Clinical and endoscopic features of Chinese reflux esophagitis patients

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AIM: To analyze the clinical and endoscopic features of Chinese patients with reflux esophagitis (RE).

METHODS: A total of 1405 RE patients were analyzed retrospectively. Data on gender, age, presence/absence of H pylori infection and associated esophageal hiatal hernia were collected. Esophagitis was divided into different grades according to Los Angeles Classification.

RESULTS: Of 18823 patients, 1405 were diagnosed as RE. The ratio of male to female patients was 1.75:1 (P < 0.01). The mean age of male and female patients was significantly different (P = 0.01). The peak age at onset of the disease was 40-60 years. According to Los Angeles Classification, there were significant differences in the age of patients with grades A and B compared to patients with grades C and D (P < 0.01). Two hundred and seventy-seven patients were infected with H pylori, the infection rate was low (P < 0.01). Complication of esophageal hiatal hernia was found to be significantly associated with the severity of esophagitis and age in 195 patients (P < 0.01). Esophageal mucosal damages were mainly located at the right esophageal wall.

CONCLUSION: The peak age of onset of RE is 40-60 years and higher in males than in females. The mean age of onset of RE is lower in males than in females. The infection rate of H pylori is significantly decreased in patients with esophagitis. Old age and esophageal hiatal hernia are associated with more severe esophagitis. Right esophageal mucosal damage can occur more often in RE patients.
examinations in the Digestive Endoscopy Center of Beijing Friendship Hospital between September 2004 and January 2007. The unified questionnaire was established and carefully filled in by specialists mainly based on endoscopic diagnosis. The general items included in the questionnaire for RE cases were gender, age, etc. The diagnostic data about the patients with RE included endoscopic staging, presence of associated *H pylori* infection and esophageal hiatal hernia (EHH), etc.

**General data**

A total of 18823 patients (9800 males and 9023 females) underwent endoscopic examinations in the Digestive Endoscopy Center of Beijing Friendship Hospital between September 2004 and January 2007. Of them, 1405 patients (895 males and 510 females) were diagnosed as reflux esophagitis. Their age was 15-89 years.

**Diagnostic criteria**

Esophagitis was divided into different grades according to Los Angeles Classification in patients with RE. Patients with upper gastrointestinal operation-induced lumen structural changes, upper gastrointestinal obstruction, esophageal varices, achalasia of cardia, and patients undergoing esophageal stenting and those with combined reflux esophagitis following three-cavity catheter or gastric tube implantation were excluded.

*H pylori* infection was evaluated based on the diagnosis by rapid urease staining, C13 breath test or pathological silver staining. Esophageal hiatal hernia was diagnosed when dentate line shifted 2 cm or more upward under endoscope, and hernia sac was seen under intra-gastric reversal endoscope. Mucosa within the hernia sac was diagnosed as gastric mucosa. Furthermore, esophageal hiatal hernia could be definitely diagnosed according to the upper gastrointestinal contrast.

A 1:00-12:00 location mark of esophageal mucosa damage similar to the index dial was established by setting the midpoints of anterior, posterior, left and right esophageal walls as 12:00, 6:00, 9:00 and 3:00, respectively. The location of mucosal damage was expressed as the corresponding location mark.

**Statistical analysis**

*P* < 0.05 was considered statistically significant.

**RESULTS**

**Reflux esophagitis, age and grade**

A total of 1405 patients were diagnosed as reflux esophagitis, accounting for 7.46% of the 18823 patients undergoing gastroscopic examinations. The diagnosis rate was 9.13% in 895 male patients and 5.65% in 510 female patients. The ratio of male to female patients was 1.75:1 (*P* < 0.01). The age of onset of RE was 15-89 years (mean age: 54.56 ± 14.19 years). The mean age of male and female patients was 53.82 ± 14.19 years and 55.85 ± 14.08 years, respectively (*P* = 0.01). From the age of 20 to 90 years, 10 years were identified as one age stage. The number and percentage of patients in each stage were 56 and 3.99%, 160 and 11.39%, 341 and 24.27%, 343 and 24.41%, 277 and 19.72%, 194 and 13.81%, and 27 and 1.92%, respectively. There were 7 patients at the age of less than 20 years, accounting for 0.5% (Figure 1). According to Los Angeles Classification, there were 710 patients with grade A (mean age 53.35 ± 13.90 years), 556 with grade B (54.53 ± 14.19 years), 94 with grade C (60.50 ± 13.68 years) and 45 with grade D (61.44 ± 14.97, Figure 2). Patients with grades A and B accounted for 90.1% of all the patients. There was no difference in the age of patients with grades A and B (P = 0.138) or with grades C and D (P = 0.712). However, there were significant differences in the age of patients with grades A and B compared with those with grades C and D (P < 0.01, Table 1).

**Reflux esophagitis and *H pylori* infection**

Of the 18823 patients undergoing endoscopic examination, 7190 were infected with *H pylori*, the infection rate was 38.2%. Of the 1405 patients with reflux esophagitis, 277 were infected with *H pylori*, the infection rate was 19.7%, etc.

**Figure 1** Percentage of patients at different age stages.

**Table 1** Comparison of age in patients with different grades of reflux esophagitis.

| RE LA grade | LA-A | LA-B | LA-C | LA-D |
|-------------|------|------|------|------|
| Mean age    | 53.35b | 54.53b | 60.50 | 61.44 |
| SD          | 13.90 | 14.19 | 13.68 | 14.97 |

b*P* < 0.01 vs the age of patients with grades C and D of RE. LA-A: Los Angeles Classification grade A; LA-B: Los Angeles Classification grade B; LA-C: Los Angeles Classification grade C; LA-D: Los Angeles Classification grade D.
which was significantly lower than that (38.2%) of all patients undergoing endoscopic examinations during the same period. Of the 277 patients infected with H. pylori, 188 were males and 89 were females. There was no gender difference in H. pylori-infected patients with esophagitis (P = 0.109). Of the 277 H. pylori-infected patients with esophagitis, 137 had grade A, 116 had grade B, 15 had grade C, and 9 had grade D, respectively. The severity of esophagitis was not associated with H. pylori infection (P = 0.71, Table 2).

**Reflux esophagitis and esophageal hiatal hernia**

Of the 1405 patients with reflux esophagitis, 195 had esophageal hiatal hernia (EHH+), accounting for 13.9%. Their mean age was 62.03 ± 14.11 years. There was a significant difference in the age between patients with and without esophageal hiatal hernia (P < 0.01). No statistical significance was found in 122 male and 73 female patients (P = 0.722). Of the 195 patients with esophageal hiatal hernia, 29 were infected with H. pylori. The occurrence of esophageal hiatal hernia was not associated with the presence of H. pylori infection (P = 0.08). In the 195 patients with esophagitis and esophageal hiatal hernia, 48 had grade A, 74 had grade B, 48 had grade C, and 25 had grade D, respectively. There was no difference in the detection rate of esophageal hiatal hernia between patients with grades C and D (P = 0.717), while there were significant differences in the detection rate of esophageal hiatal hernia among the other patients (P < 0.01, Table 3).

**Esophageal mucosal damage in reflux esophagitis patients**

In the present study, the number and location of esophageal mucosal damages in patients with grades A and B reflux esophagitis were analyzed. In the 710 patients with grade A, 453 had only a mucosal damage, 184 had 2 damages, 60 had 3 damages and 13 had 4 damages (Figure 3A and B). In the 556 patients with grade B, 115 had only a mucosal damage, 230 had 2 damages, 137 had 3 damages, 67 had 4 damages, and 7 had 5 or more damages (Figure 3), indicating that a mucosal damage occurred mainly in patients with grade A and two or more mucosal damages occurred mainly in patients with grade B.

A 1:00-12:00 location mark similar to the index dial was established by setting the midpoints of anterior, posterior, left and right esophageal walls as 12:00, 6:00, 9:00, and 3:00, respectively. The location of mucosal damage was expressed as the corresponding location mark. The number of mucosal damages at the corresponding location of 1:00-12:00 was 184, 385, 288, 301, 185, 258, 212, 88, 96, 91, 97, and 157, respectively (Figure 4). The esophageal mucosal damages were mainly located at the right esophageal wall.

**DISCUSSION**

Population-based studies suggest that GERD is a common condition with a prevalence of 10%-20% in Western Europe and North America 
[10,11]. The prevalence rates in South America (10%) and Turkey (11.9%) are similar to those in European countries 
[12-14]. In Asia, the prevalence is generally lower. Chen et al. 
[15] reported that the prevalence of heartburn occurring weekly is 6.2% while Wong et al. 
[16] have found a lower prevalence of 2.3%. With the deepening of studies and understanding of gastroesophageal reflux disease, the number of such patients is increased in clinical practice. The significantly decreased quality of life in GERD patients has increasingly attracted extensive attention 
[17]. It was reported that the quality of life deteriorates as the severity of GERD increases 
[17]. In the present study, all the patients undergoing endoscopic examinations in our hospital between September 2004 and January 2007 were analyzed. The detection rate of reflux esophagitis was 7.46%, which

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**Table 2** Relationship between reflux esophagitis and H. pylori infection

| H. pylori+ | Male | Female | LA-A | LA-B | LA-C | LA-D |
|-----------|------|--------|------|------|------|------|
| 7190      | 188  | 89     | 137  | 116  | 15   | 9    |
| 11633     | 1128 | 707    | 421  | 576  | 440  | 79   |
| 38.2%     | 19.7%| 21.01% | 17.45%| 19.3%| 20.86%| 15.96%|
| Total     | 18823| 1405   | 895  | 510  | 710  | 556  |

*P < 0.01 vs H. pylori infection rate in all patients undergoing endoscopic examination. RE: Reflux esophagitis; LA-A: Los Angeles Classification grade A; LA-B: Los Angeles Classification grade B; LA-C: Los Angeles Classification grade C; LA-D: Los Angeles Classification grade D; H. pylori+: Infected with H. pylori; H. pylori-: Not infected with H. pylori.

**Table 3** Relationship of reflux esophagitis and esophageal hiatal hernia

| EHH+ | Male | Female | LA-A | LA-B | LA-C | LA-D |
|------|------|--------|------|------|------|------|
| 195  | 62.03 ± 14.11 | 73 | 48 | 74 | 48 | 25 |
| 1210 | 53.35 ± 13.83 | 773 | 437 | 662 | 482 | 46 | 20 |
| 13.9 | 13.63 | 14.31 | 6.76 | 13.31 | 51.06 | 55.56 |

**Total** | 1405 | 54.56 ± 14.19 | 895 | 510 | 710 | 556 |

*P < 0.01 vs the age of patients with esophageal hiatal hernia; *P = 0.717 (no difference in the detection rate of grades C and D of RE; *P < 0.01 (significant differences in the detection rate of esophageal hiatal hernia among the other patients; EHH+: Associated esophageal hiatal hernia; EHH-: No esophageal hiatal hernia.
was higher in males than in females. The ratio of male to female was 1.75:1, suggesting that males have a higher susceptibility to RE than females. In comparison to the Italian general population, the prevalence of over-weight and obesity is increased in female RE patients but not in male RE patients\(^{18}\). Furthermore, RE tends to occur at a younger age of male patients, which may be related to the differences in life style between males and females. A study demonstrated that the prevalence increases linearly with age among women, and peaks among men at the age of 50-70 years and thereafter declines\(^{19}\). In the present study, the patients with grades A and B of RE accounted for 90.1%, suggesting that the disease is mild in most patients. Although reflux esophagitis can occur at all age stages, most patients are 40-60 years old. Esophagitis aggravates with the age of patients with reflux esophagitis. In this study, no statistical difference was found in items such as onset age and gender between patients with grades A and B of RE. Endoscopic examination is difficult to assess the length of esophageal mucosal damage. The esophageal mucosal damage in patients with grades A and B of RE was extended along the long axis of esophagus, which was different from transversal and vertical extension of damages in patients with grades C and D of RE. These results suggest that grades A and B of RE can be considered a same grade. According to the standards set at Yantai Meeting, reflux esophagitis can be divided into grade 0 = normal mucosa (histological changes may be observed), grade 1 = punctiform or strip redness and erosion without integration, grade 2 = punctiform or strip redness and erosion with integration but non-entire pattern, grade 3 = extensive lesions, redness, erosion integration with entire pattern or ulcers. Grade 1 is equivalent to grades A and B in Los Angeles Classification. It was reported that changes in esophageal motility and response to PPI therapy are similar between patients with grades A and B of RE\(^{20,21}\). Therefore, we believe that the standards set at Yantai Meeting are more practical. In the present study, the \(H\) pylori infection rate was significantly decreased in patients with reflux esophagitis. \(H\) pylori infection had no clear relationship with gender, age and severity of reflux esophagitis. There is evidence that \(H\) pylori infection is not associated with gastroesophageal reflux disease and \(H\) pylori-related inflammation does not affect sphincter motility, namely \(H\) pylori-positive patients have normal LES pressure and the normal frequency of transient LES relaxation\(^{22}\). Long-term PPI therapy can aggravate atrophic gastritis in patients infected with \(H\)
For *H. pylori*-positive patients with gastroesophageal reflux disease, long-term PPI therapy should be preceded by the eradication of *H. pylori*. During the long-term PPI therapy for GERD, *H. pylori* infection can speed up the progress of gastric atrophy. Some investigators have proposed that *H. pylori* should be eradicated in these patients. Nevertheless, eradication of *H. pylori* does not have a clear effect on reflux symptoms in some GERD patients. A study by Spanish scientists showed that treatment of non-erosive gastroesophageal reflux disease with lansoprazole has no effect on *H. pylori* infection. According to the randomized controlled trial by Schwerzer et al., symptoms of *H. pylori*-positive GERD patients occur earlier than *H. pylori*-negative patients and those on eradication therapy for *H. pylori* infection, suggesting that *H. pylori* increases the sensitivity of esophagus and accelerates recurrence of symptoms. In contrast, Moayyedi et al. have not found any significant differences in the recurrence after eradication of *H. pylori* in a large sample of patients. It was also reported that the infection rate of *H. pylori* is higher in Chinese than in white Americans.

Esophageal hiatal hernia is diagnosed mainly based on the upper gastrointestinal contrast. Although no recognized standards are available for endoscopic diagnosis of EHH, we can find some specific changes in EHH at endoscopic examination, including upward shift of the dentate line, hernia sac under intra-gastric reversal endoscope and gastric mucosa appearance within hernia sac. In the present study, the detection rate of esophageal hiatal hernia in those with reflux esophagitis was 13.9%. Esophageal hiatal hernia in patients with reflux esophagitis was not associated with *H. pylori* infection or gender. The age of patients with reflux esophagitis and esophageal hiatal hernia was higher than that of those with simply reflux esophagitis. Esophagitis in patients with associated esophageal hiatal hernia was more serious. It was reported that hiatal hernia (HH) is closely associated with GERD, and isolated distal esophageal reflux is seen more in patients with HH than in patients without HH. Hiatal hernia, in combination with other reflux conditions and symptoms, is associated with the risk of esophageal adenocarcinoma. It was reported that no single factor or combined factors are capable of predicting mucosal damage with clinically sufficient certainty.

In the present study, most patients with grade A of RE had one mucosal damage while those with grade B of RE had 2 or more mucosal damages. It was found that the most frequent location of mucosal damages in reflux esophagitis patients was the right esophageal wall, especially at the points of 2:00 and 4:00. This pathological change may be due to the anti-reflux role of oesophagogastric angle (His angle) and Gubaroff valve, which makes the left esophageal wall suffer from less gastric acid erosion. In contrast, the right esophageal wall is eroded and damaged by gastric contents more easily because of its direct connection with cardia ventriculi and the lack of valvar protection. Katsube et al. reported that the circumferential location of esophageal mucosal breaks differs significantly among different grades of esophagitis, suggesting that reflux of gastric contents into the esophagus can be effectively improved after a valve is added to cardia ventriculi by means of endoscopy or surgical technique.

In conclusion, the peak age of RE onset is 40-60 years and higher in males than in females. The mean age of RE onset is lower in males than in females. The infection rate of *H. pylori* is significantly lower in patients with esophagitis, but the severity of esophagitis is not associated with *H. pylori* infection. Old age and combined esophageal hiatal hernia are associated with more severe esophagitis. Right esophageal mucosal damage can occur more often in patients with reflux esophagitis.

**COMMENTS**

**Background**

Gastroesophageal reflux disease (GERD) affects at least 5%-7% of the global population. The characteristics of GERD of white and yellow race are different. The characteristics of GERD in white people have been described, but the characteristics of GERD in Chinese are not sufficiently described.

**Research frontiers**

The clinical and endoscopic features of Chinese patients with reflux esophagitis (RE) were analyzed. The relationship between RE and patient’s gender and age, between RE and *H. pylori* infection, between RE and hiatal hernia (HH) was discussed. The main location of esophageal mucosa damages to esophageal wall was found.

**Innovations and breakthroughs**

The clinical and endoscopic features of Chinese patients with reflux esophagitis (RE) were analyzed. The peak age of RE onset was 40-60 years and higher in males than in females. The mean age of RE onset was lower in males than in females. The infection rate of *H. pylori* was significantly lower in patients with esophagitis, but the severity of esophagitis was not associated with *H. pylori* infection. Old age and combined esophageal hiatal hernia were associated with more severe esophagitis. Right esophageal mucosal damage can occur more often in patients with reflux esophagitis.

**Applications**

The characteristics of Chinese patients with RE were compared to those of people in other countries. Based on the fact that ‘right esophageal mucosal damage can occur more often in patients with reflux esophagitis’, new methods to cure GERD with endoscopy or surgery should be recommended.

**Peer review**

In this manuscript, the authors analyzed the clinical and endoscopic features of Chinese patients with reflux esophagitis (RE) and described the low infection rate of *H. pylori* in RE patients, the association of hiatal hernia with the severity of reflux esophagitis, but the severity of esophagitis was not associated with *H. pylori* infection. Old age and combined esophageal hiatal hernia were associated with more severe esophagitis. Right esophageal mucosal damage can occur more often in patients with reflux esophagitis.

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