

Functional Gastrointestinal Symptoms Are Associated with Higher Serum Total IgE Levels, but Less Atopic Sensitization

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Abstract

Background The relation of gastrointestinal (GI) complaints to IgE-mediated allergy is not well understood. Increased numbers of “IgE-armed” mast cells have been observed in duodenal mucosa of patients with functional GI complaints.

Aims To explore whether total IgE and atopic sensitization were associated with functional GI complaints.

Methods Levels of serum total and specific IgE and GI complaints were measured in 161 patients and in a general population sample of 478 persons. Standard inhalant allergens were measured in the patient group, and selected inhalant allergens in the general population. GI complaints

were assessed by two standardized questionnaires. The associations between GI complaints and total IgE were analyzed in multiple regression models.

Results GI complaints were positively associated with higher total IgE levels (all: $b = 0.028$, $p = 0.012$; patient group: $b = 0.038$, $p = 0.072$; general population: $b = 0.038$, $p = 0.005$), but negatively associated with atopic sensitization (all: $b = -11.256$, $p = 0.181$; patient group: $b = -85.667$, $p < 0.001$; general population: $b = -14.394$, $p = 0.083$). The relationship between total IgE and GI complaints was consistent among sensitized and non-sensitized persons, among men and women, and across age groups.

Conclusion Serum total IgE was positively associated with GI complaints, while atopic sensitization was inversely associated with GI complaints. This suggests that IgE-mediated immunology plays a role in the pathophysiology of functional GI complaints. The biological mechanisms reflected in higher total IgE levels, but less atopic sensitization, warrant further studies.

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Introduction

Functional gastrointestinal (GI) disorders, especially irritable bowel syndrome (IBS), are increasingly common among the population in Western societies, and the conditions are recognized as primary causes of reduced quality of life [1]. Abdominal pain, bloating, and change in bowel habits are the most common GI symptoms in IBS, and women are affected more than men [1, 2].

Despite a low prevalence of classical IgE-mediated allergy among patients with functional GI complaints, it is often observed that patients with atopic conditions (i.e., asthma, allergic rhinoconjunctivitis, atopic eczema, urticaria, oral allergy syndrome) report more GI complaints than with non-atopic [3, 4], thus indicating a potential pathophysiological link between functional bowel disorders and the serum levels of IgE antibodies [5, 6]. Elevated levels of IgE antibodies might indicate a higher susceptibility to develop hypersensitivity reactions, even though the patients do not have clinical symptoms of allergy [7]. A recent study on atopic patients revealed a significant correlation between serum total IgE levels and number of mast cells with adherent IgE in duodenal mucosa, thus proposing a potential triggering effect of “IgE-armed” mast cells on the intestinal immune system in patients reporting perceived food hypersensitivity [5, 8]. Additionally, the study also found an increased intestinal permeability in patients with an atopic background compared with non-atopic patients. The presence of similar histological changes and intestinal dysfunction is also observed in previous studies of patients with atopic diseases such as dermatitis, birch pollen allergy, asthma, or allergic rhinitis, thus indicating a potential association between elevated total and specific IgE levels, atopic sensitization, and the GI manifestations observed in patients with functional GI disorders [8–10].

Hence, the main goal of this study was to investigate whether serum total IgE levels and atopic sensitization to inhalant allergens were associated with functional GI complaints. Additionally, we wanted to explore whether there were gender or age differences when it comes to the current associations.

Materials and Methods

Participants

Patient Population

A total of 161 patients referred to the Section for Clinical Allergology, Haukeland University Hospital, for suspected allergy were consecutively recruited in this study and responded to questionnaires about GI symptoms. Patients with organic disease which could explain abdominal symptoms, and pregnant or lactating women were excluded. Further details of the patients according to diagnosis at referral are presented in Appendix.

General Population

Four hundred and seventy-eight persons who participated in Bergen in the second follow-up of the population-based

multicenter study European Community Respiratory Health Survey (ECRHS) responded to questionnaires on GI symptoms. ECRHS is a multicenter, international study initially set up in the early 1990s to assess the prevalence of asthma and allergy in young- to middle-aged adults. Random population samples were selected within administrative boundaries in each study center. The present analysis used data from Bergen ECRHS from Norway. In 1992–1994, a random population sample of 4300 persons was invited to a screening questionnaire, and a subsample of 1200 responders was invited to a clinical examination of which 935 subjects took part. Six hundred subjects were re-investigated in 2000–2001. In 2011, 478 persons participated in the clinical follow-up, investigated with interview, lung function measurements, blood samples, skin prick tests, and self-filled in questionnaires. In Bergen, questionnaires assessing GI complaints were added to the protocol.

Allergologic Examination

In both the patient group and the general population, levels of total IgE and allergen-specific IgE antibodies were analyzed using the ImmunoCAP System (Thermo Fischer Scientific, Uppsala, Sweden). IgE antibodies to inhalant allergens were measured using Phadiatop® (birch, timothy, *Cladosporium herbarum*, cat, dog, horse, mugwort, and *Dermatophagoides pteronyssinus*) in the patient group, and analysis of IgE antibodies to *Dermatophagoides pteronyssinus*, cat, and timothy in the general population. Atopic sensitization was defined as having increased levels of IgE antibodies (≥ 0.35 kU_A/L) to at least one allergen.

Questionnaires Assessing GI Complaints

All participants, in the patient group and the general population, were asked to fill in two questionnaires to assess their GI complaints:

IBS Symptom Severity Scale (IBS-SSS)

The IBS-SSS contained five questions that were rated on a 100-point visual analogue scale (VAS): the severity of abdominal pain, the frequency of abdominal pain, the severity of abdominal distension, dissatisfaction with bowel habits, and interference with quality of life [11]. All five components contributed to the score equally yielding a theoretical range of 0–500, with a higher score indicating a worse condition. Previous studies have established that scores below 175 represent mild IBS symptoms, scores between 175 and 300 represent moderate severity, and scores above 300 represent severe IBS [11]. A decrease of

50 points on the IBS-SSS has been shown to correlate with improvement in clinical symptoms.

The Questionnaire for Rome III Criteria and Functional GI Complaints

The questionnaire included the short form of the Rome III criteria and IBS symptom questionnaire (IBS-SQ), both of which are widely used in diagnosing IBS and in quantification of functional GI disorders [12–14]. The IBS-SQ contained six symptoms which were rated on a scale of 0–10, with 0 = no symptoms and 10 = severe. A total score of 15 or higher defined severe IBS. In addition, the questionnaire also included four IBS criteria providing support for IBS diagnosis, four symptoms requiring further consideration, three criteria for functional dyspepsia, and two symptoms supporting heartburn diagnosis.

Statistical Analysis

Statistical analyses were performed by using Statistical Product and Service Solutions, version 21 (IBM SPSS Statistics 21, Inc., Chicago, IL, USA). Pearson's correlation coefficient was used to assess the correlation between relevant parameters. Student's unpaired *t* tests were used for comparisons of means in different groups. Linear regression models were used to evaluate the association between total IgE levels and GI complaints (IBS-SSS), adjusting for atopic sensitization, gender, age, and sample in multiple regression models. $p < 0.05$ was considered as a significant value. The regression models were considered as robust, given that the coefficients did not change front signs and had no dramatically different values in the second model with statistical adjustments. All changes in Δ values in the regression and interaction analyses were calculated as new value minus old value, and levels of confidence intervals (CI) are set at 95 % for all unstandardized regression coefficients.

Ethical Approval

The clinical study was approved by the Regional Committee for Medical Research Ethics, and all patients and the Bergen ECRHS III study participants have given written informed consent.

Results

Clinical and Demographic Data

Table 1 presents demographic data for the participants. Total IgE levels were higher in the patient group compared

with the general population, as expected given that the patient group was referred to a section of allergology. Among patients, abdominal pain was the most common GI symptom, affecting 123 patients (76.4 %), followed by bloating (61.5 %) and changes in frequency of stool (59 %) (Table 2). In the general population, bloating (41.4 %) and diarrhea (38.6 %) were the most common GI symptoms. In the patient group, 71.4 % filled the criteria for IBS according to Rome III, whereas 20.5 % had symptoms of severe IBS (IBS-SSS > 300). In the general population, one-third had IBS; most of these individuals had mild to moderate symptoms of IBS, whereas only 1.88 % suffered from severe IBS (Table 1).

Univariate Regression Analyses

In the patient group, positive correlations between total IgE and IBS-SSS ($r = 0.072$, $p = 0.379$) and between total IgE and IBS-SQ ($r = 0.084$, $p = 0.311$) did not reach statistical significance. In the general population, a significant correlation was found between total IgE and IBS-SSS ($r = 0.102$, $p = 0.029$), but not between total IgE and IBS-SQ ($r = 0.059$, $p = 0.201$).

There were significant differences in IBS-SSS scores ($p = 0.004$) and IBS-SQ scores ($p = 0.019$) between atopic and non-atopic individuals in the patient group (Fig. 1a, b), where non-atopic patients on average reported significantly more GI complaints (mean; IBS-SSS = 236.02, IBS-SQ = 22.37) than atopic (mean; IBS-SSS = 172.64, IBS-SQ = 17.58).

The same tendency was observed in the general population (Fig. 1a, b), but the differences did not reach statistical significance in univariate analyses.

Multiple Regressions Analyses of Predictors of GI Complaints

IBS-SSS and IBS-SQ scores were highly correlated in both the patient group ($r = 0.798$, $p < 0.001$) and the general population ($r = 0.664$, $p < 0.001$). Thus, IBS-SSS scores were used as a marker of GI complaints in the following regression models.

In the patient group, total IgE was positively and borderline significantly associated with GI complaints when adjusting for atopic sensitization, sex, and age ($b = 0.038$, $p = 0.072$) (Table 3). Measured by the p values, atopic sensitization was the largest contributor, which was significantly associated with less GI complaints ($b = -85.667$, $p < 0.001$). Total IgE and atopic sensitization could together explain 6.2 % of total variance in GI complaints in a multiple regression model only adjusting for levels of total IgE and atopic sensitization ($\Delta R^2 = 0.062$, $p = 0.003$).

Table 1 Demographic and clinical data in the study populations, a patient group and a general population sample

	Patient group	General population
<i>N</i>	161	478
% Women	70.2 % (<i>n</i> = 113)	44.7 % (<i>n</i> = 214)
% Men	29.8 % (<i>n</i> = 48)	55.3 % (<i>n</i> = 264)
Age, mean years (range)	36.90 (15–75)	52.51 (40–64)
IBS symptom questionnaire (IBS-SQ) (mean)	19.05	5.92
IBS symptom Severity Scale (IBS-SSS) (mean)	193.07	70.77
IBS-SSS		
>300 (severe)	20.50 % (<i>n</i> = 33)	1.88 % (<i>n</i> = 9)
175–300 (moderate)	32.30 % (<i>n</i> = 52)	5.65 % (<i>n</i> = 27)
75–175 (mild)	18.63 % (<i>n</i> = 30)	25.70 % (<i>n</i> = 123)
<75 (no IBS)	22.98 % (<i>n</i> = 37)	62.34 % (<i>n</i> = 298)
Allergy		
Total IgE (mean)	312.94	75.5
Total IgE levels >120 kU/L	49.07 % (<i>n</i> = 79)	12.97 % (<i>n</i> = 62)
Atopic sensitized (%)	67.7 % (<i>n</i> = 109) ^a	21.5 % (<i>n</i> = 103) ^b
% with an atopic condition ^c	67.1 % (<i>n</i> = 108)	

^a Percentage with elevated IgE antibody levels (≥ 0.35 kU_A/L) to at least one inhalant allergen (Phadiatop)

^b Percentage with elevated IgE antibody levels (≥ 0.35 kU_A/L) to one of the following inhalant allergens: grass, cat, or *Dermatophagoides pteronyssinus*

^c Rhinoconjunctivitis, urticaria, eczema, asthma

Table 2 Specific GI complaints in the study populations

	Patient group	General population
% with abdominal pain or discomfort last 3 months	76.4 % (<i>n</i> = 123)	29.0 % (<i>n</i> = 139)
% change in frequency of stool	59.0 % (<i>n</i> = 95)	22.3 % (<i>n</i> = 107)
% with bloating and/or abdominal distention	61.5 % (<i>n</i> = 99)	41.3 % (<i>n</i> = 198)
% with defecation at night	14.3 % (<i>n</i> = 23)	2.7 % (<i>n</i> = 13)
% with diarrhea predominant	50.9 % (<i>n</i> = 82)	38.6 % (<i>n</i> = 185)
% with constipation predominant	21.7 % (<i>n</i> = 35)	15.4 % (<i>n</i> = 74)
% med functional dyspepsia	44.7 % (<i>n</i> = 72)	15.9 % (<i>n</i> = 76)
% with heartburn	40.4 % (<i>n</i> = 65)	28.8 % (<i>n</i> = 138)

In the general population, total IgE was significantly associated with IBS-SSS (Table 3), and the size of the estimate was similar to what we found in the patient group ($b = 0.038$ and $b = 0.036$, respectively). A negative association with atopic sensitization was also indicated in the general population ($b = -14.394$, $p = 0.083$), similar as in the patient group. Total IgE and atopic sensitization could together explain 1.9 % of total variance in GI complaints in a multiple regression model only adjusting for levels of total IgE and atopic sensitization ($\Delta R^2 = 0.019$, $p = 0.014$).

In the total study population, combining the patient group and the general population (Table 3), two notable modifications in the regression models were made, namely the definition of atopic sensitization and introduction of a group sample variable. Total IgE was significantly associated with more GI complaints ($p = 0.012$) in the

regression model, and atopic sensitization was significantly associated with less GI complaints ($p < 0.001$). No significant interaction effect of sample on the association between total IgE and GI complaints was found ($p = 0.736$).

Stratified Analysis and Analysis of Interaction

Stratified analyses according to gender were performed in order to investigate whether the associations of GI complaints with total IgE levels differed between men and women. Similarly, stratified analyses were performed according to atopic sensitization and age groups (Table 4). Approximately the same consistent direct effect of total IgE on GI complaints was observed in all strata. Women had more GI complaints than men, but the interaction effect by gender was not significant

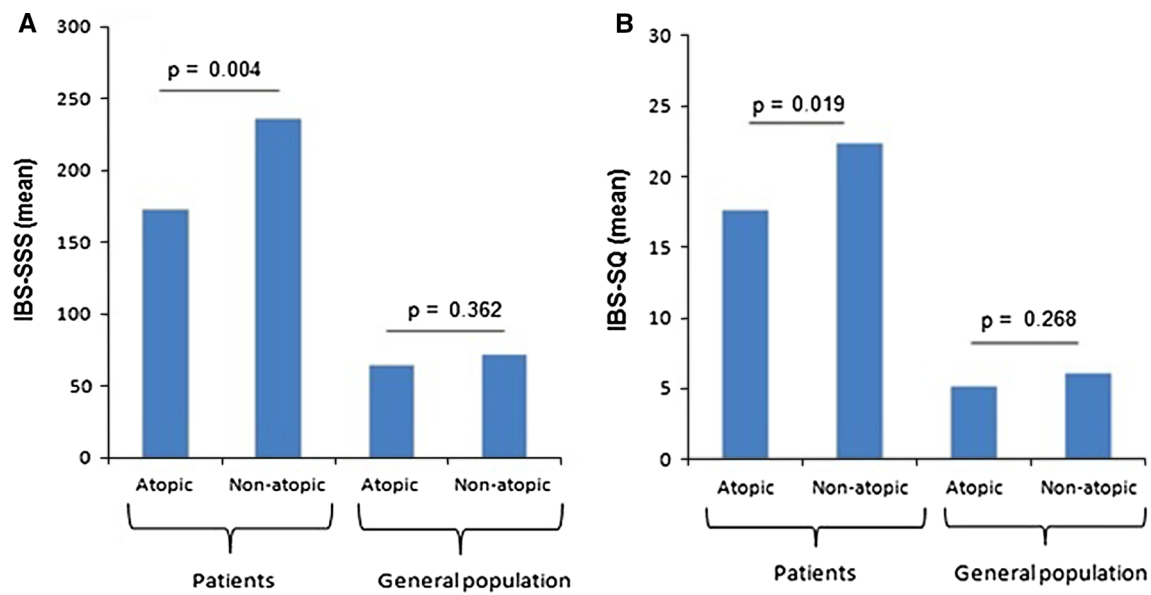


Fig. 1 Mean IBS-SSS score (a) and mean IBS-SQ score (b) between atopic sensitized (defined specific IgE ≥ 0.35 kU_A/L) and non-atopic in the patient group and the general population

Table 3 Association between GI complaints (IBS-SSS and IBS-SQ), total IgE, and atopic sensitization in the patient group and the general population

	IBS-SSS adjusted <i>B</i> (95 % CI) ^a	<i>p</i> value	IBS-SQ adjusted <i>B</i> ^a (95 % CI)	<i>p</i> value
Patient population				
Total IgE ^d	0.038 (−0.004, 0.080)	0.072	0.003 (−0.001, 0.007)	0.089
Atopic sensitization ^b	−85.667 (−132.192, −39.161)	<0.001	−5.659 (−9.869, −1.448)	0.009
General population				
Total IgE	0.038 (0.012, 0.064)	0.005	0.003 (0.000, 0.005)	0.057
Atopic sensitization ^c	−14.394 (−30.670, 1.883)	0.083	−1.385 (−3.033, 0.263)	0.099
Total study group				
Total IgE	0.028 (0.006, 0.049)	0.012	0.002 (0.000, 0.004)	0.035
Atopic sensitization ^c	−11.256 (−27.758, 5.245)	0.181	−0.889 (−2.451, 0.674)	0.264

The values in bold are defined as statistically significant with $p < 0.05$

^a *B* = beta coefficient with 95 % confidence interval from linear regression, adjusted for total IgE, atopic sensitization, sex, and age. In the total study group, the model was also adjusted for group sample

^b Defined as elevated IgE antibody levels (≥ 0.35 kU_A/L) to at least one inhalant allergen (Phadiatop)

^c Percentage with elevated IgE antibody levels (≥ 0.35 kU_A/L) to one of the following inhalant allergens: grass, cat, or *Dermatophagoides pteronyssinus*

^d Increase in IBS score per unit increase in total IgE

($p = 0.721$). Furthermore, non-atopic subjects appeared to have more GI complaints than atopic; however, no significant interaction effect by atopic sensitization was found ($p = 0.556$). Additionally, we observed that the younger participants appeared to have more GI complaints than those somewhat older; however, no significant interaction effect by age was found ($p = 0.241$). Thus, the association between total IgE and GI complaints appeared to be consistent in all strata according to gender, atopic status, or age.

Discussion

To our knowledge, this is the first study where the association between functional GI complaints and total IgE levels and atopic sensitization has been investigated. We found that GI complaints were significantly associated with both total IgE and atopic sensitization. The observations that GI complaints were associated with higher total IgE, but less atopic sensitization, are puzzling, but seem relatively convincing as these observations were consistent in

Table 4 Association between GI complaints (IBS-SSS) and total IgE in selected subgroups, analyzed with multiple regression analysis and adjusted for total IgE, ^aatopic sensitization, sex, age, and sample

Subgroup	Direct effect of total IgE on IBS-SSS <i>b</i> (95 % CI)	<i>p</i> value
Men (<i>n</i> = 296)	0.026 (−0.003, 0.056)	0.079
Women (<i>n</i> = 304)	0.045 (0.013, 0.078)	0.006
Atopic (<i>n</i> = 202)	0.040 (0.014, 0.065)	0.003
Non-atopic (<i>n</i> = 398)	0.044 (−0.029, 0.118)	0.236
Individuals aged under 50 (<i>n</i> = 286)	0.050 (0.018, 0.082)	0.002
Individuals aged over 50 (<i>n</i> = 314)	0.020 (−0.010, 0.049)	0.191

b = unstandardized beta coefficient

^a Atopic sensitization was defined as having elevated IgE antibody levels (≥ 0.35 kU_A/L) to one of the following inhalant allergens: grass, cat, or *Dermatophagoides pteronyssinus*

both a patient population and a general population. GI complaints were measured with standardized questionnaires and IgE with standard methodology, in both study populations. No significant interaction effects of atopic sensitization, sex, or age were found for the association between total IgE and GI complaints, suggesting that the association was consistent also in subgroups according to atopic status, sex, and age.

There was a positive, but nonsignificant, association between GI symptoms and total IgE in patients, whereas this association was significant in the general population. The general population group was a larger sample, which could explain the differences in the significance levels. Nevertheless, a significant correlation between GI complaints and levels of total IgE was found in patients when restricting the analysis to investigate the association of total IgE with mild to moderate IBS symptoms ($r = 0.224$, $p = 0.015$). Thus, an association between total IgE and GI complaints appeared to be driven by an association with moderate IBS symptoms, consistent with the findings from the general population where the IBS symptoms were generally less severe. Additionally, we found that there was a negative relationship between GI symptoms and atopic sensitization, which was significant in the patient group, but not in the general population. This could be related to the fact that sensitization to a larger number of allergens was measured in the patients group, while only data for sensitization to three main allergens were available from the general population sample. Measured by *p* values, atopic sensitization had the greatest contributive effect in a combined group comprising all participants, indicating no vital role of allergic sensitization to inhalant allergens in the actual development of functional GI complaints. When analyzing men and women separately, we found similar consistent associations between total IgE and GI complaints. The association between the parameters was stronger in women; however, no significant interaction effect of gender was found. We detected the same associations between total IgE and GI complaints among atopic sensitized and non-atopic, whereas no interaction effect of

atopic sensitization was observed. Hence, the positive association was consistent, although the relationship was stronger among atopic sensitized individuals. Additionally, total IgE was positively associated with GI complaints in groups separated by age, where the strongest association was found among younger; however, no interaction effect of age was observed. In the current study, total IgE and atopic sensitization could together explain 6.2 % and 1.9 % of total variance in GI complaints in the patient group and the general population, respectively.

The prevalence of atopic diseases among patients with functional GI disorders is highly recognized [5, 9, 15–17], and vice versa, GI symptoms are also frequently reported in allergic individuals [18–20], and the overlap between atopic conditions and functional GI disorders, particularly IBS, has been newly shown [19]. Hence, potential links between them are proposed, and future studies might include manipulation of the atopic pathway among the treatment options of functional GI disorders. A significantly increased number of colonic mast cells were shown in IBS patients, indicating that mast cells play a key role in the development of functional GI disorders [21]. Interestingly, the number of duodenal IgE-positive cells was significantly higher in patients with an atopic background compared with non-atopic, and these appeared to be “IgE-armed” mast cells [5]. Thus, according to various studies, “atopic IBS” was recently proposed as a new subgroup of IBS with a distinct role of activated mast cells [5, 9], and identifying atopic manifestations in patients with IBS symptoms was suggested as an important link in elucidating the pathophysiology of IBS. It has also been shown that disturbances in the gut microbiota, enteric dysmotility and fermentation problems are important pathological factors contributing to GI complaints. It seems as if the colon is not compatible to function properly, either because of disturbed bacterial flora or due to increased supply of undigested carbohydrate from the small intestine [5, 22–25]. Newer studies therefore support that alterations in the gut microbiota are of considerable interest, at least in selected subgroups of IBS [24].

The present study suggests a potential pathological link between functional GI complaints and increased total IgE levels. However, atopic sensitization to inhalant allergens appeared to have no vital influence on GI symptoms in both group samples, in contrast to previous studies linking atopic diseases and IBS. In fact, our results indicated a significant negative association between atopic sensitization and GI complaints among patients. These observations suggest that specific IgE-mediated processes and allergy may have slighter impact on functional GI complaints than previously assumed. Although patients with IBS previously have been shown to have an increased number of mast cells located in the gut, it is not anticipated that classical specific IgE-mediated sensitization is the cause of their GI symptoms [21, 26]. Mast cells encompass membrane high-affinity IgE receptors, capable of attaching circulating IgE antibodies regardless of the primary stimulus [27], and in accordance with the documentation of a significant correlation between IgE-armed mast cells and serum total IgE by Lillestøl et al., it is conceivable that the increased number of mucosal armed mast cells may induce intestinal hypersensitivity to a variety of mechanical stimuli, including bloating, distension, and water retention [5]. Visceral hypersensitivity is commonly found in patients with IBS, and several studies indicate abdominal symptom relief after the administration of mast cell stabilizing drugs [28]. Whether the cause of the increased number of IgE-armed mast cells in intestinal mucosa is in concordance with increased levels of total IgE in serum is yet uncertain, and we do not know whether our findings reveal total IgE as a predictor of GI complaints is yet of any clinical significance. However, we do believe that the term “atopic bowel” may be of particular interest in patients with less severe IBS complaints. Conversely, the actual role of total IgE levels in the development of functional GI complaints should be investigated further by mechanistic and epidemiological studies in order to clarify possible causes for increased total IgE levels, and whether high total IgE is a primary or secondary effect cause of functional GI complaints. Nevertheless, evidence from the current study shows that levels of total IgE and atopic sensitization could together explain a relatively small proportion of the total variance in GI complaints in the included patients, whereas approximately 94 % of the total variance in symptom severity remains unexplained. This supports the view that other mechanisms are involved in the pathophysiology of functional GI disorders.

A main strength of this study is that the research question, the association between IgE and GI complaints, was investigated both in a patient population and in a general population. The observation of similar trends in both study populations improved the solidity and generalizability of

the conclusions. Both the exposure and the outcomes were measured with state-of-the art methodology, comparative in the two study populations; GI symptoms were equally defined in the patient group and the general population using international standardized tools, and IgEs were measured using similar methodology. The size of the total study population is another strength of the study. While several sensitizations were measured in the patient group, only specific IgE levels to the three most common inhalant allergens were measured in the general population. This difference in definition of atopic sensitization is a weakness of the study and may account for the less consistent findings in the general population as to atopic sensitization. However, a negative association between GI complaints and atopic sensitization was detected also in this group, consistent with the findings in the patient group.

In conclusion, higher total IgE was a significant predictor of GI complaints, consistent in analyses of both a patient population and a general population, in men, women, younger, and older persons, and among persons with or without atopic sensitization. Atopic sensitization to inhalant allergens was inversely related to GI complaints. The findings support a role for IgE-related immunology in functional GI disorders. In addition, the results regarding atopic sensitization and GI complaints may indicate that the role of IgE in GI complaints is not mediated by specific IgE processes. Nevertheless, multiple factors can be involved in the association between total IgE and GI complaints, and our results should be further investigated in mechanistic studies of the role of total IgE in functional GI disorders. In particular, it might be useful to investigate further the puzzling observation that GI complaints were related to higher total IgE, but less atopic sensitization.

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Compliance with ethical standards

Conflict of interest None.

Appendix

Details of the patients according to the primary cause of reference [patients who were referred to allergologic examination with GI complaints as primary cause of reference ($n = 81$) and patients who were referred to allergologic examination with other allergic symptoms as primary cause of reference ($n = 80$)] are provided below (Tables 5, 6).

Table 5 Demographic and clinical data in patient subgroups

	With GI complaints	With other complaints
<i>N</i>	81	80
% Women	72.8 % (<i>n</i> = 59)	67.5 % (<i>n</i> = 54)
% Men	27.2 % (<i>n</i> = 22)	32.5 % (<i>n</i> = 26)
Age, mean years (range)	36.51 (17–75)	37.29 (15–71)
IBS symptom questionnaire (IBS-SQ) (mean)	23.74	13.96
IBS symptom severity scale (IBS-SSS) (mean)	267.49	116.67
IBS-SSS		
>300(severe)	33.3 % (<i>n</i> = 27)	7.50 % (<i>n</i> = 6)
175–300 (moderate)	42.0 % (<i>n</i> = 34)	22.50 % (<i>n</i> = 18)
75–175 (mild)	16.0 % (<i>n</i> = 13)	21.25 % (<i>n</i> = 17)
<75 (no IBS)	3.7 % (<i>n</i> = 3)	42.5 % (<i>n</i> = 34)
Allergy		
Total IgE (mean)	279.79	336.22
Total IgE levels >120 kU/L	45.7 % (<i>n</i> = 37)	52.5 % (<i>n</i> = 42)
Atopic sensitized (%) ^a	55.6 % (<i>n</i> = 45)	80.0 % (<i>n</i> = 64)
% with an atopic condition ^b	60.4 % (<i>n</i> = 49)	73.8 % (<i>n</i> = 59)

^a Percentage with elevated IgE antibody levels (≥ 0.35 kU_A/L) to at least one inhalant allergen (Phadiatop)^b Rhinoconjunctivitis, urticaria, eczema, asthma**Table 6** Specific GI complaints in patient subgroups

	With GI complaints	With other complaints
% with abdominal pain or discomfort last 3 months	96.3 % (<i>n</i> = 78)	56.3 % (<i>n</i> = 45)
% change in frequency of stool	79.0 % (<i>n</i> = 64)	38.8 % (<i>n</i> = 31)
% with bloating and/or abdominal distention	76.5 % (<i>n</i> = 62)	46.3 % (<i>n</i> = 37)
% with defecation at night	19.8 % (<i>n</i> = 16)	8.8 % (<i>n</i> = 7)
% with diarrhea predominant	61.7 % (<i>n</i> = 50)	40.0 % (<i>n</i> = 32)
% with constipation predominant	27.2 % (<i>n</i> = 22)	16.3 % (<i>n</i> = 13)
% med functional dyspepsia	65.4 % (<i>n</i> = 53)	23.8 % (<i>n</i> = 19)
% with heartburn	49.4 % (<i>n</i> = 40)	31.3 % (<i>n</i> = 25)

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