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Original Article

Autoantibody Positivity in Children with Chronic Diarrhea

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ABSTRACT

Aim: We aimed to determine the frequency of autoantibody antinuclear (ANA), peripheral anti-neutrophil cytoplasmic antibody (p-ANCA), anti-saccharomyces cerevisiae antibody (ASCA), anti-pancreatic exocrine gland antibody (PAb), goblet cell antibody (GAb) positivities in children with the complaint of chronic diarrhea and inflammatory bowel disease (IBD). We also purposed to explore the role of these autoantibodies in the differential diagnosis of IBD.

Materials and Methods: In our study, serum samples of 51 patients with the complaint of chronic diarrhea and 35 healthy controls were analyzed. Clinical and laboratory data at the time of serum sampling were collected and a differential diagnosis was made as the results of performed tests were recorded. For all patients, ANA, p-ANCA, ASCA, GAb, PAb positivities were evaluated by indirect immunofluorescence. The chronic diarrhea group was divided into two groups, namely, the IBD group and non-IBD group.

Results: In the chronic diarrhea group, 11 (21.6%) patients had ANA, 3 (5.9%) had p-ANCA, 1 (2%) had PAb, 1 (2%) had Gab and 1 (2%) had ASCA positivity. From the 35 cases of the control group, 8 (22.9%) had ANA, 7 (20%) had ASCA positivity. In the control group, ASCA was found to be high (p=0.007). Six cases were diagnosed as IBD; 1 (16.7%) had ANA, 1 (16.7%) had p-ANCA, 1 (2%) had Gab and 1 (2%) had ASCA positivity. ASCA and GAb positivities were significantly more frequent in the IBD group (p=0.006, p=0.006, respectively).

Conclusion: ASCA was determined to be significantly higher in the control group. High positivity in the control group showed that the percentage of nonspecific positivity may be high for this test. ASCA and GAb of those patients with a diagnosis of IBD were found significantly higher. The serologic tests which depend on p-ANCA, ASCA, PAb, GAb can be supportive of diagnoses and differential diagnoses of IBD. Autoantibodies in IBD may be used as a supportive diagnostic tool in selected cases, rather than as the diagnosis of IBD as routine practice.

Keywords: Chronic diarrhea, inflammatory bowel disease, autoantibody, PAb, GAb

Introduction

Diarrhea is one of the most important causes of mortality and morbidity in children all over the world, particularly in developing countries. For children, diarrhea can be defined as an immediate increase in their usual frequency of defecation and a decrease in their usual stool consistency (1). Diarrhea lasting more than four weeks is defined as chronic diarrhea (1).

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Inflammatory bowel diseases (IBD), one of the chronic inflammatory diseases which can involve various areas and layers of the gastrointestinal tract, manifests with remissions and exacerbations. Its exact causative mechanisms are still obscure. Crohn's disease (CD) and ulcerative colitis (UC) are the most common subtypes of IBD. A complete classification is still not possible in 10-15% of cases despite the exclusion of other gastrointestinal diseases by endoscopic, radiological and histopathological examinations, laboratory tests, and patient and family history in the differential diagnosis of UC and CD (2). Although the differential diagnosis of UC or CD in the medical treatment of IBD is not completely crucial, these two diseases differ significantly in terms of prognosis and complications. The role of antibodies against intestinal goblet cells in IBD pathogenesis is still unclear (2). Anti-pancreatic antibodies (PAb), perinuclear anti-neutrophil cytoplasmic antibody (p-ANCA), anti-saccharomyces cerevisiae antibody (ASCA), intestinal goblet cell antibody (GAb), antibodies against extracted nuclear antigens, or antinuclear antibodies are seen not only in CD or UC patients but also in healthy first-degree close relatives of these patients (2,3). Acute phase reactants frequently used for the diagnosis and monitoring of intestinal inflammation have a weak association with intestinal disease activity. The correlation of IBD with p-ANCA or ASCA has been demonstrated in various studies (4-9). Therefore, serological markers have become important in the diagnosis and follow-up of IBD (2).

In our study, the levels of the antinuclear antibody (ANA), serum p-ANCA, ASCA, GAb PAb were examined in order to investigate a possible increase in their frequency compared to a control group and chronic diarrhea patients without IBD.

Materials and Methods

A total of 51 patients with the diagnosis of chronic diarrhea aged between 6 months and 18 years who presented at our clinic between 2009 and 2011, and 35 healthy subjects similarly aged between 6 months and 18 years were enrolled in the study. Previous medical history reviews and physical examinations of the patients were performed after informed consent was obtained from the families during outpatient clinic visits. The presence of consanguinity between parents, duration of breastfeeding, duration of diarrhea, and accompanying symptoms such as abdominal pain, tenesmus, weight loss, fever, bleeding, and aphthous stomatitis were questioned in the medical history of the patients. Patients with underlying chronic diseases other than diarrhea were excluded from the study. Cases with chronic diarrhea were also evaluated as either IBD or non-IBD.

Information on complete blood count, alanine aminotransferase (ALT), aspartate aminotransferase (AST), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), fecal occult blood (FOB), fecal parasite and stool culture were obtained from each patient included in the study. For hemoglobin (Hb), ALT, AST, CRP and ESR, the lower and upper limit values of the measurement method of the biochemistry laboratory were considered as the standard reference range. Abdominal ultrasonography, endoscopy and colonoscopy were performed and biopsy samples were collected and evaluated for eligible cases.

ANA, GAb, PAb, ASCA and p-ANCA were studied using the immunofluorescence (IF) Titerplane technique in the pediatric immunology laboratory for both the patients and the controls. IF assays for ANA were performed using CIBD profile kits (Euroimmun AG, Lubeck, Germany). A serum dilution of 1:100 was made for ANA for the test. For the CIBD profile tests, as substrates, primate intestinal tissues were used to assess intestinal goblet cells, while primate pancreatic tissue, Saccharomyces cerevisiae and primate liver cells were used to assess acinar cells. For the CIBD profile tests, serum dilutions of 1:10 and 1:100 for IgA and serum dilutions of 1:10 and 1:1000 for IgG were used. In the study phase, titers were determined by performing a series of dilutions (1:160, 1:320 and 1:640) when the IF ANA test results were positive. Titers above 1:100 were considered significant.

The study was started after the Ethics Committee approval numbered 09-9/12 dated 10/23/2009 from the Ege University Faculty of Medicine Clinical Trials Local Ethical Committee was obtained.

Statistical Analysis

Statistical analysis was performed using SPSS 17.0 software (SPSS Inc., Chicago, IL, USA). All data were given as mean ± standard deviation and median values [interquartile range (IQR)]. The distribution of the data was assessed using the Kolmogorov-Smirnov test. Student t-test and Mann-Whitney U test were used for the comparisons of the data with and without normal distribution, respectively. A chi-square test was used to compare the group's ratios. Pearson correlation analysis was used to determine the relationships between variables. An alpha error level below 0.05 was considered as statistically significant.

Results

Fifty-one cases with the complaint of chronic diarrhea and 35 healthy subjects were included in the study. Of the patients with chronic diarrhea, 30 (58.8%) were male and 21 (41.2%) were female. The mean age of the patients was 60.9±59.8 [median: 52 (87)] months. Twenty-two (62.9%) of the patients in the control group were male and 13 (37.1%) were female. The mean age of the control subjects was 65.2±52.8 [median: 52 (87)] months (Table I).

Of the 35 subjects in the control group, ANA positivity in eight (22.9%) subjects and ASCA positivity in seven (20%) subjects were determined. No p-ANCA, GAb, PAb positivity was detected. Of the 51 patients presenting with chronic diarrhea, 11 (21.6%) were determined to have ANA positivity, 3 (5.9%) had p-ANCA positivity, 1 (2%) had PAb positivity and 1 (2%) had ASCA positivity (Table I). In the ANA typing of the patients presenting with chronic diarrhea, one fine speckled (granular), one coarse granular, four cytoplasmic and two nucleolar ANA positivities were determined. Of the 11 patients with ANA positivity, 1/100 titer was determined in nine patients and 1/160 titer was determined in two patients.

There was no statistically significant difference between chronic diarrhea and control groups in terms of ANA, p-ANCA, PAb and GAb positivity (p=0.545, p=0.203, p=0.593, p=0.593 respectively) (Table I). ASCA positivity was determined to be significantly higher in the control group when compared with those patients with the complaint of chronic diarrhea (p=0.007) (Table I).

Those patients presenting with chronic diarrhea had an average diarrhea duration of 12.62±23.09 [median: 6 (10)] months. Sixteen (31.4%) patients had consanguineous parents. The clinical and laboratory characteristics of these cases are summarized in Table II.

Endoscopy was performed in 20 (39.2%) of the 51 patients with chronic diarrhea. Endoscopic biopsy findings revealed that five (25%) of 19 cases had IBD, nine (45%) had esophagitis-gastritis-duodenitis and three (15%) had non-specific findings, three (15%) had normal endoscopic findings. Six (11.7%) (4 UC, 2 CD) of the patients presenting with the complaint of diarrhea were diagnosed with IBD. The diagnosis of IBD was based on the first endoscopic biopsy findings in five of these cases and the clinical and laboratory findings obtained at follow-up in one of these cases. Diagnosis distributions other than IBD were recorded as follows: Nine (17.6%) cases with esophagitis-gastritis-duodenitis, four (7.8%) with infection, two (3.9%) with lactose intolerance, three with (5.8%) IgA deficiency, one (1.9%) with hypogammaglobulinemia, one (1.9%) with abetalipoproteinemia, one (1.9%) with cow's milk allergy, one (1.9%) with non-specific colitis, one (1.9%) with lipid malabsorption, one (1.9%) with colitis secondary to congenital cytomegalovirus infection and one (1.9%) with polyp.

The mean age of the patients diagnosed with IBD was 138.1±63 months [median: 145 (104) months] and the mean duration of diarrhea was 7.1±9.1 months [median: 2.5 (8) months]. Four (66.7%) of the six patients diagnosed with IBD were female, and two (33.3%) were male. Of

Table I. Comparison of the demographic and laboratory findings of chronic diarrhea and control groups

	Chronic diarrhea (n=51)	Control (n=35)	p
Age (months)	29 (87)	52 (87)	0.570*
Gender (M/F)	30/21	22/13	0.707**
ANA	11 (21.6%)	8 (22.9%)	0.545**
pANCA	3 (5.9%)	0	0.203**
ASCA	1 (2%)	7 (20%)	**0.007****
PAb	1 (2%)	0	0.593**
GAb	1 (2%)	0	0.593**

*Mann-Whitney U test, **chi-square test. The data were given as median (IQR) values, M: Male, F: Female, ANA: Antinuclear antibody, pANCA: Serum perinuclear anti-neutrophil cytoplasmic antibody, ASCA: Anti-saccharomyces cerevisiae antibody, PAb: Anti-pancreatic antibodies, GAb: Intestinal goblet cell antibody

Table II. Clinical and laboratory characteristics of the cases diagnosed with chronic diarrhea

n=51	n (%)
Abdominal pain	30 (58.8)
Weight loss	24 (47.1)
Growth retardation	22 (43.1)
Fever	19 (37.3)
Bleeding	11 (21.6)
Recurrent aphtha	4 (7.8)
Tenesmus	3 (5.9)
Anemia	19 (31.3)
FOB positivity	9 (17.6)
Parasite in the stool	2 (3.9)
Positive stool culture	1 (2)
CRP positivity	10 (19.6)
Elevated ESR	12 (23.5)

FOB: Fecal occult blood, CRP: C-reactive protein, ESR: Erythrocyte sedimentation rate, n: Number

these six patients, all had abdominal pain (100%) and weight loss (100%), four had a fever (66.7%), and growth retardation (66.7%), and one had tenesmus (16.7%). These six patients with IBD had no recurrent aphthous stomatitis. Of the patients presenting with chronic diarrhea, the ones diagnosed with IBD had significantly higher rates of abdominal pain, weight loss and bleeding (p=0.036, p=0.007, p<0.001 respectively). There was no significant relationship between IBD and fever, growth retardation or tenesmus (p>0.05). The other demographic, clinical and laboratory findings of the 51 patients with chronic diarrhea according to the diagnosis of either IBD or non-IBD are presented in detail in Table III.

Table III. Comparison of demographic, laboratory and clinical data of the cases with inflammatory bowel disease and the other chronic diarrhea

	IBD (n=6)	Other (n=45)	p
Gender (M/F)	2/4 (33.3%/66.7%)	17/28 (37.7%/62.3%)	0.177**
Age (months)	145 (104)	22 (68)	**0.003***
Age of symptom onset (months)	174 (114)	13 (30)	**0.002***
Follow-up period (months)	2.5 (8)	0 (1)	**0.037***
Breastfeeding duration (months)	12 (6.75)	11 (7.5)	0.746*
Duration of diarrhea (months)	2.5 (14)	6 (10)	0.252*
Hemoglobin (g/dL)	9.6 (1.8)	11.60 (1.4)	**0.006***
ALT iu/L	16.0 (18.0)	17.0 (13.5)	0.977*
AST iu/L	27.5 (27.8)	30 (20)	0.471*
CRP (mg/dl)	1 (1)	0 (0)	**0.002***
ESR mm/h	35.0 (24.7)	10.0 (7.5)	**0.000***
Anemia	4 (66.7%)	15 (30%)	0.179**
FOB positivity	5 (83.3%)	4 (8.8%)	**0.000****
Parasite in the stool	1 (16.7%)	1 (2.2%)	**0.006****
Positive stool culture	1 (16.7%)	0 (0%)	**0.006****
CRP positivity	4 (66.7%)	6 (13.3%)	**0.020****
Elevated ESR	6 (100%)	6 (13.3%)	**0.000****
ANA	1 (16.7%)	10 (22.2%)	0.756**
pANCA	1 (16.7%)	2 (4.4%)	0.232**
ASCA	1 (16.7%)	0	**0.006****
PAb	0	1 (2.2%)	0.712**
GAb (n-%)	1 (16.7%)	0	**0.006****

*Mann-Whitney U test, **Chi-square test. The data were given as n (%) and median (IQR). F: Female, M: Male, IBD: Inflammatory bowel disease, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, CRP: C-reactive protein, ESR: Erythrocyte sedimentation rate, FOB: Fecal occult blood, ANA: Antinuclear antibody, pANCA: Serum perinuclear anti-neutrophil cytoplasmic antibody, ASCA: Anti-saccharomyces cerevisiae antibody, PAb: Anti-pancreatic antibodies, GAb: Intestinal goblet cell antibody, n: Number

ANA, p-ANCA and GAb positivities were observed in one patient diagnosed with UC and ASCA positivity was seen in another patient diagnosed with CD. No autoantibody positivity was detected in the other four IBD patients. ANA positivity, p-ANCA positivity and PAb positivity were not significant in IBD (p=0.756, p=0.232 and p=0.712 respectively). ASCA positivity and GAb positivity were significantly higher (p=0.006 and p=0.006, respectively) (Table III). The ANA titer in IBD was found to be significantly higher than the ANA titer in other chronic diarrhea cases (p=0.026). Other autoantibody titers were not significantly higher in IBD (p>0.05).

Treatment and diet were recommended for 25 of the 51 patients with appropriate clinical and laboratory findings. Seven (13.7%) patients were treated with steroid and salazopyrine, nine (17.6%) patients with diet regulations, two (3.9%) cases with H2 receptor blockers and seven (13.7%) patients with antibiotics-antiparasitic agents. Polypectomy was performed for one case with polyps.

ASCA positivity was significantly higher in the control group, and GAb positivity was significantly higher in the IBD group when compared to IBD, other chronic diarrhea and control groups (p=0.001 and p=0.008, respectively) (Table IV).

There was no statistically significant relationship between ASCA, p-ANCA, PAb, GAb positivity, and the age of the patients, age of symptom onset or diarrhea duration. A positive correlation was detected between elevated CRP levels and ASCA, p-ANCA, PAb, GAb positivity (p=0.043, p=0.036, p=0.043 and p=0.043, respectively).

Table IV. Comparison of frequency of autoantibody positivity of the cases with inflammatory bowel disease, the other chronic diarrhea, and control groups

	IBD (n=6)	Other chronic diarrhea (n=45)	Control (n=35)	p
ANA	1 (16.7%)	10 (22.2%)	8 (22.9%)	0.944
pANCA	1 (16.7%)	2 (4.4%)	0	0.106
ASCA	1 (16.7%)	0	7 (20%)	**0.008**
PAb	0	1 (2.2%)	0	0.631
GAb	1 (16.7%)	0	0	**0.001**

Chi-square test. The data were given as n (%), IBD: Inflammatory bowel disease, ANA: Antinuclear antibody, pANCA: Serum perinuclear anti-neutrophil cytoplasmic antibody, ASCA: Anti-saccharomyces cerevisiae antibody, PAb: Anti-pancreatic antibodies, GAb: Intestinal goblet cell antibody, n: Number

There was no statistically significant relationship between ASCA, p-ANCA, PAb, GAb positivity and ALT, AST, Hb, ESR ($p>0.05$).

Discussion

Consistent with other studies, the mean age of those patients diagnosed with IBD in our study was found to be 138.1±63.6 months (10,11). In our study, it was found that diarrhea duration was shorter in patients diagnosed with IBD, which was statistically insignificant. This may be explained by the fact that the disease is diagnosed more rapidly when the findings are more severe despite the shorter duration of diarrhea in IBD patients.

Nowadays, acute phase reactants such as CRP and ESR are used to monitor intestinal inflammation in order to diagnose the disease, to determine its activation and to predict the treatment response. In our study, the rates of elevated ESR levels were found to be 100%, elevated CRP levels were 66.7% and anemia frequency was 66.7% in those patients diagnosed with IBD. Compared to the non-IBD chronic diarrhea group, low levels of Hb and elevated levels of ESR and CRP were determined as statistically significant. These findings were found to be consistent with other studies (12).

Today, it is known that CRP, ESR and other acute-phase reactants frequently used for diagnosis and monitoring of intestinal inflammation have poor correlation with intestinal disease activity. Therefore, serologic markers have become important in the diagnosis and follow-up of IBD. After the detection of ANCA in patients with vasculitis in the 1980s, the correlation between IBD and ANCA in recent years has been highlighted. In the late 1980s, p-ANCA was found to be positive in patients with UC and this was accepted as a subclinical indicator for UC (13). Likewise, IgA and IgG antibodies (ASCA IgA and IgG) to a protein found in the outer wall of Saccharomyces cerevisiae used in the preparation of fermented foods, beer and winemaking were found to be positive in the serum of patients with CD (14). Usually, ASCA positive and ANCA negative serology is suggestive of CD while ASCA negative and ANCA positive serology is suggestive of UC (5).

In various studies, the association between IBD and p-ANCA or ASCA has been frequently demonstrated. In UC patients, the incidence of p-ANCA has been reported to be between 50-80% (5,6,8). In a study conducted by Kovacs et al. (7), 72.3% ASCA positivity was determined in patients with CD. In various pediatric studies, ASCA positivity was found to be between 44-76% in CD (4,9). In a study conducted by Kiliç et al. (5) on the Turkish population, the prevalence of p-ANCA for UC was found to be 65%. The prevalence of ASCA was found to be 63.9% in patients diagnosed with CD and no correlation was found between ASCA and the clinical activity of the disease. ASCA positivity was 43.7% in patients with UC. In the same study, p-ANCA (+) and ASCA (-) tests were found to have a lower positive predictive value, negative predictive value and sensitivity compared to p-ANCA for UC alone. Similarly, the positive predictive value, negative predictive value and sensitivity of p-ANCA (-) and ASCA (+) association were also found to be low (5). In our study, p-ANCA positivity was 16.7% and ASCA positivity was 16.7% in those patients diagnosed with IBD. When non-IBD chronic diarrhea patients and IBD patients were compared, there was no statistically significant difference in p-ANCA positivity. Similar to other studies, ASCA positivity was found to be significantly higher in IBD cases (7,8). There was no significant difference in p-ANCA positivity when our control group and chronic diarrhea group were compared. ASCA was determined to be significantly higher in the control group. The increase in ASCA positivity of the control group suggests that the percentage of nonspecific positivity may be high and the method used may not be efficient in the measurement of this auto-antibody. The positivity in the control group compared to the diarrhea group may also be due to the low number of subjects in the healthy control group.

Although antibodies against pancreatic secretion and exocrine pancreas are also suggested as CD markers, these antibodies have not been demonstrated to be associated with the development of pancreatitis in CD, and have not been proven to have direct effects on the pathogenesis of the disease and have been considered to be the result of a cross-reaction against intestinal flora due to impaired mucosal immune response (15). In some studies, PAb positivity was found to be between 31-40% in patients with CD, and it was concluded that the presence of PAb in CD is a specific marker but its sensitivity is low (3,7,16,17). Stocker et al. (18) showed that the prevalence of pancreatic antibodies is 25% in patients diagnosed with CD within the previous 2.5 years. In addition to this, in those patients diagnosed with CD more than 2.5 years previously, the incidence of the pancreatic antibodies was determined to be 46%. Klebl et al. (16) reported that PAb is a particular marker for CD. However, Koutrabakis et al. (19) reported that PAb is also highly prevalent in UC and not only in CD (41.6 and 24.7%, respectively) and that PAb should be used to differentiate IBD from diseases that cause non-IBD intestinal inflammation rather than CD. In contrast, in a study by Zhang et al. (8), PAB positivity was higher in CD

patients compared to both UC and control patients, and PAb was stated as a specific marker that could be used to differentiate CD from UC. In other recent studies, it was determined that the specificity of PAB positivity in IBD was high but its sensitivity was low (7,20). In our study, PAb positivity was not significantly higher in the 51 patients with chronic diarrhea compared to the control group. Also, in our study, it was shown that PAb positivity was not significantly higher in those patients diagnosed with IBD compared to other chronic diarrhea patients. This may be due to the relatively small number of IBD cases in our study.

The positivity of antibodies against intestinal goblet cells in UC is determined by an indirect IF method using fetal intestinal tissue from appropriate primates. The role of the antibodies against intestinal goblet cells in IBD pathogenesis is still unclear, and quite different results on the prevalence of GAb in IBD have been reported. In various studies, it was determined to be 0-33% in CD, 29-39% in UC and 0-2% in healthy controls (21-23). In one study, it was argued that GAb should be used for the diagnosis of IBD and not IBD classification, and may indicate a genetic predisposition (21). In some studies, GAb was considered as a significant marker in the differentiation between CD and UC, whereas in other studies there was no significant difference in the prevalence of the two diseases (8,21-23). In a study by Kovacs et al. (7), 12.2% of patients with UC and 1.9% of patients with CD were GAb positive. In a study by Homsak et al. (13), 46.4% of patients with UC, 2.3% of patients with CD and 0% of healthy controls were GAb positive. These findings suggest that GAb can be used in the differential diagnosis of IBD. In our study, GAb positivity was determined in one patient with UC and GAb positivity was significantly higher in those patients with IBD compared to the non-IBD cases. When we compared those patients presenting with the complaint of chronic diarrhea with the control group, there was no statistically significant correlation between GAb positivity and chronic diarrhea.

Pancreatic and goblet cell antibodies are significant because of their organ specificity and their association with the disease. Both antibodies have direct pathogenic autoimmunity against intestinal goblet cells in UC and the secretion produced by the pancreas in CD (3). However, neither GAb nor PAb had a significant correlation with either age at diagnosis, duration of the disease, area of involvement, the activity of the disease, acute phase reactants or the drugs used (19,23).

In our study, PAb positivity was determined in a patient with non-IBD chronic diarrhea. There was no statistically significant relationship between PAb positivity and the age of the patients, age of symptom onset or diarrhea duration. The patient with PAb positivity was observed to have a long follow-up period. A positive correlation was determined between PAb positivity and elevated CRP levels. There was no statistically significant relationship between PAb positivity and ALT, AST, Hb, or ESR. There was no statistically significant relationship between GAb positivity and the age of the patients, the age of symptom onset, the duration of the follow-up period or diarrhea duration. A positive correlation was determined between GAb positivity and elevated CRP levels. There was no statistically significant relationship between GAb positivity and ALT, AST, Hb or ESR. This makes the role of both autoantibodies in disease pathogenesis disputable. All these data suggest that these two antibodies are a non-pathogenic phenomenon independent of inflammation rather than contributing to the pathogenesis of IBD.

Study Limitations

In addition, studies on various antibodies as serological markers in IBD have been performed. For example, PAb, p-ANCA, ASCA, GAb, antibodies against extracted nuclear antigens, or antinuclear antibodies have been shown not only in CD or UC patients but also in healthy first-degree close relatives of these patients. These individuals were considered to be at high risk for the development of IBD (3).

Conclusion

In conclusion, in the light of these data, we think that autoantibodies in IBD may be used as an adjunctive diagnostic tool in selected cases, rather than in the diagnosis of IBD as a routine practice.

In a study performed by Kovacs et al. (7) in 152 pediatric patients diagnosed with IBD (103 CD, 49 UC); 72.8% ASCA positivity, 33% p-ANCA positivity, 34% PAb positivity and 79.6% GAb positivity were determined for CD while 26.5% ASCA positivity, 77.5% p-ANCA positivity, 20.4% PAb positivity and 12.2% GAb positivity were determined for UC. In our study, we aimed primarily to investigate autoantibody positivity in chronic diarrhea. There is no study in the literature that evaluates all autoantibodies (p-ANCA, ASCA, GAb, PAb) in childhood chronic diarrhea in relation to IBD. In our study, ASCA positivity was significantly higher in the control group compared to the chronic diarrhea group. There was no statistically significant difference in the prevalence of ANA, p-ANCA, GAb and PAb when both of the groups were compared. ASCA and GAb of those patients with the diagnosis of IBD were found significantly higher, while they were negative in patients with chronic diarrhea.

The ANA titer in IBD was found to be significantly higher than the ANA titer in other chronic diarrhea cases. CRP, as an inflammatory marker was also positively correlated with the titrations of these antibodies.

Antibodies in this context are noninvasive and sensitive markers for disease follow-up in patients diagnosed with IBD. We hope that with the more routine use, they will serve as a useful adjunct to the diagnosis of chronic diarrhea patients suggestive of IBD in larger multicenter study groups.

Ethics

Ethics Committee Approval: The study was started after the Ethics Committee approval numbered 09-9/12 dated 10/23/2009 from the Ege University Faculty of Medicine Clinical Trials Local Ethical Committee was obtained.

Informed Consent: Informed consent was obtained from the families during outpatient clinic visits.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Concept: N.K., G.A., F.Ç., Design: N.K., G.A., F.Ç., Data Collection or Processing: H.T., A.A., Ç.E., Analysis or Interpretation: E.A., N.K., Literature Search: E.A., N.K., Writing: H. T.

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