ORIGINAL ARTICLE

Frequency of Asthma and Atopic Diseases in Inflammatory Bowel Disease and Celiac Disease

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ABSTRACT

Objective: To compare the frequency of asthma and allergic diseases in patients with inflammatory bowel disease and Celiac disease using international study of asthma and allergies in childhood questionnaire.

Study Design: Cross-sectional, descriptive study.

Place and Duration of Study: Pediatric gastroenterology outpatient clinics and pediatric pulmonology outpatient clinics, from May 2015 to August 2015.

Methodology: Patients aged between 6 and 18 years with the diagnoses of celiac and inflammatory bowel disease were included in the study. After recording the socio-demographic characteristics of all patients, the International study of asthma and allergies in childhood questionnaire was applied and required information collected.

Results: Eighty-three patients (31 males, 52 females) diagnosed with celiac, 42 patients (24 males, 18 females) diagnosed with ulcerative colitis, and 28 patients (11 females, 17 males) diagnosed with Crohn's disease were included. No significant difference was found between the groups in terms of the frequency of wheezing, wheezing in the last year, lifelong allergic rhinitis, long-term use of nasal steroids, and history of eczema ($p > 0.05$). The frequency of atopic dermatitis was significantly higher in the celiac disease group than the other groups.

Conclusion: The frequencies of asthma and atopy are similar in patients with celiac disease and inflammatory bowel disease.

Key Words: *Asthma, Rhinitis, Eczema, Inflammatory bowel diseases, Celiac disease.*

INTRODUCTION

Asthma is a heterogeneous disease characterised by chronic airway inflammation, which is most commonly seen in children. It is described by variable severity over the time for respiratory symptoms such as wheezing, shortness of breath, chest tightness and cough, and different grades of accompanying expiratory airway obstruction. It has been reported that the prevalence of asthma and allergic diseases are increased in developed countries.[1] There has been an important yet unmet need in terms of interpretation of results and establishment of a relationship between the scientific studies, since no standards have been used to describe allergic diseases and to determine methodology in many epidemiological studies conducted up to now. At this point, the International Study of Asthma and Allergies In Childhood (ISAAC) was suggested as a protocol to facilitate collaboration in the international platform by standardising the epidemiological studies.[2] While the prevalence of asthma is highly variable worldwide, studies conducted using the ISAAC questionnaire reported that the prevalence of wheezing in the last 12 months is in a range between 0.8% and 32.6%.[3]

Th2-type immunity, production of IL-4, IL-5 and IgE in response to common environmental antigens plays a role in the development of atopic asthma associated with eosinophilia. However, Th1-type immunity is responsible for many autoimmune diseases such as celiac disease (CD), inflammatory bowel disease (IBD), insulin-dependent diabetes mellitus and rheumatoid arthritis. Since they develop through different regulatory pathways, it is expected that the frequency of atopic diseases, such as asthma and allergy, should be reduced in autoimmune diseases. However, there are studies that demonstrated increased frequency of asthma and atopic diseases in celiac patients.[4-6] Similarly, there are many studies that demonstrated increased frequency of asthma and atopic diseases in IBD patients.[7-10]

Studies that investigated the relationship of celiac disease with asthma and allergic diseases and found a positive correlation suggest that this relationship may be explained by the genetics, and environmental and social common risk factors of these two diseases.[4-6,11]

Similarly, it has been suggested that there is a relationship between asthma and IBD because of the presence of common risk factors such as not being breastfed as a child, antibiotic use during infancy, genetic factors such as SMAD3 that is involved in the pro-inflammatory pathway, and microbiota.[12,13]

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To the best of the authors' knowledge, there is no published research comparing asthma and atopy frequency in celiac and IBD cases. The aim of this study was to compare the frequency of asthma and atopic diseases using the ISAAC questionnaire in patients with CD and IBD.

METHODOLOGY

This cross-sectional study was performed between May 2015 and August 2015 at the Pediatric Gastroenterology Outpatient Clinic, after approval from the Ethics Committee of the Hospital. Patients aged between 6 and 18 years with the diagnoses of celiac and inflammatory bowel disease were included in the study. Those who declined to participate in this study, and with missing data, were excluded. A validated ISAAC questionnaire was used in the study,[14] containing questions relating to asthma, allergic rhino conjunctivitis, and atopic dermatitis. After obtaining informed consent from the subject and/or his/her guardian, the same physician provided the necessary explanations about the questions to the parents and children. The physician imitated the wheezing sound to facilitate better understanding by the families. The allergic salute was described to the families in the questions relating to allergic rhinitis. Blood was collected from the subjects for total IgE and inhalant panel tests.

For specific IgE-inhalant allergens, tree pollens, betula berrucosa, meadow pollens, weed pollens, house dust, dermatophagoides pteronyssinus, dermatophagoides farinae, fungi, yeast and mold and animal epithelia were investigated. Specific IgE inhalant allergens were determined to be normal or high, based on the reference values. The serum total IgE levels were determined to be normal or high, based on the participants' age.

The SPSS 15.0 for Windows software was used for the statistical analysis. In the descriptive statistics, the normally distributed variables were expressed as mean, standard deviation; whereas, non-normal distributed variables were expressed as median and interquartile range, and the categorical variables were expressed as number and percentage. The comparisons for more than two independent groups were performed using the One-Way ANOVA, if the numerical variables met the normal distribution condition; or using Kruskal-Wallis test, if the numerical variables did not meet the normal distribution condition. The subgroup analyses of more than 2 groups were performed using the Tukey's test for parametric tests, and using Mann-Whitney U-test for non-parametric tests, and interpreted using Bonferroni correction. The rate comparisons in the independent groups were performed using the Chi-square analysis. If the conditions were not met, the Monte Carlo simulation was applied. Statistical alpha significance level was considered as $p < 0.05$.

RESULTS

Of the 153 subjects, [70 (46%) with IBD and 83 (54%) with CD] included in the study, 81 (53%) were females and their mean age was 13.21 ±3.80 years. The demographic characteristics of the subjects are shown in Table I. The number of female patients in the group with CD included in the study was higher compared to the other groups, but the mean age, weight, height, age

Table I: Demographic features of the study groups.

	Celiac disease	Ulcerative colitis	Crohn's disease	p**
Gender [n (%)]				
Male	31 (37.3)	24 (57.1)	17 (60.7)	0.031
Female	52 (62.7)	18 (42.9)	11 (39.3)	
Age				
Median (Q1-Q3)	12 (9-16)	15.5 (12-17)	15 (13.3-16)	0.004
Weight (kg)				
Mean ±SD	38.7 ±15.7	51.9 ±18.7	49.2 ±12.5	<0.001#
Weight percentile				
<3p	26 (31.7)	5 (11.9)	8 (28.6)	0.053*
>3p	56 (68.3)	37 (88.1)	20 (71.4)	
Height (cm)				
Median (Q1-Q3)	144 (130-160)	162 (147.3-171.3)	159 (154.3-166)	<0.001
Height percentile				
<3p	16 (19.5)	4 (9.5)	3 (10.7)	0.588*
>3p	66 (80.5)	38 (90.5)	25 (89.3)	
BMI				
Median (Q1-Q3)	17.6 (15.7-20.5)	19.4 (16.8-22.6)	19.6 (17.1-21.9)	0.050
BMI groups				
Underweight	20 (24.4)	6 (14.3)	7 (25.0)	0.725*
Normal	49 (59.8)	26 (61.9)	17 (60.7)	
Overweight	11 (13.4)	7 (16.7)	3 (10.7)	
Age at diagnosis				
Median (Q1-Q3)	8 (3.5-10)	12 (7.8-15.3)	14 (11-14.8)	<0.001
Follow-up period				
Median (Q1-Q3)	60 (12-93)	24 (12-60)	24 (12-24)	0.006

*BMI = Body mass index; *Chi-square; **Kruskal Wallis test; #One Way ANOVA.*

Table II: Socio-demographic characteristics and the family history of asthma, celiac disease, and inflammatory bowel disease (IBD) in the study groups.

	Celiac disease	Ulcerative colitis	Crohn's disease	p**
Number of people living at home Median (Q1-Q3)	5 (4-6)	4 (4-5)	4 (4-5)	0.077**
Consanguinity n (%)	24 (28.9)	11 (26.2)	8 (28.6)	0.948
Smoke exposure n (%)	43 (51.8)	26 (61.9)	18 (64.3)	0.381
Pets at home n (%)	8 (9.6)	3 (7.1)	7 (25.0)	0.081
Family history of asthma n (%)	19 (22.9)	5 (11.9)	10 (35.7)	0.062
Family history of AR or eczema n (%)	26 (31.3)	7 (16.7)	10 (35.7)	0.139
Family history of Celiac/ IBD n (%)	3 (3.7)	7 (16.7)	4 (14.3)	0.030
Hospital admission due to asthma exacerbation n (%)	4 (4.8)	3 (7,1)	1 (3.6)	0.794

*AR: Allerjic rhinitis; *Chi-square; **Kruskal Wallis test;*

Table III: International study of asthma and allergies in childhood (ISAAC) questionnaire.

	Celiac disease		Ulcerative colitis		Crohn's disease		p*
	n	%	n	%	n	%	
Wheezing (at any time)	24	28.9	10	23.8	7	25.0	0.808
Wheezing (in the last 12 months)	16	19.3	7	16.7	5	17.9	0.936
Exercise-induced wheezing	17	20.5	11	26.2	7	25.0	0.740
Use of asthma medication	17	20.5	9	21.4	6	21.4	0.990
Night-time coughing	12	14.5	8	19.0	6	21.4	0.639
Physician-diagnosed asthma	14	16.9	7	16.7	4	14.3	0.712
Allergic rhinitis	28	33.7	17	40.5	12	42.9	0.606
Allergic rhino-conjunctivitis	21	25.3	13	31.0	10	35.7	0.537
Allegic salute	13	15.7	2	4.8	3	10.7	0.195
Physician-diagnosed allergic rhinitis	7	8.4	3	7.1	1	3.6	0.842
Nasal steroid use (>2 weeks)	15	18.1	5	11.9	6	21.4	0.541
H/o atopic dermatitis	10	12.0	1	2.4	0	0	0.039
Eczema	20	24.1	16	38.1	11	39.3	0.153
Total IgE							
Normal	48	78.7	31	77.5	22	88.0	0.541
High	13	21.3	9	22.5	3	12.0	
Inhalant panel							
Negative	50	82.0	25	65.8	19	79.2	0.172
Positive	11	18.0	13	34.2	5	20.8	

**Chi-square*

at diagnosis and duration of diagnosis were significantly lower compared to the subjects with UC and CD. No significant difference was found between the groups in terms of weight percentile, height percentile, mean BMI values and BMI groups.

The sociodemographic characteristics of the subjects included in the study and the family history for asthma, celiac and IBD are shown in Table II. No significant difference was found between the groups in terms of the number of people living at home, consanguinity, smoke exposure, pets at home, family history of asthma, AR and eczema, and number of hospitalisation for asthma. In this study, when family history of celiac in the celiac group and family history of IBD in the IBD group were questioned, the family history IBD in the UC and CD groups was significantly higher compared to the subjects with CD (p=0.030) alone.

The results of the ISAAC questionnaire applied to the subjects are provided in Table III. When wheezing episode at any time, wheezing episodes in the last 12 months, exercise-induced wheezing, previous use of asthma medications, nocturnal cough, physician-diagnosed asthma, physician-diagnosed AR and long-term (2 weeks or longer) use of nasal steroids were questioned in all subjects by the ISAAC questionnaire, no significant difference was found between the groups (p>0.05). In the questions relating to eczema, the history of atopic dermatitis was statistically significantly higher in the CD group compared to the other groups (p=0.039). No significant difference was found between the groups when frequency of eczema was questioned (p>0.05). No statistically significant difference was found between the total IgE and inhalant panel values of the subjects (p>0.05).

DISCUSSION

While autoimmune diseases such as CD and IBD are associated with T helper cell 1 expression, T helper cell is involved in the pathophysiology of allergic diseases such as asthma. It has been suggested that both autoimmune and allergic diseases can be seen together due to the common genetic risk factors and environmental factors.[4,11,15] Increased incidence of the diseases other than UC point to common environmental risk factors.[3,16] It is suggested that autoimmune and atopic diseases pose a risk for each other according to studies on large series.[4,17] Based on the results of this study that compared the frequency of asthma and atopy in CD, UC and Crohn's disease, using the ISAAC questionnaire, no significant difference was found between the groups in terms of asthma and atopy symptoms and prevalence. The frequency of atopic dermatitis was significantly higher in CD compared to the other groups.

In this study, the number of female patients in the group with CD was higher compared to the IBD group, which is consistent with the literature.[17] The mean age at diagnosis in the celiac group was lower than that of the IBD group, which is also consistent with the literature.[18] Since the mean age in the celiac group was lower than the other groups, the mean weight and height were also lower in the celiac group. The findings that the weight and height percentiles, mean BMI and BMI groups were similar in all subjects, suggests that there is no significant difference between the groups in terms of growth and developmental retardation. While growth retardation is expected in all CD, UC and Crohn's disease groups, no significant difference was found when the groups were compared with each other.[18,19] There are studies in the literature demonstrating that the family history is an

important risk factor in both CD and IBD.[20,21] However, no studies were conducted to compare the frequency of family history in the two patient groups. In the present study, there was a positive family history in both groups, but the rate of family history in the subjects with IBD was significantly higher compared to the subjects with celiac disease.

In literature, majority of the publications support relationship between CD and asthma, allergic rhinitis and atopic dermatitis.[4-6,22] But, there are a few studies that do not support such relationship.[23-24]

Some of the publications investigating the relationship of IBD with asthma, allergic rhinitis and atopic dermatitis suggest a significant relationship between IBD and asthma and atopy, while others found no relationship.[7-10] Although there are some publications that investigated the relationship of celiac and IBD with atopy and asthma, there was no study that compared CD and IBD in terms of asthma and atopy. Therefore, there was opportunity to perform a head-to-head comparison of the results of this study. While there was no significant difference between the CD and IBD patients in terms of the frequency of asthma, allergic rhinitis and eczema, the frequency of atopic dermatitis was significantly higher in the CD group.

The strength of this study is that we believe that our study, in which the frequency of asthma and atopy was investigated in children followed-up with the diagnosis of CD and IBD, provides a significant contribution to the literature. To the best of the authors' knowledge, this is the first study to compare the frequency of asthma and atopy symptoms in CD and IBD. The limitation of our study is the absence of a healthy control group.

CONCLUSION

Children with CD, UC and Crohn's disease had similar frequency of asthma and atopy.

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