



Blood Group and Incidence of Asthma and Chronic Obstructive Pulmonary Disease

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Abstract

Chronic respiratory diseases are determined by genetic predisposition, and environmental and socioeconomic variables. One genetic factor underlying susceptibility to such diseases can be the ABO blood group system. The purpose of this study was to investigate the hypothesis that there would be a relationship between the blood group and risk of developing asthma and chronic obstructive pulmonary disease (COPD). We reviewed medical history files of patients with the diagnosis of COPD or asthma, including those suffering from a cancerous disease accompanied by asthma or COPD, hospitalized from January 2016 to July 2017. The study involved 248 adult patients (85 women and 163 men; median age 65, range 20–95 years) with COPD (177; 71.4%) and asthma (71; 28.6%) with a known blood type. We found that the most

frequent was blood type A (97; 39.1%) and the least blood type AB (26; 8.0%). The distribution of individual blood types in asthma was not different from that in COPD patients. Significant differences were found between the distribution of O and pooled non-O blood types (A, B, and AB); the pooled category was more frequent in both asthma and COPD patients. We conclude that the blood type is not a prognostic differentiating between the occurrence of asthma or COPD, although both are less common in people with blood type O. Further investigation is required to set the predisposing role of the ABO antigens for chronic respiratory diseases.

Keywords

Asthma · Blood group · Cancer · COPD · Genetic predisposition · Phenotype · Respiratory disease

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1 Introduction

Chronic obstructive pulmonary disease (COPD) and asthma are the most common chronic respiratory diseases; they involve inflammation within the lower airways, leading to bronchial obstruction (Kim and Rhee 2010). Respiratory diseases are the third leading cause of death in the EU. The annual mortality rate for COPD in Poland was 52.1 *per* 100,000 people in 2015 (Global Disease Burden 2013). According to WHO (2017), chronic obstructive pulmonary disease (COPD) affects approximately 210 million people throughout the world, of whom 3 million die each year. COPD has been the third most common cause of death in the world. Estimates show that 2 million people in Poland, 5.3% of the population, suffer from this condition, but as many as 80% of them have not been diagnosed. Some COPD cases are caused later in life by persistent asthma, which worsens health status and hinders the therapeutic process (Mathers and Loncar 2006). As opposed to COPD, asthma usually starts during the first years of life, but its severity does not substantially change over time (Castro-Rodriguez et al. 2000). The incidence of asthma in Poland is 1,250 patients *per* 10,000 people, which means that about 4.5 million Polish people suffer from asthma symptoms (Samoliński et al. 2014). Asthma is a heterogeneous disease. The guidelines emphasize the need to differentiate asthma phenotypes in terms of etiology and clinical issues (GINA 2017). Both asthma and COPD are complex conditions, characterized by a changeable clinical course (Guerra 2009; Kant and Gupta 2008; Seifart and Plagens 2007). They can be regarded as sharing many aspects of pathophysiology, clinical symptoms, and treatment (Gerhardsson et al. 2015). Shaya et al. (2008) have shown that therapy of these diseases requires a considerable financial outlay.

The incidence of respiratory diseases depends on genetic predisposition and environmental factors, such as allergens that favor the development of asthma, cigarette smoke, and the most important cause of COPD, atmospheric air pollution (Chen et al. 2005; Ronchetti et al. 2001;

Kauffmann et al. 1996; El-Mehairy and El-Tarabishi 1966). Other contributors to the development of these conditions include socio-economic factors, in particular poverty and malnutrition marked by a substantial weight loss (Kant and Gupta 2008). Apart from the environmental hazards, a global increase in the incidence of COPD and asthma can be underlain by genetic predisposition (Kalsheker and Chappell 2009; Wood and Stockley 2006). One of the potential genetic underlying risk factors might be having a definite blood type. Hirszfeld and Hirszfeld (1919) demonstrated that the frequency of A and B blood types varies between populations. This observation has become a starting point for considering the relationship between the ABO blood groups and proneness to some diseases (Franchini and Lippi 2015; Franchini and Liumbruno 2013; Anstee 2010; Maurant et al. 1976). The ABO blood type antigens are complex carbohydrate molecules on the extracellular surface of the erythrocyte cell membrane. However, aside from their expression on erythrocytes, these antigens are also strongly expressed on the surface of various human cells and tissues, including the epithelium, sensory neurons, thrombocytes, and vascular endothelium. The clinical significance of the ABO blood groups thus goes beyond transfusion medicine. Several reports have suggested that this system plays a role in the development of cardiovascular, oncological, and other diseases (Cozi et al. 2017; Zhang et al. 2012).

The ABO blood type system may be a genetic factor associated with vulnerability to chronic respiratory diseases in some populations (Chen et al. 2005; Ronchetti et al. 2001; El-Mehairy and El-Tarabishi 1966; Kauffmann et al. 1996). The O and non-O blood types are regarded as genetic contributors to susceptibility to asthma. Denborough and Downing (1968) have sought for the confirmation of the relationship between ABO blood type agglutinins and the occurrence of respiratory allergic diseases, such as asthma and hay fever, in a group of 435 sick, compared with 411 healthy individuals. They show no appreciable differences in the secretory status or

isoagglutinin titer in the serum and saliva depending on the ABO blood types. A similar study, carried out by Brachtel et al. (1979) has compared the blood types of children and adults with asthma and found that A and B blood types are related to various atopic states. Baiardini et al. (2008) have demonstrated that asthma and allergic rhinitis share analogous immunopathologic mechanisms, which indicates that both diseases are manifestations of a single syndrome with a wide spectrum of severity. Bijanzadeh et al. (2011) and Togias (2003) have suggested that genetic and environmental determinants of asthma also entail greater vulnerability to allergic rhinitis.

The majority of studies that consider the potential influence of blood typing on the risk of chronic respiratory diseases date from before 2000, and the most recent reports focus on childhood asthma, which, according to WHO (2003), is one of the most common chronic childhood diseases. Denborough and Downing (1968) have described a significant difference in the frequency of ABO blood types and related secretory phenotypes in adults with asthma. Similar findings have been reported for COPD by Cohen et al. (1977) who have indicated that the absence of blood type B and the presence of type A are related to COPD in white individuals. Other studies have demonstrated a higher frequency of A and B erythrocyte phenotypes in adult patients with various atopic states than that in the control groups. Additionally, O blood type has been found to entail proneness to asthma among Taiwanese and Italian children (Chen et al. 2005; Ronchetti et al. 2001), as well as adult Europeans (Kauffmann et al. 1996). Evidence of a connection between blood types and susceptibility to COPD and asthma is not sufficient to draw explicit conclusions (Liumbruno and Franchini 2013). Therefore, in this study we seek to determine the relationship between the ABO blood groups and the incidences of asthma and COPD in adult patients. Our working hypothesis in the study was that asthma and COPD could be associated with a definite blood type.

2 Methods

The research was performed in line with the Declaration of Helsinki and was approved by the Bioethics Committee of the Pomeranian Medical University in Szczecin, Poland (approval no. KB-0012/20/16).

2.1 Study Design

This study was a retrospective review of the statistical data from the Asseco Medical Management Solutions (AMMS), a public institution that runs an integrated and comprehensive system for hospitals and clinics in Poland, and from medical files of patients with the diagnosis of COPD or asthma, including those suffering from a cancerous disease with concomitant asthma or COPD, hospitalized from January 2016 to July 2017. The analysis concerned the patients whose digital and hardcopy files included information on the ABO blood groups. Data were gathered from 248 patients. The patients were hospitalized in the tuberculosis and pulmonary disease ward (95 patients; 38.3%), general and transplantation surgery ward (49 patients; 19.8%), and urology and urological oncology ward (104 patients; 41.9%) in the Public Provincial Hospital in the city of Szczecin, Poland. The inclusion criterion was the diagnosis of at least one chronic respiratory disease (COPD or asthma) as the main disease, or as a condition coexisting with cancerous diseases. Patients' sex, age, blood type, and comorbidities were obtained from a review of medical files.

2.2 Sociodemographic and Health Structure of Study Sample

Table 1 illustrates the structure of the study sample, including the diagnosis and blood types. The median age of patients was 65 years (min–max: 20–95 years), with no appreciable difference

Table 1 Sociodemographic and clinical features of study patients ($n = 248$)

Age (years)	
Median	65
Q ₁ –Q ₃	60–70
Min–max	20–95
n (%)	
Gender	
Female	85 (34.3)
Male	163 (65.7)
Blood type	
A	97 (39.1)
B	56 (22.6)
O	69 (27.8)
AB	26 (10.5)
COPD	177 (71.4)
Asthma	71 (28.6)
Cancerous diseases	
Renal cancer	42 (34.7)
Bladder cancer	7 (5.8)
Prostate cancer	22 (18.2)
Gastric cancer	3 (2.5)
Pancreatic cancer	3 (2.5)
Colon cancer	18 (14.8)
Breast cancer	26 (21.5)

between men and women. The majority of patients (177; 67.0%) suffered from COPD and asthma (71; 33.0%). One hundred and twenty one patients were hospitalized for cancerous diseases, of whom 40 (33.1%) had asthma and 81 (66.9%) had COPD.

2.3 Statistical Analysis

Data are shown as medians with upper and lower quartiles and minimum-maximum ranges. Distribution of continuous variables was determined using the Shapiro–Wilk normality test. Categorical data are shown as the number and percentage. The Wilcoxon rank–sum test, chi–square test, and Fisher exact test were employed to compare proportions. The odds ratio (OR) with 95% confidence intervals were calculated. The statistical significance was set to $\alpha = 5\%$ ($p < 0.05$).

The analysis was performed using the statistical package R version 3.4.0.

3 Results

The A, B, O, and AB blood types were found in 39.1%, 22.7%, 27.8%, and 10.5% of the patients, respectively. These results differed from those obtained for the general Polish population, where blood type B is found in 17% and O in 37%. The differences in the distribution of blood types between the study sample and the general population were significant ($p = 0.007$).

Asthma was more common among younger patients (below 65 years of age) and COPD was among those over 65 years of age. Over two thirds (49; 69.0%) of asthma patients and less than half of COPD patients (79; 44.6%) aged ≤ 65 . The difference in the age-related prevalence of both diseases was significant ($p < 0.001$) (Table 2).

The distribution of individual blood types in the asthma group did not differ from that in the COPD group of patients ($p = 0.717$) (Table 3). The blood types that predominated in asthma were A (26; 36.6%) and O (22; 31.0%) ($p = 0.02$) and in COPD they were A (71; 40.1%), O (47; 26.6%), and B (42; 23.7%) ($p < 0.001$). We then divided the blood types into two general categories: O and non-O (including A, B, and AB). The non-O category predominated in both asthma ($\text{Chi}^2 = 10.27$, $p = 0.001$) and COPD groups ($\text{Chi}^2 = 38.92$, $p < 0.001$). Hence, we draw a conclusion that the blood type is not a prognostic differentiating between the occurrence of asthma or COPD, although diseases are less common in people with blood type O.

Cancerous disease was observed in 121 (48.8%) of patients. Forty (56.3%) patients with asthma and 81 (45.8%) with COPD had a concomitant cancerous disease. There was no relationship between the incidence of asthma and cancerous disease ($p = 0.286$) or between

Table 2 Relationship between age and sex, and the incidence of asthma, COPD, and cancerous diseases

	Age ≤ 65; n (%)	Age > 65; n (%)	*p <	OR	95% CI
Asthma	49 (69.0)	22 (31.0)	0.001	0.36	0.19–0.67
COPD	79 (44.6)	98 (55.4)	0.001	2.75	1.49–5.21
Cancerous diseases	64 (52.9)	57 (47.1)	0.705	0.91	0.53–1.54
Gender					
Female	45 (52.9)	40 (47.1)	0.302	1.37	0.74–2.51
Male	83 (50.9)	80 (49.1)			

*Fisher's exact test; OR odds ratio; 95% CI 95% confidence intervals

Table 3 Blood type frequency in asthma and chronic obstructive pulmonary disease (COPD)

	Asthma	COPD	Total
Blood type	n (%)	n (%)	n (%)
A	26 (26.8)	71 (73.2)	97 (38)
B	14 (25.0)	42 (75.0)	56 (17)
O	22 (31.9)	47 (68.1)	69 (38)
AB	9 (34.6)	17 (65.4)	26 (8)
Total	71	177	248

Fisher's exact test: $p = 0.717$; $\chi^2 = 9.96$, $df = 3$, $p = 0.02$ (asthma); $\chi^2 = 33.24$, $df = 3$, $p < 0.001$ (COPD)

COPD and cancerous disease ($p = 0.160$). However, we found a significant difference in the incidence of cancerous disease depending on the blood type. Cancerous disease was more frequent among patients with the non-O (A and B) blood types (86; 71.1% patients) than in the O group (35; 28.9% patients) ($p < 0.001$).

3.1 Odds Ratios

The odds ratio for COPD in patients with non-O blood type was significantly higher than in those with blood type O (OR = 1.24, 95% CI: 1.64–2.36), with the 73.4% and 26.6% of patients with either blood type, respectively ($p < 0.05$). The odds ratio for asthma was about the same in patients with non-O and O blood types (OR = 0.81, 95% CI: 0.42–1.56), with the 27.4% and 31.9% of patients with either blood type, respectively ($p < 0.05$).

The odds ratio for asthma in younger patients (≤ 65 years) was significantly higher than in those ≥ 65 years of age (OR = 1.36, 95% CI: 0.19–0.67; $p < 0.001$), with the 38.3% and

18.3% of patients of either age category, respectively ($p < 0.001$). The odds ratio for COPD in patients ≥ 65 years of age was nearly three times as higher as that in younger patients (≤ 65 years) (OR = 2.75, 95% CI: 1.49–5.21), with the 81.7% and 61.7% of patients of either age category, respectively ($p < 0.001$).

The odds ratio for COPD was the same in women and men (OR = 1.37, 95% CI: 0.74–2.51), with the 67.1% and 73.6% of female and male patients, respectively ($p = 0.302$). Likewise, the odds ratio for asthma was the same in women and men (OR = 0.73, 95% CI: 0.40–1.35), with the 32.9% and 26.38% of female and male patients, respectively ($p = 0.302$). The odds ratio for cancerous disease in women was about three times as high as that in men (OR = 2.9, 95% CI: 1.63–5.24) ($p < 0.001$) and it was similar in both age-groups (OR = 0.91, 95% CI: 0.53–1.54).

4 Discussion

The working hypothesis in this study was that respiratory diseases could associate with ABO blood groups. However, the findings failed to support this hypothesis. The only significant finding was that pooled non-O blood types, i.e., A, B, and AB, predominated in patients with asthma as well as COPD. The blood group system is a genetically determined characteristic of the immune system. The system plays an essential, widely described role in transplantology and hemotherapy, but the role it could play in the development of other diseases, particularly of the inflammatory, infectious, or neoplastic vein, is not entirely understood (Guerra 2009; Garratty 2005). The present study

was concerned with the plausible relation of two chronic respiratory disorders, COPD and asthma, with the blood groups. Particularly, COPD is a condition that has barely been studied in this context (Cohen et al. 1980; Kauffmann et al. 1996). Blood type B and O distribution in our study sample differed from the normal distribution assumed for Poland (22% vs. 17% for B, and 27.8% vs. 37% for O). Most asthma patients had blood type A or O, the differences between the two was significant to the advantage of A ($p = 0.02$), while the blood types in COPD patients were more diverse, including A, O, and B ($p < 0.001$). We also found that COPD and asthma were more common among patients with the non-O blood types (i.e., A, B, and AB).

A study conducted by Chen et al. (2005) in Taiwan, encompassing 136 asthmatic children and 161 control subjects, has revealed that blood type O is conducive to the occurrence of asthma. The authors conclude that O may contribute to the development of environmental allergies in children. In contradistinction, Bijanzadeh et al. (2009) have reported that blood groups do not appreciably associates with asthma in the populations of Mysore, Karnataka, and South India. Liunbruno and Franchini (2013) have reviewed the subject and conclude that there is evidence that the blood group system may be at play in various cardiovascular, neoplastic, and infectious disorders. However, diverse and sometimes opposing findings make it hard to draw a definite judgment. On the association side, Wu et al. (2008) have found that non-O blood types are related to vascular disorders, with OR of 1.25, which was confirmed by Franchini et al. (2013) who have described an increased risk of ischemic heart disease in the carriers of these blood types. The incidence of cancer and the ABO blood types has attracted understandable attention. Joh et al. (2012) have reported a non-significant association between non-O blood type and increased risk of renal cell cancer in a combined group of men and women; the association was significant in women evaluated separately. Suadicanani et al. (2007) have

carried out a 16-year-long study to assess the risk of death due to lung cancer, lifestyle, and occupational factors with respect to the ABO phenotype in a group of 3346 men aged 53–74 years. The authors have found that 170 (5.1%) of men died from lung cancer and the death rate was significantly greater in men with blood type O (84; 5.9%) than those with type A (70; 4.9%, or types B/AB (16; 3.2%). In contradistinction, Jaff (2010) has indicated that individuals with blood type O suffer from lung cancer less often than those with type A, which suggests that having type O might provide some protection against lung cancer.

Genetic and epidemiological studies of COPD patients focusing on such variables as age, sex, race, and smoking have pointed to the multifactorial background of the disease (Seifart and Plagens 2007). The presence of blood type A or the absence of type B are quoted by some authors as possible risk factors (Cohen et al. 1980). The knowledge that a multitude of genetic and environmental factors may influence the intensity of pulmonary disorders makes it important to seek for more specific phenotypes that can be tied to the ABO genotype; as exemplified by worse outcomes in females in case of renal cell carcinoma (Joh et al. 2012).

In the present study, we found no statistically significant gender-dependent differences in the distribution of the ABO blood types between men and women. Kauffmann et al. (1996) have assessed the influence of ABO genotype on respiratory variables in patients with chronic lung diseases and demonstrated that the lungs of patients with blood type A function worse. Ronchetti et al. (2001) have investigated the ABO/Secretor phenotype in asthmatic children, which controls mucosal secretion and adhesion of infectious agents in bronchial epithelium, and found that a proportion of O/nonSecretor was greater than that in healthy subjects. The association between O/nonSecretor phenotype and asthma has also been found in adult asthmatics (Kauffmann et al. 1996). Chen et al. (2005) have

indicated that blood type O combined with the Sese gene is a risk factor for asthma in children (OR = 2.7; 95% CI: 1.13–6.03). Ronchetti et al. (2001), on the other hand, have demonstrated a positive correlation between the possibility of developing asthma in children with non-O blood types and the Sese gene during the first 3 years of life. El-Mehairy and El-Tarabishi (1966) have assessed the influence of blood types on the incidence of allergic diseases, including bronchial asthma, in a study of 500 patients. They noticed that blood type AB is more common among the unhealthy participants (7.45%) than in healthy controls (14.2%). In the present study, the majority of individuals with asthma and COPD had blood type A or O. However, non-O blood type visibly predominated over type O among patients with asthma and COPD. The differences between our results and the findings reported by El-Mehairy and El-Tarabishi (1966) may be caused by the difference in blood type distribution between races. Falsarella et al. (2011) have evaluated gender differences concerning the blood types and susceptibility to allergenic factors in adults. The authors reported a significant difference in the frequency of blood type phenotypes between males with allergic rhinitis and healthy males. No such relationship is observed in females. In males, phenotype A protects against allergic rhinitis (OR = 0.44, 95% CI: 0.20–0.94; $p = 0.049$) and blood type O predisposes to it (OR = 2.79, 95% CI: 1.38–5.62; $p = 0.01$).

Our results show that men suffered from COPD more often than women ($p = 0.048$). Another determinant of asthma and COPD was patient age. Asthma was more common among younger people (< 65 years of age) and COPD among those over 65 years of age ($p < 0.001$). Likewise, Rodriguez-Pecchi et al. (2012) have found that men are more often former or current smokers, suffer several-fold more often from COPD, and if they do, they are in severer stages of the disease than women. However, women

have a greater prevalence for COPD without exposure to cigarette smoke than men have (64.7 vs. 7.2%, respectively; $p < 0.001$), which may suggest that women are more sensitive to the development of the disease. That notion finds support in a study of Silverman et al. (2001) who show that women exposed to cigarette smoke in childhood are more likely to suffer from COPD.

We conclude that non-O blood types, i.e., A, B, and AB, predominate in chronic obstructive respiratory diseases, such as asthma and COPD. The corollary is that both asthma and COPD are less common among people with blood type O. However, the blood type is not a prognostic differentiating between the occurrence of asthma or COPD. Further exploration is required concerning the predisposing role of the ABO antigens for chronic respiratory diseases. Nonetheless, unraveling the possible relationship between the blood group and the pathogenesis of respiratory diseases would enhance the predictive power for the development of such diseases.

Conflicts of Interest The authors declare no conflicts of interest in relation to this article.

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