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Association Between Food Specific IgG Antibodies with Clinical Activity in Patients with Inflammatory Bowel Disease: A Cross-Sectional Study

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Abstract: *Background and aim:* Inflammatory Bowel Disease (IBD) is an autoimmune disease that is influenced by food, an important factor in accelerating its clinical disease activity because of intestinal inflammation trough formation of antigen-antibody complex. Food-specific IgG examination can identify the types of person foods consumes that are maybe responsible for disease activity. It is useful in treating IBD without risking malnourishment as it is tailored to the individual immune profile. *Methods*: This is a cross-sectional study involving 113 patients diagnosed with IBD by colonoscopy. Examination of serum IgG specific for 220 types of foods was performed using ELISA and immuno-array techniques. Disease clinical activity was assessed using the Mayo Index and Crohn Disease Activity Index. *Results:* The highest proportion of dietary IgG in Chron's disease was peas (100%), barley (97.9%), eggs (95.9%), milk (81.6%), and corn (75.5%); while in ulcerative colitis it was barley (98.4%), peas (96.8%), egg whites (92.2%), corn (82.8%), and prunes (78.1%). In ulcerative colitis, there was a weak negative correlation between cashew nuts IgG (r = -0.347, p=0.041) and chickpeas IgG (r =-0.473, p=0.017) with clinical disease activity; while in Chron's disease, a weak positive correlation with disease activity was seen in barley (r = 0.261, p = 0.042). *Conclusion:* There was a weak negative correlation between cashew and chickpea-specific IgG antibodies with clinical activity of ulcerative colitis, and a weak positive correlation between barley-specific IgG antibodies and Chron's disease clinical activity.

Keywords: Food-Specific IgG Antibodies, Clinical Disease Activity, IBD

1. Introduction

Inflammatory Bowel Disease (IBD) occurs as a result of chronic inflammation triggered by immune system disorders and loss of tolerance to food intake, leaky gut that occurs in the intestinal epithelium, environmental factors, and changes in the composition of gut microbiota due to continuous exposure to food in people who are susceptible to genetic changes, characterized by phases of remission and relapse. IBD is classified into two main types that is, ulcerative colitis (UC) and Crohn's disease (CD) [1-5]. The incidence and prevalence of IBD continue to increase every year throughout the world. There were 6.8 million cases of IBD in 2017 worldwide, with a prevalence of 84.3% per 1000 population [7, 8]. It is estimated that 3 million people (1.3%) of the US population currently suffer from IBD. The incidence of IBD

is also increasing in Asian countries such as Japan, South Korea, and China, following the westernization of lifestyle [7]. Meanwhile, in Indonesia, the prevalence of IBD is 0.88 per 100,000 population [6]. IBD is more common in women (57%) than men (43%), can occur at any age, and is usually diagnosed at the age of 15-40 years [6].

Diet plays an important role in the pathogenesis of IBD. The "Western diet", predominantly consisting of sugar, omega-6 polyunsaturated fats, and fast food; with little amounts of fruits, vegetables, and fibers, can increase pro-inflammatory cytokines, modulate gut permeability, and alter gut microbiota, resulting in low-grade chronic inflammation in the gut, thereby triggering UC and CD [5, 8]. Intestinal inflammation can affect the clinical activity of IBD. Much of today's food supply is processed, modified, stored, and transported over great distances, in contrast to the traditional Eastern (Mediterranean) diet which is rich in fiber and fruits, seeds, and nuts consumed immediately after harvest [6]. Existing dietary studies that place greater emphasis on micronutrients and macronutrients such as that by Sakamoto et al, found that people who habitually consume sweet, fatty foods, including monounsaturated and polyunsaturated fatty acids, are at risk of developing IBD [6, 9]. However, dietary restrictions based on macro and micronutrients carry a blanket risk of causing intolerant patients to become malnourished, aside from the fact that many types of foods must be avoided [5, 10]. Food-specific IgG examination checks IgG antibody levels based on antibody-antigen binding (ELISA technique) from many food antigens so as to obtain types of food that represent intestinal inflammation individually. In this way, patients do not have to avoid foods that do not cause inflammation in their intestines, thus minimizing the risk of malnutrition [6].

Diet can also directly affect the immune system. Dysregulation of the gut mucosal immune system plays an important role in the pathogenesis of IBD [11, 12]. Of the various types of inflammatory cells, CD4+ T cells are thought to play a major role in both the induction and perpetuation of chronic inflammation by producing proinflammatory cytokines [11]. Previous studies have shown that T-associated cytokines helper Th1 (TNF-∝, IFN-γ, interleukin IL-12), as well as Th17-associated cytokines (e.g., IL-17A, IL-21, IL-23), were markedly elevated in the Crohn's disease mucosa. UC appears to exhibit increased production of Th2-associated cytokines such as IL-4 and IL-13. The adaptive immune system plays a major role in the pathogenesis of IBD either through increased pro-inflammatory cytokines by the T-helper (Th) subset or through ineffective anti-inflammatory regulatory T-cells (Tregs). Naive T cells (Th0) activation will differentiate into Th1, Th2, or Th17. Th1 responds to CD pathogenesis while Th2 to UC [13-14]. Pro/anti-inflammatory cytokine imbalance contributes to intestinal mucosal inflammation. Recent studies have found that several proinflammatory cytokines (e.g., IL-12, IL-18, IL-21, and IL-23) are significantly increased in the inflamed mucosa in CD patients and that several inhibitory cytokines (TGF-β, IL-10, IL-25, IL-33, and IL-37) were significantly reduced. The involvement of Tregs in IBD is their ability to inhibit Th1, Th2, and Th17 through the release of IL-10 and TGF cytokines so that they function as anti-inflammatory substances. In IBD, there is a reduction of Tregs in the peripheral blood and colonic mucosa as well as impaired Treg signalling by TGF-β [13-15] Loss of Foxp3+ Treg and FoxP3-IL-10+ CD4+ proteins was also found in the inflamed IBD mucosa. This results in the inability to maintain immune tolerance of the intestinal mucosa and further increases the local intestinal mucosal immune response, which leads to intestinal mucosal injury [1]. Activation of the natural and adaptive immune systems due to the presence of food antigens in the intestinal lumen causes damage to intestinal cells [2-3]. Intestinal inflammation that occurs can be determined using a fecal calprotectin test. Inflammation that occurs in the intestines can result in severe disease symptoms, which can be determined using a clinical activity score.

Dietary antigens have been shown to contribute to the etiopathogenesis of IBD, but their clinical value is still unclear. There is still controversy over the measurement of food IgG as a diagnostic tool for food allergies because food IgG can also increase in healthy people. Food intolerance is an asymptomatic delayed immune response to a specific food antigen mediated by immunoglobulin G (IgG), unlike food allergy, which is an immediate and rapid immune response mediated by immunoglobulin E (IgE). A retrospective study by Cai et al and Wang et al reported that patients with IBD had higher levels of IgG antibodies compared to healthy individuals and significantly elevated IgG antibodies compared to IgE [4, 14]. The benefit of eliminating certain foods from the daily diet was refocused in the present study [10].

2. Method

This study is a descriptive-analytic study with a cross-sectional method to determine the relationship of food-specific IgG antibodies with clinical disease activity in IBD patients. The subjects of this study were patients over 18 years old who were diagnosed with IBD by colonoscopy and histopathology, who did not receive antibiotics, had no history of surgery in the previous 3 months, had no history of cancer, who received outpatient treatment at the Gastroenterology Polyclinic and the Allergy Immunology Polyclinic, dr. Cipto Mangunkusumo Hospital, Jakarta, during the period July to September 2021. There were 113 IBD patients for examination of food-specific IgG serum using 200+ Food IgG tests from Cambridge Nutritional Sciences. Thirty healthy controls were recruited. IBD clinical activity was assessed using the Crohn Disease Activity Index (CDAI) for Crohn's disease and the Mayo Score Index for ulcerative colitis. All patients were also tested with qualitative stool calprotectin assays as a marker of intestinal inflammation.

200+ Food IgG Test is a food intolerance test with semiquantitative ELISA technique for 220 unique food

allergens, including rice, egg, cow milk, jelly, red peanut, Arabic peanut, malt, plum, oat, corn, gliadin, potato, peanut, wheat, and many others. The test was performed according to the operation manual by Cambridge Nutritional Science. IgG concentration of less than 23 IU/mL was considered normal, 24-30 IU/mL borderline, and >30 IU/mL high.

Univariate analysis was conducted to present the demographic characteristics of the subjects. Bivariate analysis was performed to see the relationship between the independent variable (IgG antibodies) and the dependent variable (clinical activity of IBD), which was performed using the Chi-square test. The strength of the relationship between the variables was calculated and presented as prevalence ratio (PR) along with the 95% confidence interval (CI) to predict the relationship between food-specific IgG levels and IBD disease activity. Statistical analysis was performed using the Social Package for Social Sciences (SPSS) version 25.0. This research was approved by the Medical Ethics Committee of Cipto Mangunkusumo Hospital, Faculty of Medicine, University of Indonesia. This study is the first food-specific IgG antibody study in Indonesia.

3. Result

Table 1. *Demographic data of all subjects.*

Variable	UC (n=64)	CD (n=49)	Control (n=30)
Sex n (%)			
Men	19 (29.7)	19 (38.8)	
Woman	45 (70.3)	30 (61.2)	
Age, mean (SD)	48.22 (13.87)	43.04 (15.78)	38.73 (10.32)
Age, n (%)			
< 40 age	18 (28.1)	23 (46.9)	16 (53.3)
> 40 age	46 (71.9)	26 (53.1)	14 (46.6)
Age at diagnosis, mean (SD)	44.72 (14.17)	40.28 (15.14)	-
Duration of disease, n (%)			
< 1 years	28 (43.8)	13 (26.5)	
1-5 years	29 (45.3)	30 (61.2)	
5-10 years	5 (7.8)	3 (6.1)	
> 10 years	2 (3.1)	3 (6.1)	
Disease activity, n (%)			
Remission	24 (38.1)	34 (70.8)	
Mild Activity	28 (44.4)	12 (25.0)	
Moderate Activity	10 (15.9)	2 (4.2)	
Severe Activity	1 (1.6)	0 (0.0)	
Mayo Score, Median (Range)	3 (2-5)		-
CDAI Score, Mean (SD)	-	128.4 (66.05)	-
Fecal Calprotectin, n (%)			
Positive	35 (55.6)	24 (49.0)	
Negative	28 (44.4)	25 (51.0)	
Location			
L1 (Ileum)	-	16 (32.6)	
L2 (Colon)	-	4 (8.2)	
L3 (Ileo-colon)	-	29 (59.2)	
E1 (Rectosigmoid)	15 (23.4)	-	
E2 (Left-Side Colitis)	15 (23.4)	-	
E3 (Pancolitis)	33 (51.5)	-	

[a]UC: ulcerative colitis. [b]CD: Crohn's disease

Table 2. *Proportion of food-specific antibodies in patients with inflammatory bowel disease.*

Antigen	Inflammatory Bowel Disease	
	Ulcerative Colitis (n=64)	Crohn's Disease (n=49)
Cow's milk	42 (65.6)	40 (81.6)
White Egg	59 (92.2)	47 (95.9)
Jelly	38 (59.4)	34 (69.4)
Peas	61 (96.8)	49 (100.0)
Barley	61 (56.5)	47 (43.5)
Corn	53 (82.8)	37 (75.5)
Gliadin	26 (40.6)	27 (55.1)
Cashews	43 (67.2)	34 (69.4)
Peanuts	25 (39.1)	25 (51.0)
Almond nut	32 (50.0)	29 (59.2)
Rice	14 (22.2)	21 (42.9)
Plum	50 (78.1)	29 (59.2)

Antigen	Inflammatory Bowel Disease	
	Ulcerative Colitis (n=64)	Crohn's Disease (n=49)
Red beans	31 (48.4)	27 (55.1)
Chickpeas	29 (45.3)	22 (44.9)
Potatoes	26 (40.6)	26 (53.1)
Oat	28 (43.8)	30 (61.2)
Wheat	30 (46.9)	33 (67.3)
Soybeans	24 (37.5)	18 (36.7)
Malt	28 (43.8)	28 (57.1)
Sunflower seeds	33 (51.6)	23 (46.9)
Snapper fish	1 (1.6)	5 (10.2)

Table 3. *Relationship between food-specific IgG antibodies and disease activity.*

IgG Food-Specific (>30 U/mL)	Ulcerative Colitis (n=64)		Crohn's Disease (n=49)	
	r	*p*	*r*	*p*
Cow's milk	-0.288	0.150	0.008	0.960
White Egg	-0.170	0.244	-0.023	0.864
Jelly	-0.009	0.960	-0.196	0.244
Peas	-0.228	0.112	0.110	0.400
Barley	-0.027	0.112	0.261	0.042
Corn	-0.170	0.308	0.020	0.885
Gliadin	-0.178	0.355	0.128	0.543
Cashews	-0.347	0.041	0.193	0.216
Peanuts	-0.230	0.239	0.117	0.586
Almond nut	-0.193	0.335	0.176	0.343
Rice	-0.256	0.164	0.285	0.120
Plum	-0.146	0.507	0.023	0.942
Red beans	0.127	0.503	-0.093	0.527
Chickpeas	-0.473	0.017	-0.040	0.839
Potatoes	-0.208	0.298	-0.029	0.889
Oat	-0.009	0.960	-0.038	0.852
Wheat	0.041	0.816	0.049	0.801
Soybeans	-0.363	0.138	0.281	0.184
Malt	-0.051	0.790	-0.227	0.255
Sunflower seeds	-0.129	0.538	0.069	0.706
Snapper fish	-0.300	0.624	-	-

Table 4. *Relationship between food-specific IgG and fecal calprotectin.*

IgG antibody (+) (>30 U/mL)	Fecal Calprotectin		p
	Positive (n = …)	Negative (n = …)	
Cow's milk	43 (72.9)	39 (72.2)	0.937
Egg	56 (94.9)	50 (92.6)	0.708*
Jelly	38 (64.4)	34 (63.0)	0.873
Peas	57 (96.6)	53 (100.0)	0.497
Barley	57 (96.6)	51 (94.4)	0.669*
Corn	49 (83.1)	41 (75.9)	0.347
Gliadin	26 (44.1)	27 (50.0)	0.528
Cashew	42 (71.2)	35 (64.8)	0.468
Peanut	29 (49.2)	21 (38.9)	0.273
Almond Nut	35 (59.3)	26 (48.1)	0.234
Rice	19 (32.2)	16 (30.2)	0.818
Plum	43 (72.9)	36 (66.7)	0.472
Redbean	29 (49.2)	29 (53.7)	0.629
Chickpeas	30 (50.8)	21 (38.9)	0.202
Potatoes	33 (55.9)	19 (35.2)	0.027
Oat	31 (52.5)	27 (50.0)	0.787
Wheat	33 (55.9)	30 (55.6)	0.968
Soybean	25 (42.4)	17 (31.5)	0.231
Malt	29 (49.2)	27 (50.0)	0.928
Sunflower seed	32 (54.2)	24 (44.4)	0.298
Snapper fish	3 (5.1)	3 (5.6)	0.911

*fisher exact test

Table 5. *Relationship between fecal calprotectin and IBD disease activity.*

Fecal calprotectin	Disease activity, n (%)		PR (CI 95%)	p
	Active (n=53)	Remission (n=60)		
Positive	35 (66.0)	24 (40.0)	1.780 (1.155-2.742)	0.010
Negative	18 (34.0)	35 (66.0)		

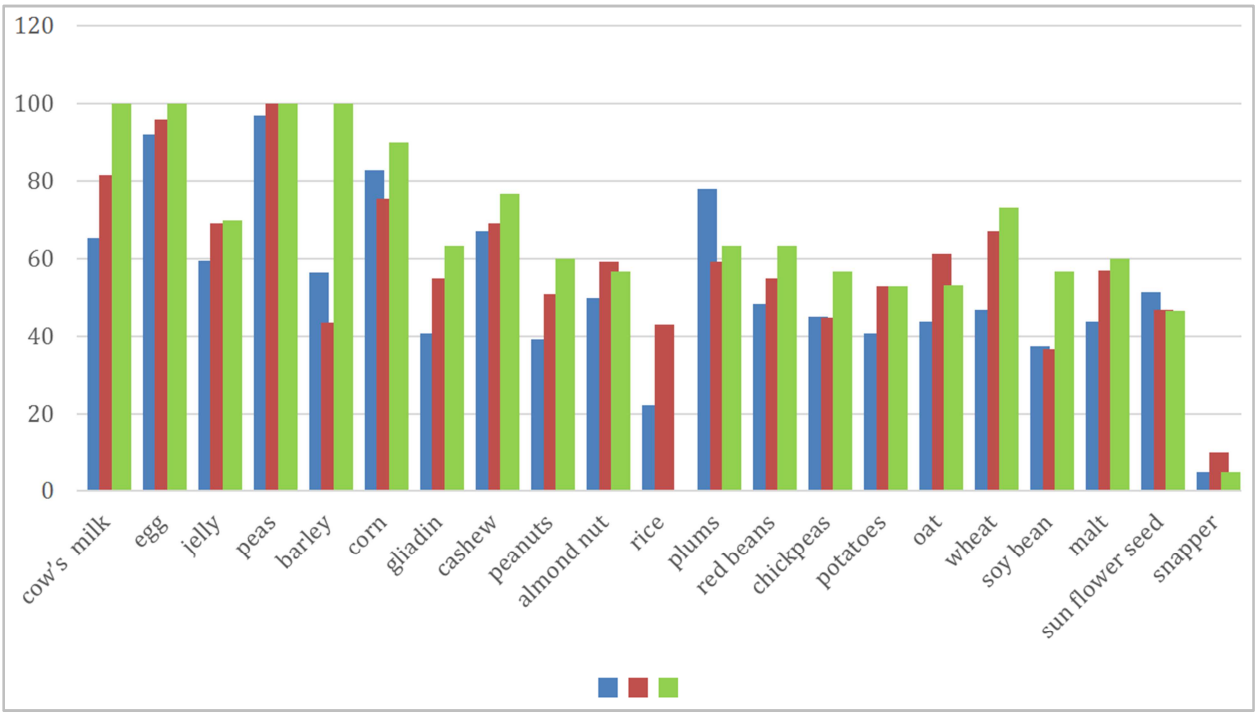

Figure 1. *Proportion of food-specific antibodies in patients with IBD and in healthy control.*

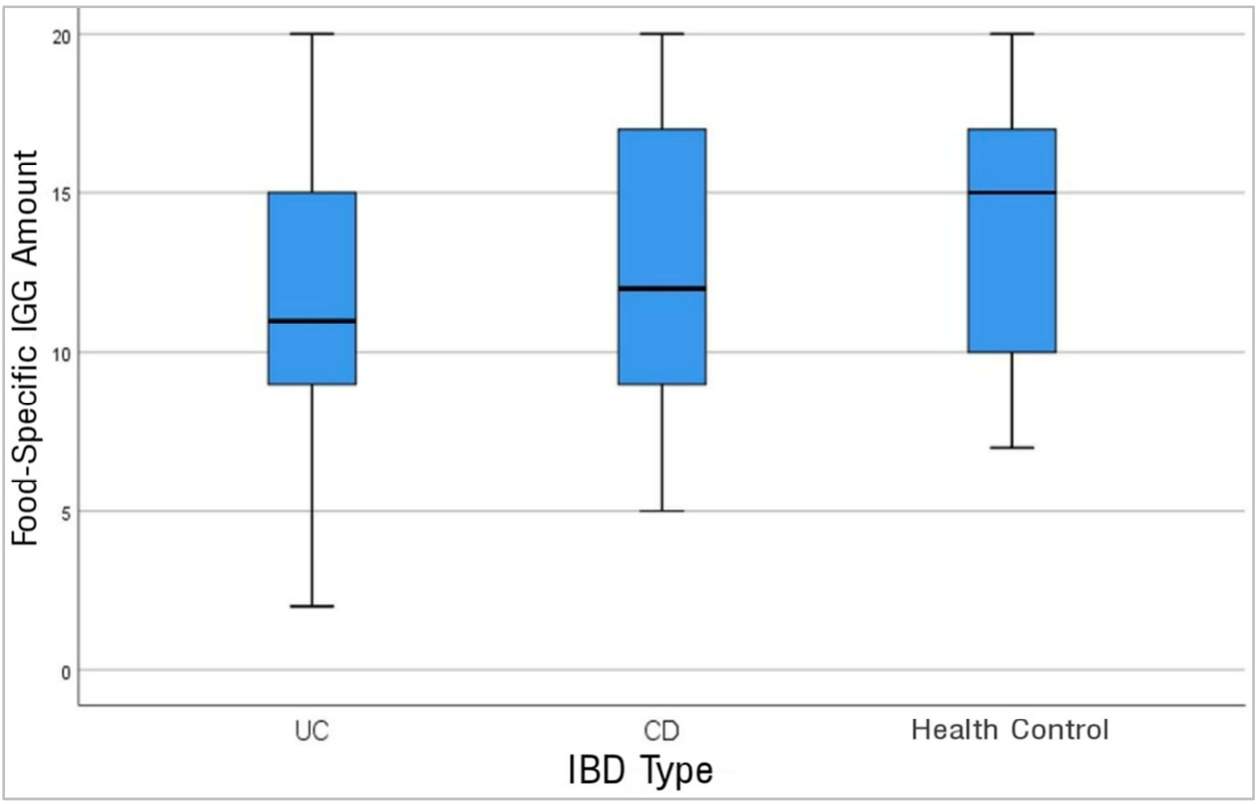

Figure 2. *Distribution of the number of positive allergen(s) with positive rate of food-specific IgG antibodies in patients with inflammatory bowel diseases (IBD) and healthy controls (HC).*

4. Discussion

In this study, the number of female participants was greater (66.37%) than that of male (33.62%). In the ulcerative colitis (UC) group there were 19 (29.7%) males and 45 (70.3%) females, while in Crohn's disease (CD) group 19 (38.8%) were males, and 30 (61.2%) were females. The gender incidence in this study was different from that of UC and CD in Asia, but the same as that of CD in the Western population. However, unlike our study, no gender proportion differences were seen in the UC group in the Western population [12]. We found that the ratio of men to women in the entire population of IBD subjects was 1:1.97. Specifically, in the UC group the ratio was 1:2.3 and in the CD group 1:1.5. In China, the ratio of male to female in UC and CD was 1.15:1 and 2.4:1 respectively [12]. The risk of UC in men was also higher in Korea [12].

Our study found that the mean age was 48.2 (SD 13.87) years in the UC group and 43.04 (SD 15.78) years in the CD group, while in the 30 healthy controls the mean age was 38.7 (SD 10.32) years. This is in contrast to the study by Cai et al from China where the median age of IBD subjects was younger, being 40.7 (35.9-45.7) years in the UC group and 36.5 (33.6-39.4) years in the CD group. A study by Wang et al even found a younger mean age of 34.22 (SD 12.50) in UC and 33.51 (SD 11.77) years in CD [13]. The age range in this study was not different from that of Cai et al's study, being 18-76 years in UC and 18-71 years in CD, while in Cai's study, the age ranges in the UC group were 18-58 years and in CD group 17-23 years [4].

The largest percentage of duration of illness in this study was one to five years (45.3% in UC and 61.2% in CD). This was different from the study by Cai et al. with duration of illness was 33,3% in UC and 48,1% in CD. It is known that patients with IBD are more prone to developing malignancy. People with Crohn's disease have a higher rate of small bowel malignancy, while patients with pancolitis, particularly ulcerative colitis, have a higher risk of developing colonic malignancy after 8-10 years of the disease. Most patients in the UC group showed ileo-colon predilection (E3=53.1%), while in the CD most had pancolitis (L3=59.2%). As such, the current standard of practice is to screen patients by colonoscopy at one to two year-interval after they have had the disease for more than ten years [15]. Bewtr et al reported an all-cause mortality SMR (Standardized Mortality Ratio) which varied from 0.44 to 7.14 for UC and 0.71 to 3.20 for CD [3].

Proportion and association of food-specific IgG antibodies with disease activity in IBD.

Patients in the UC group were found to have high IgG antibodies specific to ten types of food, namely barley (98.4%), beans (96.8%), eggs (92.2%), corn (82.8%), plums (78.1%), cashews (67.2%), milk (65.6%), sunflower seeds (51.6%), almonds (50%), and kidney beans (48.4%) (Table 2). Meanwhile, patients in the CD group had high IgG antibodies specific to peas (100.0%), barley (97.9%), eggs (95.9%), milk (81.6%), corn (75.5%), agar-agar (69.4%), cashews (69.4%), wheat (67.3%), oats (61.2%), and almonds (59.2%). No significant difference was seen in the proportion of food-specific IgG antibodies in IBD patients and in healthy group (Figure 1).

The difference between our results and those of Cai's and Wang's may be due to a different analysis, as we analyzed only foods with high IgG levels, while Cai's and Wang examined all types of food allergen (14 allergens). There are several allergens in Cai's and Wang's studies that we did not analyze, namely beef, chicken, pork, mushrooms, shrimp, and crab. On the other hand, there are several types of foods in our study that were not found in Cai's and Wang's studies, such as barley, cashews, chickpeas, gliadin (flours), oats, and sunflower seeds. Furthermore, the tools and reagents that we used were different from those that Cai and Wang used. In our study, we utilized a food intolerance test kit with a foodprint of 220 food allergens from CNS (Cambridge Nutrition Science). In Cai's study, Euroimmun AG diagnostic tool was used, and in Wang's study, Biomerica was used.

In our research, food-specific IgG levels (analyzed numerically) had a weak negative correlation with clinical disease activity, shown in cashew nuts and chickpeas in the UC group (Table 3) ($r=-0.347$; $p=0,041$ for cashews and $r= -0.473$; $p=0,017$ for chickpeas). In contrast, IgG levels to barley in the CD group showed a weak positive correlation with clinical activity of the disease ($r=0.261$; $p=0,042$). Future interventional dietary studies are necessary to observe that cashews and chickpeas cause a decrease in IBD disease activity. The inverse correlation between chickpeas and cashew nuts with clinical disease activity is supported by the prevalent knowledge that the Mediterranean diet is rich in fiber, fruits, whole grains, nuts, mono and polyunsaturated fatty acids. It is a dietary pattern that is thought to reduce intestinal inflammation in people with IBD. [8] Unfortunately, cashews and chickpeas are rarely consumed, possibly due to a cross hypersensitivity reaction triggered by similar protein forms contained in cashews and chickpeas with those in peanuts, which also had high antibody levels in this study.

The diagnosis and management of food hypersensitivity are complicated by the abundance of homologous, cross-reactive proteins in edible foods and aeroallergens. This causes the patient to experience allergic sensitization (positive test) to many biologically-related foods. However, many are sensitive to food without showing clinical reactivity [15]. Although molecular diagnostics has improved our ability to identify clinically relevant cross-reactivity, the optimal approach for patients requires an understanding of the epidemiology of clinically relevant cross-reactivity, as well as food-specific (degree of homology, protein stability, abundance) and patient-specific factors (immune response, augmentation factors) that determine clinical relevance [16].

There was no difference in the proportion of food-specific IgG levels between IBD patients and healthy controls. Only

IgG to cow's milk showed higher levels in healthy controls compared to that in IBD patients (p=0.001). This result could be due to a research bias, as subjects tried to restrict their diet from certain types of food that can affect their clinical disease activity, such as beef and cow's milk. This might have led to low exposure to these foods, hence the low IgG levels.

To further the analysis, we established a different clinical parameter of disease activity from Cai et al. In our study, as many as 98 out of 113 (86.7%) subjects were in remission or mildly active disease phase, while in Cai's study, most of the subjects (66.9%) were in mild to moderate disease clinical activity. In our study we found a remission phase in 51% of the subjects, while in Cai's study, remission was only in 8.9% of the subjects. There was even a heavy active phase of the disease in 29.1% patients in Cai's study, compared to only 1.6% in our study. We consider that the non-significant relationship between IgG levels in IBD patients and those in healthy control in our study was because most of the subjects were in remission and some had only mild clinical activity. This is the same as the hypothesis of this study that an increase in food-specific IgG antibodies is associated with an increase in clinical disease activity in IBD patients. In the same way, low food-specific IgG levels in this study were associated with mild clinical activity or remission of the disease, thereby also explaining the absence of a relationship between food-specific IgG antibodies and fecal calprotectin, a local intestinal inflammation marker.

The cross-sectional research design poses a limitation to this study, making it difficult to describe the course of the disease and prove a strong relationship between food-specific IgG levels and the clinical activity of the disease. A prospective cohort study that employs an interventional diet, avoiding foods that have high IgG, will be very useful to confirm the relationship.

Fecal Calprotectin (FC), a biomarker of local intestinal inflammation, is an inflammatory protein found in the cytosol of human neutrophils, macrophages, and fecal monocytes of IBD patients. It is a noninvasive, easy, inexpensive, and reliable examination technique. Apart from being a marker of inflammation, FC can be used as a diagnostic tool to distinguish IBD from IBS, determine disease activity, response to therapy, and the presence of recurrent inflammation or relapse after bowel surgery. An ongoing inflammatory process will increase FC levels in the body, which can be explained by migration of neutrophils to the digestive tract [17]. Food-specific IgG in this study did not have a significant relationship with fecal calprotectin, except for potatoes (p=0.027). This should be followed up by restricting potato consumption and assessing pre-and post-intervention fecal calprotectin as well as repeated colonoscopy to assess inflammation. Although Table 5 shows a significant relationship between fecal calprotectin and disease activity, the lack of research samples might have reduced the reliability of this finding.

Our subjects showed a significant difference from healthy controls (p=0.028) in terms of the type of food consumed with high IgG. On average, the UC group had 11 types of foods with high IgG levels, the CD group had 12, and the healthy controls had 15. There were significant differences between the healthy controls and the UC group in terms of distribution of the number of positive allergen(s) and positive rate of food-specific IgG antibodies (p=0.01) (Figure 2).

Several things can be noted that may affect the results of this study and become limitations of this study. Some blood and stool samples could not be taken at the same time so that it might have affected the assessment of the results of the study. The study was conducted during the COVID-19 pandemic with all the limitations and also because of the reluctance of most subjects to go back and forth to the hospital. The greater distribution of clinical activity of the subjects in the remission phase was thought to be the main factor causing a significant or strong correlation between food-specific IgG antibodies and clinical disease activity. The cross-sectional method used in this study could not describe the course of the disease because only one IgG antibody measurement was performed, which affected clinical activity results. The bias of this study is that patients tended to avoid foods they thought were harmful to their condition, such as meat, dairy, chilli, and sour taste. Lastly, qualitative assessment of fecal calprotectin might bias the results of the study because it is influenced by subjective assessments.

5. Conclusion

There was a weak negative correlation between cashew and chickpea-specific IgG antibodies with clinical activity of ulcerative colitis, and a weak positive correlation between barley-specific IgG antibodies with clinical activity of Crohn's disease.

For future studies, we suggest choosing naive patients with moderate and severe degrees of IBD using a prospective cohort study method.

Competing Interests

The author declare that they have no competing interests.

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