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Prevalence of Hypofibrinogenemia Among Patients With Acute Gastrointestinal Bleeding: A Cross-Sectional Study

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Abstract

Objectives: Hypofibrinogenemia can worsen the outcome of patients with gastrointestinal bleeding (GIB). There are a few domestic surveys on the issue. We conducted this study to evaluate the prevalence of hypofibrinogenemia and its effect on the outcome of patients with acute GIB.

Materials and Methods: In this cross-sectional study, all data about the patients with acute GIB admitted to the emergency departments of hospitals of Shahid Beheshti University of Medical sciences in 2016 were collected and analyzed using SPSS statistical software version 21.0 and all tests were considered significant at P value ≤ 0.05.

Results: From the patients under the study, 69% were male and the mean age was 53.38±13.18 years old. Mean levels of haemoglobin, international normalized ratio (INR), and fibrinogen were 10.68, 1.65, and 250.43, respectively. Moreover, most cases of hypofibrinogenemia had liver disorders or lower GIB ($P<0.05$). While, fibrinogen level had no significant effect on mortality.

Conclusions: In summary, afibrinogenemia is mostly correlated with liver diseases and lower GIB, and can cause severe morbidity.

Keywords: Hypofibrinogenemia, Gastrointestinal bleeding, Fibrinogen, Blood

Introduction

Gastrointestinal bleeding (GIB) is one of the most frequent causes of hospital and intensive care unit admissions worldwide. It is also one of the most prevalent emergent diagnoses in emergency department with the admission rate of 1% of all population. Despite the fact that 80% of GIBs are self-limited, 20% need an aggressive treatment and immediate intervention. Severity of haemorrhage, patients' hemodynamic stability, and comorbidities not only affect treatment plans, but also can increase risk of disease morbidity and mortality (1,2).

Increase of both fibrinolytic activity and afibrinogenemia in the patients with GIB may lead to continuous bleeding and poor outcome (3,4).

Although congenital afibrinogenemia can cause severe bleeding, most cases with severe bleeding might suffer from acquired afibrinogenemia due to the consumption or dilution of fibrinogen in blood. Pure afibrinogenemia is also very rare and majority of the patients have a combination of coagulopathies (5).

Some studies have shown that hypofibrinogenemia in the patients with GIB can worsen their outcome and early fibrinogen replacement can have a positive effect on the management of these patients (6).

There are a few studies on the prevalence of hypofibrinogenemia in the patients with GIB in Iran. Therefore, the aims of this study were to evaluate the prevalence of afibrinogenemia in the patients with acute GIB, and to assess its association with liver diseases and lower GIB.

Methods and Materials

Patients

All patients with chief complaint of upper or lower GIB who were admitted to the emergency departments of Shohada-e-Tajrish, Imam Hossein, and Loghman hospitals of Shahid Beheshti University of Medical Sciences, Tehran, in 2016, were included in the study. On the contrary, the patients with any possible diagnoses rather than upper or lower GIB (hemoptisia, vaginal bleeding, etc), gastrointestinal surgery within the last two weeks, or disagreement to participate in the study were excluded. An oral consent for participation was obtained from all the patients. The minimum sample size was 221, which was calculated by the following formula:

$$N = pqz^2/d^2 = (0.05 * 0.95)\ (2.73)^2/(0.04)^2 = 221$$

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Along with primary resuscitation and treatment, a 5-mL blood sample was collected before any fluid injection to measure the plasma fibrinogen levels in all the patients.

A check list including the demographic features, comorbidities, past medical and drug history, social habits such as smoking and alcohol consumption, vital signs, hemostasis and laboratory abnormalities, source of bleeding, laboratory and endoscopic results, fibrinogen level, complications, transfusion of blood products, surgical or emergent endoscopic interventions, and patients final outcome (discharge, admission to the floor or ICU, death) was completed for each patient. Data were analyzed with IBM SPSS 16, and parametric and non-parametric tests including *t* test, ANOVA, chi-square, and Kruskal-Wallis were used for analyzing the data. *P* value ≤0.05 was considered to be statistically significant.

Results

Total number of the patients included in this study was 300 with the mean age of 53.38 ± 13.81 years old, from which 69% were male. Hypertension, diabetes mellitus, and hyperlipidemia were the most frequent co morbidities (27%, 23%, and 19.7%, respectively). In addition, smoking (22.3%), nonsteroidal anti-inflammatory drugs (NSAIDs), and other anti-coagulants (26.3%) were the most prevalent risk factors. Furthermore, 64 patients had hemodynamic instability (Table 1), and gastric erosions and duodenal ulcers were the most frequent causes of bleeding.

In this study, the mean level of fibrinogen was 242.32± 77.80 mg/dL. In addition, mortality rate was 11.7%, and 53 % of the patients were discharged within the first 24 hours. Moreover, the mean level of hemoglobin and international normalized ratio (INR) were calculated to be 10.68± 2.81 and 1.65 ± 0.38, respectively.

It was also found that most patients with hypofibrinogenemia had liver disease or lower GIB (*P*<0.05, Table 2).

Table 1. Demographic Features, Comorbidities, and Risk Factors of Patients with Acute GIB Admitted to the Hospitals

Variable		No.	%
Sex	Male	208	69.3
	Female	92	30.7
Age	≤40	33	11
	41-50	61	20.3
	51-60	81	27
	61-70	71	23.7
	≥70	54	18
Comorbidity	Hypertension	81	27
	Pulmonary disease	17	5.7
	Diabetes mellitus	69	23
	Renal insufficiency	15	5
	Hyperlipidemia	59	19.7
	Cancer	30	10
	Liver Disease	34	11.3
Risk factors	Smoking	67	22.3
	Alcohol abuse	7	2.33
	NSAIDs/anti-platelates/etc.	80	26.6
Cause of bleeding	Upper GIB	204	68
	Lower GIB	96	32
Fibrinogen level	≤100	12	4
	101-399	280	93.3
	≥400	8	2.7
Intervention	Blood transfusion	124	41.3
	Emergent endoscopy	119	39.6
	Surgery	20	6.6
Outcome	Discharge within 24 hours	159	53
	Admission to the floor	59	19.6
	ICU admission	47	15.6
	Death	35	11.7

Discussion

GIB is one of the most prevalent diseases in the community and emergency department, and more than half of the patients inflicted are the elderly. [7] Although bleeding is self-limited in most patients, 20% of cases need an aggressive endoscopic treatment and surgical intervention due to severe bleeding and hemodynamic compromise.

In this study, mean age of the patients was 53.38±13.81 years old and most patients were in sixth decade of their life. Male to female ratio was 2.25 (69.3 vs 30.7), and hypertension, diabetes mellitus, smoking, and NSAIDs were the most frequent comorbidities and risk factors. Gastric erosions and duodenal ulcers were also the most frequent causes of bleeding.

In the study of Ghanadi et al, 67% of the patients were male and most cases were between 60 and 79 years old. NSAIDs (3.8%) and cirrhosis (61.5%) were the most common prevalent risk factors and underlying diseases predisposing bleeding in these patients. In addition, GI ulcer (42.7%) was the main cause of bleeding (8).

Minakari et al studied on a total of 4747 patients with GIB in Isfahan, Iran. In their survey, 69.2% of the patients were male, mean age was 55.46 ± 21.98 years old, hematemesis was the most frequent presenting symptom (63.5%), and peptic ulcer (duodenal ulcer in most cases) was the main cause of upper gastrointestinal bleeding (42.4%). They concluded that comorbidities, hemodynamic instability, high-risk endoscopic stigmata, smoking and NSAIDs, and gastric and esophageal malignancies might be important predisposing factors for re-bleeding and mortality in the patients with UGIB (9).

Masoodi and Saberifiroozi reviewed the etiology and outcome of GIB in Iran in 2012. They concluded that gastric and duodenal erosions accounted for 16.4%-25% of the etiologies. Variceal hemorrhage, Mallory-Weiss tears, and arterial and venous malformations were the other important causes of GIB. However, in 9%-13.3% of the patients, the endoscopy was normal (10).

Sharifian et al studied the endoscopic findings of the patients with UGIB referred to Taleghani hospital, Shahid Beheshti University of Medical Sciences, during 2010-2012. Out of 990 patients, 594 (60%) were male and mean age of the patients was 54 ± 17.2 years old. The authors

Table 2. The relationship Between Fibrinogen Disorder and Causes of GIB

Variable		Afibrinogenemia		Normal fibrinogen		*P* Value
		No.	%	No.	%	
Sex	Male	7	3.4	201	96.6	0.399
	Female	5	5.4	87	94.6	
Liver disease	Positive	5	14.7	29	85.3	0.002
	Negative	7	2.6	259	97.4	
Sites of bleeding	Upper GI	5	2.5	199	97.5	0.04
	Lower GI	7	7.3	89	92.7	
hemodynamic stability	Stable	8	3.4	228	96.6	0.3
	Unstable	4	6.2	60	93.8	
Blood transfusion	Positive	5	41.7	84	29.2	0.353
	Negative	7	58.3	204	70.8	
Survival status	Discharged	10	3.8	255	96.2	0.582
	Dead	2	5.7	33	94.3	

found out that peptic ulcer disease followed by esophageal and gastric varices were the most frequent causes of GIB in Iranian population. They also concluded that in the patients under the age of 70, duodenal ulcer was the most frequent cause of GIB; while over the age of 70, gastric ulcers and esophageal and gastric varices were the most important causes based on endoscopic findings (11).

In this study, demographic features, risk factors, and causes of bleeding corresponded to those of other studies in the domestic realm. Male sex predominance can be caused by either sex-related genetic factors or different lifestyles. Moreover, higher rate of smoking as well as exposure to risk factors in males rather than females in Iran could be the other contributing factors. Higher prevalence of GIB between 50 and 70 years old can be best explained by higher consumption of NSAIDs, aspirins, and anticoagulants in this group of patients.

In our study, 11.3% of the patients had liver disorders, and afibrinogenemia was significantly high in this group. Mean fibrinogen level was 242.32 mg/dL and 4% had hypofibrinogenemia. There was also found a significant relationship between lower GIB and afibrinogenemia.

A metanalysis by Kozek-Langenecker et al showed that in 70% of trials, fibrinogen replacement had a positive effect on reducing re-bleeding rate, and fibrinogen transfusion in comparison with fresh frozen plasma could reduce the volume of blood loss, duration of hospital stay, and ICU admission more than 50% (12).

Leal-Noval et al conducted a trial on the transfusion of fibrinogen concentrate (FBNc) for refractory bleeding in massively transfused, non-trauma patients with coagulopathy. They concluded that late administration of low FBNc dosage was not associated with decreased blood transfusion or an increased post-infusion fibrinogen level. As fibrinogen levels at the time of admission and target fibrinogen levels were associated with decreased blood transfusion, earlier administration and higher doses of FBNc were possibly needed.[13]

Siddiqui et al reported that among the patients with liver disease, 88% had prolonged PT, 71% had prolonged PTT, and 67% had both pathway disorders, of whom 15% had hypofibrinogenemia.[14]

Danes et al in their observational study on the administration of FBNc to the patients with acquired hypofibrinogenemia and unresponsive, life-threatening haemorrhage concluded that FC transfusion improved laboratory coagulation tests, and might also be life-saving. There was also a positive relationship between plasma fibrinogen levels and survival status in acquired fibrinogen deficiency.[15]

In our study, mortality rate was 11.7%, however there was no significant relationship between higher mortality rate and dysfibrinogenemia. None of the patients received FBNc.

Conclusions

To conclude, afibrinogenemia is mostly correlated with liver diseases and lower GIB, and can cause severe morbidity. Further longitudinal studies as well as clinical trials are required to ascertain a clear relationship between fibrinogen levels and survival status, as well as proving benefits of fibrinogen transfusion in the patients with GIB.

Limitations

This study was a cross-sectional study, whose results should be attested with longitudinal studies and clinical trials.

Conflict of Interests

Authors have no conflict of interests.

Ethical Issues

This cross-sectional study was approved by the Ethics Committee of Shahid Beheshti University of Medical Sciences (Code of Ethics: IR.SBMU.MSP.REC.1395.73).

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