THE ASSOCIATION OF ABO BLOOD GROUPS IN PATIENTS WITH ALLERGIC RHINITIS

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Abstract

ABO blood groups have been associated to increased susceptibility in allergic diseases, including asthma and atopic dermatitis. Although few studies demonstrated the association of ABO blood groups with allergic rhinitis, the evidences are still generally scarce and involved certain population. Therefore, this study aimed to investigate the association of ABO blood groups and allergic rhinitis in the Malaysian population. Further analysis was conducted to investigate the association between ABO blood groups and specific allergens, such as house dust mites, in patients with allergic rhinitis. A total of 163 patients with allergic rhinitis and 163 controls were recruited from AMDI, USM, Penang and HUSM, Kelantan. Blood samples were collected from both groups, and ABO phenotypes were identified using the tube method. The Pearson Chi-square test was employed to determine the association. Statistical significance was set for an alpha error of 5% (p-value < 0.05). O blood was identified as the most common blood group. However, no significant associations of ABO blood groups were observed in the allergic rhinitis patients. The result was also not significant with the O blood group being the highest prevalence and the AB blood group being the least prevalence to house dust mites allergy. This study provides beneficial information for future studies on the predictive role of blood groups in clinical practices. In our study, most of the participants recruited were Malays which might cause genetic bias. Therefore, employing a multi-centered and multiracial approach with larger sample size is recommended for future research.

Keywords: ABO blood groups, Allergic rhinitis, House dust mites

Introduction

Allergic rhinitis (AR) is a symptomatic condition when the epithelial lining of the nose is inflamed that is stimulated by the immunoglobulin E (IgE) mediated-immune response after exposure to the allergens and characterized by one or more symptoms, including blocking of the nose, watery nose, itchiness of the nose, and sneezing (1). AR affects people of all ages and different ethnic groups worldwide, including the younger generation in Asian countries (2). It is estimated that AR has affected about 400 million people worldwide, that is between the range of 10-40% of the world population (3), making it one of the most common chronic conditions globally.

AR is a multifactorial disease and can be caused by many factors. The risk factors of this disease include genetic predisposition and familial history, early life exposure, ethnicity, allergens exposure, pollutants, and social class (3). In addition, the interactions between the environmental and genetic factors have been identified as one of the causes of the increased susceptibility to AR.

ABO blood group has been considered as one of the genetic risk factors associated with the increased susceptibility to asthma in some populations (4). Asthma and AR are recognized as allergic and respiratory diseases which share similar immunopathological mechanisms. Due to this, ABO blood group is potentially linked to the increased susceptibility to AR.

This is what was reported in a scoping review by Dahalan et al. which demonstrated a correlation between ABO blood groups and allergic diseases, including AR, asthma, atopic dermatitis, and food allergies (5). Three out of four studies reviewed in their study indicated the correlation between, mainly, the O blood group and AR, whereas the other one study did not find any significant correlation (5).

The ABO blood group system consists of four main

antigens (A, B, AB, O) known as oligosaccharide antigens which act as a surface marker on the membrane of the red blood cells (5, 6). These antigens are widely expressed on the red cells, saliva and body fluid, as well as several cells and tissue types (5, 6). Although the exact biological function of the blood groups is not fully understood, these antigens were reported to potentially serve as receptors or coreceptors for substances such as microorganisms, toxins, or allergens which may increase the susceptibility of individuals to certain diseases (7).

Although various studies have been conducted on the association of ABO blood groups with AR, there were lack of studies that involved certain populations and thus the evidence are still generally scarce. Therefore, this study aimed to investigate the association of ABO blood groups with AR in the Malaysian population which may provide useful information representing the various populations of the Asian countries. In addition, this study also further investigated the association of ABO blood groups with specific aeroallergen, particularly house dust mites.

Materials and Methods

Study population and criteria

This study is a prospective case-control study. A total of 163 patients and 163 healthy controls were recruited from two medical centers in Malaysia, namely Advanced Medical and Dental Institute(AMDI), Universiti Sains Malaysia (USM), Penang and Hospital USM (HUSM), Kelantan. The inclusion criteria for the patients were given as: i) age from 18 – 60 years old; ii) males and females; and iii) those who had been diagnosed by the ENT specialists according to the ARIA guidelines which include the following symptoms: a) symptoms of allergic rhinitis which occurred more than four days a week for five consecutive weeks; and b) cardinal symptoms such as nasal congestion, watery rhinorrhea, sneezing, pruritus of nose, and eyes. Meanwhile, patients excluded from the study were those with organic and systemic diseases, such as hypertension, diabetis mellitus, bronchial asthma, and any malignancies.

As for the healthy controls, the inclusion criteria were given as: i) age from 18 – 60 years old; ii); without allergic rhinitis; and iii) healthy with no chronic illnesses, such as bronchial asthma, diabetis mellitus, hypertension, and any malignancies.

Sample size calculation

The sample size was calculated based on the double proportion formula using PS Power and Sample Size Calculation Version 3.0 software. The calculation was done based on the proportion of ABO blood groups among patients with allergic rhinitis from a previous study conducted by Topno et al. (8) and based on the requirements for significance level (α), 0.05 and power (1-β), 0.8. An estimation of 10% missing data was added to the final figure. A group of patients with allergic rhinitis and a group of healthy controls were recruited in this study, with 163 cases each, making a total of 326 cases obtained for further data analysis.

Skin prick test

Skin prick test (SPT) was performed on patients with allergic rhinitis. A panel which includes positive and negative controls for the *Blomia tropicalis*, *Dermatophagoides farinae*, and *Dermatophagoides pteronyssinus* allergens was chosen in this study. Prior to the skin prick test, patients were asked to refrain from taking antihistamine for seven days. First, a tape was placed on the patients' forearm and then labelled accordingly. Next, a droplet of tested allergen was placed on their forearm. A lancet was used to prick the skin so that the allergen droplet would seep into the skin. Finally, the results of the test were read after 15 minutes. A positive result was observed when the wheal formation was larger than 3mm in diameter, while a negative result was obtained when the size is otherwise.

Blood collection and blood group typing

A total of 3 ml of whole blood were collected from both 163 patients with allergic rhinitis and 163 healthy controls who fulfilled the inclusion and exclusion criteria. The tube method was employed for blood group typing which was carried out for both cell grouping and serum grouping. For cell grouping, a drop of 3% cell suspension was added into four different test tubes, each contained different antisera (anti-A, anti-B, anti-A, B, and anti-D). For serum grouping, two drops of plasma were added with A, B, and O reference cells in three different test tubes. Then, all test tubes were centrifuged at 1000rpm for 30 seconds. The agglutination reaction was read and interpreted according to the agglutination grading table to determine the blood groups.

Statistical analysis

Statistical analysis was performed by using SPSS version 27.0. The associations between the ABO/rhesus blood groups and allergic rhinitis and specific allergens were determined using the Pearson Chi-square test. The level of significance was set at a p-value of 0.05.

Results

As depicted in Figure 1, the highest prevalence of the blood groups found in patients with allergic rhinitis was the O blood group with 66 cases (40.5%), followed by the B blood group with 50 cases (30.7%), A blood group with 40 cases (24.5%), and AB blood group with 7 cases (4.3%). In healthy controls, a similar pattern of ABO blood group distribution was observed in which the highest number was recorded by the O blood group with 66 cases (40.5%), followed by the B blood group with 49 cases (30.1%), A blood group with 33 cases (20.2%), and AB blood group with 15 cases (9.2%) (Figure 1).

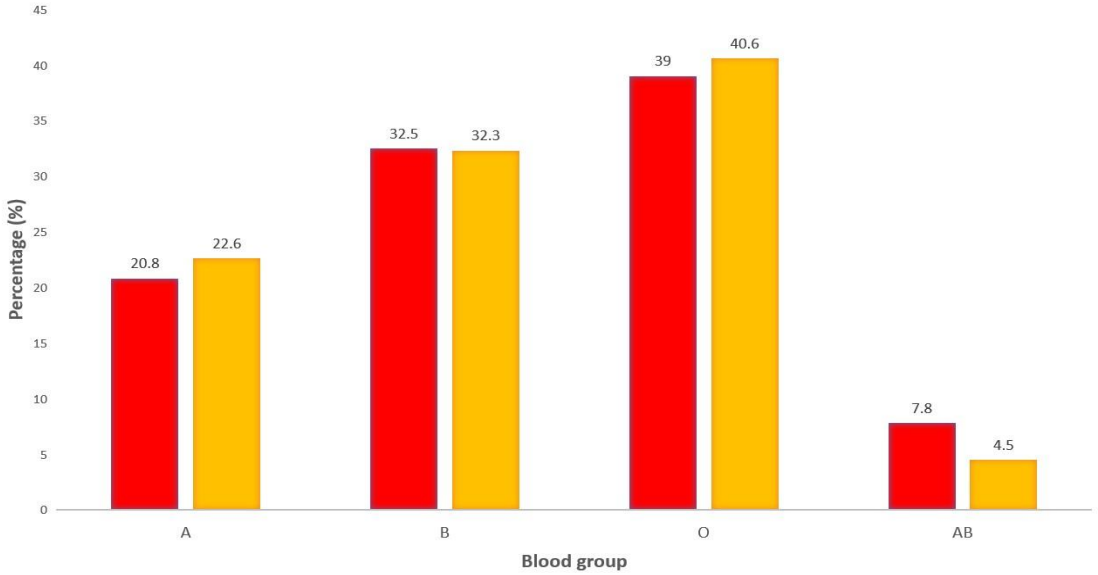

Figure 1: Frequency of ABO blood groups (in %) in AR patients and healthy controls
AR patients, Healthy controls

Then, the association of the ABO blood groups with allergic rhinitis was analyzed using the Pearson Chi-square test, with a level of significance of 0.05. Based on the analysis, the p-value obtained from the association is 0.309, thus indicating that there is no significant association between the ABO blood groups and allergic rhinitis (Table 1).

Table 1: Association of ABO blood group and allergic rhinitis. *Pearson Chi-square test was performed, level of significance= 0.05

Blood group	Patient		Healthy Controls		X^{2*}	df	p-value
	n	%	n	%			
A	40	24.5	33	20.2	3.590	3	0.309
B	50	30.7	49	30.1			
O	66	40.5	66	40.5			
AB	7	4.3	15	9.2			

Further analysis was done to investigate the prevalence of the ABO blood groups in the allergic rhinitis cases by different types of house dust mites, namely *Blomia tropicalis, Dermatophagoides farinae,* and *Dermatophagoides pteronyssinus*. The analysis revealed that the O blood group has the highest prevalence, while the AB blood group has the lowest prevalence in the cases of allergy to house dust mites (Figure 2).

Furthermore, the Pearson Chi square result also demonstrated that none of these house dust mites allergens (*Blomia tropicalis, Dermatophagoides farinae,* and *Dermatophagoides pteronyssinus*) showed a significant association with the ABO blood groups, with the p-values of 0.406, 0.617, and 0.155 respectively (level of significance = 0.05) (Table 2).

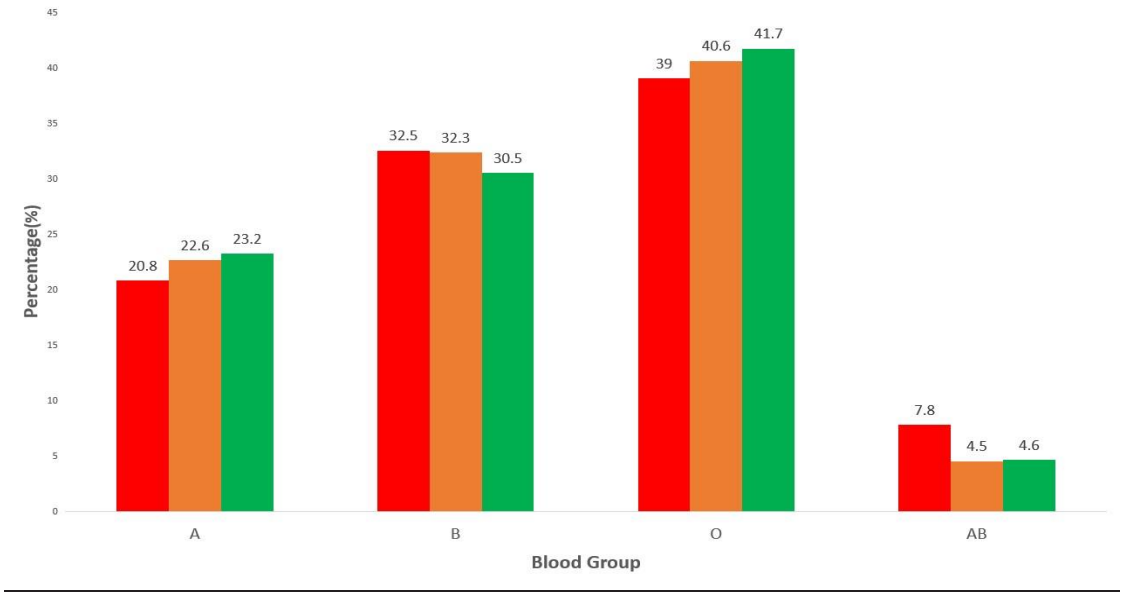

Figure 2: Frequency of ABO blood groups (in %) to house dust mites (*Dermatophagoides pteronyssinus, Dermatophagoides farinae, Blomia tropicalis)* in allerfgic rhinitis patient

Dermatophagoides pteronyssinus, *Dermatophagoides farinae,* *Blomia tropicalis*

Table 2: Association of ABO blood groups and house dust mites (*Dermatophagoides pteronyssinus, Dermatophagoides farina, Blomia tropicalis)* in allergic rhinitis patients. *Pearson Chi-square test was performed, level of significance= 0.05

Blood Groups	*Dermatophagoides pteronyssinus* n *(%)*	*Dermatophagoides farinae* n *(%)*	*Blomia tropicalis* n *(%)*
A	16 (20.8)	30 (22.6)	35 (23.2)
B	25 (32.5)	43 (32.3)	46 (30.5)
O	30 (39)	54 (40.6)	63 (41.7)
AB	6 (7.8)	6 (4.8)	7 (4.6)
x^2	5.24	1.89	2.90
p-value	0.155	0.617	0.406

Discussion

The studies by Falsarella et al. and Topno et al. revealed the significant association between the O blood group and susceptibility to allergic rhinitis (4, 8). Allergic rhinitis and asthma, which are both considered as respiratory and allergic disease, have similar pathophysiology mechanism; thus, it is suggested that genetic factors like the ABO blood group system may influence the susceptibility to asthma, and likewise the susceptibility to allergic rhinitis (4). Findings by these two studies were in agreement with other studies conducted in asthma patients in which similar statistically significant association of the O blood group were observed in Taiwanese (9), Italian children (10), and European adults (11). Furthermore, our study observed the highest prevalence of the O blood group in allergic rhinitis cases, which is consistent with other studies (4, 8, 12). However, our study did not identify any significant association of the ABO blood groups with allergic rhinitis.

Similarly, Kumar et al. and Brachtel et al. also reported the highest number of the O blood group in the allergic rhinitis patients in their studies, but they did not observe any statistically significant difference between the blood groups and the disease (13, 14). Another study by Bijanzadeh et al. found that O blood is the most common blood group of their asthma patients, but the differences among the groups were also not statistically significant (15). Although several studies demonstrated the significant association of the O blood group with allergic rhinitis which may suggest a protective value (4, 8, 12), the possibility of role and mechanism of the ABO blood group system in leading to susceptibility to allergic rhinitis still remains unclear.

Meanwhile, house dust mites are major indoor aeroallergens that can cause allergic reactions. Common house dust mites, such as *Dermatophagoides pteronyssinus, Dermatophagoides farinae,* and *Blomia tropicalis,* were reported as the most prevalent allergens which result in positive reactions in skin prick test among allergic rhinitis patients in Malaysia (16, 17). Therefore, this highlights the importance for research to specifically study on the relationships between the ABO blood groups with these common house dust mites allergens. Based on our results, the O blood group was found to have the highest prevalence, whereas the AB blood group has the lowest prevalence in terms of the allergic rhinitis patients' allergy to house dust mites. Nevertheless, the associations between all the blood groups and house dust mites were not statistically significant. The evidence on the association of the ABO blood groups to specific allergens are indeed very scarce. To the best of our knowledge, this study is the first study that investigated specifically on the associations of the ABO blood groups with house dust mites allergens in allergic rhinitis patients, particularly in Malaysia.

The allergic rhinitis patients and controls who were recruited in this study came from two different geographical area; the first area is AMDI, Penang which is located at the northwest coast of peninsular Malaysia, while the second one is HUSM, Kelantan which is located at the north-eastern corner of Malaysia. According to the Department of Statistic Malaysia's report on "2010 Population and Housing Census of Malaysia", Kelantan's ethnic composition are 95.0% *bumiputra* (including Malays), 3.8% Chinese, and 0.3% Indian, while Pulau Pinang is comprised of 42.5% *bumiputra*, 46.5% Chinese, and 10.6% Indian (18). Evidently in this study, more samples were collected from the *bumiputra* group compared to other races due to the geographical distribution in Malaysia, which may not be indicative of the Malaysian population as a whole. This may contribute to genetic bias, which also possibly explain our result on the statistically insignificant associations of the ABO blood groups with allergic rhinitis. Therefore, further studies that include a larger sample size with multiracial samples and in different settings are needed to develop more conclusive evidence on the prevalence of aeroallergens as well as the association between the ABO blood groups and allergic rhinitis in Malaysia.

Conclusion

Our study is the first study that investigated the association of ABO blood groups with allergic rhinitis in the Malaysian population. The results showed that the O blood group has the highest prevalence of allergic rhinitis, while the AB blood group has the least prevalence of the disease. However, no significant associations of the ABO/rhesus blood groups were observed in patients with allergic rhinitis. It is recommended that future research be undertaken to further explore this association for the benefits in clinical practices. The results provide useful information and preliminary guidance which can be utilized in identifying people who are at risk of developing allergic rhinitis, and thus helpful for developing strategies toward improving the management and prevention of the disease. Nonetheless, employing a multi-centered and multiracial approach with larger sample size is recommended for future research in order to generate more comprehensive and conclusive evidence pertaining to the predictive role of the ABO blood groups as a risk factor of allergic rhinitis.

Acknowledgment

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Ethical Clearance

This study was approved by the Research Ethics Committee of Universiti Sains Malaysia (USM/JEPem/20090472). Written consents were obtained from all participants, including patients and healthy controls.

Competing Interests

The authors declare that there is no conflict of interest in this study.

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