ORIGINAL ARTICLE

# A Physiologic Events' Cascade: Irritable Bowel Syndrome May Even Terminate with Chronic Gastritis

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**SUMMARY**

**When specifically asked, about one third of people report recurrent upper abdominal discomfort, and irritable bowel syndrome (IBS) and chronic gastritis (CG) maybe the most frequently diagnosed ones among all. Consecutive patients with upper abdominal discomfort applying to the Internal Medicine Polyclinic were included into the study. IBS was diagnosed according to Rome II criteria and CG was diagnosed histologically. All cases with IBS were compared with the age and sex-matched randomly selected cases without IBS. One hundred and fifty-six patients with IBS and 179 patients without IBS were studied. CG was detected in 72.4% (113 cases) of cases with IBS, and only 36.3% (65 cases) in patients without IBS (p<0.001). IBS probably is a cascade of many physiological events, being initiated by infection, inflammation, psychological disturbances-like many stresses and eventually leading to dysfunctions of gut and other systems of the body via a low-grade inflammatory process. CG may be one of the terminating points of the physiological events' cascade, IBS. This may explain the high prevalence of IBS in society. Keeping in mind this association will be helpful during prevention, treatment, and follow up of these common pathologies in Primary Health Centers and Internal Medicine and Gastroenterology Polyclinics for physicians.**

**KEY WORDS:**
*Irritable bowel syndrome, Chronic gastritis, Abdominal discomfort*

## INTRODUCTION

When asked specifically, about one third of people report recurrent upper abdominal discomfort, and one of most frequent applications to primary health centers are due to this complaint [1]. Irritable bowel syndrome (IBS), chronic gastritis (CG), gastroesophageal reflux disease (GERD), esophagitis, duodenal and/or gastric ulcers, erosive gastritis and/or duodenitis, celiac disease, chronic pancreatitis, and malignancies are other possible causes of this complaint, but IBS and CG are probably the most frequently diagnosed ones. Flatulence, periods of diarrhea and/or constipation, repeated toilet visits due to urgent evacuation or early filling sensation, excessive straining, feeling of incomplete evacuation, frequency, urgency, reduce feeling of well being, and disturbed social life due to the gastrointestinal and urinary tract symptoms are often reported by IBS patients. Although many patients relate onset of symptoms to intake of food and often incriminate specific food items, a meaningful dietary role in IBS is doubtful, but it seems that IBS patients usually suffer from CG, too and the exacerbations of IBS with specific food items may actually be a result of a close association of the disease with CG. We tried to understand whether or not there is a significant etiopathogenetic relationship between IBS and CG.

## MATERIALS AND METHODS

Consecutive patients with upper abdominal discomfort applying to the Internal Medicine Polyclinic of the Dumlupinar University between September 2006 and March 2007 were included into the study. A routine check up procedure including routine hematologic and biochemical tests, thyroid function tests, markers of hepatitis viruses A, B, and C and human immunodeficiency virus, urinalysis, electrocardiography, chest x-ray graphy, fresh fecal sample examination, abdominal X-ray graphy in supine position, abdominal ultrasonography, and serum levels of IgA was performed and medical pasts including alcohol consumption were learnt. A questionnaire for IBS was performed in all cases, and IBS is diagnosed according to Rome II criteria in the absence of red flag symptoms, which are not typical for IBS, such as pain or diarrhea that often awakens/interferes with sleep, weight loss, fever, or abnormal physical examination findings. An upper gastrointestinal endoscopy was performed, and sample biopsies were taken in suspected cases. CG is diagnosed histologically, and infiltration of neutrophils and monocytes into gastric mucosa is the hallmark of CG [2]. Additionally, microscopic examination shows stereotypical changes in epithelium such as degeneration, focal intestinal metaplasia, dysplasia, and glandular atrophy [2]. Because of highly variable clinical severity of celiac disease and high sensitivity and specificity of IgA antiendomysial antibodies [3], they were used as a screening test for celiac disease, and jejunal biopsy was planned just for the antibody positive cases to see absence of villi and elongated crypts. The IgA antiendomysial antibodies were determined by the immunofluorescent method using a preparation of primate GIT smooth muscle from IMMCO (USA) (evaluation: positive/negative, sensitivity 97-100%, specificity 90-100%). A detailed history was taken for GERD,

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and thinning of squamous mucosal layer and basilar cell hyperplasia are accepted as esophagitis. Columnar mucosal changes are features of Barrett's metaplasia. Eventually, all cases with IBS were put into one group and the age and sex-matched and randomly selected cases without IBS were put in the other group. Incidences of CG were compared between the groups with and without IBS. Student t-test was used as the method of statistical analysis.

## RESULTS

One hundred and fifty-six patients with IBS and 179 patients without IBS were studied. Their mean ages were 41.8 ± 11.1 (range 15-66) and 41.1 ± 13.3 (range 15-65) years, respectively ($p>0.05$). Interestingly, 61.5% (96 cases) of the IBS cases were female, so IBS was observed more frequently in females. CG was detected in 72.4% (113 cases) of cases with IBS, whereas this ratio was only 36.3% (65 cases) in the patients without IBS ($p<0.001$) (Table I). On the other hand, 47 cases with gastric and/or duodenal ulcers were detected in both groups totally, and one of the gastric ulcers was malignant histologically. Erosive gastritis and/or duodenitis was the diagnosis in another three cases. Thirty-six cases with giardiasis were diagnosed via fresh fecal samples but cysts in 33 and trophozoites in three cases were seen. On the other hand, although in a previous study authors concluded that celiac disease must be considered in all newly diagnosed IBS cases regardless of the nature of presenting symptoms, especially in areas with high prevalence of celiac disease[4], we detected no case of IgA deficiency or IgA antiendomysial antibody positivity in this study. We detected GERD, esophagitis, Barrett's metaplasia, urolithiasis, pyelonephritis, and cholecystitis in both groups but not acute or chronic pancreatitis.

## DISCUSSION

Approximately 10-20% of the general population have IBS[5], and as also shown here, it is more common among females for unexplained reasons. Psychological factors seem to precede onset or exacerbation of gut symptoms, and many potentially psychiatric disorders such as anxiety, depression, and sleep disorders frequently coexist with IBS[6]. For example, thresholds for sensations of initial filling, evacuation, urgent evacuation, and utmost tolerance, recorded via a rectal balloon, significantly decreased by focusing the examiners' attention on gastrointestinal stimuli by reading pictures of malignant gastrointestinal disorders in IBS cases, however no remarkable change was observed in the other group[7]. So although IBS is described as a physical - not psychological - disorder according to Rome II guidelines, psychological factors may be crucial for triggering of the physical disorder, IBS.

Although underlying causes of pathophysiologic changes remain unclear, low-grade inflammation and abnormal intestinal motility are accepted mechanisms altering gut functions and generating symptoms[8]. According to the Rome II criteria, IBS is not a disease in stead a functional disorder, and it is actually defined as a brain-gut dysfunction, but just as a personal opinion, IBS is a more complex condition than this view, and it may affect various systems of the body with a low-grade inflammatory state. We had detected in a previous study that IBS may lead to urolithiasis in a significant proportion of cases[9]. Other authors have studied the role of inflammation in 77 of cases with IBS and colonic biopsies were taken for conventional histology and immunohistology. Thirty-eight had normal histology, 31 demonstrated microscopic inflammation, and eight fulfilled criteria for lymphocytic colitis. However, in the group with "normal" histology, immunohistology revealed increased intraepithelial lymphocytes as well as increased CD3+ and CD25+ cells in lamina propria, as evidence of immune activation. These features were even more evident in the microscopic inflammation group, who additionally revealed increased neutrophil, mast cell, and natural killer cells. All of these immunopathological abnormalities were most evident in the lymphocytic colitis group, who also demonstrated HLA-DR staining in crypts and increased CD8+ cells in lamina propria[10]. A direct link between immune activation and symptoms was provided by work of Barbara and colleagues, who demonstrated not only an increased prevalence of mast cell degranulation in colon, but also a direct correlation between proximity of mast cells to neuronal elements and pain severity in IBS[11]. In addition to these findings, there is some evidence for extension of the inflammatory process beyond the mucosa. Tornblom and colleagues addressed this issue in ten patients with severe IBS by examining full-thickness jejunal biopsies obtained via laparoscopy[12]. They detected a low-grade infiltration of lymphocytes in myenteric plexus in nine cases, four of whom had an associated increase in intraepithelial lymphocytes and six demonstrated evidence of neuronal degeneration. Nine patients had hypertrophy of longitudinal muscles and seven had abnormalities in number and size of interstitial cells of Cajal. The finding of intraepithelial lymphocytosis was consistent with the reports of Chadwick and colleagues in colon and of Wahnschaffe and colleagues in duodenum[13]. So IBS maybe due to a cascade of many physiologic events, being initiated with psychological disturbances like stresses and terminating with dysfunctions of the whole gut via a low-grade inflammatory process.

As a similar process to the IBS, infiltration of neutrophils and monocytes into gastric mucosa is the hallmark of CG[2]. Gastric acid is probably not involved in the etiology but the psychological factors seem to be crucial for CG, too. Although diet is implicated as regards predisposition to constipation, colorectal cancers, and diverticular disease, a meaningful dietary role is doubtful in CG, too. Although some dietary habits may be the triggering factor for CG, this relationship does not always seen even in the same individuals. The most important etiologic association of CG is chronic infection by bacillus Helicobacter pylori (H. pylori) for today. Although H. pylori is linked to CG, peptic ulcer, gastric carcinoma, and mucosa-associated lymphoid tissue-lymphoma and it is recognised as a class I gastric carcinogen and it infects over 50% of world population[14-17], only a small subset of infected persons experience H. pylori-associated disorders[18]. Thus, a possible symbiotic relationship has been thought, and the debate has been further intensified with some studies, which have posed possibility that H. pylori infection may be beneficial for some humans[19]. This hypothesis is based on the elevated incidence of GERD, Barrett's esophagus, and adenocarcinoma of esophagus following H. pylori eradication in some countries[19]. So the colonization may either be beneficial or of low biological cost

**Table I: Comparison of the cases with and without irritable bowel syndrome**

| Variable | Cases with IBS* | Cases without IBS | p-value |
|---|---|---|---|
| Number | 156 | 179 | |
| Female ratio | 61.5% (96) | 61.4% (110) | >0.05 |
| Mean age and range (year) | 41.8 ± 11.1 (15-66) | 41.1 ± 13.3 (15-65) | >0.05 |
| Chronic gastritis | 72.4% (113) | 36.3% (65) | <0.001 |

*Irritable bowel syndrome

to the host. As a result, the underlying etiology and/or clinical appearance of the CG could not fully be explained neither by the gastric acid nor by the diet or H. pylori infection alone, and the giant gap about the underlying etiology and/or clinical onset of CG may be fulfilled by the high prevalence of IBS in society.

As a conclusion, IBS probably is a cascade of many physiological events, being initiated by infection, inflammation, psychological disturbances and stresses and eventually leading to dysfunctions of the gut and additional systems of the body by means of a low-grade inflammatory process. CG may be one of the terminating points of the physiological events' cascade, IBS. This may be explain by the high prevalence of IBS in society.

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