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Biopsy-Proven Gastric Pathological Findings in Mechanically Ventilated Intensive Care Unit Patients

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Elvan Tekir Yılmaz [1], Bilge Olgun Keleş [1]

1. Anesthesiology and Reanimation, Giresun University the Faculty of Medicine, Giresun, TUR

Corresponding author: Elvan Tekir Yılmaz, elvanty28@hotmail.com

Abstract

Objectives

Helicobacter pylori (H. pylori) is known to affect a large proportion of the world population. It plays a role in the pathogenesis of peptic ulcer (PU) and increases the likelihood of bleeding. In critically ill patients in intensive care units (ICUs), the risk of bleeding may be much higher due to many concomitant factors. The study aimed to determine the activation of *H. pylori* in mechanically ventilated (MV) intensive care patients and compare this with the general population.

Methods

This study was performed retrospectively by screening patients who underwent esophagogastroduodenoscopy and histopathological sampling in our hospital between January and June 2023. The study included 79 patients aged between 18 and 85 years. The patients were categorized into two groups: 35 patients in the ICU with mechanical ventilation (MV) support (E_{MV}) and 44 patients who presented to the gastroenterology department due to dyspeptic symptoms and underwent endoscopy ($_{ED}$). Age; sex characteristics; laboratory parameters such as hemoglobin (Hb), hematocrit (Htc), mean cellular volume (MCV), white blood cell (WBC), neutrophil, platelet, glucose, urea, creatinine, aspartate transaminase (AST), alanine transaminase (ALT), C-reactive protein (CRP), albumin, ferritin, thyroid-stimulating hormone (TSH), anti-hepatitis C virus (HCV), hepatitis B surface antigen (HBsAg), anti-HIV; and biopsy results (*H. pylori* positivity, intestinal metaplasia, and atrophy) were recorded.

Results

A total of 79 patients who underwent gastric biopsy were assessed. There were 35 patients in the E_{MV} group and 44 patients in the E_D group. There was no difference in gender and age distribution between the groups. Hb and Htc were significantly lower in E_{MV} compared to E_D (p=0.001). Hb was 9.4±1.7 g/dL in E_{MV} and 10.8±2.1 g/dL in E_D. Htc was 29.6±5.1 in E_{MV} and 33.5±5.7 in E_D. MCV, WBC, glucose, urea, AST, ALT, CRP, and ferritin values were statistically significantly higher in E_{MV} (p<0.05). Albumin and creatinine levels were statistically significantly lower in E_{MV} (p<0.05). There was no significant difference between the groups in terms of neutrophils, platelets, and TSH. In the E_{MV} group, *H. pylori* activity was negative in 31 (88.6%) patients and positive in four (11.4%) patients. In the E_D group, *H. pylori* activity was negative in 30 (68.2%) patients and positive in 14 (31.8%) patients. There was a statistically significant difference between the groups in terms of *H. pylori* positivity (p=0.032).

Conclusions

The prevalence of *H. pylori* in MV patients in the ICU is low compared to the average population. The incidence of atrophic gastritis and intestinal metaplasia is the same. The present study supports that ICU cases do not have a higher risk of gastric premalignant lesions compared to the average population.

Categories: Gastroenterology, Anesthesiology
Keywords: mechanical ventilation, intensive care units, peptic ulcer, helicobacter pylori, gastrointestinal hemorrhage

Introduction

Peptic ulcer disease (PUD) represents a significant concern for the general population, as well as for patients in the intensive care unit (ICU). This concern may be slightly higher in ICU patients for several reasons. The presence of pre-existing comorbidities also increases the risk of developing PUD [1]. Comorbidity is included in scoring systems predicting mortality from upper gastrointestinal (GI) bleeding and increases risk [2,3]. One of the factors leading to augmented risk in the ICU is age. The risk of upper GI bleeding in cases over 60 years is 10 times higher than in younger ones. As such, mortality is also higher in this age group [4]. The risk

of peptic ulcer (PU) bleeding in these patients is also increased by the use of multiple medications, antiplatelet, anticoagulant, and corticosteroid treatment. Gastric mucosal ischemia is also an essential factor leading to mucosal damage, which factors leads to stress ulcers and bleeding in 1-9% of ICU cases [5]. *Helicobacter pylori* (*H. pylori*) is the most common cause of PU, and studies have shown that it doubles the risk of bleeding from it [6-8]. *Helicobacter pylori* infection contributes to the development of PU by disrupting the mucus structure and mucosal integrity of the stomach [9]. Eradication of *H. pylori* has been shown to reduce the development of PU [10,11]. The use of proton pump inhibitors (PPIs) is quite common in the ICU, with no effect on length of stay, pneumonia risk, and mortality, while reducing the risk of GI bleeding by 50% [12]. There are studies suggesting that all patients in the ICU with or without MV (mechanical ventilation) should receive gastroprotective therapy [13]. Although multiple factors contribute to the development of GI bleeding in critically ill patients by disrupting mucosal integrity, the incidence is reported to be low compared to the average population [14]. As such, gastroprotection and low prevalence of *H. pylori* in ICU cases might make these outcomes likely. Nevertheless, no study based on gastric biopsy results has been reported to date. The present study aimed to demonstrate *H. pylori* activity in histopathological samples obtained by endoscopy in cases followed up in the ICU with MV. We believe that the results compared with samples from the normal population will shed light on this discussion.

Materials And Methods

This study was approved by the local Training and Research Hospital Clinical Research Ethics Committee. In this study, the results of patients who underwent gastric biopsy for reasons such as percutaneous endoscopic gastrostomy opening, gastric intolerance and bleeding while being followed up in the ICU with MV support of a tertiary education and research hospital between January and June 2023 were retrospectively compared with the results of daily patients who underwent gastric biopsy for dyspeptic complaints in the endoscopy unit. Thirty-five ICU patients on MV were defined as E_{MV}, and 44 patients who presented with dyspeptic complaints and underwent upper GI endoscopy were defined as E_D. Exclusion criteria were as follows: i) under 18 and over 85 years of age, ii) patients with bleeding with impaired hemodynamic parameters, iii) patients with more than four units of erythrocyte suspension replacement, iv) patients with a diagnosis of gastric cancer, and v) patients with previous gastric surgery. Age, sex characteristics, laboratory parameters such as hemoglobin (Hb), hematocrit (Htc), mean cell volume (MCV), white blood cell (WBC), neutrophil, platelet, glucose, urea, creatinine, aspartate transaminase (AST), alanine transaminase (ALT), C-reactive protein (CRP), albumin, ferritin, thyroid stimulating hormone (TSH), anti-hepatitis C virus (HCV), hepatitis B surface antigen (HBsAg), anti-HIV; and gastric biopsy results (*H. pylori* positivity, intestinal metaplasia, and atrophy) were recorded. Furthermore, data pertaining to the antibiotics administered to ICU patients during their hospitalization, the reasons for their hospitalization, and the length of their hospital stay were also recorded. The E_D group was formed by selecting patients with complete data among patients who used PPIs and underwent endoscopy for dyspeptic complaints in the same six-month interval. Furthermore, we used PPIs in patients undergoing intensive care with mechanical ventilation (MV) support. In the E_{MV} and E_D groups, all patients were on PPIs.

Statistical analyses were performed using SPSS Version 23 (IBM Corp., Armonk, NY). Normality analysis of quantitative data was performed using the Kolmogorov-Smirnov test. The comparison of normally distributed data was performed using the independent sample t-test, and the comparison of non-normally distributed data was performed using the Mann-Whitney U test. Qualitative data were compared using the Pearson chi-square test. Data were presented as n (%) and mean (±) standard deviation. The relationships between the data were analyzed by the Pearson correlation analysis. The statistical significance value was accepted as $p<0.05$.

Results

The mean age was 71±17 years in E_{MV} and 75.1±9.5 in E_D, which was not significantly different (p=0.577) (Table *1*). There was no statistically significant difference between the two groups, although there were more men in E_{MV} and more women in E_D (Table *2*). The Hb value was 9.4±1.7 g/dL in E_{MV} and 10.8±2.1 g/dL in E_D. However, Htc was 29.6±5.1% in E_{MV} and 33.5±5.7% in E_D. Hb and Htc were significantly higher in E_D (p=0.001). In addition, albumin (29.1±5.5 g/dL) and creatinine (0.81±0.67 mg/dL) in E_{MV} were significantly lower than in E_D ($p<0.00$ and p=0.014, respectively), whereas MCV, WBC, glucose, urea, AST, ALT, CRP, and ferritin levels were significantly higher in E_{MV} ($p<0.05$). Neutrophil, platelet, and TSH levels were not different between them (Table *1*).

	E_{MV}		E_D		p-Value
	n	Mean ± SD	n	Mean ± SD	
Age	35	71 ± 17	44	75.1 ± 9.5	0.577
Hemoglobin (g/dL)	35	9.4 ± 1.7	44	10.8 ± 2.1	0.001
Hematocrit (%)	35	29.6 ± 5.1	44	33.5 ± 5.7	0.001
MCV (fL)	35	93.6 ± 7.2	44	85.4 ± 6.6	<0.001
WBC (/mcL)	35	9.79 ± 4.55	44	7.65 ± 2.44	0.020
Neutrophil (/mcL)	35	70 ± 20.9	44	62.7 ± 24.9	0.064
Platelet (/mm^3)	35	268 ± 120	44	256 ± 97	0.393
Glucose (mg/dL)	35	129 ± 46	44	104 ± 24	0.006
Urea (mg/dL)	35	73 ± 40	44	47 ± 35	0.001
Creatinine (mg/dL)	35	0.81 ± 0.67	44	0.97 ± 0.64	0.014
AST (U/L)	35	34 ± 29	44	21 ± 8	0.009
ALT (U/L)	35	26 ± 22	44	16 ± 10	0.025
CRP (mg/dL)	35	80.08 ± 76.73	44	25.61 ± 48.76	<0.001
Albumin (g/dL)	35	29.1 ± 5.2	44	38.7 ± 7.7	<0.001
Ferritin (mL/ng)	35	690.5 ± 534.5	44	114.3 ± 187.7	<0.001
TSH (mIU/L)	35	2.29 ± 4.59	44	1.57 ± 1.32	0.945

TABLE 1: Patients' laboratory results

MCV, mean corpuscular volume; WBC, white blood cell; AST, aspartate aminotransferase; ALT, alanine aminotransferase; CRP, C-reactive protein; TSH, thyroid-stimulating hormone

In E_{MV}, 31 (88.6%) cases were negative and four (11.4%) were positive in *H. pylori* activity, while in E_D, 30 (68.2%) patients were negative and 14 (31.8%) were positive in *H. pylori* activity. A significant difference in *H. pylori* positivity (p=0.032) and no difference in the frequency of intestinal metaplasia and atrophic gastritis were recognized (p=0.220, p=0.666, respectively). The number of cases with chronic inflammation was higher in the E_{MV} group (p<0.001). However, the anti-HCV and anti-HIV positivity did not differ (p=0.201, p=0.108, respectively), while HBsAg positivity was higher in E_D (p=0.039) (Table *2*). In the correlation analysis, a low-level negative correlation was detected between MCV and *H. pylori* positivity (Table *3*). Antibiotics administered to ICU patients during hospitalization, reasons for hospitalization, and length of hospital stay are shown in Table *4*.

	E_{MV}, n (%)	E_D, n (%)	p-Value
Sex (female/male)	15 (42.9)/20 (57.1)	25 (56.8)/19 (43.2)	0.218
Anti-HCV (+)	0 (0)	2 (4.5)	0.201
HBsAg (+)	0 (0)	5 (11.4)	0.039
Anti-HIV (+)	2 (5.7)	0 (0)	0.108
Helicobacter pylori (+)	4 (11.4)	14 (31.8)	0.032
Intestinal metaplasia (+)	3 (8.6)	8 (18.2)	0.220
Atrophy (+)	6 (17.1)	6 (13.6)	0.666
Chronic inflammation (+)	33 (94.3)	2 (4.5)	<0.001

TABLE 2: Gastric biopsy and ELISA results

HCV, hepatitis C virus; HBsAg, hepatitis B surface antigen; ELISA, enzyme-linked immunosorbent assay

	E_{MV}		E_D	
	r	p-Value	r	p-Value
Age	0.015	0.930	-0.202	0.189
Hemoglobin (g/dL)	0.039	0.824	0,057	0.712
Hematocrit (%)	0.097	0.581	0,079	0.610
MCV (fL)	-0.360	0.034	-0.087	0.574
WBC (/mcL)	-0.115	0.509	0.019	0.905
Neutrophil (/mcL)	0.041	0.815	-0.159	0.303
Platelet (/mm^3)	0.076	0.663	-0.254	0.096
Glucose (mg/dL)	-0.132	0.450	0.024	0.877
Ürea (mg/dL)	0.126	0.470	-0.294	0.053
Creatinine (mg/dL)	0.406	0.016	-0.203	0.187
AST (U/L)	-0.128	0.463	0.223	0.145
ALT (U/L)	0.062	0.724	0.200	0.194
CRP (mg/dL)	-0.043	0.806	0.030	0.847
Albumin (g/dL)	-0.010	0.954	0.032	0.839
Ferritin (mL/ng)	-0.129	0.461	0.230	0.134
TSH (mIU/L)	-0.028	0.875	0.214	0.164

TABLE 3: Correlation analysis of H. pylori positivity with laboratory data

MCV, mean corpuscular volume; WBC, white blood cell; AST, aspartate aminotransferase; ALT, alanine aminotransferase; CRP, C-reactive protein; TSH, thyroid-stimulating hormone

	E_{MV} (n=35)
Length of ICU stay (mean±SD)	39.29±16.02
Reason for ICU hospitalization (n)	
RS diseases	4
CNS diseases	20
CVS diseases	2
Post-CPR	9
Used antibiotics (n)	
Penicillin group antibiotics	12
Tetracycline group antibiotics	4
Quinolone group antibiotics	15
Other antibiotics	15

TABLE 4: Characteristics of patients in the ICU

ICU, intensive care unit; RS, respiratory system; CNS, central nervous system; CVS, cardiovascular system; CPR, cardiopulmonary resuscitation

Discussion

The present study retrospectively evaluated 79 cases who had undergone gastric biopsy and found that the prevalence of *H. pylori* was lower in ICU patients than in the average population with dyspeptic complaints. The incidence of atrophic gastritis and intestinal metaplasia did not differ between the groups.

Gastric biopsy remains the most valid option to determine the frequency of *H. pylori* infection. However, the usability of each method on different patient populations is limited. The selection of the method is influenced by the patient's general condition, location within the hospital, and the invasiveness of the procedure. The diagnosis of *H. pylori* infection is based on non-invasive methods such as serology, 13C-urea breath test, stool antigen test, and methods requiring gastric biopsy during endoscopy (histopathology, culture, rapid urease test, polymerase chain reaction) [15]. The rapid urease test is specific but less sensitive (80-90%). The 13C-urea breath test is difficult to perform in ICU patients, especially those on MV. The performance of the fecal antigen test is close to that of the urea breath test and might be more suitable for use in ICU cases [16]. Serological tests are inexpensive and are mostly used for screening. However, there is insufficient evidence to support the use of any of these tests in place of histopathological diagnosis [17,18]. Biopsy culture helps to determine antimicrobial resistance and susceptibility and to guide treatment planning. It allows the identification of mucosal lesions and gastric inflammatory processes [15]. Therefore, endoscopy seems to be the most valid and effective method.

Stress-related gastrointestinal mucosal injury is most prevalent in patients with acute hepatic failure, anticoagulant use, severe burns, coagulopathy, lack of enteral nutrition, recent gastroduodenal ulcer, corticosteroid use, *H. pylori* infection, neurological injury, trauma, nonsteroidal anti-inflammatory drug use, mechanical ventilation, shock, and sepsis. Furthermore, it has also been found that the presence of *H. pylori* immunoglobulin antigen detected by the ELISA (enzyme-linked immunosorbent assay) method was a contributing factor for upper GI bleeding in cases treated in the ICU [17]. However, the prevalence of gastric premalignant disorders such as atrophic gastritis, intestinal metaplasia, and *H. pylori* infection remains controversial, especially among patients with MV.

Robert et al. conducted a prospective, multicenter, epidemiological study that enrolled 1,776 ICU patients and reported that *H. pylori* antigen seropositivity detected by rectal swab (fecal antigen test) was higher in female subjects than their male counterparts [16]. In our study, we found no difference between the two groups in terms of gender and age.

In a Dutch prospective observational study of 300 consecutive MV cases, the prevalence of *H. pylori* infection decreased from 38% during hospitalization to 0% one week later, probably due to the use of intensive antibiotic therapy for intestinal decontamination [11]. In contrast, a study of 100 ICU patients found that the rate of *H. pylori* infection was higher than in controls, regardless of age and disease severity scale or stress ulcer risk score [18]. Furthermore, a large-scale ICU study including 4,341 patients reported that *H. pylori* infection was more frequent in patients with bleeding than in matched controls [19]. In this study, we found

a low prevalence of *H. pylori* in patients with MV and hypothesized that the use of antibiotics to treat other diseases may have contributed to this finding. However, there has not been a study including both atrophic gastritis and intestinal metaplasia among ICU patients with MV. In this study, no difference was found between the E_{MV} group and the E_D group. Based on these findings, we concluded that patients followed with MV do not constitute an additional risk factor for gastric premalignant diseases. Nguyen et al. reported that hemoglobin concentration decreased >0.5 g/dL/day during the first days of ICU stay, and this decrease continued in cases with high APACHE II scores [20]. In our study, Hb and Htc values were lower in E_{MV}. This may contribute to perfusion impairment and ischemia by decreasing oxygen supply to tissues. In this study, high WBC, CRP, and ferritin levels in patients on MV can be attributed to the existing infections of the patients. AST and ALT elevations may be associated with the drugs used and hypoxia.

In the present study, GI bleeding occurred in only two patients in the E_{MV} group. Similar to other studies (1-9%), the incidence of bleeding was 5.8% [5]. The decreased incidence of bleeding in the ICU compared to the average population suggests that it is a factor that may reverse the disadvantage caused by factors such as mucosal ischemia, age, and anticoagulant use. In addition to the widespread use of PPIs as stress ulcer prophylaxis, it may be due to the low prevalence of *H. pylori*.

Limitations

This study retrospectively analyzed patients on mechanical ventilation in the ICU who underwent endoscopic intervention. As this procedure was performed in conformity with the indication, the number of cases is limited.

Conclusions

The prevalence of *H. pylori* infection detected by gastric biopsy was low in ICU cases. Of note, the presence of atrophic gastritis and intestinal metaplasia was similar in both E_D and E_{MV}. Therefore, the results of our preliminary report support that despite many stressors, cases in the ICU on MV do not have a higher risk of gastric premalignant lesions compared to the average population.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Elvan Tekir Yılmaz

Acquisition, analysis, or interpretation of data: Elvan Tekir Yılmaz, Bilge Olgun Keleş

Drafting of the manuscript: Elvan Tekir Yılmaz

Critical review of the manuscript for important intellectual content: Elvan Tekir Yılmaz, Bilge Olgun Keleş

Supervision: Elvan Tekir Yılmaz, Bilge Olgun Keleş

Disclosures

Human subjects: Consent was obtained or waived by all participants in this study. Giresun Training and Research Hospital Ethics Committee issued approval 140 10.07.202\12. Giresun Training and Research Hospital Ethics Committee Issue : E-53593568-771-219537440 12.07.2023Subject : KAEK Decision (Dr. Lecturer Elvan TEKİR YILMAZ)Dear Dr. Lecturer. Prof. Dr. Elvan TEKİR YILMAZ Your application titled "Retrospective Analysis of Stomach Histopathology Samples of Patients Who Underwent Upper Stomach Endoscopy While Being Followed in Intensive Care" numbered KAEK-140 was evaluated at our meeting on 10.07.2023. The applicability in terms of compliance with ethical principles and rules was unanimously decided by the participants of the meeting with the decision number 10.07.202\12. **Animal subjects:** All authors have confirmed that this study did not involve animal subjects or tissue. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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References

1. Lau JY, Sung J, Hill C, Henderson C, Howden CW, Metz DC: Systematic review of the epidemiology of complicated peptic ulcer disease: incidence, recurrence, risk factors and mortality. Digestion. 2011, 84:102-13. 10.1159/000323958
2. Kerbage A, Nammour T, Tamim H, et al.: Impact of blood transfusion on mortality and rebleeding in gastrointestinal bleeding: an 8-year cohort from a tertiary care center. Ann Gastroenterol. 2024, 37:303-12. 10.20524/aog.2024.0877
3. Blatchford O, Murray WR, Blatchford M: A risk score to predict need for treatment for upper-gastrointestinal haemorrhage. Lancet. 2000, 356:1318-21. 10.1016/S0140-6736(00)02816-6
4. Thorsen K, Søreide JA, Kvaløy JT, Glomsaker T, Søreide K: Epidemiology of perforated peptic ulcer: age- and gender-adjusted analysis of incidence and mortality. World J Gastroenterol. 2013, 19:347-54. 10.3748/wjg.v19.i3.347
5. Krag M, Perner A, Wetterslev J, et al.: Prevalence and outcome of gastrointestinal bleeding and use of acid suppressants in acutely ill adult intensive care patients. Intensive Care Med. 2015, 41:833-45. 10.1007/s00134-015-3725-1
6. Hooi JK, Lai WY, Ng WK, et al.: Global prevalence of Helicobacter pylori infection: systematic review and meta-analysis. Gastroenterology. 2017, 153:420-9. 10.1053/j.gastro.2017.04.022
7. Crowe SE: Helicobacter pylori Infection . N Engl J Med. 2019, 380:1158-65. 10.1056/NEJMcp1710945
8. Huang JQ, Sridhar S, Hunt RH: Role of Helicobacter pylori infection and non-steroidal anti-inflammatory drugs in peptic-ulcer disease: a meta-analysis. Lancet. 2002, 359:14-22. 10.1016/S0140-6736(02)07273-2
9. Peek RM Jr, Blaser MJ: Pathophysiology of Helicobacter pylori-induced gastritis and peptic ulcer disease . Am J Med. 1997, 102:200-7. 10.1016/s0002-9343(96)00273-2
10. Kanno T, Moayyedi P: Who needs gastroprotection in 2020? . Curr Treat Options Gastroenterol. 2020, 18:557-73. 10.1007/s11938-020-00316-9
11. van der Voort PH, van der Hulst RW, Zandstra DF, Geraedts AA, van der Ende A, Tytgat GN: Suppression of Helicobacter pylori infection during intensive care stay: related to stress ulcer bleeding incidence?. J Crit Care. 2001, 16:182-7. 10.1053/jcrc.2001.30164
12. Alshamsi F, Belley-Cote E, Cook D, et al.: Efficacy and safety of proton pump inhibitors for stress ulcer prophylaxis in critically ill patients: a systematic review and meta-analysis of randomized trials. Crit Care. 2016, 20:120. 10.1186/s13054-016-1305-6
13. Wang Y, Ye Z, Ge L, et al.: Efficacy and safety of gastrointestinal bleeding prophylaxis in critically ill patients: systematic review and network meta-analysis. BMJ. 2020, 368:l6744. 10.1136/bmj.l6744
14. De Korwin JD: [Advantages and limitations of diagnostic methods for H. pylori infection] [Article in French] . Gastroenterol Clin Biol. 2003, 27:380-90.
15. Nocon M, Kuhlmann A, Leodolter A, Roll S, Vauth C, Willich SN, Greiner W: Efficacy and cost-effectiveness of the 13C-urea breath test as the primary diagnostic investigation for the detection of Helicobacter pylori infection compared to invasive and non-invasive diagnostic tests. GMS Health Technol Assess. 2009, 5:Doc14. 10.3205/hta000076
16. Robert R, Gissot V, Pierrot M, et al.: Helicobacter pylori infection is not associated with an increased hemorrhagic risk in patients in the intensive care unit. Crit Care. 2006, 10:R77. 10.1186/cc4920
17. Preslaski CR, Mueller SW, Kiser TH, Fish DN, MacLaren R: A survey of prescriber perceptions about the prevention of stress-related mucosal bleeding in the intensive care unit. J Clin Pharm Ther. 2014, 39:658-62. 10.1111/jcpt.12208
18. Robertson MS, Cade JF, Clancy RL: Helicobacter pylori infection in intensive care: increased prevalence and a new nosocomial infection. Crit Care Med. 1999, 27:1276-80. 10.1097/00003246-199907000-00010
19. Maury E, Tankovic J, Ebel A, Offenstadt G: An observational study of upper gastrointestinal bleeding in intensive care units: is Helicobacter pylori the culprit?. Crit Care Med. 2005, 33:1513-8. 10.1097/01.ccm.0000168043.60624.3e
20. Nguyen BV, Bota DP, Mélot C, Vincent JL: Time course of hemoglobin concentrations in nonbleeding intensive care unit patients. Crit Care Med. 2003, 31:406-10. 10.1097/01.CCM.0000048623.00778.3F