# Epidemiology and Risk Factors for Upper Gastrointestinal Bleeding

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**KEYWORDS**

• Epidemiology • NSAIDs • Aspirin • Clopidogrel • *Helicobacter pylori* • Mortality • Risk factors • Incidence

**KEY POINTS**

- Incidence of nonvariceal upper gastrointestinal bleeding (UGIB) has been decreasing worldwide. However, nonvariceal UGIB continues to be a significant problem.
- The most common risk factors for nonvariceal UGIB include *Helicobacter pylori* infection, nonsteroidal antiinflammatory medications (NSAIDs), aspirin, selective serotonin reuptake inhibitors, and other antiplatelet and anticoagulant medications.
- More recently observed important risks for UGIB are cardiovascular disease, heart failure, left ventricular assist devices, and renal failure.
- Despite the introduction of cyclooxygenase-2 inhibitors, which were introduced to decrease UGIB, bleeding from NSAIDs continues to be a problem.
- Introduction of newer antiplatelet agents and newer oral anticoagulants has contributed to the persisting incidence of UGIB.

## INTRODUCTION

Upper gastrointestinal bleeding (UGIB) is defined as hemorrhage that involves the mouth to the duodenum proximal to the ligament of Treitz. Common causes of UGIB include peptic ulcer disease (PUD) and ulcers of the esophagus, erosions of the upper gastrointestinal (GI) tract, variceal bleeding, gastroesophageal reflux disease, Mallory-Weiss tears, vascular lesions, malignancy, and other less common

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causes. Between 40% and 50% of patients who have UGIB present with hematemesis and 90% to 98% with either melena or hematochezia.[1] The disease is commonly divided into 2 types: nonvariceal and variceal, and the primary focuses of this article are the epidemiology and risk factors of nonvariceal bleeding. Even with the use of advanced endoscopic procedures and potent medications to suppress acid production, UGIB still carries significant morbidity and mortality. Although studies have reported a decreased incidence in UGIB in the United States (96–82 per 100,000)[2,3] it still accounts for nearly 300,000 hospitalizations per year, with a mortality of approximately 5%.[3,4] PUD still accounts for most nonvariceal bleeding (37%)[5] and is higher among elderly men, those who use aspirin and nonsteroidal antiinflammatory drugs (NSAIDs), and in areas with high *Helicobacter pylori* prevalence.[3,4] In the United States in 2004, there were about 700,000 ambulatory care visits with peptic ulcer as the first-listed diagnosis, with a total cost of approximately $1.4 billion.[5]

## RISK FACTORS

The most common risk factors for nonvariceal UGIB include *H pylori* infection, NSAIDs/aspirin, and other antiplatelet and anticoagulant medication use.[4,6] *H pylori* infection and NSAID use are both independent and synergistic risk factors for peptic ulcer–related bleeding.[7] Studies from the 1980s and 1990s show that *H pylori* was present in more than 90% of patients with duodenal ulcers and approximately 70% of patients with gastric ulcers.[8,9] However, more recent Western studies have suggested that there is a changing cause of PUD, with the overall PUD incidence decreasing and the proportion of *H pylori*–negative PUD increasing.[3,10,11] A Dutch study of the incidence of duodenal and gastric ulcers in a district hospital found that the incidence of duodenal ulcer disease has been decreasing with a decline in the prevalence of *H pylori*.[11] A review of 73 worldwide published studies from 1999 to 2008 evaluating patients with duodenal ulcers showed that 88% of patients were infected with *H pylori*, with a decrease to 77% infected when including the studies from 2003 to 2008.[12] There has been an overall decline in the prevalence of *H pylori*–positive PUD and an increase in non-NSAID, non–*H pylori* PUD. According to a prospective multicenter study involving 32 hospitals in France, 40% of PUD was related to *H pylori* infection alone, 18.7% to gastrotoxic drugs alone (NSAIDs, aspirin, and/or cyclooxygenase [COX]-2 inhibitors), 19.8% had *H pylori* infection in the setting of gastrotoxic drugs, and 21.6% had neither *H pylori* infection nor gastrotoxic drug use.[13] Therefore, although *H pylori* and gastrotoxic drugs make up approximately 80% of PUD and PUD-related bleeding, there is a significant subsection of idiopathic ulcers as well.

There has been a well-established correlation between NSAID use and the increased risk of UGIB. The prevalence of PUD in patients with regular NSAID use is approximately 15% to 30%.[14] In addition to NSAID use independently increasing the risk of GI adverse effects, there are multiple other risk factors that have been associated with nonvariceal UGIB that are potentiated in the presence of NSAID use (**Fig. 1**).[15–17]

COX-2 inhibitors were first introduced in the hope that they would provide the analgesic and antiinflammatory benefits of nonselective NSAIDs without the adverse GI side effects. There is evidence that there is a reduced risk of upper GI complications and ulcers compared with those associated with nonselective NSAIDs.[18–20] However, overall, there is still an increased risk of upper GI complications and symptomatic gastroduodenal ulcers with COX-2 selective inhibitors compared with no use at all.[21,22]

Recently, a 2014 case series analysis of 7 population-based health care databases for 114,835 patients with UGIB analyzed various drug combinations with NSAIDs, low-dose aspirin, and COX-2 inhibitors. Monotherapy with nonselective NSAIDs was