Internal Medicine: Open Access

Bahardoust et al, Intern Med 2018, 8:1
DOI: 10.4172/2165-8048.1000265

Research Article Open Access

Association between ABO Blood Group and Clinical Outcomes in Patients with Gastrointestinal Bleeding

Bahardoust M, Naghshin R, Mokhtare M*, Hejrati A, Namdar P, Talebi A, Tavakoli T, Amiri H and Kiapey SH

Iran University of Medical Sciences Tehran, Tehran Iran (Islamic Republic of)

***Corresponding author:** Mokhtare M, Iran University of Medical Sciences Tehran, Tehran Iran (Islamic Republic of), Tel: 00982166554790; E-mail: marjanmokhtare@yahoo.com

Received date: January 14, 2018; **Accepted date:** January 25, 2018; **Published date:** January 30, 2018

Abstract

Introduction: Gastrointestinal (GI) bleeding is one of the most common causes of Emergency Room (ER) visits all around the world. Previous studies proved the relationship between ABO blood group and the bleeding diathesis. Distribution of ABO blood type antigens is various among the different races. This study aimed to assess the role of ABO blood group system in the development of GI bleeding in Iranian population.

Method and Material: Patients with acute upper and/or lower non-traumatic GI bleeding who admitted in ER of Rasoul-e-Akram hospital and the healthy blood donor between 2014 and 2016, were enrolled in this prospective case-control study. Demographic criteria, clinical presentation, laboratory data, endoscopic findings and GI bleeding outcome during the first 72 hours of admission were recorded. All variables were analyzed by SPSS software version 22.

Results: Overall, 513 case and 520 control groups completed the study. The risk of bleeding originated from esophageal, gastric and duodenal ulcers were significantly higher among patients with O blood group (P value=0.032, 0.021 and 0.009, respectively). Need for blood transfusion was significantly higher among patients with O blood group (P value=0.032). Older males had higher risk of developing GI bleeding (P value is 0.001and 0.003, respectively) in this study.

Conclusion: O blood type is significantly more common in Iranian patients with GI bleeding in comparison to the healthy blood donors. It seems that it is a prognostic genetic and individual risk factor for bleeding tendency in these patients, especially in those with upper GI bleeding.

Keywords: Gastrointestinal bleeding; ABO blood group; Prognosis; Autoimmune diseases

Introduction

Upper and lower gastrointestinal (GI) bleeding are one of the most common causes of ER visits all around the world. GI bleeding is estimated to have an annual incidence of 48-160 per every 100,000 people [1,2]. The most common causes of upper and lower GI bleeding include peptic ulcer disease and peri-anal disorders (e.g. hemorrhoids and fissures). Moreover, *Helicobacter pylori* infection and non-steroidal anti-inflammatory drugs (NSAIDs) use are known to play a significant role in the occurrence of GI bleeding. It seems that the presence of etiologic factors among with genetic susceptibilities is the main prognostic factors in patients with GI bleeding. Risk, severity and development of GI bleeding could be affected by ABO blood group antigens as a genetic factor [2,3]. The relationship between ABO blood group and peptic disease has been the subject of multiple studies for many years. Blood group A was found to be associated with an increased risk of gastric cancer [4]. Also, it has been determined that squamous cell carcinoma in oral cavity is more common in blood type B [5].

The possibility of the relationship between specific genetic factors and the occurrence of GI bleeding has been shown in many studies. Risk of duodenal ulcer is increased in patients with O blood type [6,7]. Recent studies have demonstrated that the same population with O blood group has additional *Helicobacter pylori* receptors compared to the general population [8]. Since the relationship between ABO blood group and the outcome of patients with GI bleeding is not clear, further studies are needed to examine the role of ABO blood group in developing GI bleeding and their effect on the outcome of patients with this disorder [9].

Many studies have proven the relationship between the ABO blood group and the bleeding diathesis. In fact, O blood type was associated with a higher bleeding potency. Moreover, the risk of venous thrombotic events was higher in non-O blood types. Furthermore, this thrombotic event was happened through the modulation of Von-Will brand Factor and Factor VIII plasma levels, which are the main risk factors for venous thrombosis. Additionally, platelet function is also compromised in O blood group [10,11]. Since the distribution of ABO blood type genes varies among different racial and ethnic groups, we designed this study to assess the role of ABO blood group system in development of GI bleeding and its short term clinical outcome in Iranian population.

Materials and Methods

All patients with acute upper and/or lower non-traumatic GI bleeding who admitted at the ER of Rasoul-e-Akram university hospital, Tehran, between 2014 and 2016, were enrolled in this

prospective case –control study. The control group was from healthy blood donors. Informed consent was obtained. The patients who we could not access to their ABO and Rh blood group were excluded. Demographic data (age and sex), presenting symptoms (hematemesis, melena, hematochezia), vital signs (pulse rate/minute, systolic and diastolic blood pressure (BP) in mmHg) were extracted from data gathering sheets. Laboratory tests were performed for the determination of ABO blood group and Rh, hemoglobin (Hb) gr/L, creatinine (Cr) in mg/dl, platelet count/μL, prothrombin time (PT), International Normalized Ratio (INR) and partial thromboplastin time (PTT) in second. Endoscopic findings and GI bleeding outcome (any need for blood transfusion, number of transfused blood products, and re-bleeding rate) during the first 72 hours of admission were recorded.

Re-bleeding was defined as overt hematemesis or hematochezia, Hb drop more than 2 gm/L within 24 hours after the first endoscopic homoeostasis and the presence of blood in the second endoscopy. This study was reviewed and approved by ethics committee of Iran University of Medical Sciences (Ethics Code; IR.IUMS.REC; 1395-8811215250).

The chi-square test, T-test and ANOVA test were used to compare qualitative an quantities variables. The logistic regression test was performed to determine the relationship between gender, age, ABO blood groups, and Rh in GI bleeding and control groups. P value less than 0.05 was considered statistically significant. The data was analyzed with SPSS (Statistical package for Social Sciences; SPSS 22; Chicago, IL, USA).

Statistical Methods

Descriptive statistical analysis was used; mean and standard deviation were used for normally distributed numerical variables, and median and minimum-maximum were used for non-normally distributed numerical variables. The Kolmogorov-Smirnov test was used for tests of normality. The t-test, Mann-Whitney U test and chi-square test were used for evaluating differences between the patient and control groups. A p-value of<0.05 was considered to be statistically significant. The SPSS 21.0 package programme (Version 21.0; Microsoft Co., Chicago, IL, USA) was used for evaluating data.

Results

Five hundred and thirteen patients with GI bleeding (65% male) and 520 healthy blood donors as control group (58% male), completed the study. Mean age of the case and control groups were 59 ± 20 (SD) and 53 ± 16(SD) years, respectively. Among patients the most common blood group was O (46%), followed by A (27%), B (18%), and AB (6%). Rh positive antigen was seen in 89% of the patients (Table 1).

ABO and Rh Blood Antigens	Frequency (N)-Case	Percent (%)-Case	Frequency (N)-Control	Percent (%)-Control
A	145	27	151	29
B	98	18	130	25.2
AB	30	6	31	6
O	240	46	208	39.8
Rh Antigen+	457	89	473	91
Total	513	100	520	100

Table 1: Distribution of ABO blood group antigens in case and control group.

Laboratory tests including Hb (gr/dL) and Cr (mg/dl), PTT, PT (second) and INR, and vital sings including heart rate/minute, systolic and diastolic BP (mmHg) and clinical presentation for each patient at the time of admission, and their relation with distribution of blood groups are shown in (Table 2).

Variables	Blood Group Antigen					P value
	A	B	O	AB	Total	
Systolic BP(M)	116.01 ± 19.05	115.5 ± 22.05	135 ± 22.0	119.04 ± 20.13	118.08 ± 21.09	NS
Diastolic BP(M)	73.08 ± 11.04	72 ± 12.06	74.00 ± 11.00	72.03 ± 12.01	73.01 ± 14.02	NS
Heart Rate(M)	88. 4 ± 15.08	85. 3 ± 14. 1	88 ± 14.05	87 ± 13.05	90.25 ± 15.24	NS
Hb(M)	9.0 3 ± 2.09	8.98 ± 2.01	10.01 ± 2.05	9.06 ± 2.6	9.32 ± 2.96	NS
Cr(M)	1.3 ± 0.6	1.06 ± 0.57	1.07 ± 0.39	1. 3 ± 0. 3	1.36 ± 0.57	NS
PT (M)	15.2 ± 2.00	14 ± 3.07	13.8 ± 2.01	13.01 ± 1.09	14.3 ± 3.00	NS
PTT (M)	31.8 ± 7.05	31.07 ± 4.9	32.12 ± 15.08	31.02 ± 5.00	31.05 ± 11.5	NS
INR (M)	1.00 ± 0.02	1.03 ± 0.03	1.02 ± 0.05	1.01 ± 0.01	1.01 ± 0.10	NS

Platelet(M)	165000 ± 20000	166000 ± 25000	166000 ± 20000	167000 ± 25000	166000 ± 20000	NS
Hematemesis(N)	72	50	18	115	255/513	0.032*
Hematochezia(N)	20	12	6	22	60/513	NS
Melena(N)	51	36	8	103	198/513	0.044*

M: Mean; N: Number; NS: Not Significant; BP: Blood Pressure; Hb: Hemoglobine; Cr: Creatinine; PT: Prothrombin Time; PTT: Partial Thromboplastine Time; INR: International Normalization Ratio; *: Statiscically Significant

Table 2: Distribution of ABO blood type based on clinical and laboratory findings at the time of admission.

Variables	**Frequency (Number)**					**P value**
Endoscopic findings	A	B	O	AB	Total	
Esophageal lesions	23	14	37	3	77	0.03*
Esophageal ulcer	10	5	17	1	33	0.04*
Esophageal varices	4	3	8	0	15	NS
Mallory-Weiss	5	5	7	0	17	NS
Erosive Disease	3	1	4	0	8	NS
Esophageal cancer	1	0	1	0	2	NS
Gastric lesions	70	28	75	14	187	0.02*
Gastric ulcer	34	13	39	5	91	0.02*
Gastric erosion	25	11	27	8	71	NS
Vascular ectasia	3	1	2	0	5	NS
Dieulafoy's lesion	1	0	2	0	3	NS
Gastric cancer	7	3	5	3	17	NS
Duodenal lesions	71	41	78	18	208	0.00*
Duodenal ulcer	38	27	48	13	126	0.00*
Duodenal erosion	28	13	26	5	72	NS
Bulbar deformity	5	1	6	0	12	NS
Normal Endoscopy	15	6	19	5	45	NS
Hemorrhoids	11	3	13	2	29	NS
Internal hemorrhoid	9	2	11	2	24	NS
External hemorrhoid	3	0	2	0	5	NS
Solitary Rectal Ulcer	2	1	4	1	8	NS
Colon Ulcer	6	4	10	4	24	NS
Benign ulcer	3	2	6	1	12	NS
Malignant ulcer	3	2	4	3	12	NS
Angioectasia	2	1	2	0	5	NS
Diverticulosis	7	1	7	1	16	NS
Bleeding from anastomosis ulcer	1	0	2	0	3	NS

Normal colonoscopy	17	8	22	7	54	NS

Table 3: Endoscopic findings and their relation with ABO blood groups.

Endoscopy and colonoscopy were performed for 472 and 136 patients respectively. Duodenal ulcers 208/472 (44.06%) and internal hemorrhoids 29/136 (21.32%) were the most common endoscopic findings for upper and lower GI bleedings (Table 3). During the hospital stay, 171 patients (34%) required blood transfusion ranging from 1 (10.8%) to 8 (0.8%) units of packed red blood cell (p-RBC). The mean number of transfused p-RBC units was 2.59 (± 1.32) among the patients (Table 4).

Variables	**Blood Group Antigens**					**P value**
Short Term Outcome	A	B	AB	O	Total	
Need for transfusion	43	40	12	76	171	0.03*
Number of transfused p-RBC	2.7 ± 1.29	2.90 ± 1.2	2.71 ± 1.30	2.52 ± 1.30	2.79 ± 1.30	NS
Re-bleeding rate	10	6	2	14	32	NS

Table 4: Short-term outcomes of GI bleeding in relation to the distribution of ABO blood group.

Distribution of Rh Antigen positive in GI Bleeding patients and in healthy blood donors was 89.7 and 91.1% respectively (P value=NS) (Table 5).

P-value	**Total**	**Non-O blood type**	**O blood type**	**ABO Blood Group Antigen**
	513	273	240	GI Bleeding patients
0.01*	520	313	207	Healthy blood donors
	1033	586	447	Total
*: Statistically significant				

Table 5: Distribution of ABO Blood Group Antigens in GI bleeding patients and healthy blood donors.

Variables		**SE**	**value**	**OR**	**95% CI for EXP(B)**	
-					Lower	Upper
Sex (male)	0.39	0.132	0.003	1.477	1.14	1.913
Age	0.018	0.003	0	1.018	1.011	1.025
Blood group O	-		0.022	-		
Blood group A	0.153	0.276	0.58	0.858	0.499	1.475
Blood group B	0.044	0.285	0.876	1.045	0.598	1.827
Blood group AB	0.365	0.293	0.214	1.44	0.81	2.559
RH+	-0.123	0.213	0.564	0.884	0.582	1.343
Constant	-1.615	1.146	0.159	5.026	-	
B: Estimate; SE: Standard Error; OR: Odds Ratio EXP(B); CI: Confidence Interval for odds ratio; *: Reference blood group						

Table 6: Relationship between blood groups and Rh Antigen in GI bleeding patients regarding age and gender (Logistic regression).

The odds ratio for age and gender variables were 1.018(95% CI=1.011-1.025) and 1.477(95% CI=1.140-1.913). It means that the

odds of having disease in males are twice compared to females. Increasing a year of age will increase the chance of GI bleeding by 2% (Table 6).

Discussion

The prognosis of GI bleeding varies from mild self-limited symptoms to severe hemodynamic instability that can leads to death [12]. This disorder is associated with morbidity and mortality. The etiologic causes and predisposing factors were properly determined [13-15]. Various risk scoring systems regarding clinical and laboratory and endoscopic findings have been developed to classify patients with GI bleeding to high- and low-risk groups [12]. Researchers have recently determined that, the genetic "host" factors might play a role in the development of GI bleeding [16-18]. Among these factors, O blood type as a genetic predisposing factor has been shown to influence susceptibility to *Helicobacter pylori* infection, duodenal ulcer and possible bleeding tendency [11] hence facilitating the development of GI bleeding [19,20].

Mortazavi et al. found that O blood type is the most frequent blood group in Iranian general population. We demonstrated that the ABO blood type distribution in this study was similar to the previous results [5,21].

The relationship between ABO/Rh blood group and development of GI bleeding was found in Bayan et al. study at 2008. They found that patients with O blood group had a higher rate for the development of GI bleeding, [22] as we determined in our study. Keramati et al. in 2013 showed inconclusive results about the risk of *Helicobacter pylori* infection in people with O blood group [23] Clark et al. performed a study in 1956 and showed that blood type A is associated with an increased risk of gastric cancer [4,24]

Hematemesis and melena was significantly more common in patients with O blood group in our study (P value less than 0.05). The risk of bleeding originated from esophageal, gastric and duodenal ulcers were significantly higher among patients with O blood group (P value is 0.032, 0.021 and 0.009, respectively). It appears that bleeding originated from upper parts of GI tract, are more prevalent in O blood type patients. Need for blood transfusion was significantly higher among patients with O blood group (P value is 0.032). The rate of re-bleeding was also slightly more common in blood type O.

The distribution of O blood type was significantly different in patients with GI bleeding patients and healthy blood donors (P value is 0.014). These results suggest that, O blood group could be considered as a genetic risk factor for bleeding tendency in Iranian patients with GI bleeding.

Previous study found that annually incidence of acute upper GI bleeding is approximately 1 person per 1000, with a higher rate in males and the elderly [25]. Multivariate logistic regression model demonstrated that older males had higher risk of developing GI bleeding (P value is 0.001, 0.003, respectively) in this study.

Meta-analysis of a very large sample of bleeding patients and controls showed that the frequency of O blood group was significantly higher in all kinds of bleedings than controls. And based on the result of this meta-analysis, O blood group was an important genetic risk factor for bleeding [26].

Conclusion

We found that, O blood type is significantly more common in Iranian patients with GI bleeding in comparison to the healthy blood donors. It seems that it is a prognostic genetic risk factor for bleeding tendency in these patients, especially in those with upper GI bleeding. Further large sample studies should be considered to evaluate the role of ABO blood type system, as an individualized risk factor, in prognostic risk scoring systems of GI bleeding.

References

1. Zhao Y, Encinosa W (2008)Hospitalizations for Gastrointestinal Bleeding in 1998 and 2006.
2. Rotondano G (2014) Epidemiology and diagnosis of acute nonvariceal upper gastrointestinal bleeding. Gastroenterol Clin North Am 43: 643-663.
3. Nagata N (2015) Risk of peptic ulcer bleeding associated with Helicobacter pylori infection, nonsteroidal anti-inflammatory drugs, low-dose aspirin, and antihypertensive drugs: A case-control study. J Gastroenterol Hepatol 30: 292-298.
4. Edgren G, Hjalgrim H, Rostgaard K (2014) Risk of gastric cancer and peptic ulcers in relation to ABO blood type: a cohort study. Am J Epidemiol 172: 1280-1285.
5. Mortazavi H, Hajian S, Fadavi E, Sabour S, Baharvand M, et al. (2014) ABO blood groups in oral cancer: A first case-control study in a defined group of Iranian patients. Asian Pacific Journal of Cancer Prevention 15: 1415-1418.
6. Loffeld RJ, Stobberingh E (1991) Helicobacter pylori and ABO blood groups. J Clin Pathol 44: 516-517.
7. Niv Y (1996) Helicobacter pylori infection and blood groups. Am J Gastroenterol 91: 101-104.
8. Boren T (1993) Attachment of Helicobacter pylori to human gastric epithelium mediated by blood group antigens. Science 262: 1892-1895.
9. Horwich L (1996) ABO blood groups in gastric bleeding. Gut 7: 680-685.
10. Lippi G, Franchini M, Brocco G, Manzato F (2001) Influence of the ABO blood type on the platelet function analyzer PFA-100. Thromb Haemost 85: 369-370.
11. Massimo F, Giuseppe L (2016) Relative risks of thrombosis and bleeding in different ABO blood groups. Semin Thromb Hemost 42: 112-117.
12. Marjan M, Vida B, Shahram A (2016) Comparison of glasgow-blatchford score and full rockall score systems to predict clinical outcomes in patients with upper gastrointestinal bleeding. Clin Exp Gastroenterol 9: 337-343.
13. Kuipers EJ, Thijs JC, Festen HP (1995) The prevalence of Helicobacter pylori in peptic ulcer disease. Aliment Pharmacol Ther 9: 59-69.
14. Marshall BJ (1994) Helicobacter pylori. Am J Gastroenterol 89: S116-S128.
15. Zuccaro G (1998) Management of the adult patient with acute lower gastrointestinal bleeding. American College of Gastroenterology. Practice Parameters Committee. Am J Gastroenterol 93: 1202-1208.
16. Papatheodoridis GV, Sougioultzis S, Archimandritis AJ (2006) Effects of Helicobacter pylori and nonsteroidal anti-inflammatory drugs on peptic ulcer disease: A systematic review. Clin Gastroenterol Hepatol 4: 130-142.
17. Musumba C (2012) The relative contribution of NSAIDs and Helicobacter pylori to the aetiology of endoscopically-diagnosed peptic ulcer disease: Observations from a tertiary referral hospital in the UK between 2005 and 2010. Aliment Pharmacol Ther 36: 48-56.
18. Piper JM (1991) Corticosteroid use and peptic ulcer disease: Role of nonsteroidal anti-inflammatory drugs. Ann Intern Med 114: 735-740.
19. Groenen MJ (2009) Incidence of duodenal ulcers and gastric ulcers in a western population: Back to where it started. Can J Gastroenterol 23: 604-608.

20. Hreinsson JP (2013) Upper gastrointestinal bleeding: Incidence, etiology and outcomes in a population-based setting. Scand J Gastroenterol 48: 439-447.
21. Montazemi K (1978) Distribution of abo blood groups in iran. Iranian Journal of Public Health 7: 39-56.
22. Bayan K (2009) Clarifying the relationship between ABO/Rhesus blood group antigens and upper gastrointestinal bleeding. Dig Dis Sci 54: 1029-1034.
23. Keramati MR (2012) Role of the lewis and ABO blood group antigens in Helicobacter pylori infection. Malays J Med Sci 19: 17-21
24. Clarke CA (1959) Secretion of blood group antigens and peptic ulcer. Br Med J 1: 603-607.
25. Nader T, Mokhtare M, Agah S (2017) Comparison of the efficacy of intravenous tranexamic acid with and without topical administration versus placebo in urgent endoscopy rate for acute gastrointestinal bleeding: A double-blind randomized controlled trial. United European Gastroenterol J 6: 46-54.
26. Dentali F, Sironi AP, Ageno W, Bonfanti C, Crestani S, et al. (2013) Relationship between ABO blood group and hemorrhage: A systematic literature review and meta-analysis. Semin Thromb Hemost 39: 72-82.