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ORIGINAL ARTICLE

# Prevalence of anemia and clinical approach in patients discharged after gastrointestinal bleeding

## Gastrointestinal kanamayla taburcu olan hastalarda anemi prevalansı ve klinik yaklaşım

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**ABSTRACT** • **Background and Aims:** Acute gastrointestinal system hemorrhages are frequent, and anemia is frequently seen in patients with acute gastrointestinal system bleeding after hospital discharge. Studies intended for patient follow-ups after discharge and anemia treatment are limited, and this topic has no guidelines. This study aimed to evaluate anemia prevalence and clinical approach in patients with acute gastrointestinal system bleeding after hospital discharge and during 3 months of follow-up. **Materials and Method:** This study retrospectively evaluated 197 patients with acute gastrointestinal system bleeding who were treated at our hospital between January 2017 and May 2018. Upon discharge, anemia was accepted as hemoglobin levels of < 13 g/dL in men and 12 g/dL in women according to the World Health Organization criteria. **Results:** Of these patients, 129 underwent upper gastrointestinal endoscopy; 3 enteroscopy; 45 lower gastrointestinal endoscopy; 8 upper and lower gastrointestinal endoscopy; 2 upper, middle, and lower gastrointestinal endoscopies; and 10 did not undergo endoscopy. Additionally, 69 patients underwent therapeutic endoscopic treatments. The mean hospitalization duration was 10 ± 13.84 days, and 67% of patients had erythrocyte transfusion with a mean value of 3.5 ± 5.89 units during hospitalization. The mean hemoglobin rate was 9.85 ± 1.67 g/dL upon hospital discharge. Of the patients, 92.4% (female: 91.1%, male: 93.2%; upper gastrointestinal bleeding: 93.9%, middle gastrointestinal bleeding: 100%, lower gastrointestinal bleeding: 86.8%) had anemia upon hospital discharge and 9.7% underwent iron deficiency treatment. Of all 197 patients, 33% were evaluated 3 months after discharge from the hospital and 80% of these patients have ongoing anemia. **Conclusions:** Anemia frequency is high when patients with acute gastrointestinal system bleeding are discharged. Most patients are discharged without receiving a prescription for anemia. In the follow-up, control applications are inadequate and anemia persists in patients. A wider range of patient studies on the treatment application and adherence, as well as guidelines from the consensus body on this issue, is necessary.

**Key Words:** Acute gastrointestinal bleeding, discharge, anemia, anemia treatment

**ÖZET** • **Giriş ve Amaç:** Akut gastrointestinal sistem kanamaları sıktır. Bu hastaların taburculukları sırasında anemi sıklıkla gözlenmektedir. Bu hastaların hem taburculuk sonrası izlemi hem de anemi tedavilerine yönelik çalışmalar kısıtlıdır ve bu konu ile ilgili kılavuzlar bulunmamaktadır. Bu çalışmada akut gastrointestinal sistem kanaması geçiren hastalarda taburcu olurken ve takip eden 3 aylık süreçte anemi prevalansı ve anemiye yaklaşım değerlendirilmiştir. **Gereç ve Yöntem:** Hastanemize Ocak 2017 - Mayıs 2018 tarihleri arasında akut gastrointestinal sistem kanamasıyla yatan 197 hasta retrospektif olarak değerlendirilmiştir. Taburculuk sırasında anemi, Dünya Sağlık Örgütü kriterlerine göre, hemoglobin değerinin erkeklerde 13 g/dL, kadınlarda ise 12 g/dL'nin altında olması olarak kabul edilmiştir. **Bulgular:** Akut gastrointestinal sistem kanama nedeniyle hastaneye yatan hastaların 129'una üst gastrointestinal sistem endoskopi, 3'üne enteroskopi, 45'ine alt gastrointestinal sistem endoskopi, 8'ine üst ve alt gastrointestinal sistem endoskopi, 2'sine üst, orta ve alt gastrointestinal sistem endoskopi uygulanmış, 10 hastaya işlem uygulanamamıştır. Hastaların 69'una endoskopik terapötik girişim yapılmıştır. Hastaların hastanede kalış süresi; 10 ± 13.84 gün iken, yatış sırasında hastaların %67'sine, ortalama 3.5 ± 5.89 ünite eritrosit süspansiyonu transfüze edilmiştir. Hastaların taburculuk sırasındaki ortalama hemoglobin değeri 9.85 ± 1.67 g/dL'dir. Hastaların %92.4'ünde (kadın %91.1, erkek %93.2, üst gastrointestinal sistem kanama %93.9, orta gastrointestinal sistem kanama %100, alt gastrointestinal sistem kanama %86.8) taburculuk sırasında anemi saptanmıştır. Anemi saptanan hastaların %9.7'sine taburculuk sırasında demir tedavisi reçete edilmiştir. 197 hastanın %33 kadarı taburculuk sonrası ilk üç ay içerisinde tekrar değerlendirilmiş ve bunların da %80'inde halen aneminin devam ettiği saptanmıştır. **Sonuç:** Akut gastrointestinal sistem kanamalı hastalar taburcu edilirken anemi oranı yüksektir. Çoğu hasta anemiye yönelik bir reçete almadan taburcu olmaktadır. İzlemde kontrol başvuruları yetersiz olup, hastalarda anemi devam etmektedir. Bu konuda uygulanacak tedavi ve takibin nasıl olması gerektiğiyle ilgili daha geniş sayılı hasta çalışmalarına ve bu konuda görüş birliğinin sağlandığı kılavuzlara ihtiyaç vardır.

**Anahtar Kelimeler:** Akut gastrointestinal kanama, taburcu, anemi, anemi tedavisi

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## INTRODUCTION

Acute gastrointestinal (AGI) bleedings are frequent in gastroenterology emergency practice. AGI bleedings are divided into 3 groups regarding bleeding site; bleedings in the GIS tract until ampulla Vateri are upper, those between ampulla Vateri and ileocecal valve are middle and those in the distal of ileocecal valve are lower AGI bleedings. Guidelines are available regarding endoscopic approach to AGI bleedings (1-4).

Anemia and particularly iron deficiency anemia are very frequent in patients with AGI bleedings (5). Although available studies on this subject are limited and old, anemia was found in more than two thirds of patients presenting with non-variceal upper GI bleeding, and anemia improved in the patients after approximately a 2-144-month follow up (6-9).

It is important to identify and correct anemia in patients presenting with AGI bleeding, because iron deficiency (ID) and ID anemia (IDA) have negative effects on the patient's quality of life and work environment. They cause frequent hospital admissions, delays in discharge and increased healthcare costs (5). In a recent local, retrospective study, anemia was noted during hospital discharge in more than 80% of patients presenting with upper AGI bleeding and only 16% of these patients received oral iron supplements (10). In recent randomized controlled studies, significant improvements were noted in hemoglobin levels in patients treated with intravenous (IV) iron therapy compared with placebo among patients presenting with GI bleeding and found to have anemia (11).

Follow up studies of patients with AGI bleeding are limited and there are not sufficient studies about rates of anemia, status of iron reserves and information regarding presence or absence of sufficient iron therapy in patients presenting and discharged with AGI bleeding mainly in our country.

In this study, it was aimed to evaluate anemia prevalence, approach to anemia and factors affecting changes in approach, if present, during discharge from hospital and the following 3 months in patients who had upper, middle and lower AGI bleeding.

## MATERIALS and METHODS

Hundred and ninety seven patients admitted to our Hospital which is a tertiary center in İzmir province of Turkey between January 2017 and May 2018 with the diagnosis of AGI bleeding were retrospectively evaluated. Primary GI bleeding was not required as the cause of hospitalization and patients with GIS bleeding who were admitted for other causes were also included in the study. This is a retrospective study and both data during hospital stay and in the three months following discharge of patients presenting to the hospital between these dates were evaluated. Patients under 18 years and with incomplete access to medical data were not included in the study. In addition, consent was obtained for this study from the ethics committee for non-invasive clinical trials of Dokuz Eylül Medical Faculty (date of consent: 13.07.2017 number: 2017/18-16). Patient data were kept confidential and the study was conducted in accordance with Helsinki declaration.

Patient related data were obtained from the hospital electronic medical records system (Probel; version 1.0; İzmir, Turkey) by entering GI bleeding related ICD diagnostic codes (ICD R58, ICD K92.0, ICD K92.1, ICD K92.2). Patient age, gender, bleeding symptoms at presentation, medications used and particularly anticoagulant drugs, related diseases, presence of prior GI bleeding, examination findings at presentation, hemogram and biochemical values, service admitted to because of bleeding, time interval between presentation and endoscopy, endoscopic findings and type of endoscopic treatment if applied, additional radiologic investiga-

tions if present, medical therapies applied for GI bleeding, blood transfusions, most recent diagnosis of GI bleeding, mortality or discharge, duration of hospital stay, final hemoglobin (Hb) and hematocrit (Htc) values at discharge, anemia treatment recommended at discharge and control Hb and Htc values within 3 months after discharge were evaluated.

According to World Health Organization's (WHO) criteria, anemia during hospital admission and at discharge has been accepted as a hemoglobin (Hb) level under 13 g/dL in men and under 12 g/dL in women (12).

The primary endpoint of this study is to establish rates of anemia induced by blood loss from GI bleeding in patients presenting or followed with the diagnosis of GIS bleeding. The secondary endpoint is to establish whether patients found to have anemia received treatment for anemia at the hospital or at discharge.

Descriptive statistics were used for interpreting the data in our study. Data were analyzed using Statistical package for the Social Sciences (SPSS) (version 22.0; SPSS Inc., Chicago, IL, USA) package program. Numerical variables were summarized with percentage distribution and quantitative variables with mean and standard deviation. Mc Nemar test was used for dependent group analysis of the numerical variables. Compatibility was analyzed with Kappa. Repeated Measures Variance Analysis was used for dependent group analysis of quantitative variables. Significance level was $p < 0.05$.

## RESULTS

Data of 197 patients admitted to our Hospital between January 2017 and May 2018 with the diagnosis of AGI bleeding were retrospectively analyzed. When demographic data of 197 patients followed because of AGI bleeding were analyzed, 118 were male and 79 were female. Mean age of the 197 included patients was 68. When bleeding sites of the patients followed with AGI bleeding were classified, 132 patients had upper GI bleeding, 57 had middle-lower GI bleeding and bleeding site could not be established in 8 patients because endoscopy could not be carried out due to of vital instability.

It was detected that chronic liver disease was present in 12.1% (n: 24) of the patients. It was observed that acute renal insufficiency developed in 46 (23.4%) of the patients after GI bleeding. It was detected that 53 patients (26.9%) had prior GI bleeding history.

The mean Hb level of 197 patients at the time of presentation is 9.3 g/dL. When the patients who were exitus (n: 28), transferred to external medical center intensive care unit (n: 3) and who refused the treatment were subtracted from 197 patients, the mean Hb level of the remaining 161 patients at the moment of discharge was found 10.1 g/dL. Anemia according to WHO criteria during discharge was detected in 147 patients (91.3%). It was seen that anemia treatment was given to only 15 (10.2%) of the 147 patients in whom anemia was detected. Within the 3 months following discharge, only 65 (40.4%) of the 161 patients who had presented with A-GIS bleeding and were followed-up came for the control follow-up visit, the mean Hb level of these patients were found 10.7 g/dL and it was seen that anemia continued in 80% of the patients at present.

Demographic data, AGI bleeding sites, Hb levels and anemia status of 197 patients with AGI bleeding are summarized in Table 1.

Hundred and thirty-one patients underwent upper GI endoscopy, 3 enteroscopy, 45 lower GI endoscopy, 8 upper and lower GI endoscopy, 2 upper, middle and lower GI endoscopy, and 8 patients could not undergo any procedures because of vi-

**Table 1** Demographic data, AGI bleeding sites, Hb levels and anemia status of the patients

| | |
|---|---|
| Males, n (%) | 118 (60.0) |
| Age at presentation (years), median (min-max) | 68 (19 - 97) |
| AGI bleeding site, n (%) | |
| Upper AGI bleeding | 132 (67.0) |
| Lower-middle AGI bleeding | 57 (28.9) |
| Unidentified bleeding site | 8 (4.1) |
| Hb level (presentation), g/dL, mean, (min-max) | 9.3 (2.4 - 15.6) |
| Hb level (discharge), g/dL, median, (min-max) | 10.1 (6.2 – 14.7) |
| Presence of anemia (discharge), n (%) | 147 (91.3) |
| Patients receiving treatment for anemia (discharge), n (%) | 15 (10.2) |
| Control patients in 3 months following discharge, n (%) | 65 (40.4) |
| Hb level in 3 months after discharge, g/dL, mean, (min-max) | 10.7 (7.7 - 14.5) |
| Presence of anemia in 3 months after discharge, n (%) | 52 (80.0) |

AGI: Acute gastrointestinal, Hb: Hemoglobin.

tal instability. The three most frequent causes of upper AGI bleeding were duodenal ulcer, gastric ulcer and esophageal variceal bleeding, respectively, and causes of upper AGI bleeding are summarized in Table 2 in order of frequency. The three most frequent causes of lower-middle AGI bleeding were hemorrhoids, diverticulae and angiodysplasias, respectively, and causes of lower-middle AGI bleeding are summarized in Table 3 in order of frequency.

Sixty nine patients underwent an endoscopic therapeutic intervention (47.8% sclerotherapy, 15.9% argon plasma coagulation, 5.8% clip application, 5.8% band ligation, 24.6% mixed procedure). Mean hospital stay was 10 ± 14 days, and 67% of patients underwent transfusion with 3.5 ± 5.89 units of erythrocyte suspension during hospital stay. Of 197 patients followed with AGI bleeding, 28 died and 3 of 169 patients were referred to the intensive care unit of another hospital, 5 refused therapy, and 161 were discharged after their post-hospitalization therapies were completed. Mean Hb levels of patients after follow up of AGI bleeding was 10.1 g/dL.

**Table 2** Causes of upper AGI bleeding

| | |
|---|---|
| Duodenal ulcer | 39 (19.8) |
| Gastric ulcer | 32 (16.2) |
| Esophageal variceal bleeding | 13 (6.6) |
| Hemorrhagic erosive gastropathy | 12 (6.1) |
| Gastric variceal bleeding | 7 (3.6) |
| Esophageal ulcer | 5 (2.5) |
| Mass lesion / cancer in stomach | 5 (2.5) |
| Dieulafoy lesion | 5 (2.5) |
| Pangastritis | 2 (1.0) |
| Mallory-Weiss | 2 (1.0) |

**Table 3** Causes of lower-middle AGI bleeding

| | |
|---|---|
| Hemorrhoid | 15 (7.6) |
| Diverticulae | 12 (6.1) |
| Angiodysplasia | 11 (5.6) |
| Malignant mass invasion | 9 (4.5) |
| Intestinal ulcer | 7 (3.5) |
| Ischemic colitis | 5 (2.5) |
| Polyps | 4 (2.0) |

147 patients (91.3%) (F 91.1%, M 91.4%, upper GI bleeding 92.8%, middle GI bleeding 100%, lower GI bleeding 87.2%) had anemia during discharge. When frequency of anemia was viewed in terms of gender, the frequency of anemia having been found as 85/93 (91.3%) in male patients and 62/68 (91.1%) in female patients, meaningful relationship was not found between prevalence of anemia and gender ($p > 0.05$). Having been found as 103/111 (92.8%) in the patient group with upper AGI bleeding and as 44/50 (88%) in the patient group with lower-middle AGI bleeding, meaningful relationship was not found in respect of frequency of anemia prevalence according to bleeding site ($p > 0.05$).

It has been seen that there is a meaningful relationship between high blood urea nitrogen (BUN) at presentation and elongated hospitalization with frequency of anemia prevalence ($p < 0.05$).

It has been seen that there is a meaningful relationship between incidence of anemia and comorbid disease in the patients followed with GI bleeding ($p < 0.05$) (Table 4). As this situation may be secondary to pre-existing chronic disease anemia, it suggests multiple drug use causing complicated lesions that will create bleeding susceptibility in GIS and chronic disease anemia and iron deficiency anemia could be overlapping. Reviewing the anemia parameters in the patients will be helpful for us to reveal this situation more clearly.

Fifteen patients noted to have anemia (10.2%) were prescribed oral (n = 12, 7.8%) and parenteral (n = 3, 1.9%) iron therapy during discharge. A mean increase of 2.96 gr/dL was observed in Hb levels of the patients given oral treatment in a three-month period. Only 1 patient of the 3 patients given IV treatment came to control visit and it was seen that there was 1 gr/dL increase in Hb level.

65 of 161 patients (40.3%) were re-evaluated in the first three months following discharge and anemia persisted in 80% of these. Of 15 patients receiving treatment for anemia, 11 came to control visits in the first 3 months after discharge and anemia was noted to resolve in 4 (36.3%) patients. Again, 54 of 132 patients not receiving treatment for anemia following discharge came to control visits in the first 3 months after discharge and anemia was noted to resolve in 9 (16.6%) patients. None of the patients followed after discharge required blood transfusion.

## DISCUSSION

In our retrospective study, anemia was noted in approximately 92% of patients presenting with AGI bleeding at discharge and treatment for ane-

**Table 4** Relationship between comorbid disease and anemia

| | | | Anemia | | |
|---|---|---|---|---|---|
| | | | Absent | Present | Total |
| **Comorbid disease** | Absent | Count | 7 | 35 | 42 |
| | | % within-comorbid disease | 16.7% | 83.3% | 100.0% |
| | | % within anemia | 46.7% | 19.2% | 21.3% |
| | Present | Count | 8 | 147 | 155 |
| | | % within comorbid disease | 5.2% | 94.8% | 100.0% |
| | | % within anemia | 53.3% | 80.8% | 78.7% |
| **Total** | | Count | 15 | 182 | 197 |
| | | % within comorbid disease | 7.6% | 92.4% | 100.0% |
| | | % within anemia | 100.0% | 100.0% | 100.0% |

mia was planned at discharge in only 10.2% of discharged patients and the large remaining patient group did not receive any treatment for anemia. It was also previously shown in the study of Bager et al. that 84% of patients presenting to the hospital with non-variceal upper AGI bleeding and discharged from intensive care unit in Denmark also had anemia during discharge and only 16% of patients received iron therapy (10). Because there are no guidelines about iron therapy that the patients followed with the diagnosis of AGI bleeding and with anemia will receive following discharge, the rate of patients receving iron therapy is rather low though the approach of clinicians is variable. Therefore, guidelines are needed on this subject and long term studies should be carried out about the course of anemia with long term iron therapy in these patients.

Similarly, anemia was noted in 91.3% of our patients and only 15 patients received iron therapy and further investigations were not carried out regarding anemia. This shows that clinicians do not need further investigations associating GI bleeding with IDA. But this will lead to failure to treat other causes of anemia in case of overlap of IDA with conditions like chronic disease anemia or B12 / folic acid deficiency. Another point is that if the patient does not have severe anemia, the clinician may not take anemia seriously and plan further investigation regarding anemia. It is important to investigate iron deficiency in patients with AGI bleeding, because it has been shown in the literature that in these patients a mean increase of 2 g/dL in Hb levels has been observed with iron therapy in a 4-week period following discharge (11). In our study also, a mean increase of 2.96 g/dL has been observed in Hb levels of the patients given oral treatment in a three-month period. Only 1 patient of the 3 patients given IV treatment came to control visits and it was seen that there was 1 gr/dL increase in Hb level.

In our study, a significant difference was not found between the rates of anemia in patients receiving (63.6%) and not receiving (83.3%) iron therapy after a 3-month follow up ($p > 0.05$). However, mean hemoglobin level of patients receiving iron therapy when anemia was noted at discharge was found to be higher than that of patients not receiving therapy and this difference was statistically significant ($p < 0.05$). In conclusion, iron therapy was shown to increase Hb levels and there may be many reasons for the lack of a significant difference between anemia rates of groups receiving and not receiving iron therapy. A follow up period shorter than 6 months being insufficient for filling iron depots is an important factor. Continuation of chronic low blood loss due to the persistence of the gastrointestinal lesion in the patient was also considered.

In addition, another factor for the failure of anemia to improve may be the low compliance of patients particularly to oral iron therapy. Selection of the type of iron therapy should depend on the clinical condition of the patient (primary GIS disorder, pathophysiology, inflammation, presence of co-morbidities and malabsorption). Timely and regular iron therapy will also reduce the need for blood tranfusions of the patients. In the case of persistence of anemia, it should also be considered that the lesion causing GIS bleeding has not fully healed during follow up and still causes blood loss.

Only approximately 1/3 of our patients followed and discharged with the diagnosis of AGI bleeding came to control visits. Being uninformed about the condition of the patients who are lost to follow up is a major healthcare problem. In addition, anemia status of the patients before AGI bleeding is not fully known because this is a retrospective study. It cannot be predicted how this can affect mean Hb levels of the patients at discharge. Nevertheless, long term anemia status of the patients could not be evaluated because we evaluated 3-month follow up data of the patients after discharge.

In conclusion, anemia is seen at a very high rate like 92% at discharge in the patients presenting with AGI bleeding in our retrospective study and most patients are discharged without receiving a prescription for the treatment of anemia. Control presentation during follow up is inadequate and anemia persists in 80% of patients coming to follow up visits. Studies with larger number of patients about the treatment and follow up to be conducted and guidelines providing consensus on this subject are needed.

***Financial Disclosures:*** *None.*

***Ethics Committee Approval:*** *This study was approved by the Dokuz Eylül University Ethics Committee on July 2017, number: 2017/18-16.*

***Conflicts of interest:*** *None.*

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