

# Physiological parameters as independent risk factors for upper gastrointestinal bleeding: A case-control study

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**Abstract:** **Background:** Gastrointestinal bleeding is one of the common causes of daily referral to hospitals worldwide. The aim of this study was to assess the risk factors of acute gastrointestinal bleeding. **Methods:** In this case-control study, the case group included patients with acute upper gastrointestinal bleeding who had referred to Rasoul-e-Akram Hospital, Tehran, Iran from 2013 to 2016, and the control group were selected among hospitalized patients with other diseases (such as rheumatologic disorders). Patients' information was extracted from patients' file and endoscopy reports. The level of significance was considered less than 0.05. **Result:** In the study, 476 patients, including 238 patients in the case group and 238 patients in the control group were evaluated. In the logistic regression model, age over 65 years (OR = 2.8; 95% CI: 1.32-4.6;  $p = 0.023$ ) and body mass index higher than 25 kg/m<sup>2</sup> (OR = 2.3; 95% CI: 1.55-3.91;  $p = 0.036$ ) were considered as the most important risk factor for acute gastrointestinal bleeding. The history of diabetes was reported as another independent risk factor for acute gastrointestinal bleeding (OR = 1.9; 95% CI: 1.14 to 3.3;  $p = 0.021$ ). **Conclusion:** The results showed that changing of lifestyle and controlling of modifiable risk factors such as obesity can be prevent gastrointestinal bleeding and reducing the complications.

**Keyword:** Upper Gastrointestinal Bleeding; Risk Factors; Case-Control

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## 1. Introduction

Gastrointestinal bleeding is one of the most main causes of daily referral to emergency wards in hospitals in recent years worldwide. Moreover, gastrointestinal bleeding with hospital admission more than 300,000 per year is one of the most commonly emergency cases of digestive system (1, 2). In 2012, gastrointestinal bleeding was among the seven main causes of referring to emergency department (3). In general, the incidence of gastrointestinal bleeding (up and down) is estimated at an average of 100-150 per 100,000 people annually in the world (4). Acute gastrointestinal bleeding is known as hematemesis, vomiting of red or bloody that has been

deformed by contact with gastric acid, is a sign of bleeding higher than ligament of Treitz (5). Hematemesis, with an average death rate of 10% in gastrointestinal bleeding, is considered one of the most commonly gastrointestinal bleeding (6, 7). Despite the improvements in diagnosis and medication in the medical field, the mortality rate of hematemesis has not decreased over the last 50 years (8). Proper management and prognosis of patients based on risk factors can be effective in reducing mortality rates of gastrointestinal bleeding and selecting appropriate treatment (6). The melena is a type of gastrointestinal bleeding, black and bitter stool, which is usually due to bleeding rate more than 500 mm, its origin can vary in each part of the digestive system, from the oropharynx to the left half of the colon (9). More than 90% of upper gastrointestinal bleedings are due to gastric peptic ulcer and varicose veins of the esophagus and stomach (10). In the world, the incidence of gastrointestinal bleeding according

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to geographical characteristics and other factors, including age, sex, demographic composition, use of painkillers such as aspirin and nonsteroidal anti-inflammatory drugs (NSAIDs), incidence of helicobacter, alcohol consumption, obesity, systolic blood pressure, stress and anxiety, quality of life and the level of education are estimated from 48 to 160 cases per 100,000 population per year (11). According to several studies, risk factors, including helicobacter pylori infection, use of NSAIDs, use of aspirin and other anti-thrombotic or anticoagulant drugs have been reported as main causes of upper gastrointestinal bleeding. While it is discussed about the role of many factors such as age, diabetes, systolic blood pressure and high weight in patients nowadays (10, 12). There are few studies that are conducted about the association between high weight [body mass index (BMI) greater than 25] and acute gastrointestinal bleeding (13). Obesity is a major risk factor for gastrointestinal malignancies. In all aspects and stages of the disease, obesity has a negative impact on the human digestive system. However, there are many gastrointestinal and liver diseases that are due to obesity (for example, liver disease in non-alcoholic fat), or an important risk factor, such as reflux and gallstones or gastrointestinal bleeding. When obesity is a risk factor, it may interfere with other mechanisms and it leads to complicated diseases. There is an increased risk or relative risk of gastrointestinal bleeding and obesity (13, 14).

Diabetic ketoacidosis is an uncontrolled acute complication of diabetes, which may be associated with gastrointestinal symptoms, including abdominal pain, nausea, vomit and bleed. Most gastrointestinal bleeding is associated with diabetic ketoacidosis, which can be a common cause for evaluating of gastrointestinal physicians (15, 16). The present study was conducted to investigate the risk factors (diabetes, obesity, blood pressure and age of patients) related with bleeding gastroesophageal refraction in patients referring to Rasoul-e-Akram hospital in Tehran. Regarding the fact that many studies have not been carried out in this field, we surveyed the relationship between the clinical and laboratory related to acute gastrointestinal bleeding.

## 2. Method

### 2.1. Study design and setting

This case-control study was performed on patients with acute upper gastrointestinal bleeding during a three-year period, from October 2015 to October 2018, referred to the Rasoul -e-Akram Hospital, Tehran, Iran. This study was approved by the Ethic Committee of Iran University of Medical Sciences. The principle of Helsinki Declaration have been respected throughout the study.

### 2.2. Participants

The case group included all gastrointestinal patients over 18 years of age with a history of hospitalization due to acute upper gastrointestinal bleeding with a reduction of 2 mg/dl in hemoglobin or requirement to blood transfusion and hospitalization. The control group was selected among patients with gastrointestinal and rheumatologic diseases. The sampling method had been consecutive. The sample size for the present study, 238 people for each group, calculated with an effect size of 0.35, a power of 80% and a 5% error using the G Power software.

### 2.3. Variables

All patient information, including demographic characteristics (age, history of blood transfusion, gender, alcohol consumption, height and weight), clinical feature of patients (type of bleeding, comorbidities, blood pressure and comorbid diseases) and laboratory findings (platelets and hemoglobin level) were extracted by referring to patients' records in the hospital archives, endoscopy and colonoscopy reports.

### 2.4. Statistical methods

The results were statistically described as mean  $\pm$  standard deviation in continuous variables. Also, frequency and percentage of categorical variables were reported. Fisher exact test was used to evaluate the relation between categorical variables. Mann-Whitney U-test and independent t-test were used to compare between means of two independent groups. Significant variables were selected in univariate logistic regression model and then stepwise multivariate logistic regression model was used to identify independent risk factors. The findings were reported as odds ratio (OR) with 95% confidence interval (95% CI). Level of significance for statistical analysis was 0.05. The SPSS version 22.0 statistical software was applied for statistical analysis.

## 3. Result

In this study, 238 patients with upper gastrointestinal bleeding and 238 patients as control group were included. The mean age of patients in case and control groups was  $57.3 \pm 23.1$  and  $55.21 \pm 19$ , respectively ( $p=0.12$ ). The level of education in 116 (48.7%) patients in the case group and 101 (42.4%) in control group were under diploma ( $p=0.11$ ). 211 (88%) patients in case and 220 (92.4%) patients in control groups were married ( $p=0.51$ ). The majority of patients were Iranian in two groups who came to the hospital from different parts of the country, majority of the foreign patients were Afghans living in Iran (Table 1). 103 (43.3%) patients in case and 102 (42.8%) patients in control groups had a history of smoking, respectively ( $p=0.18$ ). Hematemesis bleeding was the most common type of acute gastrointestinal bleeding among patients (61.8%). The frequency (percentage) of other types of bleeding was reported 71 (29.8%) melena and 20 (8.4%) hematochezia.

**Table 1:** Demographic characteristics and risk factors in the patient and control groups

Variable	Case (n=238)	Control (n=238)	P
Age (year)	57.3±22.1	55.21 ± 19.4	0.12
Sex (%)			
Male	164 (68.9)	152 (63.8)	0.40
Female	74 (31.1)	74 (36.2)	
Age (year, %)			
<30	55 (23.1)	82 (34.4)	0.003
30-60	111 (46.6)	118 (49.6)	
>60	72 (30.3)	38 (16)	
Marital status (%)			
Married	211 (88.6)	220 (92.4)	0.51
Unmarried	27 (21.4)	18 (7.6)	
Level of education (%)			
Diploma	116 (48.7)	101 (42.4)	0.11
>=Diploma	122 (51.3)	137 (57.6)	
Nationality (%)			
Native	187 (78.6)	181 (76)	0.70
Foreigners	51 (21.4)	57 (24)	
Smoking (%)			
Negative	91 (38.2)	102 (42.8)	0.18
Positive	147 (61.8)	136 (57.2)	
Hb (mg/dl)	10.2±5.21	10.2±5.21	0.028
Platelet (per microliter)	162000±92000	178000±98000	0.078
Systolic blood pressure (mmHg, %)			
<120/80	68 (28.6)	108 (45.3)	0.037
120-140.9	121 (50)	101 (42.4)	
>150	49 (21.4)	29 (12.3)	
Diabetes (%)			
Positive	78 (32.7)	46 (19.3)	0.026
Negative	105 (44.1)	142 (59.7)	
Unknown	55 (23.2)	50 (21)	
Alcohol consumption (%)			
Positive	72 (30)	61 (26)	0.059
Negative	166 (62)	177 (74)	
BMI (kg/m <sup>2</sup> , %)			
<25	72 (30)	113 (47.5)	0.022
25-30	160 (67.2)	122 (51.2)	
>30	6 (2.8)	3 (1.3)	

BMI= Body Mass Index; Hb= Hemoglobin

**Table 2:** Multivariate Logistic Regression Analysis, predictive risk factors in Acute Upper Gastrointestinal Bleeding

Variable	OR	CI 95 %		P
		Lower	Upper	
BMI>25 kg/m <sup>2</sup>	2.3	1.55	3.91	0.036
Systolic Blood Pressure	2.1	1.21	3.2	0.001
Age>60 year	2.8	1.33	4.6	0.023
Diabetes	1.9	1.14	3.3	0.021
Constant	0.023	-	-	<0.001

BMI= Body Mass Index; CI= Confidence interval; OR= Odds Ratio

The results of univariate logistic regression showed that there is significant relationship between systolic blood pressure (p= 0.037), age (p= 0.002), BMI (p = 0.022) and diabetes (P-value = 0.026) and upper gastrointestinal bleeding. The mean hemoglobin level was significantly

lower in case group than control group (p= 0.028). There was no statistically significant difference between the two groups in the mean blood platelet count (p=0.078) (Table 1).

The multivariate logistic regression analysis showed that BMI greater than 25 (OR = 2.3; 95% CI: 1.55-3.91; p =

0.036), systolic blood pressure greater than 150 mmHg (OR = 2.1; 95% CI: 1.21 to 3.2;  $p = 0.001$ ), age over 60 years (OR = 2.8; 95% CI: 1.32-4.6;  $p = 0.023$ ), and type II diabetes mellitus (OR = 1.9; 95% CI: 1.14 to 3.3;  $p = 0.021$ ) are the most important risk factors in upper gastrointestinal bleeding (Table 2).

## 4. Discussion

The findings of this study showed that BMI greater than 25, systolic blood pressure greater than 150 mmHg, age over 60 years and type 2 diabetes are the most important risk factors for upper gastrointestinal bleeding.

In the present study, the age over 65 years old was one of the major risk factors for upper gastrointestinal bleeding including melena, Hematochezia and *Hematomas*. These results are consistent with Freedman et al. who reported age as an important factor in acute gastrointestinal bleeding (7). While Gultekingil Keser et al. reported that old age as risk factor for Melena's acute gastrointestinal bleeding (17).

The results of previous studies demonstrated the role of respiratory failure and smoking consumption as a potential risk factor for acute gastrointestinal bleeding, especially in the intensive care unit while it is not surveyed in our study (18, 19). The problem can be justified because of the lack of reporting of smoking by the patient or the absence of registration of smoking in the medical records. Although some studies have investigated the role of cigarette in causing peptic ulcers and the subsequent relationship between smoking and acute gastrointestinal bleeding, there was no significant relationship between smoking and incidence of gastrointestinal bleeding in our study (20).

In total, a few studies had been done on the role of obesity and BMI in patients as a predictor of acute gastrointestinal bleeding. The results of the present study indicated a main role BMI greater than 25, as a potential risk factor, in acute gastrointestinal bleeding. These results coincide with LL Strate et al. who reported obesity in men as a potential risk factor for acute gastrointestinal bleeding (14).

Contrary to the results of previous studies that have indicated a significant relationship between alcohol and smoking with acute gastrointestinal bleeding (18, 19, 21, 22), in our study, there is a significant relationship between alcohol consumption and acute gastrointestinal bleeding by Multivariate Logistic regression analysis that can be because not responding correctly to the history of alcohol consumption by some patients. The lack of relationship between smoking and acute gastrointestinal bleeding in the present study can be explained by the lack or less of reporting of smoking in group of patients than control group.

In our study, multivariate Logistic regression analysis reported systolic blood pressure as one of the most important risk factors for predicting of acute gastrointestinal bleeding. The probability of gastrointestinal

bleeding was higher in patients with a systolic blood pressure higher than 140 mmHg. Yoo Jin Lee et al. reported high systolic blood pressure as an independent risk factor for death in patients with acute gastrointestinal bleeding, which is consistent with our study (23). While in the study of Gultekingil et al. although a relationship between the higher number of pulses per minute and the gastrointestinal bleeding, there was no significant relationship between higher systolic blood pressure and the acute gastrointestinal bleeding (17).

According to the results of current study, there was a significant relationship between diabetes and acute gastrointestinal bleeding, as an independent predictor of acute gastrointestinal bleeding which is consistent with Badipatla et al. which reported significantly higher blood glucose levels in patients (24). Due to increased life expectancy and noninvasive diseases, continuous follow-up of older patients can reduce costs and acute gastrointestinal bleeding.

In the end, identifying people at risk and predictive factors for acute gastrointestinal bleeding can play a significant role in providing preventive strategies, timely treatment of the disease and reducing its complications.

The main limitation of the present study was to design the study as retrospectively and based on patient records. Further studies can be provided by designing of study as prospective studies and accurate patient information records.

## 5. Conclusion

According to the results of this study, the age over 65 years, BMI greater than 25 kg/m<sup>2</sup>, systolic blood pressure greater than 120 mmHg and diabetes were the most important risk factors for acute gastrointestinal bleeding. Therefore, according to the results of this study, prevention of obesity, blood pressure monitoring and lifestyle changes, may decrease the chance of acute gastrointestinal bleeding.

## 6. Acknowledgment

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## 7. Conflict of interest

No conflict of interest was declared.

## 8. Funding source

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## 9. Author contribution

M.B and, S.A contributed to study design. M.B, and S.A contributed to the selection of patients and data collection. A.T performed data analysis. M.B and, A.T prepared the manuscript. S.A revised the manuscript.

## 10. Reference

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