The Relationship Between *Helicobacter pylori* Infection and the Risk of Gastroesophageal Reflux Disease (GERD) in Batak Ethnics in Boho Village, Sianjur Mulamula District, Samosir Regency, North Sumatra Province

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ABSTRACT

Introduction: Gastroesophageal reflux disease (GERD) is one of the most common disorders of the digestive tract with an increasing prevalence. Epidemiological studies have found an increased prevalence of H. pylori infection with GERD. H. pylori has a high incidence in Asian countries. In Indonesia, the incidence of H. pylori infection remains unclear and controversial.
Aim: This research aims to analyse relationship between H. pylori infection with risk of GERD in Batak ethnicity in BOHO Village, Sianjur Mulamula District, Samosir Regency, North Sumatra Province.
Methods: This research is a cross-sectional analytical study. Research subjects were asked to fill out a demographic questionnaire, GERD questionnaire, and perform a fecal antigen test (FAT).
Results: A total of 100 participants who met the criteria were included in this study. The majority of research subjects were male, had normal BMI, and had no history of smoking or taking NSAIDs. Twenty percents of participants had a risk of GERD and positive FAT results were found in 17% of participants.
Conclusion: Chi-square test showed no association between H. pylori infections and the risk of GERD with p-value of 0.741.

Keywords: GERD, H. pylori, FAT, GERD-Q

INTRODUCTION

Gastroesophageal reflux disease (GERD) is one of the most common gastrointestinal tract disorders with an increasing prevalence (1). GERD is defined as a condition resulting from reflux of gastric contents causing symptoms that can be accompanied by disturbing complications (2,3). Based on a systematic review and meta-analysis conducted by Nirwan, et al in 2020, the prevalence of GERD varies widely. On the Asian continent with a general prevalence of 12.92%, East Asia has the lowest prevalence, while the Middle East has the highest prevalence (4). Epidemiological studies have found an increasing prevalence of H. pylori with GERD. This raises suspicion on the site of infection from H. pylori and gastric acid secretion. (5) On the other hand, epidemiological data found an increase in the incidence of GERD which was associated with an increase in the success of H. pylori eradication (6). H. pylori has a high incidence in Asia with a high prevalence in China and Japan.(7) The incidence is associated with race found in Asia, there are several countries with an incidence H. pylori which is low as in ethnic Malays seen in Malaysia (8). In Indonesia, the incidence of H. pylori infection remains unclear and controversial because Indonesia is a multiethnic country (incidence ranges from 5.7 – 68%).(8,9) Papua, Batak, and

Bugis ethnicities were found to have a higher risk of H. pylori infection compared to the Javanese, Dayak, and Chinese (10). Incidence of H. pylori in children of developing countries are ranging from 30 to 50% and are increasing with age (90%). This is associated with poor sanitation and lifestyle because the transmission of these bacteria is from oral-oral and fecal-oral route. In addition to lifestyle, H. pylori infection can also be affected by low economic status, normal microbiota and flora, use of clean water, and diet (11).

MATERIALS & METHODS
Participants

Individuals aged >18 years in BOHO Village, Sianjur Mulamula District, Samosir Regency, North Sumatra Province in October 2021with positive Fecal Antigen Test (FAT) and Urea Breath Test (UBT) results, and willing to become respondents were included in this study. Individuals who had undergone *H. pylori* eradication therapy and had GERD at the time of sampling were excluded from this study. A total of 100 participants who met the inclusion and exclusion criteria were included in this study.

Procedure and ethical considerations

The Ethical Committee of University of Universitas Sumatera Utara approved of the study protocol. The researcher informed each participant about the purpose of the study. Furthermore, all participants were informed of their rights to refuse or to discontinue their participation, according to the ethical standards of the Helsinki Declaration of 1983. Participation in the study was contingent on individual verbal consent.

Measures

Research subjects were asked to fill out a demographic questionnaire and GERD-Q. Cut-off ≥9 on GERD-Q is used to determine the presence of GERD in participants. FAT examination is then carried out to assess the presence of *H. pylori* infection by asking the patient to collect the stool in the container provided. The stool specimen should not be contaminated with water or urine. The specimen is then examined as soon as possible (<18 hours). Detection of *H. pylori* antigen in feces was carried out using an Enzyme Immunoassay (EIA). This test is a rapid immunochromatographic test which is a qualitative detection of H. pylori bacteria. The kit uses a specific monoclonal antibody against *H. pylori* antigen. During the test, the stool sample will react with red latex particles coated with anti-*H. pylori* monoclonal antibodies. In the case of a positive sample, the antigen-antibody complex particles migrate along the membrane coated with anti-*H.pylori* monoclonal antibody in the area of test line. The specific antibody reacts with the antigen-antibody particle complex and forms a red line in the T-line area. The green line control indicates the test migration was successful.

STATISTICAL ANALYSIS
This research is a cross-section analytical study. A descriptive analysis was used to identify samples' characteristics. Chi-square tests of correlations were computed to compare observed frequencies with expected frequencies. All statistical analyses were performed using the Statistical Package for Social Sciences, Version 23.0 for Windows.

RESULT
Characteristics of Research Subjects

This study is conducted in 100 participants consisting of 60 males (60%) and 40 females (40%). Most of the subjects have normal BMI, namely in 38 people (38%) followed by grade I obesity, namely in 28 people (28%).

Table 1. Characteristics of Research Subjects

Characteristics	Total (n)	Percentage (%)
Age		
> 60 years	77	77
≤ 60 years	23	23
Gender		
Male	60	60
Female	40	40
Body Mass Index (BMI)		
Underweight	4	4
Normal	38	38
Overweight	27	27
Obese grade I	28	28
Obese grade II	3	3

Helicobacter pylori infection

In the FAT examination, it was found that the majority of research subjects had negative FAT results. The research subjects who had positive results were found in 17 participants (17%), while the subjects who had negative results for *H. pylori* were found in 83 participants (83%).

Table 2. Fecal Antigen Test (FAT) Examination Results.

Fecal Antigen Test (FAT)	n	Percentage (%)
Positive	18	18
Negative	82	82

Risk of Gastroesophageal Reflux Disease (GERD)

There were 20 participants (20%) who were at risk for GERD and 80 participants (80%) who did not have a risk for GERD.

Table 3. Risk of Gastroesophageal Reflux Disease (GERD)

GERD-Q	n	Percentage (%)
At risk	20	20
No Risk	80	80

The Relationship between Helicobacter pylori Infection and the Risk of Gastroesophageal Reflux Disease (GERD)

Chi-square test showed no relationship between age and the results of the FAT examination with a p-value of 0.757. Gender and nutritional status were also showing no relationship to the FAT examination with p-values of 0.534 and 0.219.

Table 4. Relationship of *Helicobacter pylori* infection based on *Fecal antigen test* (FAT) with GERD Risk

Variable	Fecal Antigen Test (FAT)		p value
	Positive	Negative	
Age			0.757[a]
< 60 years old	15	62	
≥ 60 years old	3	20	
Gender			0.534[a]
Male	10	52	
Female	8	30	
Nutritional status			
Underweight	1	3	0.219[a]
Normoweight	5	33	
Overweight	5	22	
Obese grade I	5	23	
Obese grade II	2	1	

[a]*p-value* is consider significant if <0.05

The Relationship between Risk Factor and the Gastroesophageal Reflux Disease (GERD) Test on Helicobacter pylori infection variables based on the results of the Fecal antigen test (FAT) with the risk of GERD using the Chi-Square test shows no relationship between *Helicobacter pylori* infection and the risk of GERD with a p-value of 0.367.

Variable		Stool Antigen Test		Total	P value
		Positive	Negative		
GERD-Q	Yes	6	19	25	
	No	12	63	75	0.367[a]
Total		18	82	100	

[a]*p-value* is considered significant if <0.05

DISCUSSION

The role of *H. pylori* (HP) infection for GERD was first reported by Labenz in 1997. The pathogenesis of GERD is based on its potential to increase gastric acid secretion (12). The Fecal Antigen Test (FAT) is a non-invasive test that is easy, fast and inexpensive and can assess response to antimicrobial treatment with a sensitivity of 94% and a specificity of 92%. FAT is widely used in Indonesia. Enzyme immunoassay (EIA) is a FAT method based on polyclonal antibodies and has been shown to have high accuracy. EIA-based tests, such as the Premier Platinum HpSA commercial kit, can be used in Indonesia (15).

In this study, Fecal Antigen Test (FAT) were dominantly positive in samples aged <60 years, namely 15 samples, while in those aged ≥60 years, only 3 samples were positive. In the data analysis conducted, it

was found that there was no relationship between age risk factors and FAT (p-value 0.757). This is in line with research conducted by Kabido *et al.* where H.pylori infection was not related to age (p>0.05). This may also imply that all age groups have additional risk of exposure (16).

Genetiano & Magtibay conducted a similar study on 104 participants ranging from 15 – 76 years old. In this study, the ages were classified into 13-18 years, 19-59 years and ≥60 years. Positive FAT was more dominant in those aged <60 years, namely 62 samples aged 19-59 years and 6 samples aged 13 – 18 years. Whereas in the age category ≥60 years, only 2 samples were detected positive. These findings support the result that *H. pylori* seroprevalence increases with age. It is estimated that *H. pylori* infection affects more than half of the adult population worldwide and is now responsible for 75% of all stomach cancer cases (17).

In this study, the dominance of positive FAT results was obtained in males (10 samples) compared to females (8 samples). The results of the chi-square analysis obtained a p-value of 0.534, which means that there is no significant relationship between gender and FAT. Research by Temeshkel *et al.* (2018) found that no association was observed between gender and *H. pylori* infection (p=0.284) (18). These results are not in accordance with the research conducted by Eidha & Huda (2021) on 100 research samples which stated that there was a significant relationship between male (p=0.035) on the incidence of *H. pylori* using FAT examination. Because of this variation, further research is needed to look at the sex-specific relationship to positive FAT results (19).

In this study, each BMI category of normoweight, overweight and obesity grade I had 5 research samples with positive FAT results. Whereas in Obese grade II, there were 2 research samples that had positive FAT results and 1 study sample with positive FAT result who had an underweight

BMI. From the results of the research analysis conducted, there was no significant relationship between BMI and FAT (p= 0.219). Similar research was also conducted in 2018 by Alzahrani *et al.* which was carried out on 2 different types of subjects, namely subjects with type 2 diabetes mellitus and non-diabetic subjects. Significant results were found in non-diabetic subjects so that there was a relationship between BMI in *H. pylori* infection, which was higher in samples with overweight and obesity (p= 0.013). Meanwhile, in the study sample with type 2 diabetes mellitus, no significant results were obtained with respect to age, gender or BMI (20).

In this study, the results were obtained for patients with a risk of Gastroesophageal Reflux (GERD) who were assessed using the GERD-Q. In the age category <60 years, there were 20 samples and ≥60 years were 5 research samples. The results of the chi-square analysis also showed no significant difference between age and the risk of GERD (p=0.681). Research conducted by Alrashed *et al.* in 400 students aged 18 – 27 years revealed that GERD is a common problem in this population with a prevalence of 23.8%. Previous study has shown that university students have a higher prevalence of GERD when compared to the general population. This is likely due to the fact that students are more exposed to various risk factors for GERD namely stress and higher consumption of caffeine. However, due to the narrow age range in this population it is understandable that age as a GERD factor is not statistically significant in this study. However, general study population reports indicate that GERD prevalence is associated with increasing age (21).

In contrast, research by Carlos *et al.* (2020) in 1,069 subjects found that age is associated with the incidence of GERD (p <0.001). GERD can develop in a younger age population but remains a disease whose severity increases with age with the highest incidence being found between the ages of

60 – 69 years. GERD in the elderly is associated with physiological changes in the digestive tract, increased gastric acid secretion, and delayed peristalsis and gastric emptying (22).

The results of the study showed that the number of samples with male gender was greater in the results of the GERD-Q examination, namely 16 research samples compared to 9 female samples. Chi-square analysis shows a p-value of 0.812 so it was concluded that there was no significant relationship between gender risk factors and GERD risk. In a study conducted by Alrashed, regarding the relationship between gender and GERD risk, male students have a higher risk of developing GERD than female students (21).

This study obtained a dominant sample with positive results with a normoweight Body Mass Index (BMI) interpretation of 8 research samples followed, 7 samples with Obese grade I BMI, 6 overweight samples and research samples with underweight BMI and Obese grade II with respectively - each as many as 2 research samples. The results of the analysis also showed that there was no significant relationship between BMI risk factors and GERD (p = 0.299). Research conducted by Carlos *et al.* also showed an insignificant relationship (p=0.162). Obesity and BMI are risk factors for reflux disease (especially in Western populations). The relationship between these two variables is not coincidental because the pathophysiology of GERD is mostly related to overweight and obesity (23).

In a study conducted on a population of all individuals who were infected with *H. pylori* on Samosir Island in October 2021. At a minimum calculation of 52 samples were taken which had to meet the criteria of the study, namely individuals aged 18-50 years, samples that would later carry out examination of the Fecal Antigen Test (FAT) and all of these samples were willing to become respondents and signed an informed consent. Individuals who had undergone H. pylori eradication therapy and who had experienced GERD at the time of sampling were the exclusion criteria in this study. In a study conducted by Alzoubi *et al,* it was concluded that FAT can be used in individuals who have undergone eradication therapy to assess the success of treatment of H. Pylori infection. Therefore, individuals who meet these criteria are excluded because they can affect the results of the study (24).

The Fecal Antigen Test in this study showed that more research subjects had negative results for Helicobacter pylori infection than subjects who had positive results. The study subjects who had positive results on the Fecal Antigen Test (FAT) were as many as 18 people (18%), while the subjects who had negative results was 82 people (82%) .

Based on the GERD-Q score, 20 people (20%) are at risk for GERD and 80 people (80%) do not have GERD risk. Research conducted by Simarmata *et al.,* in 2020 showed a significant correlation between GERD-Q in patients suspected of having GERD in the Endoscopy unit of Hasan Sadikin Hospital (25).

In this study a test was carried out on the *H. pylori* infection based on the results of the Fecal antigen test with the risk of GERD using the Chi-Square test. The significance value indicates that there is no relationship between *H. pylori* infection and the risk of GERD with a p-value of 0.367. These results are in line with a study conducted by Niknam *et al* on 1916 patients where 45.6% of the respondents were diagnosed with GERD which found no significant difference from *H. pylori* findings in patients with GERD and without GERD (26).

Another study conducted in healthy young Japanese volunteers, conducted by Tanaka *et al.,* aimed to determine the prevalence and risk factors for *H. pylori* and GERD and their risk factors. This study was in line with our study where *H. pylori* infection had no effect on the prevalence of GERD, but obesity was a risk factor for GERD.

Research conducted by Kurniawan *et al* in 2019 also showed no differences in *H. pylori* antigen in GERD and non-GERD patients at Atma Jaya Hospital (27). Based on the results of this study and the findings of other studies that have been presented in this section, it is also necessary to consider other risk factors other than *H. pylori* infection. Infection from *H. pylori* is still a controversy as a definite causative factor for GERD, both from its mechanism as a protective or aggressive factor. Age, gender, and even obesity are other factors that can be considered as the development of GERD

CONCLUSION

This study shows that there is no relationship between H. pylori infection and the risk of GERDThere are Batak ethnic groups on Samosir Island, but the data available does not provide sufficient evidence to determine the true relationship between the two. Therefore, further research is needed that considers risk factors for GERD other than HP infection.

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