

## Analysis of the Gastrointestinal Symptoms of Uninvestigated Dyspepsia and Irritable Bowel Syndrome

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**Background/Aims:** Epidemiological studies suggest that there is a considerable overlap between functional dyspepsia (FD) and irritable bowel syndrome (IBS). The aim of this study was to examine concurrent gastrointestinal symptoms in FD and IBS. **Methods:** A total of 186 college students filled out a questionnaire regarding whether they had uninvestigated dyspepsia (UD, FD without endoscopic examination) and IBS based on Rome-II criteria. Gastrointestinal symptoms were measured using the Gastrointestinal Symptom Rating Scale (GSRS) questionnaire. **Results:** A total of 181 students (98 males, mean age 24.6 years) completed both questionnaires. The prevalence of UD, IBS, and UD+IBS overlap was 12 (6.7%), 40 (22.1%), and 8 (4.4%), respectively. A significant UD+IBS overlap was observed (66.7% IBS in UD, 20.0% UD in IBS). Reflux scores of GSRS in either UD or IBS were significantly greater than in those without. Gastroesophageal reflux disease (GERD), defined as weekly occurring moderate symptoms of heartburn and/or acid regurgitation and evaluated using the GSRS, was found in 16 (8.8%) of the subjects. The prevalence of IBS was significantly higher in GERD patients than in non-GERD patients (50.0% vs 19.4%). **Conclusions:** The considerable overlap not only between UD and IBS, but also between GERD and IBS, suggests the involvement of common pathophysiological disturbances in the two conditions. (*Gut and Liver* 2009;3:192-196)

**Key Words:** Dyspepsia; Irritable bowel syndrome; Gastroesophageal reflux; Overlap; Gastrointestinal symptom rating scale

## INTRODUCTION

Functional dyspepsia (FD) and irritable bowel syndrome (IBS) are two major functional gastrointestinal (GI) disorders. Both conditions are determined by heterogeneous factors, and FD and IBS are regarded as separate entities with unknown etiology; however, several common pathophysiological disturbances in FD and IBS have recently been identified, such as visceral hypersensitivity,<sup>1</sup> and indeed FD coexists in one- to two-thirds of IBS subjects.<sup>1-7</sup> Based on such common disturbances, a few recent review articles suggested that FD and IBS represent different manifestations of a single entity.<sup>2,3</sup> Surveys of concurrent upper and lower GI symptoms are useful to support this idea; however, the overlap of FD and IBS has not been examined in Japan.

The aim of this study was to examine GI symptoms in FD and IBS. We conducted a survey of FD and IBS in our medical students after a lecture on these diagnoses. The severity of various GI symptoms was assessed using the GI Symptom Rating Scale (GSRS), which is a validated, self-administered questionnaire.<sup>8,9</sup>

## MATERIALS AND METHODS

### 1. Subjects

One hundred eighty-six consecutive 5th-year medical students in our college (100 males, 24.5±3.0 years old) were recruited between June 2005 and December 2007. This survey was conducted when small groups of 5 or 6 students entered our Division of Gastroenterology for clinical training.

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## 2. Survey

### 1) *Helicobacter pylori* (*H. pylori*)

To examine the influence of *H. pylori* on the development of FD or IBS, blood was collected, and serum anti-*H. pylori* immunoglobulin G antibodies were measured by an enzyme-linked immunosorbent assay.

### 2) GSRS

Students filled out the GSRS questionnaire anonymously. GSRS includes 15 questions on a scale of 1 to 7, depending on how inconvenient it had been during the previous week. A higher score indicates more inconvenient symptoms. Combination scores among 15 questions can assess the following five domains: reflux syndrome (heartburn and acid regurgitation), abdominal pain (stomach ache, gastric hunger pains and nausea), indigestion syndrome (gastric borborygmus, gastric bloating, eructation and increased flatus), diarrhea syndrome (diarrhea, loose stools and urgent need to defecate) and constipation syndrome (constipation, hard stools and feeling of incomplete evacuation).<sup>8</sup>

The presence of gastroesophageal reflux disease (GERD) was also assessed by GSRS. GERD was considered when the either heartburn score or acid regurgitation score was 4 or greater. This condition indicates moderate symptoms of heartburn and/or acid regurgitation occurring at least once per week, which corresponded to the Montreal definition for the diagnosis of GERD in population-based studies.<sup>10</sup>

### 3) Our questionnaire

After the GSRS questionnaire, a small group was given an intensive lecture on FD and IBS diagnoses for half an hour. These diagnoses were based on Rome II criteria. In brief, FD was defined as follows: at least 12 weeks within the preceding 12 months of dyspepsia defined as pain or discomfort centered in the upper abdomen; no evidence of organic disease likely to explain the symptoms; and no evidence that dyspepsia is exclusively relieved by defecation or associated with the onset of a change in stool frequency or stool form.<sup>11</sup> FD was subdivided into symptom subgroups, ulcer-like (pain-predominant), dysmotility-like (unpleasant or irritating non-painful sensation-predominant) and unspecified (no symptoms of the above) dyspepsia. IBS was defined as follows: at least 12 weeks in the preceding 12 months of abdominal discomfort or pain with two of three features: relieved with defecation; and/or onset associated with a change in defecation frequency; and/or onset associated with a change in stool forma-

tion.<sup>12</sup> IBS was also subdivided into symptom subgroups, diarrhea-predominant and constipation-predominant IBS.

Subsequently, students filled out our questionnaire about whether they had uninvestigated dyspepsia (UD, defined as FD without endoscopic investigation) and IBS anonymously. The questionnaire also included age, gender and the use of nonsteroidal anti-inflammatory drugs (NSAIDs). NSAID users were defined as subjects who had taken NSAIDs on at least 3 days over the previous week.

Exclusion criteria from this study were that students did not complete both GSRS and our questionnaires.

## 3. Statistics

The results are reported as the mean±standard deviation. Fisher's exact probability test and the Wilcoxon test were performed using JMP software (SAS Institute Inc., Cary, NC, USA).  $p < 0.05$  was considered significant.

## RESULTS

### 1. Prevalence

One hundred eighty-one of 186 students completed both questionnaires (97.3% response rate). Five students were excluded due to incomplete responses to our questionnaire. Subject characteristics are summarized in Table 1. This survey revealed that 12 (6.7%) and 40 (22.1%) of 181 subjects had UD and IBS, respectively. *H. pylori* infection was recognized in 15 subjects (8.3%).

UD coexisted with IBS in 8 (4.4%) subjects. In 12 UD subjects, IBS was significantly prevalent than in non-UD

**Table 1.** Demographics of Students Who Completed the Survey (n=181) and Prevalence of UD, IBS, and UD+IBS

Demographics	Male:Female (%)	98:83 (54:46)
	Age (years [SD], range)	24.6±3.1 (21-43)
Prevalence	<i>H. pylori</i> infection (%)	15/181 (8.3)
	NSAID user (%)	5/181 (2.8)*
	UD (%)	12/181 (6.7) <sup>†</sup>
	Ulcer-like (%)	5/12 (41.7)
	Dysmotility-like (%)	7/12 (58.3)
	IBS (%)	40/181 (22.1)
	Diarrhea-predominant (%)	26/40 (65.0)
	Constipation-predominant (%)	14/40 (35.0)
	UD+IBS overlap (%)	8/181 (4.4)

UD, uninvestigated dyspepsia; IBS, irritable bowel syndrome; SD, standard deviation; *H. pylori*, *Helicobacter pylori*; NSAID, nonsteroidal anti-inflammatory drug.

\*All 5 NSAID users were on-demand users; <sup>†</sup>None had unspecified UD.

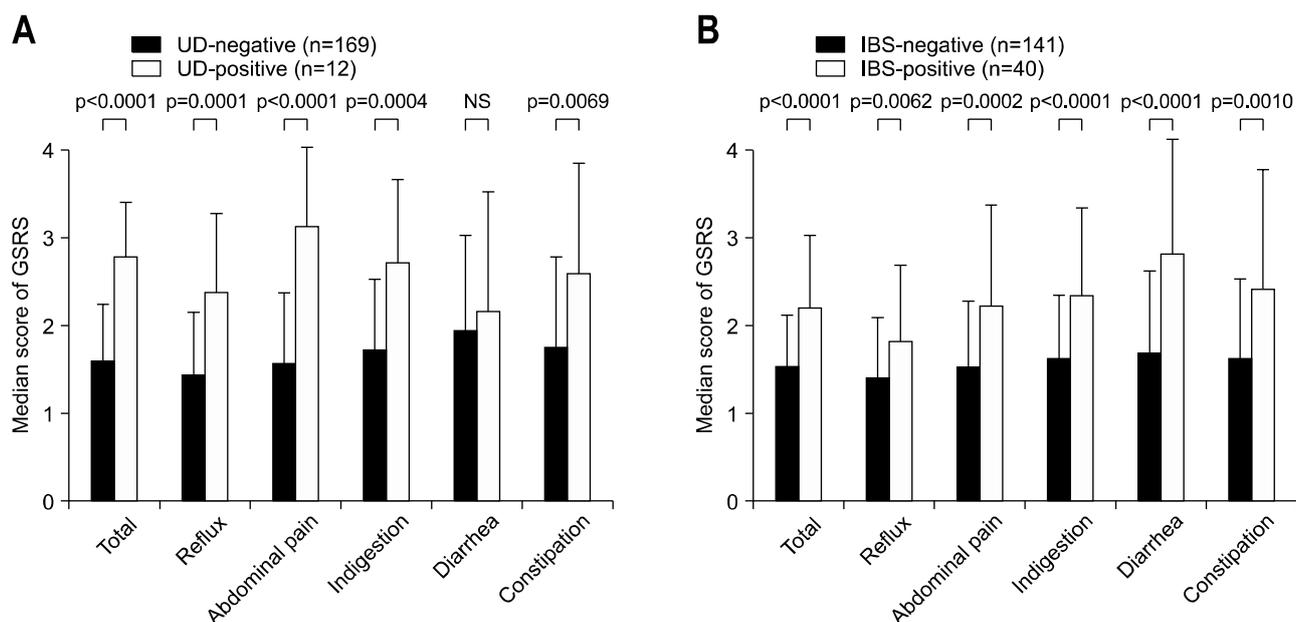


Fig. 1. GSRs scores for (A) UD and (B) IBS. Data are mean and standard deviation values.

GSRs, Gastrointestinal Symptom Rating Scale; UD, uninvestigated dyspepsia; IBS, irritable bowel syndrome; NS, not significant.

subjects (8/12 [66.7%] vs 32/169 [18.9%],  $p=0.0008$ ). Conversely, in 40 IBS subjects, UD was significantly more prevalent than in non-IBS subjects (8/40 [20.0%] vs 4/141 [7.1%],  $p=0.0008$ ).

## 2. Characteristics

Demographic comparisons either between UD and non-UD cases or between IBS and non-IBS cases showed no statistically significant differences in age, sex, *H. pylori* status, and NSAID use (*data not shown*). Comparisons between UD+IBS overlap and non-overlap cases showed similar results, except a sex difference. Seven (87.5%) of 8 students with UD+IBS overlap were women, which was significantly predominant compared with non-overlap (vs 76/173 [43.9%],  $p=0.0247$ ). Also in subdivided IBS, the characteristic of constipation-predominant IBS was significantly prevalent in women (12/14 [85.7%] vs 71/167 [42.5%],  $p=0.0036$ ).

## 3. Symptoms

The severities of GI symptoms in UD and IBS are shown in Fig. 1. In UD subjects, not only abdominal pain but also constipation were significantly more inconvenient than in subjects without UD. Also in IBS subjects, not only diarrhea and constipation but also abdominal pain indicating upper abdominal symptoms (stomach ache, gastric hunger pains and nausea) were significantly more inconvenient than in non-IBS subjects.

The reflux scores in subjects with UD or IBS were sig-

Table 2. The Prevalence of UD, IBS, and UD+IBS in GERD (as Estimated by the GSRs)

Disorder	GERD-negative (n=165)	GERD-positive (n=16)	p-value
UD (%)	9 (5.5)	3 (18.8)	NS
Ulcer-like (%)	2 (1.2)	3 (18.8)	0.0051
Dysmotility-like (%)	7 (4.2)	0 (0)	NS
IBS (%)	32 (19.4)	8 (50.0)	0.0095
Diarrhea-predominant (%)	22 (13.3)	4 (25.0)	NS
Constipation-predominant (%)	10 (6.1)	4 (25.0)	0.0240
UD+IBS overlap (%)	6 (3.6)	2 (12.5)	NS

UD, uninvestigated dyspepsia; IBS, irritable bowel syndrome; GERD, gastroesophageal reflux disease; GSRs, Gastrointestinal Symptom Rating Scale; NS, not significant.

nificantly greater than in those without. If GERD was defined as weekly moderate symptoms of heartburn and/or acid regurgitation, 16 (8.8%) of 181 subjects were considered as having GERD estimated by GSRs. In GERD subjects, the prevalence of IBS, especially the constipation type of IBS, was significantly greater than in non-GERD subjects (Table 2).

The overlaps among UD, IBS and GERD are shown in Fig. 2. GERD coexisted with IBS in 4.4% of our population. Not only UD and IBS but also GERD and IBS considerably overlapped.

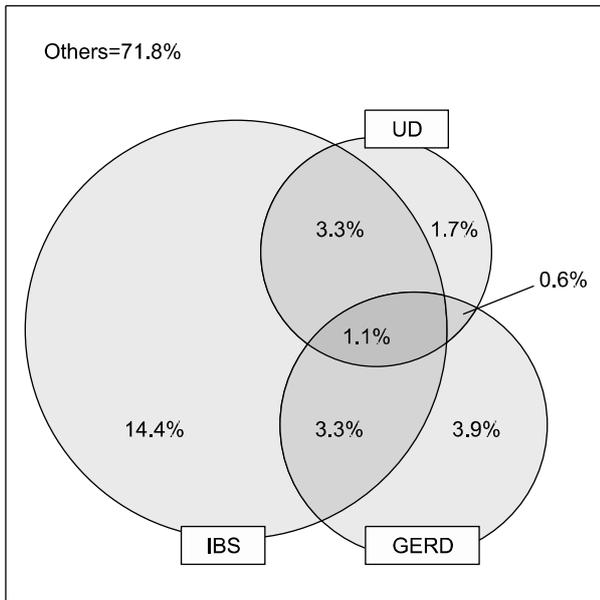


Fig. 2. Overlap between UD, IBS, and GERD (as estimated by the GRSR) in 181 students.

UD, uninvestigated dyspepsia; IBS, irritable bowel syndrome; GERD, gastroesophageal reflux disease; GRSR, Gastrointestinal Symptom Rating Scale.

## DISCUSSION

This survey found considerable overlap, not only between UD and IBS but also between GERD and IBS. GERD+IBS overlap rather than FD+IBS overlap has been recently highlighted, and this considerable overlap has been advocated in several review articles.<sup>13,14</sup> The prevalence of IBS in GERD has been reported to be 19-71%, and that of GERD in IBS as 11-79%<sup>4,13-17</sup>; in this study they were 50% and 20%, respectively. A population-based study revealed that the prevalence of GERD+IBS overlap was 2.8% in men and 4.4% in women, and the authors concluded that GERD+IBS overlap did not occur by chance, because these rates were greater than the expected prevalence<sup>15</sup>; the prevalence in our population was similar (4.4%). A systemic review showed that the prevalence of IBS in the non-GERD population was estimated to be only 5.1%, much lower than in the whole population, 11.2%,<sup>13</sup> indicating that IBS could be relatively uncommon in the absence of GERD, and vice versa.

The reason for the strong overlap between GERD and IBS remains unknown. Two main hypotheses have been proposed as follows: GERD and IBS are two distinct disorders with a common pathophysiologic process; and IBS symptoms are part of GERD manifestations.<sup>14</sup> GERD is defined as a condition that develops when the reflux of stomach contents causes irritating symptoms and/or com-

plications,<sup>10</sup> and is an organic disorder; however, general GERD studies might often include functional disorders, such as functional heartburn. Unfortunately the prevalence of IBS was reported to be similar in patients with functional heartburn vs non-erosive reflux disease (NERD) (46% vs 50%),<sup>16</sup> or in patients with NERD probably including functional heartburn vs erosive GERD (35% vs 36%)<sup>17</sup>; therefore, GERD symptoms may be generated by an "irritable gut" as a common pathophysiologic process rather than the greater extent of reflux or mucosal injury.

Common pathophysiologic processes have been reported in the overlap of FD and IBS, such as visceral hypersensitivity and delayed gastric emptying.<sup>2,3</sup> In a visceral hypersensitivity study, patients with FD+IBS overlap were found to have hypersensitivity to gastric distension compared to those with FD alone (44% vs 28%).<sup>1</sup> In a gastric emptying study, gastric emptying rates were lower in IBS patients than in controls (33%/h vs 40%/h), whereas those in patients with IBS alone were similar to those in controls (37%/h vs 40%/h, but 31%/h in IBS with dyspepsia).<sup>5</sup> Although these results suggest the existence of common disturbances between FD and IBS, these significant but limited data seem to be weak if FD and IBS are regarded as a single entity. Our results also appeared similar in the significant but limited overlap. Rather, the possible existence of a novel entity between FD and IBS should be addressed, such as irritable gut. The prevalence of UD+IBS overlap was reported to be 5.0% in an outpatient population,<sup>6</sup> and 4.9% in a GERD population,<sup>7</sup> similar to 4.4% in this study. Significant female predominance in the overlap was found in our study, and a few articles have shown a similar result.<sup>1</sup>

A high prevalence of IBS (22.1%) was found in this study. The prevalence of IBS in population-based studies is around 10%.<sup>4</sup> IBS mainly affects adolescents and younger adults, and IBS development in this population is about twice as frequent as in a presenile population.<sup>18</sup> Hence, the high prevalence seems to be due to the younger age of our study subjects. Our result of significant female predominance in constipation-predominant IBS is the same as in previous studies.<sup>19</sup>

In contrast, a low prevalence of UD (6.7%) was found in this study. The prevalence of UD in population-based studies is around 24% using Rome II criteria.<sup>20</sup> Although the peak prevalence of FD was noted at ages 40-49 in Japan, the prevalence at a younger age of 15-29 stayed about the same (about 14% vs 13%).<sup>21</sup> Since a cross-national study pointed out that the prevalence of upper GI symptoms in Japan was the lowest (9.4%) of the 7 countries (28.1% on average),<sup>22</sup> Japanese may have fewer symptoms of dyspepsia.

In summary, significant UD+IBS overlap was observed in 4.4% with female predominance. Subjects with GERD symptoms more frequently had IBS than those without. Considerable overlap between UD and IBS or between GERD and IBS could indicate the involvement of common pathophysiological disturbances. Investigating such common disorders could be a breakthrough to identify the pathogenesises.

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