ORIGINAL ARTICLE

Association between ABO Blood Groups and Severity of Dyspepsia in Gunungsitoli, Indonesia

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ABSTRACT

Background. Human blood groups may play a key role in various human diseases. An association has been found between ABO blood groups and both infectious and non-infectious diseases of the gastrointestinal tract and other organs. Dyspepsia is one of the most common encountered gastrointestinal complaints.

Aims. To investigate the association between ABO blood groups and severity of dyspepsia symptoms in a specific ethnic group.

Study Design. Cross-sectional study.

Methods. Consecutive adult Nias tribe dyspepsia outpatients in the General District Hospital, Gunungsitoli Nias, Indonesia, were interviewed using a structured questionnaire between May–June 2018. The severity of dyspepsia was assessed with the Porto Alegre Dyspeptic Symptoms Questionnaire (PADYQ) scoring instrument. ABO blood groups were determined by a standard direct agglutination test. Upper gastrointestinal endoscopy was performed in all participants. Data were statistically analyzed using statistical software. P value less than 0.05 was considered as statistically significant.

Results. Of 66 patients, 54.5% were males, with median age of 47 years (range, 23–67). Majority of the participants had blood group O (48.5%). The most encountered dyspepsia symptom was epigastric pain (66.7%). Participants with blood group type B had significantly more severe dyspepsia symptoms based on total PADYQ score (p=0.017). Participants with blood group type O were more prone to epigastric pain (p=0.015), while blood group type B to bloating (p=0.01) and early satiation (p=0.02).

Conclusion. In outpatients from the Nias tribe with dyspepsia, those with blood group type B had more severe dyspepsia symptoms.

Key Words: ABO blood groups, dyspepsia symptoms, PADYQ score, Porto Alegre Dyspeptic Symptoms Questionnaire

INTRODUCTION

Human blood group antigens are glycoproteins and glycolipids expressed on the surface of red blood cells (RBC) and a variety of human tissues.[1] Blood group antigens are permanent, fixed, lifelong hereditary biological markers, and play a vital role in transfusion safety, genetics, inheritance pattern and disease susceptibility.[2] The association of different blood groups with diseases is important as some of the blood groups are particularly prone to developing certain diseases.[3] The ABO blood type (discovered by Landsteiner, Decastello and Sturli) is the main type of blood group.[4] Studies of relationship between ABO blood groups and diseases have interested researchers since decades.[3]

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Association between ABO blood groups and both non infectious and infectious diseases of the gastrointestinal tract and other organs have been found, although the exact biologic basis for this association remains unknown.[5]

Dyspepsia is one of the most commonly encountered gastrointestinal complaint in outpatients and inpatients.[6] It is a heterogenic abnormality, presenting as one or more complaints or symptoms in upper abdominal area.[7] Based on Rome IV criteria, dyspepsia is the presence of one or more complaints of postprandial fullness, early satiation, epigastric pain and epigastric burning during the past three months and those symptoms must be present for more than six months.[8] The symptoms of dyspepsia could be due to an important structural pathology such as chronic peptic ulcer disease, gastroesophageal reflux, malignancy or it might also present as functional dyspepsia.[6] Due to these pathologies, upper gastrointestinal (UGI) endoscopy is the first approach in differentiating between structural and functional dyspepsia.[9]

Over 80% of the population is affected by dyspepsia at some time in their life. Worldwide investigations have shown that the prevalence of dyspepsia is in the range of 14.5-45%.[6] Dyspepsia is a common finding in Indonesia, with an estimated 30% of cases diagnosed in general practice and 60% in medical specialist practice.[10] Based on the Indonesian Health Profile 2013, in Gunungsitoli, the capital of Nias Island, Sumatera Utara Province, dyspepsia was highly prevalent and ranked 5th in the category of most common diseases.[11]

The presence of etiologic factors with genetic susceptibilities seem to be the main prognostic factors in patients with dyspepsia, where severity and development of dyspepsia might be affected by ABO blood group antigens as a genetic factor.[12] Since the relationship between ABO blood group and dyspepsia is not clear, further study is needed to examine the role of ABO blood group in developing dyspepsia,[3] particularly related to ethnic diversity in Indonesia, especially in Sumatera Utara Province. The aim of our current study was to investigate the association between ABO blood groups, the severity of dyspepsia symptoms, and endoscopic findings in Nias tribe, the indigenous inhabitants of Nias Island.

METHODS

This observational cross-sectional study was carried out at the Department of Internal Medicine, Gunungsitoli General District Hospital, Nias District, Sumatera Utara Province, Indonesia, between May–June 2018. This study followed the Declaration of Helsinki, and was approved by the Health Research Ethical Committee Medical Faculty of University of Sumatera Utara and Haji Adam Malik Central General Hospital (492/TGL/KEPK FK-USU-RSUPHAM/2018). Written informed consent was obtained from all participants.

We included all adult Nias tribe outpatients, aged more than 18, with dyspepsia based on Rome IV criteria; fulfilled by presence of one of the symptoms of postprandial fullness (fullness, discomfort after normal size meal), early satiation (unable to finish normal size meal), epigastric pain, epigastric burning, in which those symptoms has been experienced in the last 3 months with the onset of symptoms at least 6 months before diagnosis. We excluded those with predominant symptoms of gastroesophageal reflux disease (GERD), alarm symptoms (weight loss more than 10% of the previous weight, persistent vomiting, anemia (hemoglobin was less than 13 g/dL for men, and less than 12 g/dL for women), history of upper gastrointestinal bleeding, stomach malignancy), dysphagia, history of peptic ulcer, stomach surgery which omitted some part of gastric mucosa, biliary colic, pregnancy, breast feeding, systemic decompensated disease (congestive heart failure, coronary heart disease, liver failure, diabetes mellitus, thyroid disease, acute or chronic respiratory failure, hematological diseases), major psychiatric disorders, use of non steroid anti-inflammatory drugs (NSAIDs) including low dose treatment up to one week before study inclusion, use of antibiotics, bismuth-containing compounds, proton pump inhibitors (PPIs) or H2-blockers for more than two weeks before study enrollment, impediment to UGI endoscopy and difficulty to understand the aims and procedures of the study.

The patients were interviewed by two trained investigator physicians using structured questionnaire for information on gastrointestinal symptoms, body mass index (BMI), demographic factors and socioeconomic status. Scoring of the severity of dyspepsia symptoms was performed using 11-item Porto Alegre Dyspeptic Symptoms Questionnaire (PADYQ), to evaluate dyspepsia symptoms, including epigastric pain, nausea, vomiting, fullness, and early satiation. Epigastric pain, nausea, upper abdominal bloating was evaluated by its intensity, duration, and frequency; vomiting and early satiation were evaluated by its frequency. Scores for each symptom were averaged and summed. Scores ranged from 0 (no symptoms) to 44 (severe symptoms).[13]

Blood samples were collected by finger prick with a sterile lancet after cleaning the puncture site with 70% ethyl alcohol by conventional glass slide method. ABO blood group determination was performed using commercial monoclonal antibodies kit in a direct agglutination test (ReiGed Diagnostics, UK).

Upper gastrointestinal endoscopy was performed on all consecutive participants using Fujinon Fujifilm EPX2500 video processor and EG530WR forward-viewing gastroscopes by two experienced endoscopists. Endoscopic findings for each participant were recorded. Gastric antral biopsy was taken for rapid urease test (Pronto Dry®, Gastrex, France) to determine *H. pylori* infection.

Data were analyzed using IBM Statistical Package for Social Sciences (IBM SPSS) version 24.0 software. Descriptive statistics were used to characterize patient demographic features; mean and standard deviation (SD) were used for normally distributed numerical variables, and median and minimum-maximum were used for non-normally

distributed numerical variables. Kolmogorov-Smirnov test was used for test of normality. Chi-squared test, Fisher's exact test, T-test, Mann-Whitney U test, One way ANOVA, Kruskal-Wallis test were used wherever applicable. A p-value less than 0.05 was considered statistically significant.

RESULTS

We included 66 consecutive adult outpatients, 36 of whom were males (54.5%). The most encountered dyspepsia symptoms were epigastric pain (66.7%), followed by nausea-vomiting (63.6%), bloating (57.6%) and early satiation (51.5%) with a total median score of PADYQ 31.0 (27.0–36.0) (Table 1). Participants with blood group B had significantly higher PADYQ score than those with other blood groups (p=0.017). There was a significant difference in dyspepsia symptoms scoring between epigastric pain, nausea-vomiting and bloating between ABO blood groups. In epigastric pain symptom, there was a significant difference in scores between blood group A vs AB (p=0.008), B vs O (p=0.006) and AB vs O (p=0.006). For the nausea-vomiting symptom, there was a significant difference in score between blood group B vs O (p=0.015) and AB vs O (p=0.019). For the bloating symptom, there was a significant difference of score between blood group A vs AB (p=0.013), A vs O (p=0.014), B vs AB (p=0.008) and B vs O (p=0.03). The most common identifiable endoscopic lesions were gastritis in 58 patients (81.8%), followed by esophagitis in 14 patients (21.2%) and duodenitis in 10 patients (15.2%). Gastric ulcer, gastritis atrophy and duodenal ulcer were noted in two patients (3.0%) respectively. Dyspepsia symptoms and endoscopic findings based on ABO blood groups distribution are displayed in Table 2.

The PADYQ score was higher in female subjects, age more than 40 years, single marital status, low level education, underweight, current/former smoker, current/former alcoholic consumption and household crowding more than five persons. Blood group type O was more prone to epigastric pain (39.4%, p=0.015), while blood group type B to bloating (30.3%, p=0.01) and early satiation (27.3%, p=0.02). (Table 3)

Blood group type O had more prevalent lesions in esophagus compared to other blood group types (p=0.465), while in gaster and duodenum no difference endoscopic lesions were found statistically within blood groups. (Table 4)

Table 1. General characteristics of study participants (N=66)

Characteristics	n (%)	PADYQ score Median (Range)	p-value
Sex			
Male	36 (54.5)	31.0 (27.0–36.0)	0.68*
Female	30 (45.5)	32.0 (27.0–35.0)	
Age (years)			
≤ 40	26 (39.4)	31.0 (28.0–36.0)	0.22*
> 40	40 (60.6)	31.0 (27.0–34.0)	
Marital status			
Married	56 (84.8)	30.5 (27.0–35.0)	0.047*
Single	10 (15.2)	32.0 (31.0–36.0)	
Level of education			
Low	48 (72.7)	31.0 (28.0–36.0)	0.11*
High	18 (27.3)	30.0 (27.0–33.0)	
Blood groups			
A	4 (6.1)	29.0 (28.0–30.0)	0.017†
B	26 (39.4)	33.0 (29.0–36.0)	
AB	4 (6.1)	29.0 (27.0–31.0)	
O	32 (48.5)	31.5 (27.0–34.0)	
Helicobacter pylori status			
Positive	2 (3.0)	31.5 (29.0-34.0)	0.784*
Negative	64 (97.0)	31.0 (27.0-36.0)	
Body Mass Index (BMI)			
Underweight (< 18.5 kg/m^2)	14 (21.2)	31.0 (29.0–36.0)	0.32†
Normal (18.5–24.9 kg/m^2)	36 (54.2)	31.5 (27.0–35.0)	
Overweight (>25 kg/m^2)	16 (24.2)	30.0 (27.0–33.0)	
Occupation			
Employee	18 (27.3)	30.0 (27.0-33.0)	0.006†
Retired	6 (9.1)	28.0 (28.0-31.0)	
Housewife	16 (24.2)	29.5 (27.0-35.0)	
Entrepreneur	12 (18.2)	32.5 (29.0-36.0)	
Farmer	14 (21,2)	32.0 (30.0-34.0)	
Family monthly income (IDR)			
≤2.500.000	44 (66.7)	31.0 (28.0–36.0)	0.96*
>2.500.000	22 (33.3)	31.0 (27.0–35.0)	
Smoking status			
Current/former	20 (30.3)	31.5 (30.0–36.0)	0.03*
Never smoked	46 (69.7)	30.0 (27.0–35.0)	
Alcohol consumption			
Current/former	16 (24.2)	32.0 (27.0–35.0)	0.046*
No consumption	50 (75.8)	30.0 (27.0–36.0)	
Household (no. of persons)			
≤5	34 (51.5)	31.0 (27.0–36.0)	0.60*
>5	32 (48.5)	32.0 (27.0–35.0)	

PADYQ, Porto Alegre dyspeptic symptoms questionnaire
**Mann-Whitney U test; †Kruskal-Wallis test with post hoc Mann-Whitney U test, data expressed as median (minimum-maximum); p< 0.05*

DISCUSSION

Nias is an island located on the western coast of Sumatera, administratively are part of Sumatera Utara Province, Indonesia. Nias Island covers an area of 5,121.3 km^2/1,977.3 sq mi (including the minor offshore islands). The population in this area was 788,132 inhabitants in January 2014 including Ono Niha (the indigenous inhabitants of the island), Malay, Batak, and Chinese.[14] This current study about the association between ABO blood groups, severity of dyspepsia symptoms and endoscopic findings in Nias tribe dyspepsia patients is the first one conducted in Gunungsitoli, Nias Island.

Mahadeva et al. in a population-based study reported that male-to-female ratio in dyspepsia was generally

Table 2. Distribution of ABO blood groups based on dyspepsia symptoms and endoscopic findings (N=66)

	Blood groups				Total	p-value
	A	B	AB	O		
Dyspepsia symptoms (PADYQ score)						
Epigastric pain						
n (%)	4 (6.1)	14 (21.2)	0 (0.0)	26 (39.4)	44 (66.7)	
Median (range)	9.0 (9.0–9.0)	9.0 (8.0– 10.0)	8.0 (8.0– 8.0)	9.0 (8.0-12.0)		0.003†
Nausea-vomiting						
n (%)	2 (3.0)	20 (30.3)	4 (6.1)	16 (24.2)	42 (63.6)	
Median (range)	11.0 (9.0–13.0)	12.0 (9.0–14.0)	12.0 (12.0–12.0)	9.5 (9.0–13.0)		0.035†
Bloating						
n (%)	4 (6.1)	20 (30.3)	0 (0.0)	14 (21.2)	38 (57.6)	
Median (range)	10.5 (10.0–11.0)	10.0 (9.0– 12.0)	9.0 (9.0–9.0)	9.0 (8.0–11.0)		0.001†
Early satiation						
n (%)	0 (0.0)	18 (27.3)	2 (3.0)	14 (21.2)	34 (51.5)	
Median (range)	1.0 (1.0–1.0)	2.0 (1.0–4.0)	1.5 (1.0–2.0)	1.5 (1.0–3.0)		0.059*
Median PADYQ score	29.0 (28.0–30.0)	33.0 (29.0–36.0)	29.0 (27.0–31.0)	31.5 (27.0–34.0)		0.017†
Endoscopic findings						
Esophagus						
Normal	4 (6.1)	22 (33.3)	2 (3.0)	24 (36.4)	52 (78.8)	
Esophagitis	0 (0.0)	4 (6.1)	2 (3.0)	8 (12.1)	14 (21.2)	
Gaster						
Normal	0 (0.0)	2 (3.0)	2 (3.0)	2 (3.0)	6 (9.1)	
Gastritis erythematous	2 (3.0)	12 (18.2)	2 (3.0)	14 (21.2)	30 (45.5)	
Gastritis erosive	2 (3.0)	10 (15.2)	0 (0.0)	12 (18.2)	24 (36.4)	
Gastric ulcer	0 (0.0)	0 (0.0)	0 (0.0)	2 (3.0)	2 (3.0)	
Gastritis atrophy	0 (0.0)	0 (0.0)	0 (0.0)	2 (3.0)	2 (3.0)	
Gastropathy	0 (0.0)	2 (3.0)	0 (0.0)	0 (0.0)	2 (3.0)	
Duodenum						
Normal	0 (0.0)	20 (30.3)	2 (3.0)	32 (48.5)	54 (81.8)	
Duodenitis	4 (6.1)	4 (6.1)	2 (3.0)	0 (0.0)	10 (15.2)	
Duodenal ulcer	0 (0.0)	2 (3.0)	0 (0.0)	0 (0.0)	2 (3.0)	

PADYQ, Porto Alegre dyspeptic symptoms questionnaire
**Mann-Whitney U test; †Kruskal-Wallis test with post hoc Mann-Whitney U test, data expressed as median (minimum-maximum); p< 0.05*

Table 3. Association between dominated blood group type and dyspepsia symptoms (N=66)

Blood groups	Dyspepsia symptom		X^2	p-value
	Epigastric pain			
	Present	Absent		
O	26	6	5.95	0.02
Non O	18	16		
	Nausea/vomiting			
	Present	Absent		
B	20	6	3.27	0.07
Non B	22	18		
	Bloating			
	Present	Absent		
B	20	6	6.57	0.01
Non B	18	22		
	Early satiation			
	Present	Absent		
B	18	8	5.39	0.02
Non B	16	24		

Table 4. Association between dominated blood group type and endoscopic findings (N=66)

Blood groups	Organ		Total	p-value
	Esophagus			
	Normal	Abnormal		
O	24	8	32	0.465*
Non O	28	6	34	
	Gaster			
	Normal	Abnormal		
O	2	30	32	0.673†
Non O	4	30	34	
	Duodenum			
	Normal	Abnormal		
B	20	6	26	0.517†
Non B	34	6	40	

**Chi-square test; †Fisher's exact test*

comparable.[15] In our study male-to-female ratio was 1.2:1 which is similar to another study stating that men experienced UGI tract disease and dyspepsia more than women. Our study shows a male preponderance most probably due to the increased consumption of alcohol beverage (called Tuak Nias) and smoking, which play a key role in pathogenesis of dyspepsia. And this finding also might be attributed to the fact that women's health problems were still not given priority and fewer women present with dyspepsia to health facilities than men.[16]

In this study, it was found that the median age of dyspepsia patients was 47 years old. It was in concordance with study performed by Garg et al. and Mustapha et al. which reported that the average age of dyspepsia patients were 47 years and 47.2 years, respectively.[17,18] Very few UGI tract diseases presented before the age of 20 years, peaking in the fifth decade (i.e., more prevalent in the older age group).[19]

It has been observed that the percentage of blood groups distribution in different parts of the world varies depending upon the ethnic origin of the races. Nakao et al. reported that stomach diseases was closely linked with genotypes of human ABO blood groups.[20] In our study, blood group O was the most common blood group among dyspepsia patients, similar to previous epidemiological studies by Jaff (2011), Mohammed et al. (2015) and Baqir et al. (2016).[21–23]

Using PADYQ score as a tool to evaluate severity of dyspepsia, we found that epigastric pain was the most common symptom experienced by dyspepsia patients, followed by nausea-vomiting, bloating and early satiation. This study was in line with study from Abdeljawad et al. which concluded that epigastric pain (76.6%) was the most frequent symptom experienced by dyspepsia patients. Less patients experienced nausea-vomiting, bloating and early satiation.[24] In this current study, we found that blood group type O was significantly more prone to epigastric pain compared to other blood groups. Blood group type B in our study was more prone to nausea-vomiting, bloating and early satiation. This result is not so different from Jaff et al. and Aryana et al.[21,25] A study from Hanley showed that blood group culminates the development of secretory cell mass, reinforcing that gastric peptic cell mass is larger in particular blood groups.[26] So far, to our knowledge there has been no reasonable explanation yet for this special phenomena, which might be on a molecular level.

There was significant association between dyspepsia symptoms based on PADYQ score with marital status, smoking status and alcohol consumption. However, the association between PADYQ score to sex, age, BMI, educational level, number of household members and low socioeconomic status was not significant. These may also be due to wide social difference, dietary habits, lifestyle and the study methods, or study type.[16]

The results of endoscopic examination demonstrated that gastritis was the most common finding (81.8%). This finding is similar to the results obtained by Faintuch et al. (61%) and Jemilohun et al. (60.5%).[27,28] There was considerable overlap in the endoscopic findings in study participants as many of them with one endoscopic lesion also had other endoscopic lesions.

There are several causes of dyspepsia, including *H. pylori* infection. Many studies have demonstrated the role of *H. pylori* as the cause of dyspepsia, especially organic dyspepsia, manifested as peptic ulcer disease and gastritis. *H. pylori* may also produce varied symptoms in different people.[29] In this study, the result of positive *H. pylori* examination was only in two participants. Therefore, the association of this variable to sample size was less important.

Some limitations of this study were the short duration, unknown etiological factors like genetic, dietary differences and limited to a hospital setting. A community-based study is therefore desirable as this is usually more representative.

This study may be beneficial to predict the abnormality of UGI tract by evaluating patients' symptoms and ABO blood groups before performing UGI endoscopy.

CONCLUSION

From this study conducted in Gunungsitoli, Nias, we found that blood group type O was more prevalent in dyspepsia patients. Epigastric pain was the most encountered symptom of dyspepsia. Blood group type B had more severe dyspepsia symptoms. Blood group type O was more prone to epigastric pain, while blood group type B to nausea-vomiting, bloating and early satiation. Blood group type O had more prevalent lesions in esophagus compared to other blood types. The prevalence of *H. pylori* infection was low.

Acknowledgment

Author thanks Dr. Kanserina Dachi and staff of Department of Internal Medicine Gunungsitoli General District Hospital, Nias District, Sumatera Utara Province, Indonesia for their support to this research.

Statement of Authorship

All authors participated in drafting the protocol. OKY designed, managed the study, did endoscopy, interpreted the data, drafted and wrote the manuscript. GAS was involved in preparing and critical checking of the manuscript. LHZ analyzed data and critical checking of the manuscript. LBD took part in collection of data, laboratory works and preparation of the manuscript. All authors read and approved the final manuscript submitted.

Author Disclosure

The authors declared no conflicts of interest.

Funding Source

This paper was funded by all authors.

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