Original Article

Analysis of risk factors for ulcer recurrence and upper gastrointestinal bleeding in children with peptic ulcer treated with *Helicobacter pylori* eradication therapy

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Background: The incidence of peptic ulcer disease (PUD) has been increasing yearly, especially in the adolescent population. The eradication of *Helicobacter pylori* (*H. pylori*) may reduce recurrence and bleeding to some extent, but it does not completely change the clinical status of PUD. Therefore, this study aims to analyze the risk factors for ulcer recurrence and upper gastrointestinal bleeding after *H. pylori* eradication therapy in order to provide a reference for reducing the risk of PUD and improving the quality of life of patients.

Methods: We retrospectively analyzed 536 adolescent patients who developed peptic ulcer and received *H. pylori* eradication therapy from June 2016 to July 2021. The relationship between the clinical characteristics of the patients and gastrointestinal bleeding and recurrence was analyzed using the *t*-test and chi-squared test. Binary logistic regression was used to analyze the independent risk factors for the occurrence of bleeding and recurrence.

Results: A total of 536 patients were included in this retrospective study. Gender, history of ulcers, number, size, location and staging of ulcers, and application of nonsteroidal anti-inflammatory drugs (NSAIDs), and other characteristics were significantly different between the bleeding and nonbleeding groups ($P<0.05$); family history of upper gastrointestinal ulcer, history of ulcers, number and size of ulcers and application of NSAIDs, and other characteristics were significantly different between the recurrent and nonrecurrent groups ($P<0.05$). Binary logistic regression analysis showed that history of ulcers, number and location of ulcers, coagulation abnormalities, and other characteristics were independent risk factors for the occurrence of bleeding; the occurrence of previous bleeding, number and size of ulcers, and other characteristics were independent risk factors for recurrence.

Conclusions: In the clinical treatment of adolescent patients, it is important to pay high attention to clinical characteristics, such as the patient's previous ulcer history, the size, number and location of ulcers, and coagulation function, so as to adopt individualized treatment methods to effectively reduce the harmfulness of the disease in response to the risk factors of ulcer bleeding and recurrence after *H. pylori* eradication therapy. This can decrease the occurrence of complications and improve the prognosis of patients.

Keywords: Peptic ulcer disease (PUD); bleeding; recurrence; adolescents; *Helicobacter pylori* (*H. pylori*) eradication therapy

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Introduction

Peptic ulcer disease (PUD), a common disease of the upper gastrointestinal tract, is a mucosal rupture larger than 3–5 mm and visible in depth in the stomach or duodenum (1). It is mainly caused by an imbalance between endogenous protective factors of the gastric mucosa (mucus and bicarbonate, prostaglandin E_2, nitric oxide, sulfhydryl compounds, and antioxidant enzymes) and invasive factors (acid and pepsin secretion) (2). PUD often leads to complications of bleeding, perforation, and pyloric obstruction if not diagnosed and treated in a timely manner, thus increasing the risk of death and socioeconomic burden on patients (3).

Currently, the prevalence of PUD remains high and is increasing year by year in the adolescent population. According to previous studies, the current prevalence of PUD is about 0.2% to 0.5% in Western countries, 2% to 3% in Asian countries (4), and 24–28% in sub-Saharan African populations (5-7). It is estimated that 15,000 people die from PUD each year, which indicates that PUD still affects human health to a large extent. *Helicobacter pylori* (*H. pylori*) infection and the use of nonsteroidal anti-inflammatory drugs (NSAIDs) are recognized to be the main causes of PUD (8). It has been shown that about 80–90% of patients with gastric and duodenal ulcers have a cause related to *H. pylori* infection (9), and the lifetime risk of developing PUD is 3–10 times higher in *H. pylori*-positive individuals than in negative individuals (10). A study showed that 4.4 billion people (57.9% of the global population at that time) were infected with *H. pylori* in 2017 (11). and global reports show that the prevalence of *H. pylori* infection in patients with PUD is 14–21% in the United States, 60–70% in Asia, and 70–90% in sub-Saharan Africa (12,13). Therefore, worldwide consensus guidelines recommend mandatory *H. pylori* eradication in patients with PUD (14). Since this mandate, anti-*H. pylori* treatment has become an important part of the peptic ulcer treatment process and is widely used in clinical practice. A study found that by eradicating or suppressing *H. pylori* infection, the possibility of bleeding could be reduced (15). Subsequent studies have also confirmed that *H. pylori* eradication promotes healing and reduces the occurrence of rebleeding (16). In addition, it was also revealed that the annual recurrence rate of peptic ulcer patients with eradicated *H. pylori* is significantly lower than that of patients who fail to successfully eradicate *H. pylori* (17). The annual recurrence rate of peptic ulcers after *H. pylori* eradication has been reported to be 6.45%, while the annual recurrence rate of *H. pylori*–positive PUD can reach 23.3% (18). All of the above studies indicate that *H. pylori* eradication therapy significantly improves the prognosis of patients. However, there is less analysis of the factors influencing the occurrence of ulcer recurrence and bleeding even after anti-*H. pylori* treatment. Therefore, the aim of this study was to analyze the risk factors for ulcer recurrence and upper gastrointestinal bleeding after anti-*H. pylori* treatment for peptic ulcer in adolescents. We hope our findings can help clinicians identify the relevant clinical features as early as possible and provide a reference basis for reducing the occurrence of ulcer recurrence and upper gastrointestinal bleeding, thus improving the quality of life of adolescent patients. We present the following article in accordance with the STROBE reporting checklist (available at https://tp.amegroups.com/article/view/10.21037/tp-23-155/rc).

Highlight box

Key findings

- Some relevant clinical features of patients are independent risk factors for concomitant bleeding and ulcer recurrence after peptic ulcers. Great attention should be paid to the features in clinical work to improve their clinical symptoms and reduce the occurrence of bleeding and recurrence.

What is known and what is new?

- There are many independent risk factors affecting ulcer recurrence and upper gastrointestinal bleeding after *H. pylori* eradication therapy for adolescent peptic ulcers.
- Inflammatory indicators, ulcer number, etc. are independent risk factors for concomitant bleeding and ulcer recurrence after peptic ulcers in adolescents.

What is the implication, and what should change now?

- Clinical attention should be paid to the eradication treatment of *H. pylori* and to the different clinical characteristics of patients such as ulcer size, ulcer number and other high-risk factors, providing individualized treatment and improving the follow-up system for patients to improve the patients' prognosis.

Methods

Research participants

A total of 536 adolescent patients who developed PUD and received *H. pylori* eradication therapy at the Affiliated Hospital of Jiangnan University between June 2016 and July 2021 were included in this study.

The included participants were (I) adolescent patients

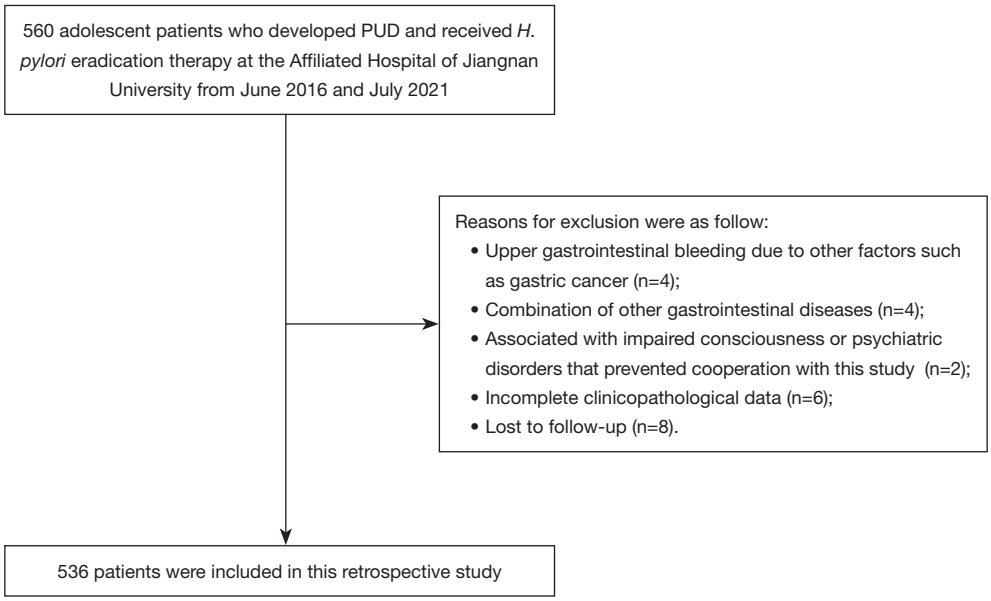

Figure 1 Flowchart of patient selection. PUD, peptic ulcer disease; *H. pylori*, *Heliobacter pylori*.

who were 12–18 years old, (II) who met the diagnosis (19) of PUD and received *H. pylori* eradication therapy between June 2016 and July 2021, and (III) who had complete clinicopathological data.

The exclusion criteria were as follows: (I) upper gastrointestinal bleeding due to other factors such as gastric cancer, (II) combination of other gastrointestinal diseases, (III) associated with impaired consciousness or psychiatric disorders that prevented cooperation with this study, and (IV) incomplete clinicopathological data (*Figure 1*).

The formula $N=(Z_{1-\alpha/2}/\delta)^2P(1-P)$ was used to calculate the sample size. In this study, the incidence of recurrence and bleeding was used as the main outcome index. According to the previous study of our group, the incidence of bleeding after *H. pylori* eradication was 10%, δ was 3%, α was 0.05(bilateral), and 10% sample loss rate was taken into account. Finally, N=423 cases were obtained. After *H. pylori* eradication, the incidence of ulcer recurrence (P) was 5%, δ was 3%, α was 0.05(bilateral), and 10% sample loss rate was taken into account. Finally, N=223 cases were obtained. Therefore, the sample size of the study population planned for this study was 560 cases. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Affiliated Hospital of Jiangnan University ethics board (No. KYLC2016113) and informed consent was taken from all the patients' guardians.

General information questionnaire

A general information questionnaire was used to collect demographic data, such as gender, age, body mass index, and clinical data (history of PUD, history of smoking, history of alcohol consumption, family history of upper gastrointestinal ulcer, number of ulcers, ulcer location, ulcer diameter, ulcer stage, dietary habits, compliance with medication, regular exercise, negative emotions, complications, gastrointestinal symptoms, and laboratory indexes, etc.).

Diagnosis of H. pylori infection, eradication regimens and Eradication criteria after H. pylori treatment

All of our included patients were confirmed to be *Hp* positive by gastroscopy or ^{14}C-urea breath test.

Patients were administered with amoxicillin capsules 25 mg/kg per time, 2 times/d; clarithromycin extended-release tablets 10 mg/kg per time, 2 times/d; colloidal bismuth capsules 2–3 mg/kg per time, 4 times/d; all patients were treated for 2 weeks, and the eradication effect was observed.

Eradication criteria: Gastroscopic review was requested in all cases 4 weeks after the end of the treatment course, and antibiotics, proton pump inhibitors (PPIs) and H_2

receptor inhibitors were not allowed to be used within 4 weeks after the review. If the patient refused to repeat gastroscopy, ^{14}C-urea breath test was performed.

Evaluation of efficacy

We classified the efficacy of therapy in patients into 4 classes: (I) recovery—clinical symptoms and signs disappear, the endoscopic ulcer disappears, and the surrounding inflammation disappears, or the ulcer turns into the scarring stage; (II) marked effective—clinical symptoms and signs improve significantly, and the endoscopic ulcer area is reduced by ≥50%; (III) moderately effective—clinical symptoms and signs improve, the endoscopic ulcer area or the number of ulcers is reduced by <50%, or the ulcer enters the healing stage; and (IV) ineffective—clinical symptoms and signs do not change significantly after treatment, the endoscopic ulcer is still in the active stage, and the ulcer area does not decrease. The total efficacy was calculated as follows: total efficacy = recovery + marked effective + moderately effective.

The last follow-up was in July 2022.

Recurrence

All enrolled patients were followed up for 1 year by telephone, internet, or outpatient appointment. Immediate hospital visits were encouraged if there was any discomfort, and endoscopy was conducted as necessary to determine if the peptic ulcer had recurred. The last follow-up visit was in July 2022.

Statistical analysis

The data of each scale were entered into a computer for score conversion, and statistical analysis was performed using SPSS 26 (IBM Corp.), with measured data expressed as mean and standard deviation and count data expressed as frequency and percentage. Statistical analysis between groups was performed using a *t*-test and chi-squared test, and factors influencing the occurrence of bleeding and ulcer recurrence were analyzed using binary logistic regression. A P value <0.05 was considered statistically significant.

Results

Baseline data

Baseline characteristics of the patients are shown in *Table 1*. Due to 24 cases of actual loss and lost to follow-up, therefore, 536 adolescent patients with PUD treated with *H. pylori* eradication therapy were included in this study, of whom 51 (9.5%) had bleeding and 25 (4.7%) had ulcer recurrence, with a mean age of 15.35±1.99 years. There were 33 males (64.7%) in the bleeding group and 237 males (48.9%) in the nonbleeding group, and there was a significant difference between the bleeding and nonbleeding groups in prevalence of male patients (P<0.05). In the bleeding group, 3 patients (12.0%) had a history of smoking, while 9 patients (1.8%) in the nonbleeding group had a history of smoking. In the ulcer recurrence group, 3 patients (5.9%) had a history of smoking, while in the nonrecurrence group, 9 patients (1.9%) had a history of smoking. Smoking history was significantly different between both the nonrecurrence and recurrence groups (P<0.05). In the recurrence group, 7 patients (28.0%) had a family history, while in the nonrecurrence group, 43 patients (8.4%) had a family history of upper gastrointestinal ulcer, representing a statistically significant between the 2 groups (P<0.05). History of ulcers, number and size of ulcers, and application of NSAIDs were significantly different between groups which did and did not experience bleeding and recurrence (P<0.05). In the bleeding group, there were 5 (9.8%) patients with ulcer history, 16 (31.4%) with multiple ulcers, 6 (11.8%) with ulcer size ≥2 cm, and 4 (7.8%) treated with NSAIDs. In the nonbleeding group, there were 10 (2.1%) patients with ulcer history, 67 (13.8%) with multiple ulcers, 18 (3.7%) with ulcer size ≥2 cm, and 12 (2.5%) treated with NSAIDs. In the relapse group, there were 3 (12.0%) patients with a history of ulcers, 9 (36.0%) with multiple ulcers, 4 (16.0%) with ulcers ≥2 cm in size, and 3 (12.0%) with NSAIDs. In the nonrecurrence group, there were 12 (2.3%) patients with a history of ulcers, 74 (14.5%) with multiple ulcers, 20 (3.9%) with ulcers ≥2 cm in size, and 13 (2.5%) treated with NSAIDs. In the bleeding group, 5 (9.8%) cases were compound ulcers, while in the nonbleeding group, 18 (3.7%) cases were compound ulcers, representing a significant difference (P<0.05). In the bleeding group, 26 (51.0%) ulcers were in the active stage, while in the nonbleeding group, 175 (36.1%) ulcers were in the active stage; 5 (9.8%) coagulation abnormalities were found in the bleeding group and only 7 (1.4%) coagulation abnormalities were found in the nonbleeding group. There was a significant difference between ulcer stage and the presence of coagulation abnormalities in the presence or absence of bleeding and nonbleeding (P<0.05). In the recurrence group, 13 (52.0%)

Table 1 Baseline data of included patients according to study group.

Item	Bleeding group	Nonbleeding group	χ^2/t	P	Recurrence group	Nonrecurrence group	χ^2/t	P
Age (years)	15.35±1.99	15.01±2.04	–1.143	0.253	15.08±2.18	15.04±2.03	–0.093	0.926
Gender			4.632	0.031			0.059	0.808
Male	33 (64.7)	237 (48.9)			12 (48.0)	258 (50.5)		
Female	18 (35.3)	248 (51.1)			13 (52.0)	253 (49.5)		
BMI (kg/m^2)	22.25±2.14	22.13±2.13	–0.371	0.711	22.42±2.31	22.13±2.12	–0.669	0.504
Course of disease			0.055	0.814			0.017	0.895
≥1 year	21 (41.2)	208 (42.9)			11 (44.0)	218 (42.7)		
<1 year	30 (58.8)	277 (57.1)			14 (56.0)	293 (57.3)		
History of smoking			3.419	0.064			11.416	0.001
Yes	3 (5.9)	9 (1.9)			3 (12.0)	9 (1.8)		
No	48 (94.1)	476 (98.1)			22 (88.0)	502 (98.2)		
History of drinking			1.301	0.254			0.652	0.419
Yes	2 (3.9)	8 (1.6)			1 (4.0)	9 (1.8)		
No	49 (96.1)	477 (98.4)			24 (96.0)	502 (98.2)		
Family history			0.015	0.902			10.809	0.001
Yes	5 (9.8)	45 (9.3)			7 (28.0)	43 (8.4)		
No	46 (90.2)	440 (90.7)			18 (72.0)	468 (91.6)		
History of peptic ulcers			10.169	0.001			8.162	0.004
Yes	5 (9.8)	10 (2.1)			3 (12.0)	12 (2.3)		
No	46 (90.2)	475 (97.9)			22 (88.0)	499 (97.7)		
Number of ulcers			10.871	0.001			8.433	0.004
≥2	16 (31.4)	67 (13.8)			9 (36.0)	74 (14.5)		
<2	35 (68.6)	418 (86.2)			16 (64.0)	437 (85.5)		
Ulcer location			4.171	0.041			0.878	0.349
Compound ulcers	5 (9.8)	18 (3.7)			2 (8.0)	21 (4.1)		
Non-compound ulcers	46 (90.2)	467 (96.3)			23 (92.0)	490 (95.9)		
Ulcer diameter			6.998	0.008			8.14	0.004
≥2 cm	6 (11.8)	18 (3.7)			4 (16.0)	20 (3.9)		
<2 cm	45 (88.2)	467 (96.3)			21 (84.0)	491 (96.1)		
Ulcer staging			4.37	0.037			1.234	0.267
Activity stage	26 (51.0)	175 (36.1)			12 (48.0)	189 (37.0)		
Healing stage	25 (49.0)	310 (63.9)			13 (52.0)	322 (63.0)		
Use of NSAIDs			4.593	0.032			7.359	0.007
Yes	4 (7.8)	12 (2.5)			3 (12.0)	13 (2.5)		
No	47 (92.2)	473 (97.5)			22 (88.0)	498 (97.5)		

Table 1 (*continued*)

Table 1 (*continued*)

Item	Bleeding group	Nonbleeding group	χ^2/t	P	Recurrence group	Nonrecurrence group	χ^2/t	P
Coagulation abnormalities			14.738	0			0.601	0.438
Yes	5 (9.8)	7 (1.4)			0 (0.0)	12 (2.3)		
No	46 (90.2)	478 (98.6)			25 (100.0)	499 (97.7)		
Preference for spicy and stimulating foods			0.915	0.339			5.2	0.023
Yes	19 (37.3)	149 (30.7)			13 (52.0)	155 (30.3)		
No	32 (62.7)	336 (69.3)			12 (48.0)	356 (69.7)		
Followed medical advice on medication			0.498	0.48			4.619	0.032
Yes	43 (84.3)	389 (80.2)			16 (64.0)	416 (81.4)		
No	8 (15.7)				9 (36.0)	95 (18.6)		
Regular exercise			1.52	0.218			0.509	0.476
Yes	17 (33.3)	123 (25.4)			5 (20.0)	135 (26.4)		
No	34 (66.7)				20 (80.0)	376 (73.6)		
With negative emotions or not			0	0.998			5.373	0.02
Yes	4 (7.8)	38 (7.8)			5 (20.0)	37 (7.2)		
No	47 (92.2)	447 (92.2)			20 (80.0)	474 (92.8)		

Data are presented as n (%) or Mean ± SD. BMI, body mass index; NSAID, nonsteroidal anti-inflammatory drug; SD, standard deviation.

Table 2 Comparison of complications between the patient groups

Item	Bleeding	Perforation	Obstruction	Carcinogenesis
Yes	51 (9.5)	22 (4.1)	18 (3.4)	0 (0.0)
No	485 (90.5)	514 (95.9)	518 (96.6)	536 (100.0)

Data are presented as n (%).

patients preferred spicy food, 16 (64.0%) followed medical advice on medication, and 5 (20.0%) had negative emotions; in the nonrecurrence group, 155 (30.3%) patients preferred spicy food, 416 (81.4%) took medication as prescribed, and 37 (7.2%) had negative emotions. There was a significant difference (P<0.05) in dietary habits, compliance with medication, and negative emotions between the recurrence and nonrecurrence groups.

Patient complications

Of all adolescent patients receiving anti-*H. pylori* treatment for PUD, 51 (9.5%) had gastrointestinal bleeding, 22 (4.1%) had gastrointestinal perforation, 18 (3.4%) had gastrointestinal obstruction, and none (0.0%) had cancer (*Table 2*).

Comparison of gastrointestinal symptoms between the patient groups

In the bleeding group, 26 (51.0%) patients had abdominal pain, 14 (27.5%) had bloating, 13 (25.5%) had nausea, 12 (23.5%) had vomiting, 23 (45.1%) had acid reflux, and 21 (41.2%) ate less food than before. The symptoms of

Table 3 Comparison of gastrointestinal symptoms between the patient groups

Item	Bleeding group	Nonbleeding group	χ^2	P	Recurrence group	Nonrecurrence group	χ^2	P
Abdominal pain			3.991	0.046			0.042	0.838
Yes	26 (51.0)	178 (36.7)			10 (40.0)	194 (38.0)		
No	25 (49.0)	307 (63.3)			15 (60.0)	317 (62.0)		
Bloating			0.899	0.343			0.584	0.445
Yes	14 (27.5)	105 (21.6)			4 (16.0)	115 (22.5)		
No	37 (72.5)	380 (78.4)			21 (84.0)	396 (77.5)		
Nausea			1.734	0.188			1.962	0.161
Yes	13 (25.5)	87 (17.9)			2 (8.0)	98 (19.2)		
No	38 (74.5)	398 (82.1)			23 (92.0)	413 (80.8)		
Vomiting			7.535	0.006			14.863	<0.001
Yes	12 (23.5)	51 (10.5)			9 (36.0)	54 (10.6)		
No	39 (76.5)	434 (89.5)			16 (64.0)	457 (89.4)		
Acid reflux			4.806	0.028			0.003	0.959
Yes	23 (45.1)	146 (30.1)			8 (32.0)	161 (31.5)		
No	28 (54.9)	339 (69.9)			17 (68.0)	350 (68.5)		
Reduced food intake			4.711	0.030			0.190	0.663
Yes	21 (41.2)	130 (26.8)			8 (32.0)	143 (28.0)		
No	30 (58.8)	355 (73.2)			17 (68.0)	368 (72.0)		

Data are presented as n (%).

abdominal pain, vomiting, acid reflux, and reduced food intake were significantly different between the bleeding and nonbleeding groups (P<0.05).

In the recurrence group, 10 (40.0%) patients had abdominal pain, 4 (16.0%) had bloating, 2 (8.0%) had nausea, 9 (36.0%) had vomiting, 8 (32.0%) had acid reflux, and 8 (32.0%) ate less food than before. The symptoms of vomiting was significantly different between the recurrence and nonrecurrence groups (P<0.05; *Table 3*).

Comparison of laboratory metrics between the patient groups

In the bleeding group, the mean laboratory metrics were as follows: platelet count (PLT) (161.53±61.89)×10^9/L, prostaglandin E_2 (PGE2) 226.27±68.91 pg/mL, hemoglobin (Hb) 107.90±13.81 g/L, albumin (Alb) 38.41±8.62 g/L, interleukin-6 (IL-6) 40.38±7.07 pg/mL, IL-8 29.97±4.88 μg/L, C-reactive protein (CRP) 20.66±9.01 mg/L, and the tumor necrosis factor alpha (TNF-α) was 20.86±4.72 ng/L. In the nonbleeding group, the mean laboratory metrics were as follows: PLT (187.35±59.47)×10^9/L, PGE2 302.85±40.67 pg/mL, Hb 128.41±13.39 g/L, Alb 41.89±8.83 g/L, IL-6 41.71±7.53 pg/mL, IL-8 30.07±5.50 μg/L, CRP 16.75±5.80 mg/L, and TNF-α 20.27±4.66 ng/L. Among these, the differences in PLT, PGE2, Hb, Alb, and CRP levels were statistically significant between the bleeding and nonbleeding groups (P<0.05).

In the recurrence group, the mean laboratory metrics were as follows: PLT (186.48±58.04)×10^9/L, PGE2 286.92±48.39 pg/mL, Hb 121.12±18.21 g/L, Alb 40.44±8.11 g/L, IL-6 52.77±10.93 pg/mL, IL-8 32.56±5.50 μg/L, CRP 21.51±9.43 mg/L, and TNF-α 24.17±7.68 ng/L. In the nonrecurrence group, the mean laboratory metrics were as follows: PLT (184.82±60.28) ×10^9/L, PGE2 295.98±49.52 pg/mL, Hb 126.72±14.48 g/L, Alb 41.62±8.90 g/L, IL-6 41.04±6.84 pg/mL, IL-8 29.94±5.41 μg/L, CRP 16.91±6.01 mg/L, and TNF-α

Table 4 Comparison of laboratory metrics between the patient groups

Item	Bleeding group	Nonbleeding group	t	P	Recurrence group	Nonrecurrence group	t	P
PLT ($\times10^9$/L)	161.53±61.89	187.35±59.47	2.938	0.003	186.48±58.04	184.82±60.28	–0.135	0.893
PGE2 (pg/mL)	226.27±68.91	302.85±40.67	7.794	<0.001	286.92±48.39	295.98±49.52	0.894	0.372
Hb (g/L)	107.90±13.81	128.41±13.39	10.377	<0.001	121.12±18.21	126.72±14.48	1.864	0.063
Alb (g/L)	38.41±8.62	41.89±8.83	2.686	0.007	40.44±8.11	41.62±8.90	0.649	0.517
IL-6 (pg/mL)	40.38±7.07	41.71±7.53	1.213	0.226	52.77±10.93	41.04±6.84	–5.315	<0.001
IL-8 (μg/L)	29.97±4.88	30.07±5.50	0.125	0.901	32.56±5.50	29.94±5.41	–2.361	0.019
CRP (mg/L)	20.66±9.01	16.75±5.80	–3.032	0.004	21.51±9.43	16.91±6.01	–2.414	0.023
TNF-α (ng/L)	20.86±4.72	20.27±4.66	–0.862	0.389	24.17±7.68	20.14±4.39	–2.602	0.015

Data are presented as mean ± SD. PLT, platelet; PGE2, prostaglandin E_2; Hb, hemoglobin; Alb, albumin; IL-6, interleukin-6; IL-8, interleukin-8; CRP, C-reactive protein; TNF-α, tumor necrosis factor alpha; SD, standard deviation.

Table 5 Comparison of treatment effect between the bleeding and nonbleeding groups

Item	Bleeding group	Non-bleeding group	χ^2	P
Recovery	7 (13.7)	77 (15.9)	34.025	<0.001
Marked effective	16 (31.4)	185 (38.1)		
Moderately effective	11 (21.6)	184 (37.9)		
Ineffective	8 (15.7)	23 (4.7)		
Recurrence	9 (17.6)	16 (3.3)		
Total efficacy rate	34 (66.7)	446 (92.0)	31.551	<0.001

Data are presented as n (%).

20.14±4.39 ng/L. Among these, the differences in IL-6, IL-8, CRP, and TNF-α levels were statistically significant between the recurrence and nonrecurrence groups (P<0.05; *Table 4*).

Comparison of treatment efficacy between the patient groups

According to the results of the chi-squared analysis, in the bleeding group, 7 (13.7%) patients were classified as recovery, 16 (31.4%) as effective, 11 (21.6%) as moderately effective, 8 (15.7%) as ineffective, and 9 patients (17.6%) as recurrence, for a total efficacy rate of 66.7%. In the nonbleeding group, 77 (15.9%) patients were classified as recovery, 185 (38.1%) as effective, 184 (37.9%) as moderately effective, 23 (4.7%) as ineffective, and 16 (3.3%) as recurrence, for a total efficacy rate of 92.0%. The treatment efficacy in the nonbleeding group was significantly higher than that of the bleeding group, and the total efficacy rate was also significantly higher than that of the nonbleeding group (P<0.05), as shown in *Table 5*.

Treatment associated with recurrence in 1 year

In the relapse group, 4 (16.0%) were treated with surgery, 21 (84.0%) were treated with PPIs, 8 (32.0%) were treated with H_2 antagonists, and 2 (8.0%) were treated with antacids. PPI, H_2 antagonist, and antacid treatment had a significant effect on whether relapse occurred (P<0.05; *Table 6*).

Risk factors of bleeding and recurrence analyzed with binary logistic regression models

Binary logistic regression analysis showed that gender, ulcer history, number and location of ulcers, abnormal

Table 6 Treatment associated with recurrence in 1 year

Item	Overall	Recurrence	No recurrence	χ^2	P
Surgical treatment or not				0.173	0.677
Yes	71 (13.2)	4 (16.0)	67 (13.1)		
No	465 (86.8)	21 (84.0)	444 (86.9)		
PPI use				8.754	0.003
Yes	513 (95.7)	21 (84.0)	492 (96.3)		
No	23 (4.3)	4 (16.0)	19 (3.7)		
H_2 antagonist use				7.531	0.006
Yes	73 (13.6)	8 (32.0)	65 (12.7)		
No	463 (86.4)	17 (68.0)	446 (87.3)		
Antacid use				4.042	0.044
Yes	134 (25.0)	2 (8.0)	132 (25.8)		
No	402 (75.0)	23 (92.0)	379 (74.2)		

Data are presented as n (%). PPI, proton pump inhibitor.

Table 7 Binary logistic regression analysis of bleeding

Related factor	B	SE	Wald	P	OR	95% CI	
						Upper	Lower
Gender	1.305	0.569	5.255	0.022	3.686	11.247	1.208
History of peptic ulcers	2.828	1.150	6.050	0.014	16.920	161.148	1.776
Number of ulcers	1.258	0.575	4.776	0.029	3.517	10.866	1.139
Ulcer location	2.155	0.890	5.857	0.016	8.627	49.407	1.506
Coagulation abnormalities	2.585	1.165	4.925	0.026	13.269	130.169	1.353
Vomiting	1.582	0.718	4.857	0.028	4.866	19.874	1.191
PGE2	–0.025	0.004	35.209	0.000	0.976	0.984	0.968
Hb	–0.120	0.022	30.851	0.000	0.887	0.925	0.850
Alb	–0.066	0.029	5.222	0.022	0.936	0.991	0.884
CRP	0.088	0.032	7.558	0.006	1.092	1.164	1.026

SE, standard error; OR, odds ratio; CI, confidence interval; PGE2, prostaglandin E_2; Hb, hemoglobin; Alb, albumin; CRP, C-reactive protein.

coagulation, vomiting, PGE2, Hb, Alb, and CRP were independent risk factors for the occurrence of bleeding in patients (*Table 7*). Bleeding, number and size of ulcers, dietary habits, compliance with medication, vomiting, IL-6, and TNF-α were independent risk factors for the occurrence of ulcer recurrence in patients (*Table 8*).

Discussion

PUD is a common medical condition with severe symptoms and a complex etiology, but the most important cause remains *H. pylori* infection (20). It has been shown that *H. pylori* is present in up to 85% of patients with PUD (21).

Table 8 Binary logistic regression analysis of recurrence

Related factor	B	SE	Wald	P	OR	95% CI	
						Upper	Lower
Bleeding	2.114	0.806	6.877	0.009	8.280	40.191	1.706
Number of ulcers	1.439	0.670	4.609	0.032	4.216	15.683	1.134
Ulcer diameter	2.436	0.910	7.160	0.007	11.429	68.072	1.919
Preference for spicy and stimulating foods	1.610	0.643	6.271	0.012	5.004	17.644	1.419
Followed medical advice for medication	–1.887	0.713	7.005	0.008	0.152	0.613	0.037
Vomiting	1.483	0.705	4.422	0.035	4.408	17.568	1.106
IL-6	0.174	0.033	27.644	0.000	1.119	1.269	1.115
TNF-α	0.160	0.052	9.575	0.002	1.173	1.298	1.060

SE, standard error; OR, odds ratio; CI, confidence interval; IL-6, interleukin-6; TNF-α, tumor necrosis factor alpha.

Because of the high prevalence of *H. pylori*, there is now a consensus to treat with *H. pylori* eradication therapy. There are various clinical manifestations of PUD, and one of the hallmark symptoms is abdominal pain (22). Patients with abdominal pain in this study had the highest proportion of all symptoms, which is consistent with the results of the previous studies. Upper gastrointestinal bleeding is a common comorbidity of PUD, and the percentage of PUD complicated by upper gastrointestinal bleeding can be 20% to 30% (23,24). Melena is the most common first symptom of upper gastrointestinal bleeding, followed by vomiting blood, with abdominal pain, fever, anemia, and hypovolemic manifestations all being concomitant symptoms (25). To sum up, peptic ulcer, as one of the most common chronic diseases of the digestive system, seriously reduces the quality of life of patients and brings great troubles to patients. Therefore, it is important to analyze the risk factors for peptic ulcer bleeding and recurrence after anti-*H. pylori* treatment to prevent peptic ulcer recurrence and improve patients' prognosis (26-28).

The results of this study showed that smoking history, ulcer history, number and size of ulcers, and application of NSAIDs were significantly different between groups that did and did not experience bleeding or recurrence. Smoking was found to be an independent risk factor for the development of peptic ulcers. Smoking inhibits bile secretion, and nicotine relaxes the sphincter, causing bile reflux and increasing the rate of *H. pylori* infection, which leads to PUD (29). Larger ulcers heal more slowly and form larger scars during treatment, resulting in degeneration of the local peptic mucosa and reduced resistance to erosion via gastric acid or proteases, which in turn causes the recurrence of the ulcer and an increased chance of bleeding. In addition, NSAID drugs can accumulate in high concentrations in cells in an acidic environment, thereby damaging mucosal cells and increasing the risk of ulcers complicated by gastrointestinal bleeding. At the same time, NSAID drugs can inhibit the effect of COX-1, leading to a decrease in PGE synthesis and vasoconstriction, which affects the blood supply to the gastric mucosa and its cell regeneration and repair, reduces the secretion of pancreatic and bile content, weakens the ability to neutralize gastric acid, and destroys the gastric protection function, which also leads to an increased probability of PUD complicated by upper gastrointestinal bleeding (30). This study demonstrated that the differences in PLT, PGE2, Hb, Alb and CRP levels were statistically different between the ulcer bleeding and nonbleeding groups, while IL-6, IL-8, CRP, and TNF-α levels were significantly different between the recurrence and nonrecurrence groups. Among these, PGE2 can inhibit gastric acid secretion, synthesize gastric mucosal protective substances, and maintain good blood circulation in gastric mucosa, thus playing a protective role against peptic ulcer bleeding (31). In contrast, *H. pylori* mainly colonizes the gastric-type epithelium and contains strong urease, which promotes the hydrolysis of urea to produce ammonia, causing gastric epithelial cells to secrete transmembrane ammonia gradients that disrupt gastric mucosal barrier function, interfere with gastric mucosal hydrophobicity, reduce antacid effects, and thus decrease

prostaglandin content. In addition, acute neutrophils infiltrate the gastric mucosal surface to varying degrees after *H. pylori* infection (32). Neutrophils and monocytes activated by *H. pylori* and its products infiltrate the *H. pylori*-infected gastric mucosa and stimulate the transcription and synthesis of several proinflammatory cytokines, such as interleukins IL-1β, IL-6, IL-8, TNF-α, and anti-inflammatory cytokines (e.g., IL-4 and IL-10) (33). One study reported that the increased production of inflammatory cytokines after *H. pylori* infection leads to enhanced inflammation of the gastric mucosa via the binding to specific receptors on target cells, which does not heal easily and thus increases the risk of bleeding and recurrence (34). This finding is consistent with our study in which IL-6 and TNF-α were independent risk factors for the development of ulcer recurrence in patients.

The prevalence of peptic ulcer is high in China, and it tends to occur in those who are younger. A large amount of clinical research indicates that patients mostly develop peptic ulcer due to *H. pylori* infection. *H. pylori* is resistant to most antimicrobial drugs, making eradication difficult and treatment generally ineffective (35). The results of this study showed that the efficacy found in the bleeding group was also significantly lower than that in the nonbleeding group. The reason for this may be that the bleeding group had a greater number of ulcers, larger ulcer diameters, and more compound ulcers. Their gastric and duodenal mucosal wounds healed relatively poorly, or because *H. pylori* eradication was not complete, which could have resulted in a significantly lower treatment effect than that in the nonbleeding group; meanwhile, their recurrence rate was higher than that of the nonbleeding group.

In conclusion, there are many factors that influence bleeding and ulcer recurrence after *H. pylori* eradication therapy of peptic ulcer in adolescents. In clinical work, great attention should be paid to the relevant clinical characteristics of patients, and sequential therapy should be used for patients with *H. pylori*-positive peptic ulcer to improve clinical efficacy and reduce the risk of bleeding and recurrence. This type of therapy can improve the clinical symptoms of patients and promote the recovery of patients' health.

The main drawback of this study is the relatively short follow-up period due to limited time and manpower. In addition, we used a retrospective design, and although the study indicators were all from the same hospital, the impact of laboratory tests and treatments on the data at different time periods was not studied due to the large time span of collection. Furthermore, ulcer recurrence was only defined clinically in this study, not endoscopically, which may have caused some errors.

Conclusions

In the clinical treatment of adolescent patients, it is important to pay particular attention to clinical characteristics of patients and to adopt individualized treatment methods in response to the risk factors of ulcer bleeding and recurrence after *H. pylori* eradication therapy, which can effectively reduce the harmfulness of the disease by decreasing the occurrence of complications and thus improve the prognosis of patients.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://tp.amegroups.com/article/view/10.21037/tp-23-155/rc

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tp.amegroups.com/article/view/10.21037/tp-23-155/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Affiliated Hospital of Jiangnan University ethics board (No. KYLC2016113) and informed consent was taken from all the patients' guardians.

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