The Correlation between New Serological Markers and Disease Phenotype and Activation in Inflammatory Bowel Disease

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Abstract

Background:
The aim of the study is to assess the correlation between a new antibody panel that is developed against glycans on Crohn's disease (CD) and ulcerative colitis (UC) differentiative diagnosis and disease properties.

Methods:
In the study, 137 CD and 122 UC patients and 90 controls were included. Anti-saccharomyces cerevisiae IgG (ASCA), anti-laminaribioside IgG (ALCA), anti-chitobioside IgA (ACCA), and anti-mannobioside IgG (AMCA) were tested in serum.

Results:
While at least 1 of the other 3 serological markers was positive in 89% of ASCA-positive patients, at least 1 of the other 3 serological markers was positive in 77% of ASCA-negative patients. Positivity ratio for a single anticarbohydrate was ALCA 18 (22%), ACCA 5 (12%), and AMCA 16 (23%). A significant correlation was found between ASCA positivity ($P<0.001$) in operated patients and between ASCA, ALCA, and ACCA positivity ($P<0.05$) in patients with stricturing and fistulizing CD. According to the ROC analysis, ASCA was found to have the highest area under the curve (0.70-0.82) (correlation coefficient interval 95%). A significant correlation was found between ASCA, ALCA, and ACCA positivity and high serum antibody levels and disease activation ($P<0.05$).

Conclusion:
ASCA, ALCA, and ACCA were found to be correlated with the disease complication and activation in CD. ASCA and ALCA were determined as the best markers in the differentiation between CD and UC.

Keywords:
Antiglycan antibodies, Crohn's disease, Ulcerative colitis

Introduction

Crohn's disease (CD) and ulcerative colitis (UC) are chronic inflammatory diseases of the digestive system. Even though the exact etiology is not known, it is thought that an environmental factor (possibly the microorganisms in the intestinal flora) causes an irregular inflammation in genetically susceptible individuals.[1] It is suggested that inflammatory bowel disease (IBD) is associated with a defect in tolerance

against commensal microorganisms; antigens bind to the receptors on white blood cells, stimulate cellular proliferation, phagocytosis, and cytokine secretion, and thus, they develop an inflammatory response.[2] More recently, novel specific seroreactivity to anti-glycan carbohydrate antibodies, containing anti-laminaribioside carbohydrate IgG antibodies (ALCA), anti-chitobioside carbohydrate IgA (ACCA), and anti-mannobioside carbohydrate IgG antibodies (AMCA) have been included into the armamentarium of current serological markers that are likely to be detected.[3] Some studies have investigated their capability to the diagnosis of CD and to differentiate CD from UC. Recent evidence has also proved that high levels of anti-glycan antibodies may lead to complicated disease behavior and a higher probability of disease-related surgery in CD.[4,5] The presence of anti-glycans most probably leads to developing a complicated IBD behavior and thus increases the risk of IBD-related surgery.[6] Today, IBD is diagnosed based on the combination of clinical, endoscopic, and histopathological findings. Existing current immunological diagnostic tests for IBD cannot detect all such patients.[7]

This study was conducted to examine serum levels of newly discovered anti-glycan antibodies, anti-laminaribioside IgG (ALCA), anti-chitobioside IgA (ACCA), and anti-mannobioside IgG (AMCA) and previously used anti-saccharomyces cerevisiae IgG (ASCA) and to investigate whether these markers are beneficial in differential diagnosis of CD and UC, disease age, complicated disease type (phenotypic discrimination), disease activity and localization classification.

Materials and Methods
Study Groups
The population of the study included 259 patients (137 with CD and 122 with UC) and 90 healthy controls.

The following criteria were used for the selection of the patient and control groups:

Inclusion criteria for the patient group:) 1) Age over 18 years, (2) Patients diagnosed with IBD endoscopically, histopathologically and/or radiologically and (3) Giving written consent to participate in the trial.

Inclusion criteria for the control group:) 1) Age over 18 years, (2) Those who do not have any known disease and had referred to the polyclinic only for general health check-up, (3) Persons who gave written consent to participate in the research.

Exclusion criteria: (1) Presence of non-IBD bowel diseases (colon malignancy, radiation colitis, ischemic colitis, microscopic colitis, intestinal tuberculosis), (2) Severe kidney, liver, or heart failure, (3) Having any diagnosed malignancy, (4) Those who are pregnant, (5) Patients with known autoimmune disease or vasculitis and (6) Patients diagnosed with primary sclerosing cholangitis

The demographic characteristics of the patients included in the study, known diseases, drugs used, disease localization, disease type and duration, previous operations, smoking and alcohol habits, and whether they had a family history of IBD or colon malignancy were recorded. Systemic examinations of all patients and control groups were performed, and pulse, blood pressure, and temperature were measured. Hemogram, C-reactive protein (CRP), and sedimentation levels were recorded from the files of those who agreed to participate in the study. Colonoscopy was performed for the participants of the study.

Patients, who were smoking more than seven cigarettes a week for at least 6 months, were defined as active smokers.[8] The demographic and illness characteristics (known diseases, medications used, localization of the disease etc.) were included in the study.

According to the Montreal classification, the age at the disease onset, localization, and type of disease (behavior) of the patients with CD were recorded. Crohn's Disease Activity Index (CDAI) was used for the assessment of the clinical activity of CD.[9] Truelove-Witts activity index was used to assess the clinical activity of UC.[10] The involvement localizations of the disease in the patients were determined according to the existing endoscopic and histopathological data.

Biochemical Analyses
Hemogram, CRP, and sedimentation levels were recorded from the files of the participants. 10 cc venous blood samples were taken to examine ASCA IgG, ALCA IgG, ACCA IgA, and AMCA IgG.

IBDX gASCA IgG ELISA kit was used to detect IgG class antibodies against *Saccharomyces cerevisiae* by

using the ELISA method (Glycominds Ltd., Israel). IBDX ALCA IgG ELISA kit was used to detect IgG class antibodies against laminaribiose carbohydrate (Glycominds Ltd., Israel). IBDX ACCA IgG ELISA kit was used to detect IgA class antibodies against chitobioside carbohydrate (Glycominds Ltd., Israel). IBDX AMCA IgG ELISA kit was used to detect IgG class antibodies against mannobioside carbohydrate (Glycominds Ltd., Israel).

Optical density (OD) was measured at 450 nm by using a Dynex MRXII Revelation double-beam spectrophotometry (Dynex Technologies, Ashford, Middlesex, UK). At first, mean OD was determined for every sample. Reactivity was non-linearly connected to the existing antibody amount. Cutting values were determined according to the manufacturer's recommendations as follows: less than 50 RU for gASCA, less than 60 RU for ALCA, less than 90 RU for ACCA, and less than 100 RU for AMCA.

The sera were incubated with fluorescein isothiocyanate-labeled rabbit anti-human IgG immunoglobulin (INOVA Diagnostics Inc., San Diego, California, USA). The preparations were evaluated by using a Leitz Wetzler Ortophlan microscope (Germany) under ultraviolet.

Statistical Analysis

In the study, statistical analyses were performed by using SPSS software for Windows version 15.0. For the evaluation of data, one-way analysis of variance, Tukey test, independent t test, chi-square test, and Pearson's correlation analysis were used. In order to determine the estimation points of the variables, the areas under the ROC curve, sensitivity, specificity, positive predictive value, and negative predictive value were calculated. Results are reported as 95% confidence interval (CI), with P values. The results were evaluated at significance levels of $P<0.05$, $P<0.01$, and $P<0.001$.

Results

Smoking in patients with UC, and the frequency of appendectomy in patients with CD were significantly higher than the other two groups ($P<0.001$). Table 1 shows the onset features and phenotypes of the CD and UC patients. Colonoscopy involvement sites and

Table 1. Onset properties and phenotypes of patients with CD and UC

	CD, No. (%)	UC, No. (%)
Female	65 (47.4)	55 (45.1)
Male	72 (52.6)	67 (54.9)
Age average	36.28±11.90	44.45±14.08
Not smoking	48 (36.1)	54 (44.3)
Quitted	71 (53.4)	23 (18.9)
Smoking	14 (10.5)	45 (36.9)
Not drinking alcohol	109 (83.2)	93 (76.2)
Quitted	17 (13)	21 (17.2)
Drinking alcohol	5 (3.8)	8 (6.6)
Family history		
None	118 (88.1)	95 (77.9)
CD	11 (8.2)	1 (0.8)
UC	1 (0.7)	17 (13.9)
Colon cancer	4 (3)	9 (7.4)
Extraintestinal involvement	27 (19.7)	12 (10.1)
Not using drugs	33 (24.1)	20 (16.4)
5-aminosalicylic acid	88 (64.2)	101 (82.8)
Corticosteroid	30 (21.9)	15 (12.3)
Immunosuppressants anti tumor necrosis	52 (38)	10 (8.2)
Factor antagonist	4 (2.9)	1 (0.8)
Operation history	50 (36.5)	8 (6.6)
Appendectomy	26 (19)	3 (2.5)
Age of disease onset<17 years	7 (5.1)	Age of disease: 54.52±60.23 months
Between 17 and 40 years old	115 (83.9)	
Over 40 years old	15 (10.9)	
Ileal (L1)	27 (19.7)	
Colonic (L2)	7 (5.1)	
Ileocolonic (L3)	103 (75.2)	
Non-stricturing – non-penetrating (B1)	60 (43.8)	
Stricturing (B2)	39 (28.5)	
Penetrating (B3)	17 (12.4)	
B1+Perianal disease	10 (7.3)	
B2+Perianal disease	6 (4.4)	
B3+Perianal disease	5 (3.6)	
CDAI<150	63 (65.6)	
CDAI≥150	33 (34.4)	
Rectosigmoid involvement		25 (20.5)
Left colon involvement		30 (24.6)
Extensive		14 (11.5)
Pancolitis		53 (43.4)
Mild activity		72 (59)
Moderate activity		41 (33.6)
Heavy activity		9 (7.4)

CD, Crohn's disease; UC, ulcerative colitis; CDAI, Crohn Disease Activity Index.

activation degrees of patients with UC are shown in Table 2. Since there was a difference between the numbers in severe, moderate, and mild involvement, no comparison was made. Antibody levels and antibody positivity rates were compared according to the Truelove Witts criteria. It has been added as a table only because there is a relationship between perinuclear anti-neutrophil cytoplasmic antibodies (pANCA) and clinical activity of the disease. pANCA positivity was significantly higher in moderately and severely active UC patients than in mildly active patients.

While ASCA positivity was significantly higher in patients with CD compared with the other two groups, ASCA, ALCA, ACCA, and AMCA positivities were significantly higher in the CD and UC patients than in the control group ($P \leq 0.001$). Table 3 and Figure 1 show the antibody positivity rates of all groups.

The positive antibody counts in the CD and UC patients were significantly higher than in the control group ($P \leq 0.001$). Table 4 shows the rate of the total positive antibody counts of all groups.

ASCA, ALCA, ACCA, and AMCA antibody levels were significantly higher in CD and UC patients compared with the control group. On the other hand, ASCA, ALCA, and ACCA and their mean values were significantly higher in CD patients compared with UC patients ($P < 0.001$). Figure 1 shows the comparison of anti-glycan antibody levels of all groups.

In differentiation of CD and UC, sensitivity was determined as ASCA: 26%, ALCA: 60%, ACCA: 31%, and AMCA: 50%, respectively; specificity as ASCA: 99%, ALCA: 98%, ACCA: 99%, and AMCA: 99%, respectively; negative predictive value as ASCA: 47%, ALCA: 62%, ACCA: 48%, and AMCA: 57%, respectively; and positive predictive value as ASCA: 97%, ALCA: 98%, ACCA: 98%, and AMCA: 99%, respectively (Table 5). In the ROC analysis, the area under the curve of ASCA and ALCA in the differentiation of CD from UC was mostly determined as 0.763 in ASCA ($P < 0.001$) and 0.646 ($P < 0.001$)

Table 2. The relationship between disease activity and pANCA in UC

UC group		pANCA (-)		pANCA (+)		P value
	Mild	60	% 63	12	% 46	
Truelove-Witts	Moderate	32	% 33	9	% 35	χ^2:7.23
	Heavy	4	% 4	5	% 19	$P=0.027$*

UC, ulcerative colitis; pANCA, perinuclear anti-neutrophil cytoplasmic antibody.
*$P<0.05$.

Table 3. Antibody positivity rates of all the groups

	Control		CD		UC		P value
	No.	%	No.	%	No.	%	
AMCA							
Negative	89	99	68	50	62	51	0.001***
Positive	1	1	69	50	60	49	
ACCA							
Negative	89	99	95	69	97	80	0.001***
Positive	1	1	42	31	25	20	
ALCA							
Negative	88	98	55	40	79	65	0.001***
Positive	2	2	82	60	43	35	
ASCA							
Negative	89	99	101	74	121	99	0.001***
Positive	1	1	36	26	1	1	

CD, Crohn's disease; UC, ulcerative colitis; mannobioside IgG antibodies; AMCA, anti-chitobioside IgA antibodies; ACCA; ASCA, anti-*Saccharomyces cerevisiae* antibodies; ALCA, anti-laminaribioside IgG antibodies.
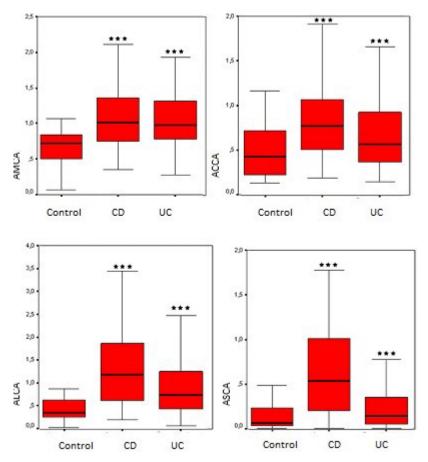***$P \leq 0.001$.

Figure 1. Distribution of antiglycan antibody levels of all the groups. AMCA, anti-mannobioside IgG antibodies; ACCA, anti-chitobioside IgA; ASCA, anti *Saccharomyces cerevisiae* antibodies; ALCA, anti-laminaribioside IgG antibodies.

Table 4. Rate of the total positive antibody counts of all the groups

Antibody positivity count	Control group		CD		UC		P value
	No.	%	No.	%	No.	%	
0	83	92	23	17	34	28	
1	7	8	43	31	40	33	
2			35	26	32	26	0.001***
3			24	17	13	11	
4			12	9	3	2	

CD, Crohn's disease; UC, ulcerative colitis.
***$P \leq 0.001$.

Table 5. Comparison of anti-glycan antibody levels of all the groups

	Control group	CD	UC	P value
	Mean±SD	Mean±SD	Mean±SD	
AMCA	0.66±0.24	1.25±0.89	1.13±0.63	0.000***
ACCA	0.48±0.28	0.87±0.52	0.71±0.47	0.000***
ALCA	0.45±0.32	1.30±0.78	0.95±0.72	0.000***
ASCA	0.18±0.22	0.63±0.48	0.23±0.22	0.000***

CD, Crohn's disease; UC, ulcerative colitis; mannobioside IgG antibodies; AMCA, anti-chitobioside IgA antibodies; ACCA; ASCA, anti-*Saccharomyces cerevisiae* antibodies; ALCA, anti-laminaribioside IgG antibodies.
***$P \leq 0.001$.

in ALCA (Figure 2). The AMCA, ACCA, ALCA, and ASCA antibody values of the CD and UC groups were significantly higher than the control group, and the mean ACCA, ALCA, and ASCA values of the CD group were significantly higher than the UC group *** $P<0.001$

In patients with CD, ASCA antibody levels were significantly higher in terms of ileocolonic involvement, complicated disease, and perianal disease than in the ALCA, ACCA, and AMCA groups ($P<0.001$).

Operational frequency ($P<0.001$), complicated disease course, and CDAI above 150 ($P<0.05$) in ASCA positive cases were significantly higher than the ASCA negative cases. ASCA values of L3 cases were significantly higher than L1 and L2 cases ($P<0.05$). ASCA antibody levels were significantly lower in the patients with inflammatory (B1) disease than in others ($P<0.05$).

The frequency of CS use in ALCA negative cases was significantly higher than in the ALCA positive cases ($P<0.05$). Complicated disease course and CDAI above 150 in ALCA positive cases were significantly higher than in ALCA negative cases ($P<0.05$).

Among patients with CD, it was found that the frequency of ASA use in ACCA negative group was significantly higher than in the ACCA positive group ($P<0.05$). Frequency of non-medication use, complicated disease course, and CDAI above 150 were significantly higher in the ACCA positive group than
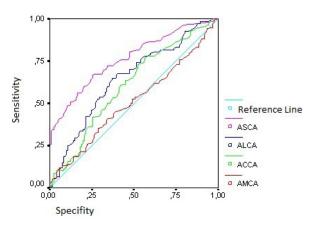

Figure 2. Comparison of antibodies with the ROC Curve Analysis in differentiating Ulcerative colitis and Crohn's disease. ROC, receiver operating characteristic; AMCA, anti-mannobioside IgG antibodies; ACCA, anti-chitobioside IgA; ASCA, anti *Saccharomyces cerevisiae* antibodies; ALCA, anti-laminaribioside IgG antibodies.

in the ACCA negative group ($P<0.05$). The frequency of colonic involvement in the ACCA positive group was significantly higher than in ACCA negative cases ($P<0.01$).

A comparison was made between colonoscopy findings and antibody levels and positivity rates according to the Montreal classification of Crohn's patients. In addition, a comparison was made between the CDAI, antibody levels, and antibody positivity rates (Table 6)

The ages of AMCA positive cases were significantly lower than the AMCA negative cases ($P<0.05$).

Discussion

Serum antibodies against microbial antigens or auto-antigens have been used as biomarkers in predicting disease course, complications, and responses to medications and surgery.[11]

In the present study, it was found that ASCA, ALCA, and ACCA antibody positivity rates and antibody serum levels were higher in the UC and CD patients than in the control group.

There is no ASCA IgG in 15%-40% of CD patients. Thus, it has been suggested that the addition of related glycan markers would increase diagnostic accuracy.[5] In the study by Malickova et al, the total sensitivity of ASCA was 67% for CD. Minimum one of the other serological markers were found to be positive in 56% of CD patients with negative ASCA. Besides, the positivity rate for a single anticarbohydrate (ALCA; 25%, ACCA 27%, and AMCA; 31%) test was lower. The combined use of ASCA and additional anti-carbohydrate tests increased the sensitivity of the immunological diagnosis in CD up to 85%.[12] In the present study, sensitivity for each of four markers in CD was determined as 26% for ASCA, 60% for ALCA, 31% for ACCA, 50% for AMCA, and specificity was found as 99% for ASCA, 98% for ALCA, 99% for ACCA, and 99% for AMCA.

In a study, it was found that although approximately three-fourths of CD patients showed seroactivity for one or more microbial glycan antibodies, reactivity was only found in 1¼ of UC patients. ASCA showed a better differentiating feature between CD and UC than other glycan antibodies. When it was compared with the classic gASCA/pANCA combination, although the

Table 6. Correlation of antibody positivity with disease properties and disease activation in patients with Crohn's disease

	ACCA Negative		ACCA Positive		P value
	No.	%	No.	%	
Patients not using drugs					
Yes	77	81	27	64	
None	18	19	15	36	
5-aminosalicylic acid					
No	27	28	22	52	
Yes	68	72	20	48	
Site of involvement					
Ileal	21	22	6	14	
Colonic	1	1	6	14	
Ileocolonic	73	77	30	72	
Type of involvement					
Non-stricturing – non-penetrating (B1)	48	51	12	29	
Stricturing (B2)	23	24	16	38	
Penetrating (B3)	11	12	6	14	
B1 and perianal disease	6	6	4	9	
B2 and B3 perianal disease	7	7	4	10	
CDAI					
<150	46	73	17	51	
≥150	17	27	16	49	
	ALCA Negative		**ALCA Positive**		**P value**
	No.	%	No.	%	
Corticosteroid					
No	37	67	70	85	0.012*
Yes	18	33	12	15	
Type of involvement					
Non-stricturing – non-penetrating (B1)	31	56	29	35	
Stricturing (B2)	14	25	25	31	
Penetrating (B3)	2	4	15	18	0.011*
B1 and perianal disease	6	11	4	5	
B2 and B3 perianal disease	2	4	9	11	
CDAI					
<150	28	82	35	56	0.011*
≥150	6	18	27	44	
	ASCA Negative		**ASCA Positive**		**P value**
	No.	%	No.	%	
Operation					
No	74	73	13	36	0.000***
Yes	27	27	23	64	
Type of involvement					
Non-stricturing – non-penetrating (B1)	53	52	7	19	
Stricturing (B2)	25	25	14	39	
Penetrating (B3)	11	11	6	17	0.013*
B1 and perianal disease	5	5	5	14	
B2 and B3 perianal disease	7	7	4	11	
CDAI					
<150	50	73	13	46	0.011*
≥150	18	27	15	54	

CDAI, Crohn's Disease Activity Index; ACCA, anti-chitobioside IgA antibodies; ALCA, anti-laminaribioside IgG antibodies; ASCA, anti-*Saccharomyces cerevisiae* antibodies.
*P<0.05, **P<0.01, ***P<0.001.

addition of ALCA resulted in only a minor development in the differentiation of CD from UC, it significantly improved the accuracy of the differentiation of IBD from healthy controls and non-IBD bowel inflammation.[13] In the present study, ASCA, ALCA, and ACCA antibody levels were significantly higher than the control and UC groups. In the UC patients, the positivity rate for a single anticarbohydrate was determined as 8 for ALCA (18.6%), 3 for ACCA (12%), and 21 for AMCA (35%). ASCA and ALCA showed the highest positivity for differentiating CD from UC. According to the ROC analysis, the largest area under the curve was ASCA.

In some studies, it was also shown that ASCA, ALCA, and anti-OmpC were related to ileal disease concerning the localization of the disease, and pANCA was associated with CD in which the isolated colon was involved.[5,14] In their study, Simondi and colleagues found that ASCA level was related to ileal disease.[15] In the present study, it was found that while ASCA antibody level was associated with ileocolonic involvement in CD patients, ACCA was related to colonic involvement.

Papp and colleagues found no significant correlation between the serological biomarkers and sex, familial disease, smoking habits, and extraintestinal involvement. In their study, significantly higher ALCA levels were determined in those with a minimum of one of their first-degree relatives was affected compared with those without family history among CD patients.[16] In our study, while AMCA negative patients among the CD patients were mostly seen in patients between 17 and 40 years old, no correlation between AMCA and other antibodies and sex, smoking, alcohol use, personal history, and extraintestinal involvement was found.

Ferrante et al reported that 373 CD patients had significantly higher antibody responses to ASCA, AMCA, and anti-OmpC by the prolongation in the disease duration.[4] Some studies revealed that the risk factors, such as genetic risk or environmental exposure affecting the correlation between the development of IBD-related antibodies and the onset of the clinical disease, may differ with age. Another possible explanation for this mutual correlation is the phenomenon of continuous B-cell activation and epitope spread. In addition, the data revealed that these antibodies could reflect the pathogenesis of IBD because it was demonstrated that they existed prior to the occurrence of the disease.[17,18] In our study, no correlation between the age of disease onset and serum anti-glycan antibody concentrations could be found. Since the present study is not a follow-up study, it is recommended to conduct prospective and longitudinal studies where serum measurements are performed with serial clinical evaluations in order to see whether the changes in the clinical phenotype of the patient change the serological profile and the associated antibody response.

It has been shown that the stricturing and penetrating phenotype of ASCA IgG were independently associated with the perianal disease of AMCA and the abdominal surgery need for ASCA and ACCA.[19] Ferrante et al found that there was a significant correlation between the increasing levels of all the five markers (ASCA, ALCA, ACCA, AMCA, and anti-OmpC) and the formation of a stricture or fistula in CD patients and the need for abdominal surgery.[4] In this study, a correlation was found between ASCA positivity and operation risk and between ASCA, ALCA, and ACCA positivity and stricturing and fistulizing disease in CD patients. The correlation between the increasing ASCA titer and ileocolonic involvement, stricture, and fistulizing type, and perianal disease was determined.

Data on the stability of serum markers over time is limited. Teml and others found that ASCA titers in mesalamine treatment remained stable over time, and they showed a decreasing tendency in corticosteroid treatment.[20] In the present study, the use of corticosteroid in ALCA negatives and the frequency of ASA use in ACCA negatives were significantly higher than the positive group. In addition, the rate of those, who did not use drugs in the ACCA positive group, was significantly higher. Follow-up studies can determine whether or not the drugs make these markers negative.

In the present study, ASCA sensitivity was low in CD patients compared with other studies. ASCA was the most accurate marker in the differentiation of UC and CD from the healthy controls. The reason is that ALCA, ACCA, and AMCA showed a higher positivity than ASCA in the control group and in the UC

patients. The combined use of ASCA and additional anti-carbohydrate tests increases the sensitivity of the immunological diagnosis in CD. In CD patients, it was found that ASCA, ALCA, and ACCA were associated with a more complicated disease (need for an abdominal surgery due to the occurrence of strictures and fistula) and disease activity. In addition, it was determined that serum antibody titers of the markers increased as the number of antibodies increased in the patients with more than one antibody positivity. A correlation was observed between high ASCA antibody levels and ileocolonic involvement, complicated course, and perianal disease.

The diagnosis of IBD depends on clinical, endoscopic, histological, radiological, and biochemical criteria, which may be invasive, time-consuming, and usually not accepted by patients with IBD.[21] Identification of novel IBD-related antigens can provide an increase in the sensitivity of current diagnostic tools. It may be beneficial to add new anti-glycans in the differential diagnosis of IBD from the healthy controls. The fact that the number of controls is lower than the number of patients is a limitation of the study. Prospective longitudinal studies are needed to determine predictive values for detecting patients requiring aggressive treatment with complicated diseases and distinguishing CD and UC in order for these antibodies to be beneficial in the clinic.

Conclusion

In conclusion, ASCA, ALCA, and ACCA were associated with more complicated disease and activity in Crohn's patients. However, the highest rate of ASCA and ALCA positivity was found in differentiating CD from UC.

Ethical Approval

The protocol of the study was approved by the Ministry of Health, Istanbul Goztepe Training and Research Hospital Research Assessment Commission.

Conflict of Interest

The authors declare no conflict of interest related to this work.

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