Korean J Gastroenterol Vol. 85 No. 4, 484-490
https://doi.org/10.4166/kjg.2025.080
pISSN 1598-9992 eISSN 2233-6869

REVIEW ARTICLE | Upper GI Tract

KJG

상부위장관 출혈의 역학과 원인

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Changing Epidemiology and Etiology of Upper Gastrointestinal Bleeding

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Upper gastrointestinal bleeding (UGIB) is defined as bleeding from the esophagus, stomach, and duodenum, whereas lower gastrointestinal bleeding originates from below the ligament of Treitz, including the small bowel and colon. The incidence of UGIB has decreased globally over the past 20 years, reaching approximately 50–150 and 47 cases per 100,000 of the global population per year for variceal and non-variceal bleeding, respectively. The eradication of *Helicobacter pylori* and the widespread introduction of proton pump inhibitors have contributed to the current improvement in epidemiological outcomes. Regarding the etiology of UGIB, peptic ulcer disease is the most common cause, accounting for 43.6% of cases, followed by gastritis and duodenitis (27.6%), esophageal variceal bleeding (8.0%), and esophagitis (5.6%). Other causes, including malignancy, Dieulafoy's lesions, and Mallory Weiss tears, collectively account for 10–12% of UGIB. In conclusion, the outcomes of *H. pylori* eradication and the widespread introduction of proton pump inhibitors have offset the effects of an aging population. In addition, the increasing indications for non-steroidal anti-inflammatory drugs, anticoagulation, and antiplatelet agents have resulted in a decrease in the incidence of UGIB. **(Korean J Gastroenterol 2025;85:484-490)**

Key Words: Upper gastrointestinal tract; Epidemiology; Etiology

INTRODUCTION

Upper gastrointestinal bleeding (UGIB) is a commonly encountered clinical manifestation that has a mortality rate ranging from 7% to 11%.[1,2] The incidence of variceal and non-variceal bleeding has reached approximately 50–150 and 47 cases per 100,000 of the global population per year. Defined as a loss of blood from the gastrointestinal tract, including the esophagus, stomach, and duodenum, UGIB is categorized and distinguished from lower gastrointestinal bleeding (LGIB) by the ligament of Treitz, which confines it to the proximal region. In contrast, LGIB covers the distal portion from the ligament of Treitz, including the jejunum, ileum, and colon. It has risk factors of age, male, smoking, alcohol consumption, and medication that interferes with the stability of the intestinal epithelium.[3-8] The clinical manifestation varies depending on the disease severity. It is typically manifested by fresh red hematemesis or coffee-ground vomiting, hematochezia, or melena. In addition, the gastrointestinal symptoms mentioned above and systemic signs associated

Received July 15, 2025. **Revised** August 2, 2025. **Accepted** August 2, 2025.
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Financial support: None. Conflict of interest: None.

with hypovolemia occur, including syncope, sweating, and orthostasis. Peptic ulcer disease is the most common cause, accounting for 43.6% of UGIB, followed by gastritis and duodenitis (27.6%), esophageal variceal bleeding (8.0%), and esophagitis (5.6%). Other causes, including malignancy, Dieulafoy's lesions, and Mallory Weiss tears, collectively account for 10–12% of UGIB cases.[9,10] This study investigated the changing global incidence and the etiology of UGIB from Western countries to the Asian region.

GLOBAL INCIDENCE OF UGIB

UGIB is more common in males than females, and the incidence increases with age (Fig. 1).[11-15] The consumption of non-steroidal anti-inflammatory drugs (NSAIDs), antiplatelet agents, and anti-coagulants is more frequently indicated in old age. Hence, the incidence of age-dependent bleeding has increased regardless of the total global UGIB tendency.[14,16]

Several population-based studies have presented declining global epidemiologic outcomes of UGIB in the recent twenty years. Most epidemiologic studies have covered Western countries, including Europe and the United States (US), to the Asian region (Table 1 and Fig. 2).[13,14,16-21] A prospective observational study conducted in Italy comparing the time trends of UGIB from 1983 to 1985 and from 2002 to 2004 reported an overall 35% decrease in incidence.[17] The overall incidence

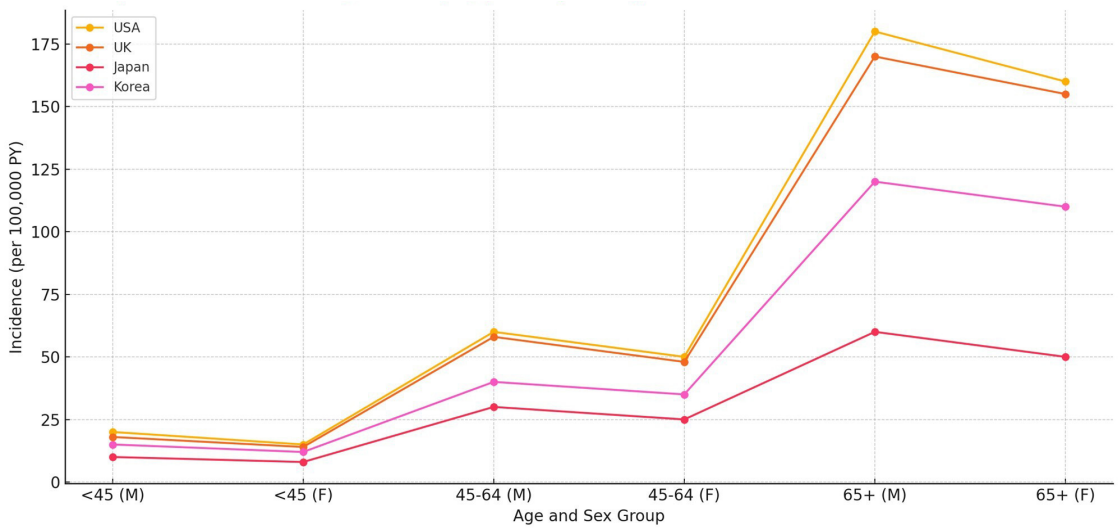


Fig. 1. UGIB incidence by age and sex group. UGIB incidence increases significantly with age, especially in individuals aged 65 and older. Males generally have higher incidence rates than females across all age groups. Western countries (USA and UK) show higher overall UGIB incidence compared to East Asian countries (Korea and Japan), particularly in elderly males. UGIB, upper gastrointestinal bleeding.

Table 1. Incidence and Outcome of Acute UGIB

Study	Region	Study design	Time frame	Incidence change (per 100,000 person-year)	Mortality
Loperfido et al.[17]	Italy	Prospective	1983–1985, 2002–2004	112.5→89.8	17.1→8.2 per 100,000/year
Abougergi et al.[18]	US	Retrospective	1989, 2009	108→78	4.5→2.1%
Theocharis et al.[16]	Greece	Retrospective, Prospective	1995, 2005	162.9→108.3	3.9→6.5%
van Leerdam et al.[19]	Netherlands	Prospective	1993/1994, 2000	61.7→47.7	15→14%
Kim et al.[14]	Korea, Republic of	Retrospective	2006–2015	34.3→30.7	3.6→3.8%
Miyamoto et al.[13]	Japan	Retrospective	1997–2008	160.8→23.6	-
Oakland[20]	Global, Spain	Retrospective	1996–2012	87→47	Decrease in global trend

UGIB, upper gastrointestinal bleeding.

has decreased from 112.5 to 89.8 per 100,000 persons. In addition, the annual mortality has decreased from 17.1 to 8.2 per 100,000 persons in 1983-to-1985 and 2002-to-2004 periods, respectively.[17]

Abougergi et al. retrospectively evaluated the incidences and mortality rates of UGIB in the US population from 1989 to 2009.[18] The incidence and mortality rates have shown a declining trend, with a decrease in incidence from 108 to 78 cases per 100,000 persons in 1994 and 2009, respectively, as well as a reduction in mortality rate from 4.5% in 1989 to 2.1% in 2009.[18]

Theocharis et al. evaluated the epidemiology and clinical outcomes of UGIB in Greece by comparing the prospective study results from 2005 with retrospective data from the same population 10 years earlier.[16] The incidence decreased from 162.9 per 100,000 population in 1995 to 108.3 per 100,000 population in 2005.[16] A prospective study in the Netherlands examined the recent trends in the incidence and outcome of UGIB in 1993/1994 and 2000.[19] They reported a decrease in incidence from 61.7 cases per 100,000 persons in the 1993/1994 period to 47.7 cases per 100,000 persons in 2000.[19]

Kim et al. evaluated the Korean National Health Insurance Service Database records of Korean patients hospitalized with peptic ulcer bleeding (PUB) from 2006 to 2015.[14] The average annual incidence of hospitalization was 34.98 per 100,000 person-year. A 2.7% decrease in total hospitalizations was observed between 2008 and 2015. In addition, the incidence of hospitalization with PUB significantly decreased, especially in men between 2008 and 2015, with an annual change of –3.4%.[14]

In Japan, Miyamoto et al. retrospectively evaluated the correlation between the incidence of UGIB from 1997 to 2008 and the frequency of usage of medicine, including proton pump inhibitors (PPIs), histamine 2 receptor antagonists, and aspirin.[13] The annual incidence of UGIB with the widespread use of PPI decreased significantly from 160.8 to 23.6 per 100,000 population.[13] Oakland et al. conducted a global review of UGIB from 1980 to 2012 and reported a decline in the incidence of UGIB in Western population-based studies.[20] Their study results included a reduction of upper gastrointestinal complication incidence from 87 to 47 per 100,000 persons between 1996 and 2005 in Spain.[20,21]

The global trend has become evident for populations with appropriate access to endoscopic facilities and hospitalization because of the advances in the gastrointestinal field, the introduction of endoscopic devices, and the application of effective endoscopic and medical therapeutic management, including injection therapy, thermal coagulation, hemoclips, hemospray, Doppler endoscopic probe, and endoscopic suturing.[22-25] The eradication of *H. pylori* and the widespread introduction and use of PPIs have led to superior treatment outcomes

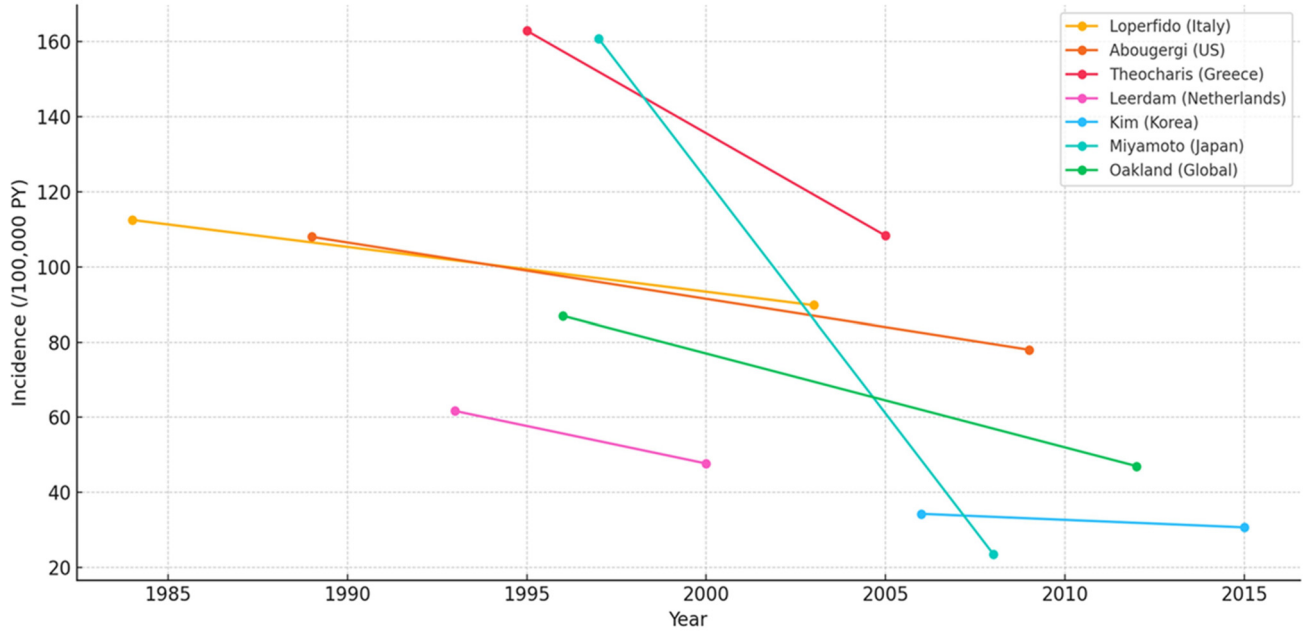


Fig. 2. UGIB incidence trends by study and region. UGIB, upper gastrointestinal bleeding.

for peptic ulcer diseases, resulting in a reduction of upper gastrointestinal complications.[26-32] The population is aging, and they are consuming increasing amounts of NSAIDs and anticoagulation and antiplatelet agents. Nevertheless, *H. pylori* eradication, the use of PPIs, and the increased use of safer COX-2 selective inhibitors may have contributed to the current changing epidemiologic outcomes.[28-34] In addition, advances in therapeutic endoscopy, including novel effective endoscopic devices and efficient approaches to endoscopic units, have contributed to the current changing epidemiologic outcomes of UGIB.[22-25] In the aspect of variceal bleeding, the incidence of variceal UGIB in the US showed a declining outcome, demonstrating a consistent worldwide trend of gastrointestinal bleeding.[35,36] In addition, despite the expanded hospitalization caused by cirrhotic underlying comorbidities, studies performed in the US evaluation on esophageal variceal bleeding based on a national inpatient sample from 2002 to 2012 showed a decreasing incidence.[37] The prophylactic management of varices with endoscopic ligation and the application of beta blockers and vasoactive agents would have resulted in the current epidemiologic outcome of variceal bleeding.

ETIOLOGY OF UGIB

Previous studies based on national observational and databases in the US and Europe as well as the Asian region have shown the global etiology of UGIB (Fig. 3).[12-15,17,38] Peptic ulcer disease is the most common cause reaching 43.6% of UGIB cases followed by gastritis and duodenitis (27.6%), esophageal variceal bleeding (8.0%), and esophagitis (5.6%). Other causes, including malignancy, Dieulafoy's lesions, and Mallory–Weiss tears, collectively account for 10–12% of UGIB.[9,10]

A prospective observational study conducted in Italy to analyze the time trends of UGIB with its etiology in 1983–1985 and 2002–2004 reported an overall decrease in the incidence of peptic ulcer disease from 32.7% to 19.5% ($p<0.001$). In addition, a decrease in the proportion of patients bleeding from peptic ulcers (347/587, 59.1% vs. 286/539, 53.1%, $p=0.12$) and gastroesophageal varices (73/587, 12.4% vs. 44/539, 8.2%, $p=0.05$) was reported.[17] On the other hand, the proportion of patients bleeding from other lesions, including esophagitis (11/587, 1.9% vs. 23/539, 4.3%, $p=0.01$), angiodysplasia, and Dieulafoy's lesion, increased in 2002–2004.[17]

According to the recent retrospective, an observational cohort study to investigate the trends in the etiology and outcome of UGIB in hospitalized patients from 2002 to 2012

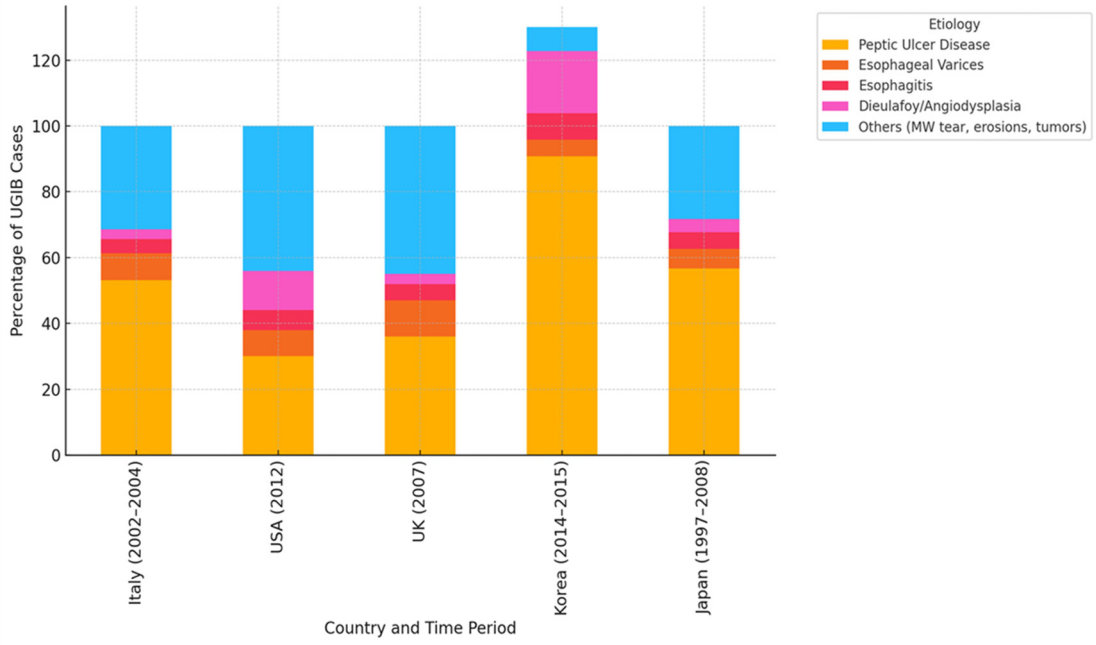


Fig. 3. Etiologic breakdown of UGIB by country. UGIB, upper gastrointestinal bleeding.

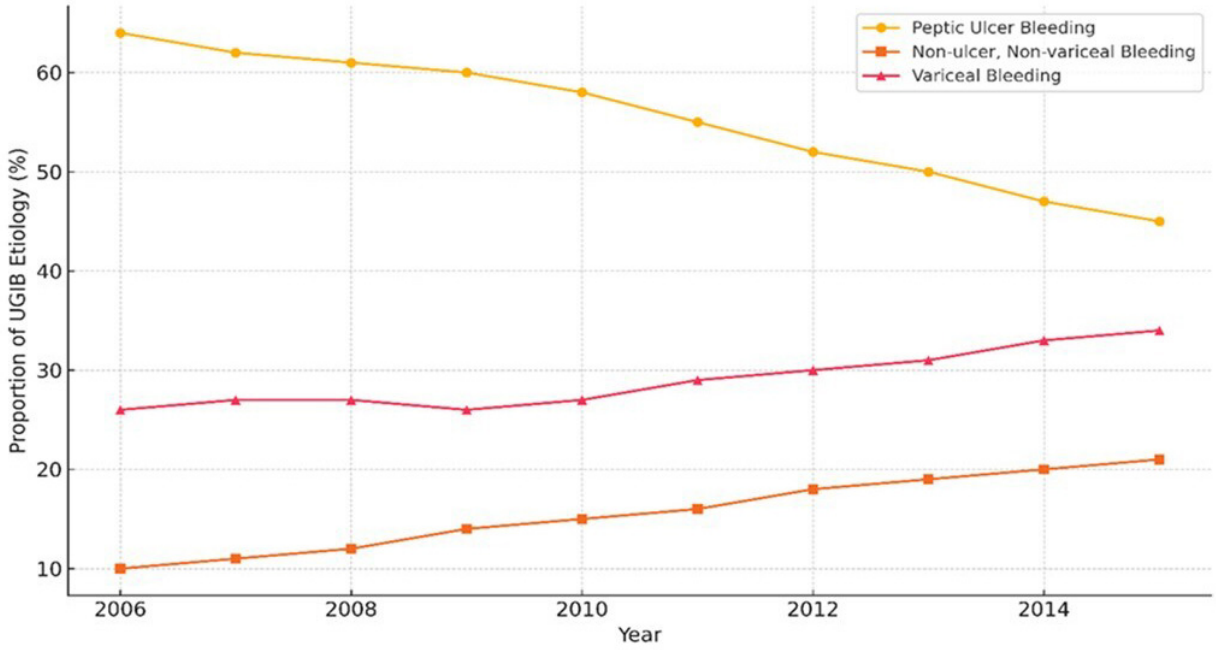


Fig. 4. Changing etiology of UGIB in Korea (2006–2015). UGIB, upper gastrointestinal bleeding.

in the US, the hospitalization rate of peptic ulcer disease decreased 30% from 41 to 30 cases per 100,000 population, in addition to an overall reduction of the hospitalization rate from 81 to 67 cases per 100,000 population.[12] Regarding trends in other etiologies, the hospitalization rate of Dieulafoy's lesions, angiodysplasia, and neoplasm increased 33%, 32%, and 50%, respectively.[12] Hearnshaw et al. performed a multi-center, cross-sectional clinical audit of the UK to assess the organization of endoscopy services for acute UGIB in 2007.[15] Six thousand and fifty patients from 208 hospitals were analyzed. The study group showed 36% with PUB as the most common cause, followed by 11% of variceal bleeding.[15]

An analysis of PUB in Korea was performed from an extensive prospectively collected database of patients with PUB who were hospitalized between 2014 and 2015 at 28 medical centers.[14] The study had 904 registered PUB patients, of which 897 patients were analyzed, with 60.9% having gastric ulcers and 29.9% having duodenal ulcers.[14] Approximately 7.1% of the patients had rebleeding with a 1.0% 30-day mortality.[14] In addition, a prospective observational cohort study reviewed prospectively collected data from 1984 patients who underwent an upper gastrointestinal endoscopy due to UGIB to assess the predictability of scoring systems for non-ulcer bleeding (NUB) and compare the outcomes of NUB and ulcer bleeding.[38] The most common cause of bleeding in Group NUB was Mallory–Weiss tears (51.1%), followed by Dieulafoy's lesions (18.9%), AGML and erosions (9%), and esophagitis (8%).[38]

The overall changing etiology of UGIB from 2006 to 2015 has shown a gradual decline of PUB, reflecting the prevalence of *H. pylori* and the widespread use of PPIs. On the other hand, the incidence of non-ulcer, non- variceal bleeding has increased slightly owing to advanced diagnostics capturing rare or atypical lesions as well as variceal bleeding, reflecting the trends of chronic liver disease (Fig. 4).[14,38] The study results from Japan, retrospectively evaluating the correlation between the use of medicine and incidence of UGIB over 12 years from 1997 to 2008, revealed a bleeding etiology, with 144 peptic ulcer patients (56.7%), including 108 gastric and 36 duodenal ulcer patients, out of 253 patients with UGIB.[13]

SUMMARY

The global epidemiologic approach and evaluation revealed a declining trend due to the influential outcome of *H. pylori* eradication and the widespread introduction of PPIs, over the effect of an aging population with increasing indication for NSAIDs, anticoagulation, and antiplatelet agent consumption. In the aspect of variceal bleeding, a prophylactic therapeutic

approach combining endoscopic ligation and medical management with beta blockers and vasoactive agents would have resulted in the current reduction trends in the epidemiological outcomes of variceal bleeding. Future follow-up studies tracing the consistency of current changes would be required to understand and assess UGIB.

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