Prevalence of H. Pylori Infection in Liver Cirrhosis Patients in Makassar: A Descriptive Study

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INTRODUCTION

Helicobacter Pylori (H. Pylori) is a common human pathogen and it is estimated that around 50% of the world's population is infected, while in developing countries the proportion reaches 90%. Data on the prevalence of H. pylori infection in Indonesia at general about 20%, but is much higher among several ethnic groups (Papuan 42.9%, Batak 40.0%, and Bugis 36.7%).[1,2]

According to WHO, H. pylori is a class I carcinogenic factor. H. Pylori is a microaerophilic, Gram-negative bacillus, resistant to gastric juice. It can be in vegetative form (spiral form) or sporulation form. H. pylori lives mainly on the surface of the prepyloric mucosal epithelial cells in the gastric, causing an increase in the pro-inflammatory cytokine interleukin (IL) in the gastric mucosa, such as IL-1, IL-2, IL-4, IL -6, IL-8, IL-10, IL-17, interferon-β, and tumor necrosis factor-α (TNF-α). This phenomenon exacerbates various systemic inflammatory reactions, one of which is in patients with liver cirrhosis.[3]

H. pylori infection affects lipid metabolism disorders, manifested by hypertriglyceridemia and hypercholesterolemia, along with a decrease in high-density lipoprotein. It is essential in hepatocyte metabolism, steatosis, and liver fibrosis. [(3)] Liver cirrhosis is the final stage characterized by the replacement of normal hepatocyte cells with fibrotic tissue. Cirrhosis is the leading cause of chronic liver disease-related deaths in the Asia-Pacific region, accounting for 630 843 (48·2%) deaths in 2015, compared with 46 941 (64·8%) in the United States and 115 075 (58·4%) people in Europe. Cirrhosis-related deaths in the Asia-Pacific region in 2015 represented 54·3% of 1 161 914 cirrhosis-related deaths globally. [4,5]

The severity of cirrhosis is related to the prognosis which can be assessed using the Child-Pugh criteria as a valid predictor in predicting patient survival. The Child-Pugh criteria consist of five parameters, namely serum bilirubin, serum albumin, ascites, prothrombin elongation which describes liver metabolic function and *hepatic encephalopathy* which describes the severity of portal hypertension.[6]

In liver cirrhosis, pathological lesions often appear on the gastric mucosa. Portal hypertensive gastropathy is the most common chronic inflammatory condition. H. pylori infection in the group of liver cirrhosis sufferers can directly influence the exacerbation of inflammatory lesions in the gastric and can indirectly cause liver function disorders, by triggering exacerbations in patients with chronic liver disease.[7]

Alarfaj SJ et al in Egypt found a prevalence of H. Pylori infection of 19.1% of 340 patients with liver cirrhosis who underwent upper gastrointestinal endoscopy (UGIE) and then examined for H. Pylori using histology. Yadav et al on 100 patients who underwent UGIE and were examined using the rapid urease test for H pylori infection, found that 46% were positively infected with this bacteria.[8,9]

Feng H et al, found in a meta-analysis study that the prevalence of H. pylori infection in liver cirrhosis patients was highest in Europe (88.98%) and lowest in Asia (31.85%). Compared with Asia (43.73%), the prevalence of H. pylori infection in liver cirrhosis patients was shown to be significantly higher in Europe (72.12%) and America (45.78%). In Indonesia itself, there has been no research data on the prevalence of H. Pylori infection in liver cirrhosis patients.[10]

Liver cirrhosis is a serious threat to public health worldwide, which can progress to hepatocellular carcinoma. Patients with cirrhosis are found to have gastric manifestations in the form of portal hypertensive gastropathy. Based on endoscopy screening, it was found that the frequency of peptic ulcers in liver cirrhosis patients increased to 5-20% compared to 2-4% in the general population. Due to the high rate of life-threatening complications such as peptic ulcers, hepatic encephalopathy (EH), and upper gastrointestinal bleeding, it is considered important to carry out prevalence research so that optimal treatment can be done, considering the large costs that must be incurred related to complications caused by comorbidities, especially cirrhosis and H. Pylori infection.[10]

H. pylori infection, diagnosed with endoscopy or biopsy and non-invasive. Invasive examinations include histological staining (hematocycline and eosin, *Alcian blue stain* , and *modified silver stain*), culture, rapid urease test, and molecular detection with DNA PCR. Meanwhile, non-invasive methods include *urease breath test* (UBT), fecal antigen test and serological test. [11]

METHODS

A cross-sectional study, hospital-based at the Gastroenterohepatology Division, HAM Akil Gastoenterohepatology and Endoscopy Center at Wahidin Sudirohusodo Hospital and the Education Network of the Department of Internal Medicine, Hasanuddin University, Makassar. A 245 diagnosed liver cirrhosis patients were included in this study. The duration of the study is 5 years (during the period January 2018 to December 2022).

Inclusion Criteria: 1. Age greater than or equal to 18 years, 2. liver Patients cirrhosis with H. pylori infection diagnosed by upper gastrointestinal endoscopy (UGIE). **Exclusion Criteria:** 1. Age < 18 years 2. Patients with incomplete clinical and laboratory data. Written informed consent was taken from all patients. Histroy taking and a physical examination is performed, the patient undergoes the following investigations: liver function tests, prothrombin time and etiology. HBsAg Viral Marker, Anti-VHC, abdominal ultrasound. All

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patients also underwent an *Upper Gastrointestinal Endoscopy* (UGIE) examination and *H. Pylori examination* (based on the histopathology results of biopsy tissue in the stomach). Patients were categorized based on different Child-Turcotte-Pugh (CTP) scoring systems. The prevalence of H pylori infection was calculated in patient subgroups.

RESULTS

The sample of 245 liver cirrhosis patients. The subjects' age was between 20 – 81 years with a mean of 52.2 ± 11.6 years, where the majority (77.6%) of liver cirrhosis patients were male.

Table 1. Patient characteristics

Characteristics	**N**	**%**
Age (years)		
20 – 29	11	4.5
30 – 39	20	8.5
40 – 49	60	24.5
50 – 59	82	33.5
60 – 69	59	24.1
>= 70	13	5.3
Gender		
Man	190	77.6
Woman	55	22.4
Etiology		
Hepatitis B	98	40
Hepatitis C	13	5.3
Non-Viral	134	54.7
Child-Turcotte-Pugh (CTP) Score		
A	78	31.8
B	149	60.8
C	18	7.3

The most common etiology of causes of cirrhosis in our study was non-viral at 54.7%, followed by viral causes such as hepatitis B virus (HBV) at 40% and hepatitis C virus (VHC) at 5.3%. Meanwhile, on average, patients who come to our hospital are already at CTP B stage, 60.8% (table 1).

The prevalence of H. Pylori in liver cirrhosis found in the study was 1.6% (4 of 245) (table 2). The prevalence of H. Pylori is highest in patients with liver cirrhosis, namely aged 50-59 years (3.7%) (table 3). H. Pylorii in liver cirrhosis is highest in men (2.1%) (table 4).

Table 2. H. Pylori

H. Pylori	n	%
Positive	4	1.6
Negative	241	98.4
Total	245	100.0

Table 3. Distribution of H. Pylori according to Age

Age (years)		H. Pylori		Total
		Positive	Negative	
20-29	n	0	11	11
	%	0.0%	100.0%	100.0%
30-39	n	0	20	20
	%	0.0%	100.0%	100.0%
40-49	n	1	59	60
	%	1.7%	98.3%	100.0%
50-59	n	3	79	82
	%	3.7%	96.3%	100.0%
60-69	n	0	59	59
	%	0.0%	100.0%	100.0%
>=70	n	0	13	13
	%	0.0%	100.0%	100.0%
Total	n	4	241	245
	%	1.6%	98.4%	100.0%

Table 4. Distribution of H. Pylori according to gender

Gender		**H. Pylori**		**Total**
		Positive	**Negative**	
Man	n	4	186	190
	%	2.1%	97.9%	100.0%
Woman	n	0	55	55
	%	0.0%	100.0%	100.0%
Total	n	4	241	245
	%	1.6%	98.4%	100.0%

Table 5. Distribution of H. Pylori according to HBV and HCV infection

H. PYLORII									
Hepatitis B			**Positive**	**Negative**	**Total**	**Hepatitis C**		**Positive**	**Negative**	**Total**
Reactive		n	2	96	98	Reactive	n	2	11	13
		%	2.0%	98.0%	100.0%		%	15.4%	84.6%	100.0%
Non Reactive		n	2	145	147	Non Reactive	n	2	230	232
		%	1.4%	98.6%	100.0%		%	0.9%	99.1%	100.0%
Total		n	4	241	245	Total	n	4	241	245
		%	1.6%	98.4%	100.0%		%	1.6%	98.4%	100.0%

Table 6. Distribution of H. Pylori according to CTP

CTP			H. Pylori		Total
			Positive	Negative	
	A	n	3	75	78
		%	3.8%	96.2%	100.0%
	B	n	1	148	149
		%	0.7%	99.3%	100.0%
	C	n	0	18	18
		%	0.0%	100.0%	100.0%
Total		n	4	241	245
		%	1.6%	98.4%	100.0%

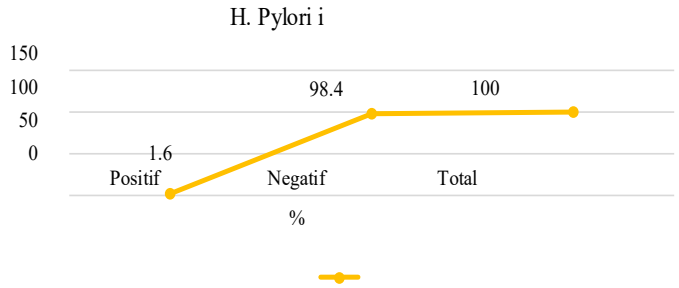

Figure 1. Graph Prevalence of H. Pylori in liver cirrhosis patients

In hepatitis C patients who experience liver cirrhosis, the incidence of H. Pylori infection is 15.4% (table 5), while for HBV infection it is 2%. The average of cirrhosis patients infected with H. Pylori was at CTP A stage (3.8%) (table 6).

DISCUSSION

The most common etiology of causes of cirrhosis in our study was non-viral, 54.7%, followed by viral such as hepatitis B virus (HBV) at 40% and hepatitis C at 5.3%. Globally the most common etiology of chronic liver disease is *Non-Alcoholic Fatty Liver Disease* (NAFLD) 59%, followed by HBV (29%), hepatitis C virus (VHC) (9%), and *Alcoholic Liver Disease* (ALD) the remaining 2% Other liver diseases, including *primary biliary cholangitis* (PBC), *primary sclerosing cholangitis* (PSC) , alpha-1-antitrypsin deficiency, Wilson's disease, and autoimmune hepatitis, noted for 1% of cases. NAFLD and ALD are tending to increase considering increasing rates of obesity, and many regions are experiencing increased alcohol consumption. Chronic HBV infection (HBV) causes more than half of cirrhosis deaths in the Asia-Pacific region, followed by alcohol consumption (20·8%), non-alcoholic fatty liver disease (NAFLD; 12·1%), and chronic hepatitis virus C infection (VHC; 15·7%). In research conducted by Pati, G et al in India, where 864 patients with liver cirrhosis found that the majority of cirrhosis cases were of non-viral causes and were male.[5,12,13]

On average, the cirrhosis patients treated in our treatment room were at the CTP B score stage, this is the same as research conducted by Tri Wulandari et al regarding a descriptive study of liver cirrhosis patients at the Wahab Sjahranie Regional Hospital Samarinda, South Kalimantan , Indonesia. Likewise, research by Nababan et al at RSCM, Jakarta, Indonesia, as many as 241 patients were analyzed; Patients were mostly male (74.3%), had hepatitis B (38.6%), and had Child-Pugh class B or C CTP cirrhosis (40% and 38%, respectively). A systematic analysis of the mortality rates of liver cirrhosis patients in 187 countries by Mokdad et al. showed a decline of 22% in the period 1980–2010 in developed countries in Europe, China and the United States, while in Indonesia this figure has increased. Lower death rates in developed countries are associated with improved preventive measures, such as hepatitis screening for blood donors, hepatitis B vaccination, and limiting alcohol consumption.[6,11]

In our study, the prevalence of H. Pylori in liver cirrhosis found in the study was 1.6% (4 of 245). Several studies conducted abroad, such as Pati, G et al in India, of 864 cases of liver cirrhosis patients, 57.4% were infected with H. Pylori, underwent UGIE and then tested for H.pylorii using *a rapid urease test* (RUT) with a sensitivity of 90% and a specificity of 93. % [(13.14)] . Abdel-Razik et al in Egypt obtained results from 558 cirrhotic patients who underwent esophagogastroduodenoscopy (EGD) and found H. pylori infection, 288 patients (51.6%) were H. pylori-negative and 270 patients (48.4%) were H. pylori- positive[15]

The H. Pylori examination method can influence the research results. The examination we carry out uses a histopathological examination with special staining (Warthin-Starry/hemactoxylin-eosin/Giemsa) where samples are taken from the antrum and corpus. The sensitivity and specificity levels of this examination reached more than 95%[14] .

Previous studies around the world have investigated the relationship between dietary patterns and H. pylori, many of which were published more than 20 years ago. Several studies have found that salty, pickled, fermented, or smoked foods increase the risk of H. Pylori infection. Fruits, vegetables or high antioxidants were found to be protective factors against infection. Eslami et al., reported that low consumption of raw vegetables was significantly associated with a higher risk of H. pylori infection in a group of Iranian students. A recent case-control study of patients with gastric ulcers in Pune, India, found that meat consumption as well as restaurant food consumption increased the risk of H. pylori infection, while chili pepper intake was protective[16] .

There are a number of countries where H. pylori infections are rare despite poor hygiene conditions (eg, Malaysia, Indonesia, and Zanzibar)[17] . The hygiene hypothesis suggests that environmental and microbial exposures can shape the developing immune system and confer protection or risk against immune-mediated diseases [17] .

In our study, in patients with HCV infection who experienced liver cirrhosis, the incidence of H. Pylori infection was 15.4% and in patients with cirrhosis due to HBV with H. Pylori infection was 2.0%. Yadav et al found that the prevalence of H pylori infection was quite common in patients with chronic liver disease. The prevalence of H pylori infection is more common in liver cirrhosis due to post-viral hepatitis (B and C) compared with other etiologies [9]. El-Shahat M, et al in Egypt in his study showed that H. pylori infection increased significantly (P = 0.03) in patients infected with VHC when compared with healthy controls, where H. pylori infection was found in 50 (55.6%) of 90 VHC-infected patients versus 26 (39.4%) of 66 healthy controls. In HCV-infected patients, the prevalence of H. pylori infection increased significantly (P = 0.04) from active chronic hepatitis to cirrhosis. H. pylori infection is found in patients with chronic active hepatitis, respectively Child-Pugh score A, Child-Pugh score B and Child-Pugh score C [(18)] . H. pylori infection significantly increased (P = 0.021) the incidence of liver fibrosis. Patients with F4 were accompanied by a significant increase (P < 0.05) in H. Pylori antigen concentration. Patients coinfected with H. pylori and VHC were 3.19 times more likely to experience cirrhosis compared with those with VHC monoinfection. Their study also found that H. Pylori infection with VHC concomitant was predominantly male (79.19%)[19] , whereas in our study 2.1% of liver cirrhosis patients experienced H. Pylori infection in males. This shows the importance of H. pylori screening in patients, especially with HCV-associated cirrhosis, to choose appropriate treatment.[19]

CONCLUSION

The incidence of H. Pylori infection in patients with liver cirrhosis according to our study was 1.6%.

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