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BRIEF ARTICLE

Prevalence and risk factors of asymptomatic peptic ulcer disease in Taiwan

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Abstract

AIM: To investigate the prevalence and risk factors of asymptomatic peptic ulcer disease (PUD) in a general Taiwanese population.

METHODS: From January to August 2008, consecutive asymptomatic subjects undergoing a routine health check-up were evaluated by upper gastrointestinal endoscopy. Gastroduodenal mucosal breaks were carefully assessed, and a complete medical history and demographic data were obtained from each patient. Logistic regression analysis was conducted to identify independent risk factors for asymptomatic PUD.

RESULTS: Of the 572 asymptomatic subjects, 54 (9.4%) were diagnosed as having PUD. The prevalence of gastric ulcer, duodenal ulcer and both gastric and duodenal ulcers were 4.7%, 3.9%, and 0.9%, respectively. Multivariate analysis revealed that prior history of PUD [odds ratio (OR), 2.0, 95% CI: 1.3-2.9], high body mass index [body mass index (BMI) 25-30: OR, 1.5, 95% CI: 1.0-2.2; BMI > 30 kg/m^2: OR, 3.6, 95% CI: 1.5-8.7] and current smoker (OR, 2.6, 95% CI: 1.6-4.4) were independent predictors of asymptomatic PUD. In contrast, high education level was a negative predictor of PUD (years of education 10-12: OR, 0.5, 95% CI: 0.3-0.8; years of education > 12: OR, 0.6, 95% CI: 0.3-0.9).

CONCLUSION: The prevalence of PUD in asymptomatic subjects is 9.4% in Taiwan. Prior history of PUD, low education level, a high BMI and current smoker are independent risk factors for developing asymptomatic PUD.

Key words: Asymptomatic; Endoscopy; Health check-up; Peptic ulcer disease

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INTRODUCTION

Peptic ulcer disease (PUD) is a common disease of the

digestive system[1]. The self-reported PUD prevalence among people aged 18 years and older in the United States was 10.3% in 1989[2], compared with 14% among people aged 20 to 81 years in Hong Kong[3].

The pathogenesis of symptom development in PUD is unclear. A few studies have revealed that several factors, such as acid, inflammation, or muscle spasm, may be related to the pathogenesis of ulcer pain[4,5]. A study in Taiwan revealed that 67% of PUD patients had no remarkable symptoms[6]. Some patients with PUD are asymptomatic until life-threatening complications (e.g. hemorrhage, perforation) develop[7]. Previous studies found that the majority of patients who died from PUD usually had no ulcer symptoms until the final fatal illness[8]. Therefore, non-symptom producing ulcers remain a clinical challenge.

Currently, the long-term consequences of silent PUD remain unclear, however, hemorrhage, perforation, and stricture are well known complications of PUD[9,10]. Therefore, identification and follow up of these asymptomatic patients is essential. Nonetheless, the risk factors for asymptomatic PUD still remain unclear. The aims of this study were to investigate the prevalence and risk factors of asymptomatic PUD in Taiwan.

MATERIALS AND METHODS

Subjects

From January to August 2008, consecutive asymptomatic subjects undergoing a routine endoscopy during a health check-up were invited to participate in this study. The eligible subjects were free of reflux and dyspeptic symptoms such as heartburn, regurgitation, dysphagia, epigastric pain, epigastric fullness, nausea and vomiting in the previous month. Exclusion criteria were (1) use of proton pump inhibitors, histamine-2 receptor antagonists, sucralfate, prostaglandin analogs and antacids within the previous month; (2) use of prokinetic or anticholinergic agents; and (3) serious medical illness.

Study design

A complete history and physical examination were performed for every subject undergoing a health check-up. All subjects were carefully interviewed regarding the presence of reflux or dyspeptic symptoms in the previous month, and subjects who responded negatively were classified as asymptomatic subjects and enrolled in this study. Endoscopies were performed by three experienced endoscopists (Hsu PI, Cheng LC, and Yu HC) using an Olympus GIF XV10 and GIF XQ200 (Olympus Corp., Tokyo, Japan) after the subjects had fasted overnight. The endoscopists were blinded as to whether the patients they were examining were symptomatic or asymptomatic. The patients were carefully examined for gastroduodenal mucosal breaks, and the length of these breaks was measured by opening a pair of biopsy forceps of known span in front of the breaks. Peptic ulcer disease was defined as a circumscribed mucosal break 5 mm or more in diameter, with a well defined ulcer crater[11].

To assess the relationships between clinical characteristics and asymptomatic PUD, the following data were recorded for each subject: age; gender; educational status; prior history of PUD; consumption of tobacco, alcohol, coffee, tea, spicy foods or betel nut, and use of non-steroidal anti-inflammatory drugs (NSAIDs) within 4 wk of endoscopy. All variables were categorized for data analyses.

Table 1 Demographics and endoscopic findings of asymptomatic subjects undergoing a routine health check-up (n = 572) n (%)

Clinical characteristics	
Age (yr)	
mean ± SD	51.5 ± 12.9
< 45	206 (36.0)
45-60	235 (41.1)
> 60	131 (22.9)
Gender	
Men	372 (65.0)
Women	200 (35.0)
Body mass index (kg/m^2)	
mean ± SD	24.3 ± 3.5
< 25	321 (55.6)
25-30	225 (38.8)
> 30	26 (4.6)
Endoscopic findings	
Peptic ulcer	54 (9.4)
Gastric ulcer	27 (4.7)
Duodenal ulcer	22 (3.9)
Gastric ulcer and duodenal ulcer	5 (0.9)

Statistical analysis

The χ^2 test or Fisher's exact test was employed to investigate the relationships between the rate of PUD and clinical characteristics. These variables included the following: gender; age (< 45, 45-60, or > 60 years); educational status (< 10, 10-12, or > 12 years); body mass index [body mass index (BMI): < 25, 25-30, or > 30 kg/m^2]; NSAID use (yes or no); history of PUD (yes or no); smoking status (no, former smoker, current smoker); consumption of alcohol, coffee, tea or spicy foods (no, ≤ 3 times per week, or > 3 times per week); betel nut habit (yes or no). A P value less than 0.05 was considered significant. Significant variables revealed by univariate analysis were subsequently assessed by a stepwise logistic regression method to identify independent clinical factors predicting the presence of PUD in asymptomatic subjects.

RESULTS

Patient demographics and endoscopic characteristics

From January to August 2008, 572 asymptomatic subjects (mean age, 51.5 ± 12.9 years; age range, 18-87 years; male/female, 372/200) were recruited into this study. Of these patients, 54 (9.4%) had PUD (Table 1). The cases of PUD consisted of 27 gastric ulcer (4.7%), 22 duodenal ulcer (3.9%) and 5 had both gastric ulcer and duodenal ulcer (0.9%).

Comparison of socio-demographic and lifestyle factors in subjects with and without peptic ulcer disease

Table 2 shows the relationships between clinical character-

Table 2 Comparison of socio-demographic and lifestyle factors in asymptomatic subjects with and without peptic ulcer disease *n* (%)

Principal parameter	Non-peptic ulcer	Peptic ulcer	*P* value
Sex			< 0.001
Men	330 (63.7)	42 (77.8)	
Women	188 (36.3)	12 (22.2)	
Age (yr)			0.082
< 45	199 (38.4)	16 (29.6)	
45-60	211 (40.7)	23 (42.6)	
> 60	108 (20.9)	15 (27.8)	
Education (yr)			0.045
< 10	118 (22.8)	18 (33.3)	
10-12	225 (43.4)	20 (37.0)	
> 12	175 (33.8)	16 (29.7)	
BMI (kg/m^2)			< 0.001
< 25	315 (60.8)	25 (46.3)	
25-30	189 (36.5)	25 (46.3)	
> 30	14 (2.7)	4 (7.4)	
NSAID use			0.628
No	471 (90.9)	50 (92.6)	
Yes	47 (9.1)	4 (7.4)	
Peptic ulcer history			< 0.005
No	370 (71.4)	30 (55.6)	
Yes	148 (28.6)	24 (44.4)	
Smoking status			< 0.001
No	359 (69.3)	27 (50.0)	
Former smoker	75 (14.5)	8 (14.8)	
Current smoker	84 (16.2)	19 (35.2)	
Alcohol drinking			0.137.
No	379 (73.2)	36 (66.7)	
≤ 3 times per week	88 (17.0)	13 (24.1)	
> 3 times per week	51 (9.8)	5 (9.2)	
Coffee drinking			0.739
No	299 (57.7)	31 (57.4)	
≤ 3 times per week	100 (19.3)	12 (22.2)	
> 3 times per week	119 (23.0)	11 (20.4)	
Tea drinking			0.209
No	222 (42.9)	19 (35.2)	
≤ 3 times per week	99 (19.1)	11 (20.4)	
> 3 times per week	197 (38.0)	24 (44.4)	
Spicy foods consumption			0.147
No	321 (62.0)	29 (53.7)	
≤ 3 times per week	121 (23.4)	14 (25.9)	
> 3 times per week	76 (14.6)	11 (20.4)	
Betel nut use			0.016
No	506 (97.7)	50 (92.6)	
Yes	12 (2.3)	4 (7.4)	

BMI: Body mass index, indicating weight in kg divided by body surface area; NSAID: Non-steroid anti-inflammatory drug.

istics and the presence of PUD. The subjects with PUD were less educated than those without ulcer. Additionally, male gender, prior history of PUD, current smoker, and betal nut chewing were significantly higher in the PUD group than in the non-PUD group ($P < 0.001$, < 0.005, < 0.001, 0.016, respectively). Furthermore, the PUD group had higher BMI than the non-PUD group. However, the two groups had similar age, alcohol, coffee, tea, and spicy food consumption and NSAID use.

Independent factors influencing the presence of peptic ulcer disease in asymptomatic subjects

Multivariate analysis with stepwise logistic regression showed that history of PUD [odds ratio (OR), 1.99; 95% CI: 1.34-2.93], low education level (years of education 10-12: OR, 0.49; 95% CI: 0.31-0.80; years of education > 12: OR, 0.57; 95% CI: 0.34-0.96), high BMI (BMI 25-30 kg/m^2: OR, 1.49; 95% CI: 1.01-2.23; BMI > 30 kg/m^2: OR, 3.64; 95% CI: 1.53-8.68) and current smoker (OR, 2.61; 95% CI: 1.56-4.38) were independent factors predicting the development of PUD (Table 3).

Table 3 Independent risk factors for the presence of peptic ulcer disease in asymptomatic subjects[1]

Risk factors	Coefficient	SE	OR (95% CI)	*P* value
Peptic ulcer history	0.686	0.199	1.99 (1.34-2.93)	0.001
Education (yr)				
10-12	-0.704	0.247	0.49 (0.31-0.80)	0.004
> 12	-0.562	0.265	0.57 (0.34-0.96)	0.034
Current smoker	0.960	0.263	2.61 (1.56-4.38)	< 0.001
BMI (kg/m^2)				
> 25	0.404	0.203	1.49 (1.01-2.23)	0.046
> 30	1.292	0.443	3.64 (1.53-8.68)	0.004

OR: Odds ratio; BMI: Body mass index, indicating weight in kg divided by body surface area. [1]Analysis for sex, education level, BMI, peptic ulcer history, smoking and betel nut consumption; CI: Confidence interval.

DISCUSSION

The clinical presentation of peptic ulcer patients is variable. Some patients with PUD are asymptomatic until life-threatening complications develop. This study demonstrated that the prevalence of asymptomatic PUD in Taiwan was 9.4%. Further analysis showed that prior history of PUD, high BMI, low education level and current smoker were independent predictors for developing asymptomatic PUD.

This study revealed a strong positive association between BMI and asymptomatic PUD. These associations remained robust even after adjusting for several important potential factors, including age, gender and lifestyle. Furthermore, a significant dose-response relationship between BMI and PUD was noted. The odds ratio of BMI 25-30 kg/m^2 (overweight) and BMI > 30 kg/m^2 (obesity) were 1.5 and 3.6, respectively. Previous studies indicated that higher BMI, considered as overweight or obese, revealed associations with more severe symptoms of reflux esophagitis[12,13] and PPI treatment response to achieve sustained symptomatic response in reflux esophagitis[14]. Little data exist on the association between obesity and PUD. The mechanism by which obesity increases the risk of asymptomatic PUD is unknown. Possible explanations include the increased intra-abdominal pressure and higher acid secretion rates in obese subjects[15]. Wisén *et al* reported that obese (nondiabetic) patients were found to have higher gastric acid secretion than non-obese patients using the gastric acid secretion test after modified sham feeding[16]. Moreover, obese subjects appear to be more sensitive to acid in the upper gastrointestinal tract than non-obese subjects[17]. In addition, studies have demonstrated that obese rats and humans have higher "somatic" pain thresholds because obese patients have a higher plasma

level of endorphins[18,19].

The present study also demonstrated that subjects with low education level have a higher risk of asymptomatic PUD. It has been well documented that PUD is associated with low socioeconomic status[20]. That association may be explained by a higher risk of *Helicobacter pylori* (*H. pylori*) infection among less educated groups, probably due to poor standards of hygiene[21]. Psychological stress, risk lifestyle behaviors, and hard physical work may be other important risk factors for PUD in low education populations[22].

NSAIDs are known to be associated with gastrointestinal injury, including erosions, ulceration and hemorrhage. During long-term administration, 60%-94% of NSAIDs users have been reported to show mucosal damage and 15%-31% to have evidence of frank gastric ulcer[23,24]. In this study, NSAID use was not identified as a risk factor for the development of asymptomatic peptic ulcer. The reasons for the lack of association between NSAIDs and asymptomatic peptic ulcer could be due to short-term use of NSAIDs in our patients, the use of selective cyclooxygenase-2 inhibitors in some subjects or a small number of cases (type Ⅱ error).

Certain lifestyle factors such as consumption of tobacco, alcohol, tea, coffee, betel nut and spicy foods are believed to stimulate gastric acid secretion, however, the findings of previous cross-sectional epidemiological studies have been inconsistent[25,26]. The current cross-sectional study revealed that only current smoking independently predicted the development of PUD in asymptomatic subjects. A Japanese study of men aged 45 years and older revealed that current smokers were at higher risk of both gastric (OR, 3.4, 95% CI: 2.4- 4.7) and duodenal ulcers (OR, 3.0, 95% CI: 1.9- 4.7), compared with nonsmokers[27]. However, another study failed to confirm these findings for PUD risk in smokers compared with nonsmokers[28]. Recent studies have suggested that tobacco smoking causes peptic ulcer only if *H. pylori* infection is present[29]. A prospective cohort study in Denmark showed that tobacco smoking remained an independent risk factor for PUD despite controlling for *H. pylori* infection status[30]. Hence, we believe that ulcer patients should be advised to cease smoking. In this study, the specific aim was to investigate the prevalence and risk factors of asymptomatic PUD in Taiwan. It is necessary to further examine the risk factors for peptic ulcer in symptomatic subjects and to investigate the differences in risk factors for PUD between symptomatic and asymptomatic subjects in the future.

Despite its contributions, this study had certain limitations. First, self-selection bias of the population in this trial was possible, because all enrolled subjects had undergone self-paid health examinations and likely had a better economic status than the general population. Second, the studied subjects may differ from subjects in a primary care hospital because our hospital is a tertiary care center. Third, the status of *H. pylori* infection was not routinely examined. Its prevalence might differ between the non-peptic ulcer group and the peptic ulcer group. Nevertheless, most asymptomatic subjects had not received an examination for *H. pylori* infection before their routine upper gastrointestinal endoscopy and did not know their *H. pylori* status. The major aim of this study was to identify the clinical factors predicting peptic ulcer development prior to endoscopic examination. The findings may be useful for identifying asymptomatic subjects at high risk for the development of peptic ulcer.

In conclusion, the prevalence of PUD in asymptomatic subjects is 9.4% in Taiwan. Prior history of PUD, low education level, a high BMI and current smoker are independent risk factors for developing asymptomatic peptic ulcer.

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COMMENTS

Background

Peptic ulcer disease (PUD) is a common disease of the digestive system and the pathogenesis of symptom development in PUD is unclear. Some patients with PUD are asymptomatic until life-threatening complications (e.g. hemorrhage, perforation) develop. The aims of this study were to investigate the prevalence and risk factors of asymptomatic PUD in Taiwan.

Research frontiers

Currently, the long-term consequences of silent PUD remain unclear, however, hemorrhage, perforation, and stricture are well known complications of PUD. Therefore, identification and follow up of these asymptomatic patients is essential. Nonetheless, the risk factors for asymptomatic PUD still remain unclear.

Innovations and breakthroughs

Helicobacter pylori (*H. pylori*) infection, smoking and non-steroidal anti-inflammatory drugs use are known risk factors of symptomatic PUD but few studies to date have reported the risk factors for asymptomatic PUD. In this study, the authors observed that prior history of PUD, low education level, a high body mass index and current smoker are independent risk factors for developing asymptomatic PUD.

Applications

The status of *H. pylori* infection was not routinely examined and the prevalence of *H. pylori* status might differ between the non-peptic ulcer group and the peptic ulcer group. Nevertheless, the major aim of this study was to identify the clinical factors predicting peptic ulcer development prior to endoscopic examination, and most of the asymptomatic subjects did not receive any tests for *H. pylori* infection.

Terminology

PUD was defined as a circumscribed mucosal break 5 mm or more in diameter, with a well defined ulcer crater. All subjects were carefully interviewed regarding the presence of reflux or dyspeptic symptoms in the previous month, and subjects who responded negatively were classified as asymptomatic subjects and enrolled in this study.

Peer review

The study was well performed and very interesting. However, it contains some serious problems which have to be answered by the authors. The reviewer considered that the comparisons should be also required between the asymptomatic peptic ulcer disease group and the symptomatic peptic ulcer disease group to investigate risk factors of asymptomatic peptic ulcer disease.

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