Association of Colonic Diverticular Disease and Irritable Bowel Syndrome in Thai Patients

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Background: *Colonic diverticular disease exhibits mucosal outpouchings through the large intestine. Common complications of this disease are diverticular bleeding and diverticulitis. Some patients with colonic diverticular disease have abdominal symptoms resembling irritable bowel syndrome (IBS). IBS is a functional gastrointestinal disorder with abdominal discomfort, bloating or pain associated with disturbed defecation and unclear etiology. Some studies have shown a high prevalence of colonic diverticular disease in patients with IBS.*

Objective: *To determine the association, clinical characteristics and factors associated with colonic diverticular disease in IBS patients compared with a control group.*

Material and Method: *A cross-sectional prospective study was conducted at the Gastroenterology Unit, Department of Medicine, Rajavithi Hospital, Bangkok during December 2007 to January 2009. The study collected data regarding clinical characteristics, demographics and colonoscopic findings of colonic diverticular disease comparing among IBS patients, defined by Rome III criteria and control group patients. The study was approved by the institutional ethics committee of Rajavithi Hospital. Demographic data of patients were collected. The presence of diverticula, their location and number from colonoscopic findings were recorded.*

Results: *One hundred and fifty patients were enrolled and analyzed. The patients comprised 75 patients in the IBS group and 75 patients in the control group. The prevalence of colonic diverticular disease in the total population was 17.3% (26 of 150). The IBS group had a higher prevalence of colonic diverticular disease than the control group with statistical significance (18 of 75, 24.0% in the IBS group vs. 8 of 75 or 10.7% in the control group, p = 0.031). Body mass index (BMI) more than 25 kg/m^2, age more than 60 years and being male were associated with colonic diverticular disease without significance (28.1% in BMI >25 kg/m^2 vs. 14.3% in BMI ≤25 kg/m^2, p = 0.071, 23.0% in age >60 years vs.13.5% in age ≤60 years, p = 0.132 and 20.3% males vs. 15.1% females, p = 0.406). Type of IBS (IBS-C vs. IBS-D) did not affect the prevalence of colonic diverticular disease (25.8% in IBS-C and 23.1% in IBS-D, p = 0.791). There were no difference in the location of colonic diverticular disease and number of diverticuli between the IBS group and control group (p = 0.149 and 0.095).*

Conclusion: *An increased frequency of colonic diverticular disease was observed in patients with IBS. Increasing age, high BMI and being male were factors associated with colonic diverticular disease. These results suggest that IBS and colonic diverticular disease may have a common pathogenesis.*

Keywords: *Irritable bowel syndrome, Colonic diverticular disease, IBS with constipation (IBS-C), IBS with diarrhea (IBS-D)*

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Colonic diverticular disease exhibits mucosal outpouchings through the large bowel wall. The prevalence increases with age, being 5.0% at age 40, 30.0% at age 60 and 85.0% at age 80[1]. Western countries have the highest prevalence rates. In Asia, the data on this disease are limited. Rajendra et al reported that the prevalence rate of colonic diverticular disease in the Asian population was 10.0% and that the right-sided location was predominant (80.0%)[2]. Common complications of this disease are diverticular bleeding and diverticulitis.

Irritable bowel syndrome (IBS) is a functional gastrointestinal disorder presenting abdominal discomfort, bloating or pain associated with change of bowel movement[3]. The diagnosis of IBS is based on the Rome III criteria for functional gastrointestinal disorder[4]. The prevalence of this disease in western countries is about 12.0-15.0%[5]. The prevalence of this disease in Thailand is about 4.8%[6]. Some patients with colonic diverticular disease have abdominal symptoms resembling IBS. Many studies have shown that colonic

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diverticular disease involves abnormal intestinal motility, abdominal discomfort and bowel habit change[7,8]. Some studies have reported a higher prevalence of colonic diverticular disease in IBS patients than in the general population[9,10]. In Thailand, no data exists of associations, clinical characteristics and factors associated with colonic diverticular disease in IBS patients. The purpose of this study was to determine the associations of colonic diverticular disease and IBS including the prevalence, clinical characteristics and endoscopic findings of colonic diverticular disease among Thai patients. This study could provide the epidemiology and associations of colonic diverticular disease and IBS in our community.

Material and Method

This cross-sectional prospective study was conducted at the Gastroenterology Unit, Department of Medicine Rajavithi Hospital, Bangkok from December 2007 to January 2009. Written consent was given. Medical history and physical examination were obtained and colonoscopy was performed. The study was reviewed and approved by the ethics review committee of Rajavithi Hospital.

Inclusion criteria included patients aged 18 years or over with clinical and physical examination compatible with IBS defined by Rome III criteria and the control group with subjects aged 18 and over who received colonoscopies for various indications. Exclusion criteria included patients with bowel obstruction, massive colon bleeding, colon perforation, inflammatory mass known colon or rectal cancer and patients with contraindication for colonoscopy. IBS patients, defined by Rome III criteria[4], and control group patients were enrolled.

Sample size was calculated using two independent proportion formulas. Prevalence of colonic diverticulosis in patients with IBS (28%)[9] and in healthy populations in Asian countries(10%)[2] was used to calculate the sample size of each group. The author indicated 80% of power and *p*-value less than 0.05 was statistically significant. The appropriate number for number of subjects was determined to be seventy-five patients.

IBS is defined by Rome III criteria as recurrent abdominal pain or discomfort at least three days a month in the past three months, associated with two or more of the following:

- Improvement with defecation.
- Onset associated with a change in frequency of stool.
- Onset associated with a change in form or appearance of stool.

Criteria fulfilled for the past three months with symptom onset at least six months before diagnosis with exclusion of organic causes.

Four subtypes of IBS were classified:

- IBS with constipation (IBS-C): hard or lumpy stool $\geq$25%/loose or watery stool <25% of bowel movements.
- IBS with diarrhea (IBS-D): loose or water stool $\geq$25%/hard or lumpy stool <5% of bowel movements.
- Mixed IBS (IBS-M): hard or lumpy stool $\geq$25%/loose or watery stool $\geq$25% of bowel movements.
- Unsubtyped IBS (IBS-U): insufficient abnormality of stool consistency to meet the above subtypes' criteria.

Colonoscopic examination

All endoscopic procedures were performed by a gastroenterologist working at Rajavithi Hospital. The bowels were prepared using either polyethylene glycol or sodium phosphate solution. Conscious sedation was administered using intravenous midazolam and pethidine. Standard colonoscopes were used for the examinations. If colonic diverticular disease were found, their location and number were recorded completely. The authors defined the right side of the colon as the cecum and the ascending and transverse colon, and the left side as the descending and sigmoid colon.

Clinical data and colonoscopic data were collected and analyzed.

Statistical analysis

Chi-square test or Fishers' exact test was used for qualitative variables and the Student t-test for quantitative variables. SPSS for Windows (SPSS, Chicago, IL, USA version 17.0) was used to analyze data. A *p*-value less than 0.05 were considered statistically significant.

Results

One hundred and fifty patients were enrolled in the present study. The IBS group (75 patients) had more females than males (46 females and 29 males), with age (mean $\pm$ SD) 54.07$\pm$13.03 years and BMI (mean $\pm$ SD) 23.98$\pm$4.70 kg/m^2. The control group had nearly equal numbers (40 females and 35 males), with a mean $\pm$ SD age of 60.48$\pm$12.09 years and BMI (mean $\pm$ SD) 23.48$\pm$4.15 kg/m^2. No difference was found in age,

sex and BMI between the IBS and the control groups (p>0.050) (Table 1). The IBS patients were classified in four subgroups (Fig. 1): 52.0% with IBS-D, 41.3% with IBS-C, 4.0% with BS-M and 2.7% with IBS-U. Most patients had symptoms 8-14 days each month: 36.0% (27 of 75) 3-7 days each month, 62.7% (47 of 75) 8-14 days each month, and 1.3% (1 of 75) more than 14 days each month (Table 2). Most patients had duration of symptom for 6-9 months: 36.0% (27 of 75) followed by 3-6 months, 57.3% (43 of 75), 6-9 months, 2.7% (2 of 75), 9-12 months and 4.0% (3 of 75) more than 12 months (Table 2).

The prevalence of colonic diverticular disease in the total population was 17.3% (26 of 150). The prevalence of colonic diverticular disease was significantly higher in the IBS group than in the control group (18 of 75, 24.0% in IBS group vs. 8 of 75, 10.7% in control group, p = 0.031). The prevalence of colonic diverticular disease was not different between patients with IBS-C and IBS-D (25.8% in IBS-C and 23.1% in IBS-D, p = 0.791) (Table 3). The locations of colonic diverticular disease were scattered among right side, left side and total colon (9 patients in left side colon, 11 patients in right side colon and 6 patients in entire colon). The patients in the IBS group had colonic diverticular disease more at the right side colon than the left side colon (9 patients in the right-side colon vs. 6 patients in the left side colon), while the control group locations of colonic diverticular disease in the control group did not differ (2 patients in the right side colon vs. 3 patients in the left side colon). However, no statistic significant differences were found in the location of colonic diverticular disease between the IBS and control groups (p = 0.149). Most patients in the IBS group had a number of colonic diverticuli, 1-5 per person (14 of 18 or 77.8%), while the patients in the control group had a number of colonic diverticuli varying from 1-5 to more than 10 diverticuli per person but no difference was observed in the IBS group (p = 0.095).

Body mass index (BMI) more than 25 kg/m^2, age more than 60 years and being male were associated

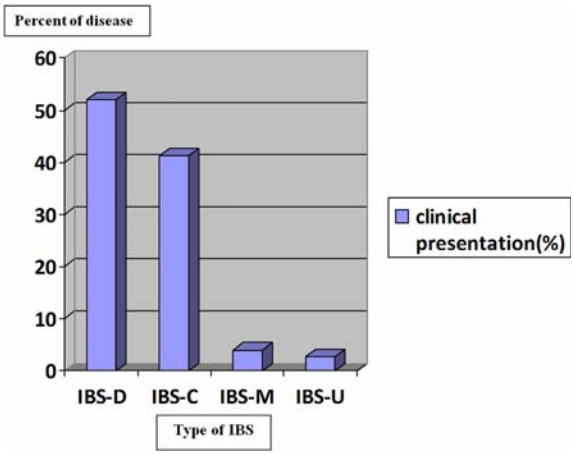

Fig. 1 Clinical presentation of patients in the IBS group.

Table 1. Baseline demographic data of the IBS and control groups

Data	IBS group (n = 75)	Control group (n = 75)	p-value
Age (mean ± SD) (years)	50.07±13.03	60.48±12.09	0.270
Gender (male/femal)	29/46	35/40	0.320
BMI (mean ± SD) (kg/m^2)	23.98±4.7	23.48±4.15	0.260

Table 2. Severity of disease and duration of presentation of patients in the IBS group

Characteristics	Number	%
Severity of clinical presentation		
3-7 days per month	27/75	36.0
8-14 days per month	47/75	62.7
More than 14 days per month	1/75	1.3
Durations of clinical presentation (month)		
3-6	27/75	36.0
6-9	43/75	57.3
9-12	2/75	2.7
>12	3/75	4.0

with colonic diverticular disease without significance (28.1% in BMI >25 kg/m^2 vs. 14.3% in BMI ≤25 kg/m^2, p = 0.071, 23.0% at age >60 year vs. 13.5% at age ≤60 year, p = 0.132 and 20.3% in males vs. 15.1% in females, p = 0.406) (Table 4).

Discussion

From the present study, the prevalence of colonic diverticular disease was 17.3%, not different from previous studies in Asia[12-14] but lower than in Western countries[9,11]. The IBS group had a higher prevalence of colonic diverticular disease than the control group with statistical significance (24.0% vs. 10.7%, p = 0.031). The finding was correlated with a recent study that reported IBS had a higher association with colonic diverticular disease[9]. The pathogenesis of IBS is uncertain but may be multifactorial. One pathogenesis of IBS is abnormal large bowel motility[15,16]. Patients with colonic diverticular disease also have abnormal large bowel motility and abnormal colonic contractility causing a thickening of the tunica muscularis in the diverticular area[17,18]. Lack of intrinsic inhibition mediated by nitric oxide may contribute to impaired muscle relaxation in IBS and colonic diverticular disease[17,19]. Another pathophysiology in IBS is visceral hypersensitivity[20,21] resembling colonic diverticular disease with a low threshold perception to colonic distension[22]. One epidemiologic study showed an association of low-fiber diet with colonic diverticular disease[23]. Low fiber diet caused stasis of bowel contents and bacterial overgrowth. Bacterial overgrowth induced chronic inflammation affecting the afferent neurons in the myenteric plexus and submucosa, causing visceral hypersensitivity and abnormal colonic contractility and colonic symptoms resembling symptoms of IBS[19,24].

The IBS group had more females than males (46 females and 29 males). This did not correlate to a recent meta-analysis that showed that the prevalence of IBS was not significantly higher in women, compared with men in South Asian, South American or African studies[25]. It may be due to geography and the criteria used to define IBS. IBS-D and IBS-C were present in a similar proportion in patients with IBS (52.0% vs. 41.3%), resembling a recent review of IBS in Asia[26]. Between patients with IBS-C and IBS-D, the prevalence of

Table 3. Association of IBS and IBS subtypes with colonic diverticular disease

Population group	Diverticular disease	%	*p*-value
Total	26/150	17.3	
IBS group	18/75	24.0	0.031*
Control group	8/75	10.7	
IBS group subtype			
IBS-C	8/31	25.8	0.791
IBS-D	9/39	23.1	

* = Significant at p<0.050

Table 4. Association between colonic diverticular disease and baseline characteristics

Baseline characteristics	Diverticular disease	%	*p*-value
Body mass index (BMI)			
>25 kg/m^2	9/32	28.1	0.071*
≤25 kg/m^2	15/105	14.3	
Age			
>60 year	14/47	23.0	0.132*
≤60 year	12/77	13.5	
Sex			
Male	13/64	20.3	0.406*
Female	13/86	15.1	

* = No significance at p<0.050

colonic diverticular disease was not different (25.8% vs. 23.1%, $p = 0.791$). This finding was different from a recent study that IBS-D was the strongest predictor of colonic diverticular disease especially after colonic infection[9]. The location of colonic diverticular disease and number of colonic diverticuli found in the IBS and the control groups did not differ. These findings showed that numbers and locations of colonic diverticular disease were not related to IBS symptoms but may be related to geographic variation.

Increased age was associated with colonic diverticular disease[27,28] due to decrease of the tensile strength of the colon wall with aging. The present study showed the correlation between prevalence of colonic diverticular disease and aging (23.0% in age >60 year vs. 13.5% in age ≤60 year). BMI was more than 25 kg/m^2 and males are potentially correlated with colonic diverticular disease but without statistical significance found. This finding is consistent with other studies in Israel[29] and Korea[30].

Some potential limitations were involved in the present study. The study population came from patients only in one hospital that may not represent the general population due to the geographic variation of the disease.

In conclusion, an increased frequency of colonic diverticular disease was found among patients with IBS. Increasing age, high BMI and being male were potentially associated with colonic diverticular disease. These results suggest that IBS and colonic diverticular disease may have a common pathogenesis.

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Potential conflicts of interest

None.

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ความสัมพันธ์ของโรคกระเปาะลำไส้ใหญ่กับโรคลำไส้แปรปรวนในผู้ป่วยไทย

สยาม ศิรินธรปัญญา, สมบุญ รุ่งจิระธนานนท์

ภูมิหลัง: *โรคกระเปาะลำไส้ใหญ่เกิดจากการยื่นของเนื้อเยื่อชั้นในของลำไส้ใหญ่เข้าไปในตัวผนังลำไส้ใหญ่ ทำให้เกิดกระเปาะที่ยื่นออกจากผนังลำไส้ ภาวะแทรกซ้อนได้แก่ เลือดออกและการอักเสบของกระเปาะลำไส้ใหญ่ ผู้ป่วยบางรายมีอาการทางช่องท้องเหมือนโรคลำไส้แปรปรวน โรคลำไส้แปรปรวนเป็นโรคทางเดินอาหารที่ไม่มีสาเหตุทางกายภาพ มีอาการไม่สบายท้อง ท้องอืด หรือปวดท้องร่วมกับการเปลี่ยนแปลงการขับถ่าย ซึ่งยังไม่ทราบสาเหตุชัดเจน บางการศึกษาพบความชุกของโรคกระเปาะลำไส้ใหญ่สูงขึ้นในผู้ป่วยโรคลำไส้แปรปรวน*

วัตถุประสงค์: *เพื่อดูความสัมพันธ์ ลักษณะทางคลินิก และปัจจัยอื่นๆ ที่เกี่ยวข้องกับการเกิดโรคกระเปาะลำไส้ใหญ่กับโรคลำไส้แปรปรวนในผู้ป่วยไทยเทียบกับประชากรทั่วไป*

วัสดุและวิธีการ: *การศึกษาแบบตัดขวางไปข้างหน้าเพื่อดูความสัมพันธ์ของข้อมูลพื้นฐาน, ลักษณะทางคลินิก และปัจจัยอื่นๆ ที่เกี่ยวข้องกับการเกิดโรคกระเปาะลำไส้ใหญ่กับโรคลำไส้แปรปรวนในผู้ป่วยไทย วินิจฉัยจากข้อตกลงโรมสามเปรียบเทียบกับประชากรทั่วไป การศึกษานี้ได้รับการอนุมัติจากคณะกรรมการจริยธรรม โรงพยาบาลราชวิถี ข้อมูลพื้นฐาน, ลักษณะทางคลินิกและการตรวจพบและลักษณะ, ตำแหน่งและจำนวนของกระเปาะลำไส้ใหญ่ การตรวจหาโรคกระเปาะลำไส้ใหญ่ทำโดยการส่องกล้องตรวจลำไส้ใหญ่จะถูกรวบรวมและนำมาวิเคราะห์*

ผลการศึกษา: *การศึกษาในผู้ป่วยจำนวน 150 ราย ประกอบด้วยผู้ป่วยกลุ่มโรคลำไส้แปรปรวน 75 ราย และกลุ่มควบคุมจำนวนเท่ากัน การวินิจฉัยโรคลำไส้แปรปรวนใช้นิยามตามข้อตกลงโรมสาม (Rome III criteria) ความชุกของโรคกระเปาะลำไส้ใหญ่โดยรวมเท่ากับร้อยละ 17.3 (26 ใน 150) ความชุกของโรคกระเปาะลำไส้ใหญ่ในผู้ป่วยที่มีโรคลำไส้แปรปรวนสูงกว่าในกลุ่มควบคุมอย่างมีนัยสำคัญทางสถิติ (ร้อยละ 24.0) ในกลุ่มโรคลำไส้แปรปรวนและร้อยละ 10.7 ในกลุ่มควบคุม, p = 0.031) ในผู้ป่วยโรคลำไส้แปรปรวนแบบท้องผูกและท้องเสีย ความชุกของโรคกระเปาะลำไส้ใหญ่ไม่แตกต่างกัน (ร้อยละ 25.8) ในผู้ป่วยโรคลำไส้แปรปรวนแบบท้องผูกและร้อยละ 23.1 ในโรคลำไส้แปรปรวนแบบท้องเสีย, p = 0.791) ไม่มีความแตกต่างกันของตำแหน่งและจำนวนกระเปาะลำไส้ใหญ่ระหว่างผู้ป่วยโรคลำไส้แปรปรวนและกลุ่มควบคุม (p = 0.149 และ 0.095) ค่าดัชนีมวลกายที่มากกว่า 25 กก./ตร.ม. อายุมากกว่า 60 ปี และเพศชายสัมพันธ์กับการเกิดโรคกระเปาะลำไส้ใหญ่แต่ไม่มีนัยสำคัญทางสถิติ (ร้อยละ 28.1) ในกลุ่มค่าดัชนีมวลกายที่มากกว่า 25 กก./ตร.ม. เทียบกับร้อยละ 14.3 ในกลุ่มค่าดัชนีมวลกายที่น้อยกว่าหรือเท่ากับ 25 กก./ตร.ม. p = 0.071, ร้อยละ 23.0 ในกลุ่มอายุมากกว่า 60 ปี เทียบกับ ร้อยละ 13.5 ในกลุ่มอายุน้อยกว่าหรือเท่ากับ 60 ปี, p = 0.132 และร้อยละ 20.3 ในเพศชายเทียบกับร้อยละ 15.1 ในเพศหญิง, p = 0.406)*

สรุป: *โรคกระเปาะลำไส้ใหญ่พบได้บ่อยขึ้นในผู้ป่วยที่มีโรคลำไส้แปรปรวน ค่าดัชนีมวลกายที่มากกว่า 25 กก./ตร.ม. อายุมากกว่า 60 ปี และเพศชายสัมพันธ์กับการเกิดโรคกระเปาะลำไส้ใหญ่ โรคกระเปาะลำไส้ใหญ่และโรคลำไส้แปรปรวนน่าจะมีพยาธิกำเนิดของโรคร่วมกัน*