

The Clinical Feature of Reflux Esophagitis Patients Visiting a Single Korean Medicine Hospital: A Retrospective Study

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ABSTRACT

Objectives: This study investigated the clinical characteristics and symptoms of patients with reflux esophagitis (RE) visiting a Korean medicine hospital.

Methods: We retrospectively reviewed the medical records of patients with an RE diagnosis who visited a Korean medicine hospital from June 15, 2020, to April 15, 2021. We analyzed the clinical characteristics and the results of a symptoms questionnaire.

Results: Our sample included 1,151 patients (711 females). The median age was 58 years; the most common age bracket was 60-69 years. A total of 837 patients (72.7%) presented with symptoms lasting more than one year, and 1,035 (89.9%) had been prescribed medications for more than three months before visiting a Korean medicine hospital. Belching (77.6%) and acid regurgitation (70.9%) were the most frequent symptoms, followed by epigastric pain (61.6%) and throat globus (58.5%). Throat globus was the most bothersome symptom, and 72.4% of the patients experienced the symptom on more than five days in the preceding two weeks. Patients with a longer symptom duration were older ($p<0.01$) and more likely to be overweight ($p=0.03$). Patients experiencing symptoms for more than five years were more likely to report throat globus ($p=0.02$), hoarseness ($p<0.01$), and coughing ($p<0.01$).

Conclusions: Most RE patients visiting a Korean medicine hospital were females in their sixties with chronic and refractory RE. Atypical symptoms (belching, epigastric pain, and throat globus) were common. Throat globus was highly prevalent in severe cases, suggesting that it warrants attention when treating RE patients.

Key words: reflux esophagitis, clinical characteristics, symptoms

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I . Introduction

Gastroesophageal reflux disease (GERD) is a common and chronic disease defined as the abnormal reflux of gastric contents into the esophagus. The

global pooled prevalence of GERD was approximately 13.98% and varies from 4.16% in China to 22.40% in Turkey¹. Although the prevalence of GERD in Asia is lower than in Western countries, it has increased rapidly since 2000 from 13.8 to 18.3%²⁻⁴. In Korea, the number of patients who visited hospitals for GERD increased by 11.6% from 4,165,789 in 2016 to 4,650,302 in 2020, and the number of outpatients at Korean medical hospitals increased by 40.4% from 15,776 in 2016 to 22,155 in 2020⁵.

GERD is usually diagnosed based on patient symptoms, an esophageal pH monitoring test, and gastrointestinal endoscopy. Heartburn and regurgitation are considered typical symptoms of GERD. However, atypical symptoms such as throat globus, chronic cough, and non-cardiac chest pain are prevalent in clinical practice, and can occur with or without typical symptoms^{6,7}. GERD is classified into non-erosive reflux disease (NERD) and erosive reflux disease (ERD) or reflux esophagitis (RE) based on the detection of erosions by upper endoscopy. Although NERD is conventionally the major subcategory of GERD, its prevalence may be overestimated because a diagnosis is based on the subjective symptoms of the patient. In Korea, endoscopy has been conducted widely during regular health check-ups and it resulted in a substantial number of GERD patients being diagnosed with RE: from 3.5% in 2001⁸ to 7.91% in 2006⁹ and 7.1% in 2007¹⁰.

GERD is conventionally treated with medications, such as PPIs and antacids and more recently, anti-reflux surgery has been suggested¹¹. However, GERD is still regarded as a highly prevalent and frequently recurrent and refractory disorder. In clinical practice, an increasing number of symptomatic RE patients visit Korean medicine hospitals out of

fear of the results of endoscopy. A previous study on the clinical spectrum of RE among Koreans undergoing health check-ups exists⁹, but there are no studies of RE patients seeking a traditional medicine. The aim of the present study was to investigate the clinical characteristics and symptoms of RE patients visiting a Korean medicine hospital.

II. Methods

1. Study design and Participants

A retrospective study was conducted to identify RE patients who had visited a GI clinic of Gangnam Weedahm Korean medicine hospital from June 15, 2020, to April 15, 2021. We used electronic medical records to carry out an extensive review of the patients' medical files, including documentation of all previous medical consultations at other hospitals. In this study, we limited the sample to RE subjects who had been diagnosed on the basis of endoscopic findings. Patients were excluded if they had previously received gastrointestinal surgery, including anti-reflux surgery, or had a cancer diagnosis. The basic clinical characteristics of the patients included sex, age, body mass index (BMI), physical exercise status, eating habits, smoking status, drinking status, and status of *Helicobacter pylori* (*H. pylori*) infection. This retrospective study was approved by the Institutional Review Board of Weedahm Korean medicine hospital (WD00009-21-CR-007).

2. Assessment of symptoms

We reviewed all patient medical records and a questionnaire that was designed to assess the severity of subjective symptoms and had been administered to all patients. The questionnaire included the two most representative GERD symptoms (heartburn

and regurgitation): atypical symptoms like chest pain, throat globus, hoarseness, cough, and insomnia; and some additional gastric symptoms, such as epigastric pain, belching, and hiccupping. The frequency of symptoms was determined based on symptom occurrence in the previous two weeks in the form of a five point Likert scale used in Neapen dyspepsia index¹² : 0=none; 1=1-4 days; 2=5-8 days; 3=9-12 days; 4=13 or more days.

3. Outcome measures and statistical analysis

Continuous data were expressed as the mean± standard deviation. The chi-squared test and Fisher's exact test were used to determine whether differences between groups were statistically significant. Differences between three groups were analyzed by a one-way analysis of variance. Pearson's correlation was used to evaluate correlations between symptoms. A p-value <0.05 was considered statistically significant. All statistical analyses were performed using SPSS version 20 (IBM, USA).

III. Results

1. The baseline characteristics

A total of 1,151 patients, including 440 males (38.2%) and 711 females (61.8%), were enrolled in this study. The median age was 58.02 years, and the greatest prevalence of GERD was in the group aged 60-69 years. The mean BMI (kg/m²) was 23.5, and 626 patients (54.4%) were overweight (BMI>23). After excluding 486 patients with an unknown status of *H. pylori* infection, 257 patients (38.6%) were *H. pylori*-positive. Most patients reported that they were not current smokers or drinkers, and the percentage of current smokers was particularly low (7.4%). More than 70% of

patients had suffered from subjective GERD symptoms for more than one year, and 477 patients (41.4%) reported symptoms lasting more than five years. A total of 1,035 (89.9%) patients had been treated with medications at other hospitals for more than three months before visiting a Korean medicine hospital (Table 1). Those who drink or smoke at the time of visiting a hospital were marked as 'current drinker' and 'current smoker'. 'Regular exercise' is defined as more than 3 times a week regardless of any type of exercise, and 'regular diet' is defined when patient eat at the right time every day.

Table 1. Characteristics of Participating Subjects (n = 1,151)

Category	Value (n)
Sex (M/F)	440/711 (38.2%/61.8%)
Age (Mean±SD)	58.02±13.02
<39 yrs (M/F)	119 (58/61)
40-49 yrs	100 (44/56)
50-59 yrs	330 (114/216)
60-69 yrs	414 (158/256)
>70 yrs	189 (66/123)
BMI (kg/m ² , Mean±SD)	23.5±3.6
< 23	525 (45.6%)
≥ 23	626 (54.4%)
<i>H. pylori</i> positive (among 665 subjects)	257 (38.6%)
Current drinker	351 (30.5%)
Current smoker	85 (7.4%)
Regular exercise	601 (52.2%)
Regular diet	716 (62.2%)
History of GERD symptoms	
<1 yr	314 (27.3%)
1 to 5 yrs	360 (31.3%)
>5 yrs	477 (41.4%)
Duration of treatment before visiting a Korean medical hospital	
≤3 months	116 (10.1%)
>3 months	1035 (89.9%)

2. Prevalence of symptoms

The symptom prevalence is shown in Fig. 1. Excessive belching was the most frequent symptom and was found in 893 patients (77.6%). The next most frequent was acid regurgitation, reported by 816 patients (70.9%); epigastric pain in 709 patients (61.6%); throat globus in 673 patients (58.5%); chest pain in 643 patients (55.9%); heartburn in 600 patients (52.1%); cough in 566 patients (49.2%); and hoarseness in 389 patients (33.8%). Only 497 patients (43.2%) presented with both heartburn and acid regurgitation. Throat globus was the most bothersome symptom, considering 72.4% reported experiencing it on more than five days in the previous two weeks among those with throat globus.

The trends in symptom occurrence were similar in each age group. In terms of frequency, the general order of symptoms was belching, acid regurgitation, epigastric pain, throat globus, chest pain, heartburn, cough, insomnia, and hoarseness. However, the frequency of throat globus and chest pain was higher in patients aged 40-49 than in other age groups (Fig. 2-A). Female patients were

significantly more likely than male patients to report epigastric pain (64.3%, $p=0.02$), belching (80%, $p=0.01$), throat globus (61%, $p=0.03$), and insomnia (49.9%, $p<0.01$) (Fig. 2-B).

The coexistence of majority of atypical symptoms was higher in patients with typical symptoms (Table 2). However, the insomnia comorbidity rate was higher in the group without typical symptoms. Furthermore, the frequency of atypical symptoms in this study compared to previous studies is shown in Table 3.

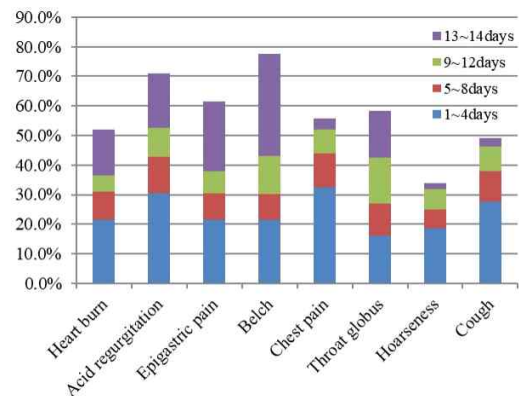


Fig. 1. Presence and frequency of symptoms in previous two weeks.

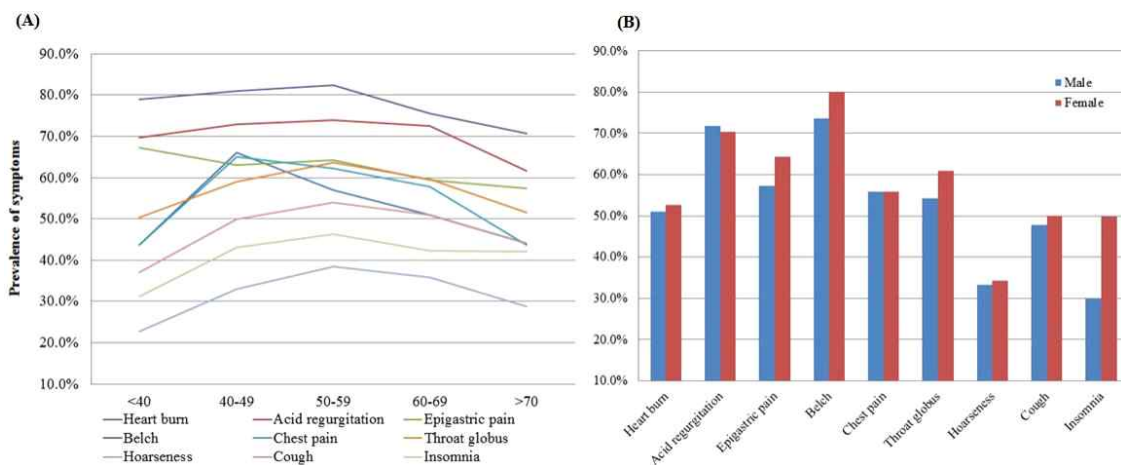


Fig. 2. Presence of symptoms according to (A) age and (B) gender.

Table 2. Frequency of Atypical Symptoms according to Existence of Two Typical Symptoms

Symptoms	Heartburn exist group (n=600)	Acid regurgitation exist group (n=816)	None of typical symptoms group (n=232)
Epigastric pain	445 (74.2%)	537 (65.8%)	94 (40.5%)
Belch	493 (55.2%)	674 (82.6%)	147 (63.4%)
Chest pain	420 (70.0%)	496 (60.8%)	81 (34.9%)
Throat globus	400 (66.7%)	511 (62.6%)	103 (44.4%)
Hoarseness	236 (39.3%)	299 (36.6%)	62 (26.7%)
Cough	347 (57.8%)	438 (53.7%)	78 (33.6%)
Insomnia	284 (58.3%)	360 (44.1%)	156 (67.2%)

Table 3. Frequency of Atypical Symptoms in Various Studies

Study	The present study	Yi et al. ¹³ (2012)	Cho et al. ⁸ (2005)
Country, target population	Korea, Patient visiting a single KM hospital	Taiwan, Patient visiting a single GI clinic	Korea, Population based study
Participants	RE n=1,151	GERD n=210 (ERD, n=90+NERD, n=120)	Frequent GERD* n=50 among 1,417 subjects
Atypical symptoms			
Chest pain	54.5%	50.5%	44.0%
Throat globus	52.2%	36.7%	14.0%
Cough	40.8%	22.1%	-
Belch	80.6%	54.6%	-
Hoarseness	26.1%	-	10.0%
Dysphagia	-	27.6%	16.0%
Extra symptoms	Epigastric pain 65.3% Arrhythmia 9.6% Insomnia 43.6%	Dyspepsia 52.9% Hiccup 55.1%	Asthma 26.0% Bronchitis 20.0%

ERD : erosive reflux disease, KM : Korean medicine, NERD : non-erosive reflux disease, *At least weekly symptoms

3. Differences among groups divided by duration of subjective symptoms

There were no significant differences in the characteristics (age, sex, BMI, alcohol/smoking habit, physical exercise status, and eating habits) or subjective symptoms of patients who had been treated for more than three months (n=1,035) versus less than three months (n=116) before visiting a Korean medicine hospital (data not shown). The only significant differences in the characteristics of three groups divided by duration of subjective

symptoms were sex, BMI, and age (Table 3). Patients with a longer duration of symptoms tended to be older (p<0.01) and were more likely to be overweight (p=0.03). Throat globus (p=0.02), hoarseness (p<0.01), and cough (p<0.01) were more common in patients suffering more than five years compared to patients with a shorter duration of symptoms (Table 4, Fig. 3). In addition, a slightly higher percentage of patients with symptoms lasting more than five years had an arrhythmia (14.5% vs. 12.3% of the overall sample), but without statistically significant (p=0.12).

Table 4. Characteristics and the Presence of Symptoms according to Symptom Duration

	Duration of symptoms ≤1 year (N=314)	Duration of symptoms <5 (N=360)	Duration of symptoms ≥5 years (N=477)	p-value
No of males (%)	33.1	47.2	34.8	0.00**
Overweight patient (%)	49.0	54.9	54.1	0.03*
Mean age	56.32	56.81	60.01	0.00**
<i>H. pylori</i> positive (%)	22.6	19.7	24.1	0.49
Current smoker (%)	6.4	8.3	7.3	0.62
Current drinker (%)	26.1	33.9	30.8	0.09
Regular exercise (%)	51.0	55.0	50.7	0.42
Regular diet (%)	62.1	64.2	60.6	0.57
Symptoms				
Heartburn (%)	48.7	54.7	52.4	0.30
Acid regurgitation (%)	68.8	69.2	73.6	0.24
Epigastric pain (%)	65.3	58.3	61.6	0.18
Belch (%)	80.6	75.3	77.4	0.26
Chest pain (%)	54.5	57.8	55.3	0.66
Throat globus (%)	52.2	62.5	59.5	0.02*
Hoarseness (%)	26.1	36.7	36.7	0.00**
Cough (%)	40.8	51.4	53.0	0.00**
Arrhythmia (%)	9.6	11.9	14.5	0.12
Insomnia (%)	43.6	39.2	43.8	0.35

Analyzed by chi-square test and Fisher's exact corrections, *p-value<0.05, **p-value<0.001

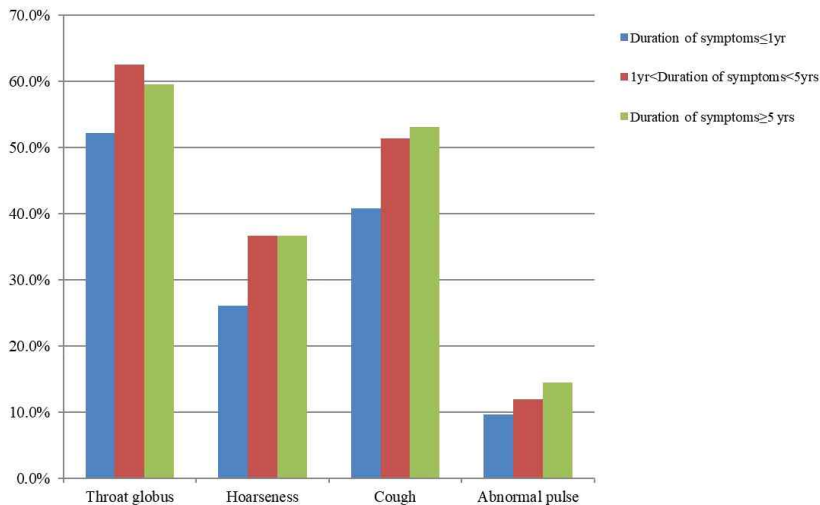


Fig. 3. Different proportions of symptoms among groups divided by duration of symptoms.

IV. Discussion

This study describes the characteristics of RE patients visiting a single Korean medicine hospital. The patients were predominantly female (61.8%) and the 60–69 year age range was the most common, compared to the previous studies reported that males were more prevalent^{3,9,13} and that patients were evenly distributed by age^{9,13}. Findings of the present study reflect the preference of women and older people for Korean medicine.

In this study, 72.7% of patients visited a Korean medicine hospital for symptoms lasting more than one year and 89.9% of patients had been prescribed PPIs, H2 blockers, or other medications for more than three months. This is consistent with the gradual increase in Korea in the use of PPIs for at least three months and 10% of patients were prescribed more than the standard dose, with a significant economic burden¹⁴. Furthermore, these findings show that the majority of patients visiting a Korean medicine hospital are experiencing chronic RE that is refractory to conventional treatment.

Trends in symptom frequency were similar across age groups, but throat globus and chest pain were relatively higher in patients aged 40–49 years compared to other age groups. Most symptoms were more frequently reported by females than by males, probably because of differential symptom perception by sex (as in Kim et al.¹⁵). Notably, 49.9% of female patients had insomnia versus 30% of male patients. A previous study reported that insomnia in GERD patients was not affected by sex, but by the severity of extra-esophageal symptoms¹⁶. The higher proportion of female insomnia patients in this study could be affected by the frequency of atypical symptoms in females. Of the characteristics

that we examined in the present study, which included BMI, alcohol, tobacco, physical exercise, and dietary habits, only BMI was correlated to duration of symptoms. A higher proportion of overweight patients was reported in groups with symptoms lasting more than five years, indicating that it is necessary to consider the need for weight control in long-term treatment of GERD. In contrast to a previous study finding that *H. pylori* infection may be negatively associated with GERD^{9,17}, the present study found no relationship between *H. pylori* infection and GERD, which is probably attributable to a lack of data.

GERD patients are reported to present with a broad range of troublesome symptoms. In the present study, 70.9% and 52.1% of RE patients presented with acid regurgitation and heartburn, respectively. Only 43.2% of patients presented with both symptoms. This percentage is far smaller than that reported in previous studies finding that typical symptoms were reported by 60–68% of patients in western countries¹⁸ and 60% of patients in Japan⁴. However, it is higher than the percentage reported in a previous Korean study that found that 33.3% of RE patients presented with heartburn and 35.6% with acid regurgitation⁹.

It is well-known that atypical symptoms are highly prevalent and found in up to 80% of patients¹⁹. Atypical symptoms were reported to be highly frequent and bothersome in the present study. Excessive belching was the most frequent symptom and was reported by 77.6% of all subjects. This is consistent with the recent studies that have increased awareness of the association between excessive supragastric belching and GERD, and of the fact that excessive belching may even be attributable to PPI-refractory GERD^{20,21}. Moreover,

epigastric pain, throat globus, and chest pain were found more frequently than heartburn. This is supported by a study of 25,536 people undergoing health check-ups in Korea, which found that epigastric soreness was the most frequent symptom in RE⁹. Tack et al.²² also found that epigastric pain was found mainly in patients with pathological acid exposure, and Cho et al.⁸ suggested it was probable that Korean patients would complain of epigastric soreness or chest pain (i.e., heartburn).

Another notable finding in this study was the importance of throat globus in GERD. 'Throat globus' means a non-painful sensation of a lump or foreign body in the throat. 58.5% of all patients presented with throat globus. This is higher than the percentages reported in other studies, which range from 14.0-55.2%⁸ or 22.8%⁹ in Korea and 36.7% in Taiwan²³. Furthermore, this symptom is relatively severe: 72.4% of patients presenting with throat globus experienced the symptom on more than five days in the previous two weeks, and patients with a longer duration of symptoms were more likely to report throat globus, hoarseness, cough, and arrhythmia. Throat globus in GERD can be explained by two mechanisms: direct irritation or inflammation of the laryngopharynx caused by gastric contents and vagovagal reflux triggered by acidification²⁴. Thus, it is necessary to assess throat globus as it can be an indicator of the severity of RE and affect treatment decisions.

In addition, we suggest consideration of the cardiovascular aspect of GERD. This is appropriate given that 12.3% of patients in the present study had an arrhythmia, which is similar to the reported incidence of atrial fibrillation, 0.62% to 14%, in GERD patients²⁵. The incidence of an arrhythmia was increased in patients with a longer duration of

symptoms. The vagovagal reflux triggered by acidification may cause an arrhythmia as well as throat globus²⁴. This can also be understood by referring to the conceptualization of GERD in Korean medicine, where it is addressed by treating 'stomach or spleen' and 'heart', as with the medication 'Ban Xia Xie Xin Tang'²⁶.

This study is meaningful in that it analyzed the clinical features of more than 1,000 RE patients who visited a Korean medicine hospital, which will be different from population-based studies or studies on patients visiting the conventional treatment. In addition, the characteristics of atypical symptoms of GERD that can be overlooked in conventional treatment were analyzed. Since most of RE patients are accompanied by atypical symptoms, it is thought that Korean medicine treatment that comprehensively considers these will be better in treating GERD patients than medications such as PPIs.

This study has several limitations. Detailed data on the endoscopic classification (such as Los Angeles classification of GERD) and types of medication taken, such as PPI or prokinetic drugs, are lacking. In addition, a certified questionnaire was not used for evaluating the severity of symptoms. As coffee consumption can affect the development of GERD²⁷, the consumption of coffee is recommended in further study.

Therefore, further study with information about medication patient used, consumption of coffee or tea, herbal prescriptions, and the rate of improvement with herbal medicine will be needed. Also, additional study with annual data involving both NERD and RE patients evaluated with verified questionnaires is required.

V. Conclusion

In conclusion, the present study shows that patients visiting a hospital for Korean medicine were predominantly females in their sixties with chronic and refractory RE. Female patients tended to have more frequent symptoms and patients aged 40-49 years had a higher prevalence of throat globus and chest pain compared to other age groups. Atypical symptoms, such as belching, epigastric pain, and throat globus, were frequent. Throat globus was particularly prevalent in severe cases, suggesting that the symptom merits careful attention when treating GERD patients.

Ethical statement

This research was reviewed and approved by the institutional review board of Weedahm Korean medicine hospital (WD00009-21-CR-007). Informed consent was obtained from all participants.

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