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The Relationship Between Rh and ABO Blood Groups Distribution and the Incidence of Gastric Cancer and Peptic Ulcer Disease: Case-Control Study

Ziad Aljarad[1], Ahmad Alhamid[2], Sara Aljarad[3], Jawhar Aljarad[4],Husam Abbas[1], Ahmad Sankari Tarabishi[2], Ahmad Mouakeh[2], Bachirbadawi Mobaid[5]

[1]Gastroenterologist, Department of Gastroenterology, Aleppo University Hospital, Aleppo, Syria.
[2]Medical Student, Faculty of Medicine, University of Aleppo, Aleppo, Syria.
[3]Hematologist, Department of Hematology, Al Assad University Hospital, Damascus, Syria.
[4]Medical Student, Faculty of Medicine, Syrian Private University, Damascus, Syria.
[5]Phd, Professor of Gastroenterology and Hepatology, Faculty of Medicine, University of Aleppo, Aleppo, Syria.
dr.ziad-aljarad@hotmail.com

***Corresponding Author:** Ziad Aljarad, MD, Gastroenterology Department, Aleppo University Hospital, Aleppo, Syria,*

Abstract

***Background:** In 1953, Aird et al. found an association between blood group A and gastric cancer, and between blood group O and peptic ulcer disease (PUD). Further research demonstrated relationships between ABO blood groups and some diseases. No studies included Rh blood groups in the analysis. In addition, a controversy exists among studies investigating the association of ABO blood groups with gastric cancer and PUD.*

***Aim:** This study aims to investigate the relationship between Rh and ABO blood groups and the incidence of gastric cancer and PUD. To our knowledge, this is the first study that includes Rh blood groups in the investigation.*

***Methods:**It is acase-control study. It involved all patients who undergone esophagogastroduodenoscopy (EGD) in Aleppo University Hospital during the study period. We did Rh and ABO blood group typing for all participants. We took biopsies from all ulcers, tumors and infiltrative lesions, and the biopsies were histologically examined. We formed four case groups: benign PUD group (n=276), benign gastric ulcer group (n=125), benign duodenal ulcer group (n=169), and gastric cancer group (n=26). the control group (n=276) consisted of participants whose EGDs were normal or revealed only gastritis or duodenitis. We used ODDs Ratio with 95% confidence interval and P-value to evaluate statistical significance of differences between groups.*

***Results:** We found no significant relationship between Rh blood groups and gastric cancer or PUD. We found no relationship between ABO blood groups and PUD. We detected an increased risk of gastric cancer among blood group A(OR=1.24, 95% CI 1.11-1.46, P=0.02). Non-A groups revealed no significant risk. 100% of biopsies showed H.pyloriinfection.*

***Conclusion:** After comparing our findings to available literature, we suggest larger-scale studies to investigate the association of non-A groups with gastric cancer, and Rh groups with gastric cancer and PUD . We recommend studying the feasibility of establishing screening programs for gastric cancer in people with blood group A, and consideringblood group A as a risk factor that may indicate EGD in the presence of upper gastrointestinal symptoms. We should determine the prevalence of H.pylori infection in the Syrian population.*

Keywords: *Rh, ABO, Peptic Ulcer Disease, Gastric Cancer*

Introduction

In 1921, Higley and Buchanan studied the relationship between ABO blood groups and some diseases, including: peptic ulcer disease (PUD), pernicious anemia, and some cancers; and found no significant relationships (1). The interest in this research question returned when Aird *et al.* In 1953 found an

association between blood group A and gastric cancer, and between blood group O and PUD (2). Further research demonstrated relationships between ABO blood groups and some diseases, like the increased risk of ovarian and pancreatic cancers among people with blood group A (3) (4), and the protective effect of blood group O from venous thrombosis and pancreatic cancer (5)(6). No studies included Rh blood groups in the analysis. In addition, a great controversy exists among studies investigating the association of ABO blood groups with gastric cancer and PUD.

This study aims to investigate the relationship between Rh and ABO blood groups and the incidence of gastric cancer and PUD. To our knowledge, this is the first study that includes Rh blood groups in the investigation. Our study included participants who underwent esophagogastroduodenoscopy (EGD) during a period of 22 months in Aleppo University Hospital.

Methods

We chose case-control study design. The study took place at Aleppo University Hospital, internal medicine department, gastroenterology ward, between January 2016 and October 2017 inclusive. The study included all patients who underwent esophagogastroduodenoscopy (EGD) during the study period, from all ages and both genders. The EGD was done by expertized specialists. We did ABO and Rh blood group typing for all participants. We diagnosed peptic ulcer disease (PUD) with EGD depending on gross appearance, considering gastric and duodenal lesions greater than 5 mm in diameter and have a grossly recognizable depth. We took biopsies from margins of all ulcers, tumors and infiltrative lesions in the stomach and duodenum. Histopathologic examination of biopsies was done. Gastric and duodenal cancer was diagnosed depending on histopathologic findings of biopsies. No data missing happened. We formed the following case groups: benign PUD group, which contains benign gastric ulcer group and benign duodenal ulcer group. We also formed a case group of gastric cancer patients. For every case in benign PUD group, we chose a control from the same gender and age group, whose EGD was normal or revealed only gastritis or duodenitis. Thus, the control group of this study was formed. We used Pearson chi-square test and Fisher exact test, whichever is applicable, to compare the distribution of blood groups between case and control groups. We used categorical binary logistic regression to calculate odds ratio. We used 95% confidence interval and P value to evaluate statistical significance of differences between groups. The level of significance is $P < 0.05$. We performed statistical analyses with SPSS (Version 22.0; SPSS Inc.: Chicago, IL, USA).

Results

2574 patients underwent EGD during the study period, 276patients of them had benign PUD, and 26 patients had gastric cancer.Among benign PUD patients, 125 cases were benign gastric ulcer (isolated or accompanied with duodenal ulcer), 169 cases were benign duodenal ulcer (isolated or accompanied with gastric ulcer), and 18 cases were accompanied benign gastric and duodenal ulcers (studied with the previously mentioned gastric and duodenal ulcers).

Benign PUD group consisted of 170 males (61.59%) and 106 females (38.41%). The mean age of this group was 49.83 years with a standard deviation of 17.71 years. Among PUD group, 118 cases (42.75%) were blood group A, 29 cases (10.51%) group B, 107 cases (38.77%) group O and 22 cases (7.97%) group AB. 248 cases (89.86%) were Rh^+ and 28 cases (10.14%) were Rh^-. Benign gastric ulcer group consisted of 71 males (56.80%) and 54 females (43.20%). The mean age of this group is 53.75 years with a standard deviation of 17.19 years. Among this group, 54 cases (43.20%) were blood group A, 12 cases (9.60%) group B, 50 cases (40%) group O and 9 cases (7.20%) group AB. 113 cases (90.40%) were Rh^+ and 12 cases (9.60%) were Rh^-. Benign duodenal ulcer group consisted of 108 males (63.91%) and 61 females (36.09%). The mean age of this group is 47.14 years with a standard deviation of 17.03 years. Among this group, 71 cases (42.01%) were blood group A, 19 cases (11.24%) group B, 64 cases (37.87%) group O and 15 cases (8.88%) group AB. 148 cases (87.57%) were Rh^+ and 21 cases (12.43%) were Rh^-. Gastric cancer group consisted of 26 cases: 21 cases were adenocarcinoma and five cases were lymphoma. 8 cases of the gastric cancer group appeared endoscopically as ulcers, 7 of them were adenocarcinoma and 1 was lymphoma. The rest of gastric cancer cases appeared endoscopically as tumors or infiltrative lesions in the stomach. Gastric cancer group consisted of 16 males (61.54%) and 10 females (38.46%). The mean age of gastric cancer group was 52.61 years with a standard deviation of 14.68 years. Among this group, 14 cases (53.85%) were blood group A, 2 cases (7.69%) were

blood group B, 9 cases (34.62%) were blood group O and 1 case (3.85%) was blood group AB. Among control group, 126 cases(45.65%) were blood group A, 27 cases (9.78%) were blood group B, 112 cases (40.58%) were blood group O, and 11 cases (3.99%) were blood group AB. 243 cases (88.04%) were Rh^+ and 33 cases (11.96%) were Rh^-.

Control group consisted of of 170 males (61.59%) and 106 females (38.41%). The mean age of this group was 51.01 years with a standard deviation of 17.03 years.Among control group, 126 cases (45.65%) were blood group A, 27 cases (9.78%) group B, 112 cases (40.58%) group O and 11 cases (3.99%) group AB. 243 cases (88.04%) were Rh^+ and 33 cases (11.96%) were Rh^-

In comparing the benign PUD group with the control group, we found no statistically significant difference between: Blood group A and non-A blood groups (OR=0.97, 95% CI 0.67-1.39, P=0.85), blood group B and non-B blood groups (OR=0.90, 95% CI 0.50-1.61, P=0.72), O blood group and non-O blood groups (OR= 0.73, 95% CI 0.76-1.49, P=0.73), AB blood group and non-AB blood groups (OR=0.83, 95% CI 0.35-1.90, P=0.63) and between Rh^+ and Rh^- blood groups (OR=0.83, 95% CI 0.49-1.41, P=0.5). (Table 1)

In comparing the benign gastric ulcer group with the control group (276 controls), we found no statistically significant difference between: Blood group A and non-A blood groups (OR=1.10, 95% CI 0.63-1.90, P=0.73), blood group B and non-B blood groups (OR=1.23, 95% CI 0.55-2.78, P=0.60), O blood group and non-O blood groups (OR= 1.00, 95% CI 0.70-1.60, P=1.00), AB blood group and non-AB blood groups (OR=1.37, 95% CI 0.56-3.38, P=0.50,) and between Rh^+ and Rh^- blood groups (OR=1.10, 95% CI 0.46-1.82, P=0.14). (Table 1)

In comparing the benign duodenal ulcer group with the control group (276 controls), we found no statistically significant difference between: Blood group A and non-A blood groups (OR=0.86, 95% CI 0.45-1.51, P=0.30,), blood group B and non-B blood groups (OR=1.05, 95% CI 0.89-1.16, P=0.61), O blood group and non-O blood groups (OR= 0.78, 95% CI 0.42-1.06, P=0.25), AB blood group and non-AB blood groups (OR=0.88, 95% CI 0.58-1.54, P=0.23) and between Rh^+ and Rh^- blood groups (OR=1.11, 95% CI 0.44-1.86, P=0.79). (Table 1)

In comparing gastric cancer group with the control group, we found that the risk of gastric cancer in blood group A was significantly higher than that in non-A groups (OR=1.24, 95% CI 1.11-1.46, P=0.02). We found no significant difference of gastric cancer risk between: blood group B and non-B blood groups (OR=0.94, 95% CI 0.78-1.35, P=0.64), O blood group and non-O blood groups (OR= 1.11, 95% CI 0.92-2.13, P=0.74), AB blood group and non-AB blood groups (OR=1.00, 95% CI 0.65-1.71, P=0.74) and between Rh^+ and Rh^- blood groups (OR=0.97, 95% CI 0.72-1.88, P=0.70).(Table 1). Notably, 100% of the biopsied patients during the study period, whether they were included in the final sample or not, were infected by H.pylori as confirmed by pathology reports.

Table 1. *The significance of differences in the incidence of gastric cancer and PUD between different ABO and Rh blood groups; demonstrated by P-value and OR with 95% CI.*

	Blood type to non-AA	Blood type B to non-B	Blood type AB to non-AB	Blood type O to non-O	Rh(+) to Rh(-)
Peptic ulcer disease patients (276)					
P value	0.851	0.722	0.639	0.73	0.498
Odds Ratio OR	0.966	0.899	0.817	1.061	0.831
95% CI	1.386-0.673	1.613-0.502	1.900-0.352	1.488-0.757	1.418-0.488
Gastric ulcer patients (125)					
P value	0.734	0.603	0.495	0.997	0.140
Odds Ratio OR	1.099	1.239	1.37	0.997	1.095
95% CI	1.890-0.639	2.778-0.553	3.378-0.555	1.577-0.699	1.818-0.456

Duodenalulcer patients (169)					
P value	0.3	0.612	0.232	0.254	0.792
Odds Ratio OR	0.864	1.053	0.877	0.783	1.112
95% CI	1.507-0.454	1.162-0.891	1.540-0.582	1.063-0.416	1.858-0.439
Gastric Cancer (26)					
P value	**0.022**	0.635	0.741	0.741	0.699
0.968	**1.24**	0.943	1.008	1.112	0.968
95% CI	**1.455-1.112**	1.345-0.781	1.712-0.645	2.129-0.923	1.881-0.728

Discussion

This is a case-control study carried out within a cohort of people who underwent EGD and their ABO and Rh blood group was detected. We found no significant relationship between Rh blood groups and PUD or gastric cancer. We also concluded that the relationship between ABO blood groups and PUD is not significant. We have confirmed the findings of many previous studies that blood group A has a significant higher risk for gastric cancer than non-A blood groups.

Even though the participants may know their blood group, it is not expected that this knowledge may influence their lifestyle. Consequently, there would not be important differences between blood groups in the prevalence of major risk factors for PUD and gastric cancer like NSAIDs use, alcohol consumption and smoking. So, these potential confounders would not affect the results of this study to a greater extent. For this reason, we did not do adjustment for lifestyle-related variables. All participants were infected with H.pylori, so we did no do adjustment fo H.pylori infection status. Many hypotheses try to explain the ABO interplay with cancer (7). In addition, many hypotheses try to explain the pathogenic mechanism by which the A blood group interplay with gastric cancer. Nakao et al. found a significant increased risk of H.Pylori infection in AA genotype(8). In addition, Shararah *et al.* found a significant relationship between infection with a cytotoxin-associated gene A-positive strain of H. Pylori in blood type A (9). This serotype of H. Pylori is associated with higher risk of gastric cancer (10) (11).However, Robertson *et al.* Concluded no significant relationship between H.pylori infection and ABO blood groups (12). Roberts *et al.* suggested that individuals with blood group A are more prone to have pernicious anemia (13)which is associated with higher risk of gastric cancer (14). Another hypothesis is that blood group A is associated with ulcers accompanied with normal or decreased free acid secretion, and these ulcers have a higher risk of malignant transformation (15). The mechanism of the relationship between ABO blood groups and cancer is still poorly understood and remains a matter of research (7).

The relationship between blood group A and gastric cancer has been concluded by several studies (2) (16) (17) (18) (19).

Some studies found no significant difference in PUD risk among ABO blood groups (8) (20). But some other studies found a significant relationship between blood group O and the development of PUD (21) (22) (18).

The small size of the gastric cancer group is a limitations of this study. In addition, infection of all participants with H.pylori prevented us from studying the difference in the distribution of this infection among blood groups, and whether this difference -if presents- is a cause of different distribution of gastric cancer among these groups. Another limitation is that we did not do adjustment for age and sex. However, this would not affect the results for a great extent, as age and sex distributions are approximate among different groups.

Conclusion

Depending on the results of this study, We found no significant relationship between Rh blood groups and PUD or gastric cancer. We also found no significant relationship between ABO blood groups and PUD. In addition, We found a significant increase in gastric cancer risk in blood group A, while we did not found a significant relationship between non-A groups and gastric cancer. We suggest further large-scale well-designed studies to investigate the relationship

between Rh blood groups and diseases, including PUD and gastric cancer. We also recommend further studies to study the association between ABO blood groups and PUD, because of the diversity of findings in the available literature. Although the correlation between blood group A and gastric cancer has been proved by several studies, we need further research that investigates the feasibility of establishing screening programs for early detection of gastric cancer among people with blood group A, or considering blood group A as a risk factor that may indicate EGD in the presence of upper gastrointestinal symptoms. Finally, we invite health organizations working in Syria to establish epidemiologic studies to detect the prevalence H.pylori infection in the Syrian population, and to take action to limit the spread of this infection, especially after the deterioration of socioeconomic status and health care during the Syrian war.

Author's contribution

Conception and design: Ziad Aljarad, Ahmad Alhamid, Ahmad Mouakeh, Ahmad Sankari Tarabishi

Analysis and interpretation of the data: Ziad Aljarad,Sara Aljarad , Jawhar Aljarad, Husam Abbas

Drafting of the article: Ziad Aljarad,Ahmad Alhamid, Ahmad Mouakeh, Ahmad Sankari Tarabishi

Critical revision of the article for important intellectual content: Ziad Aljarad,Bachir badawi mobaid

Final approval of the article: Bachir badawi mobaid

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