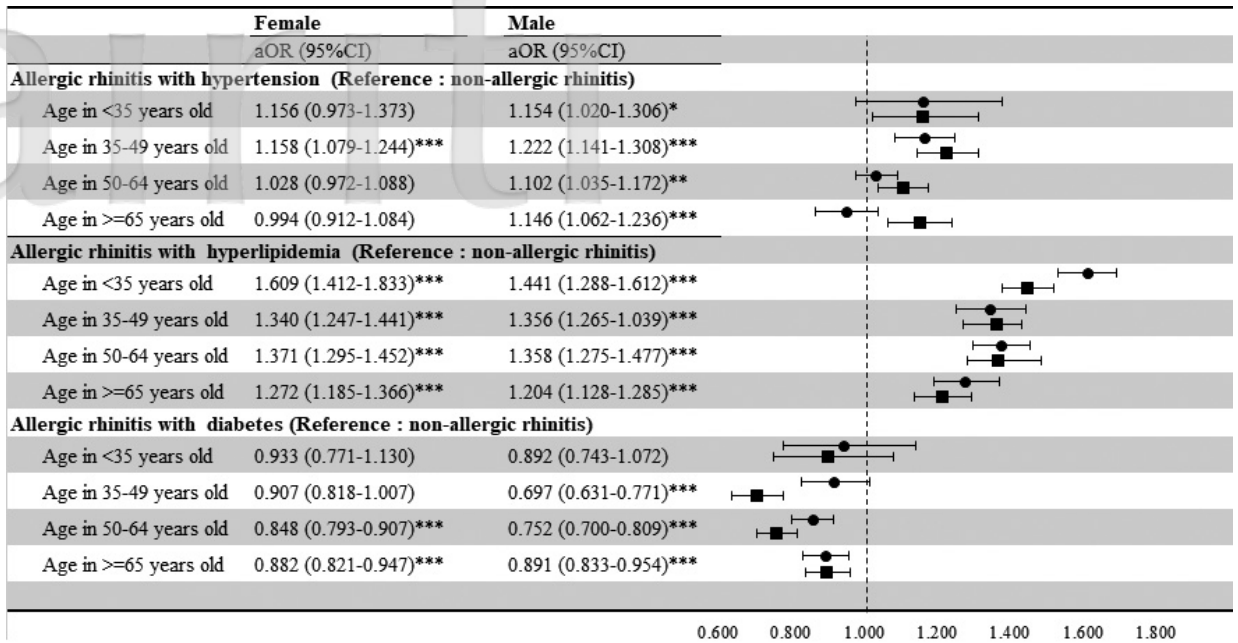


Figure 2. Logistic regression analysis of factors associated with triple H disease by gender and age. Abbreviation: aOR, adjusted odds ratio; CI, confidence interval. Adjusted for age, gender, occupational category, urbanization level, and comorbidities. Circle denotes female aOR and square denotes male aOR.

indicated that males are more susceptible to HTN or HPL associated with AR. Regardless of gender, AR is not a risk factor for hyperglycemia.

Discussion

The results of the present study suggested that AR can lead to HTN and HPL. However, it is not associated with hyperglycemia. The probabilities of patients with AR presenting with HTN and HPL are 1.273 and 1.34 aOR, respectively, which are higher than those of patients without AR.

After adjusting for gender, the ratio of female AR patients with HPL was higher than that of male AR patients with HPL. This is an interesting phenomenon and may be due to the lifestyles of Asian females [25]. In addition, after adjusting for age, occupation, and urbanization level, the risk of HTN was higher among female AR patients living in low-income households in agricultural or remote towns. Among males, military and government personnel living in agricultural and remote towns presented with a higher risk. We were curious as to why there were different occupational risks under

the same regional risk. This may be related to diet. In remote and agricultural towns of southern and central Taiwan, food tends to be salty. It has been confirmed that too much sodium in the diet causes hypertension [26]. However, we cannot explain the difference in occupational risk between males and females or determine whether diet or lifestyle is a risk factor from the information provided in the NHIRD. What is known is that AR is related to the risk of HTN.

No significant correlations were found between AR and HPL among females in different occupational categories, while males working in the military or for the government were at higher risk than males in other occupational categories. As for urbanization level, both sexes were at higher risk in highly urbanized cities. Fast food is readily available in modern cities [27]. Although it is the most convenient choice for people living a busy life, it tends to be greasy. It is known that a diet rich in greasy foods can lead to HPL [27] and this may be the reason why the risk of HPL in urbanized cities is higher. Similarly, we could not glean information about patients' diet or lifestyle from the NHIRD. It is worth noting that males working

in the military or government at risk of AR have higher risks of HTN and HPL than those in other occupations. The diet and lifestyle of military and government personnel should be further explored to explain why their risks of HTN and HPL are higher than those of people in other occupations under the influence of AR. Nevertheless, AR is relevant to the risk of HPL.

Hyperglycemia is not associated with the risk of AR in females or males. Under the influence of AR, females in low-income households are at higher risk than those in other occupational categories, similar to the results for HTN. Studies on the lifestyles and diets of low-income families are warranted to determine the reasons for the higher risks of HTN, HPL, and hyperglycemia.

AR induces asthma and apnea, which can lead to HTN. Pollinosis is significantly associated with HTN after adjusting for age [28] and abnormal IgE increases the incidence of HTN [29]. We hypothesized that AR-induced IgE generation acts as an important risk factor in AR-induced HTN. To now, the mechanism of AR-induced HPL is still unclear. However, histamine was found to be involved in HPL-induced atherosclerosis in an animal model [13]. Therefore, we suggested that AR-induced histamine secretion is a critical risk factor for AR induced-HPL. To now, the mechanism of how AR induces hyperglycemia has not yet been elucidated. IgE-induced allergic diseases can lead to hyperglycemia. Thus, we proposed that AR-induced IgE generation is a critical risk factor in AR-induced hyperglycemia [30]. The results of our study showed that AR is significantly associated with the risks of HTN and HPL, but not with the risk of hyperglycemia.

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