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Helicobacter pylori Increasing Spread of An Inflammation Cells and Gastric Mucosal Atrophy in Gastritis Patients

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ABSTRACT

Background
Helicobacter pylori (H. pylori) is a bacterium which could cause chronic gastritis and then has the capability to influence gastric mucosal atrophy. The modifications within the degree of gastric mucosal atrophy have been appreciably correlated with the degree of risk of gastric cancer. The aim of this study is to investigate the relationship among H. pylori and the spread of inflammatory cellular infiltration and gastric mucosal atrophy in gastritis patients in Banjarmasin

Method
The study was carried out in September-November 2021 using a cross-sectional method with purposive sampling, that is as many as 87 samples of histopathological slides of gastritis patients in the anatomical pathology laboratory of Sari Mulia Hospital, Banjarmasin for the period 2019. Research analysis used Kolmogorov-Smirnov. Slide preparations were stained with immunohistochemistry (IHC) and hematoxylin-eosin (HE). Inflammatory cellular clearance was measured by a scale from revised Sydney system and gastric mucosal atrophy was measured by the OLGA staging system.

Results
The results showed as many as 40 (45.98%) H.pylori-positive patients with the most chronic inflammatory cell infiltration in 24 (60%) patients at grade 3 ($p<0.001$) and for gastric mucosal atrophy as many as 29 (72, 50%) of patients at various stages ($p<0.001$).

Conclusion
H. pylori has a significant relationship with inflammatory cell infiltration and gastric mucosal atrophy. H. pylori-positive causes a growth within the severity of inflammatory cellular irritation and mucosal atrophy in gastritis patients.

Keywords: Atrophy, gastritis, Helicobacter pylori, inflammatory cells, OLGA, Sydney System

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INTRODUCTION

Gastritis is an inflammation that takes place within the gastric mucosal layer.[1,2] Gastritis is one of common digestive diseases and is a prime health problem within the social and community fields in evolved and developing countries.[3,4] Primarily based on global data, gastritis patients reach 34.7% of the population in developed countries and 50.8% of the population in developing countries.[5] Although the prevalence of gastritis in developed countries is lower than in developing countries, it remains a major health problem.[6] The incidence of gastritis sufferers in Indonesia, based totally on the outcomes of a 2009 take a look at through the Indonesian Ministry of health, indicates that gastritis is one of the ten most commonplace diseases in Indonesian hospitals in which sufferers are hospitalized with 30,154 cases. The percentage of gastritis patients was also recorded at 40.8% with prevalence data that was still high, that is as many as 274,396 incidents from 238,452,952 people.[7] Based on data from the Central Statistics Agency for the city of Banjarmasin in 2014, it showed that gastritis was ranked 5th out of 10 diseases with the most cases in Banjarmasin with a record of 25,950 cases, and then in 2019 it decreased to 25th with a record of 4,637 case.[8]

H. pylori has virulence factors, considered one of that's the enzyme urease which lets in those bacteria to continue to exist within the acidic surroundings of the stomach. The urease enzyme is able to act as a catalyst for the hydrolysis of urea into ammonia and carbonate which causes these bacteria to reduce the acidity of gastric acid in the vicinity. *H. pylori* flagella allow bacteria to penetrate into the interior of the gastric mucosal lining and adhere to the gastric epithelium to promote colonization.[9] In addition, other virulence factors which include cagPAI, cagA, and vacA which can purpose inflammatory cellular infiltration that is an inflammatory system.[10] The inflammatory process that is prolonged and tends to be multifocal results in gastric mucosal atrophy, there is a loss of the appropriate gland.[2] Loss of these glands is followed by fibrosis of the lamina propria with or without metaplasia.[11] The infection of *H. pylori* and its virulence factors are the main cause of gastric mucosal atrophy and are estimated to occur in 40–50% of infected individuals.[12]

Research that examines the increase in inflammatory cell infiltration and gastric mucosal atrophy resulting from *H. pylori* bacteria in Indonesia is still rare. Based on this background, the research was carried out using histopathological examination with IHK and HE staining from gastric samples of gastritis patients. The aims of the study were to identify *H. pylori* infection in Banjarmasin, and to analyze the relationship of *H. pylori* to the spread of inflammatory cell infiltration and gastric mucosal atrophy.

METHOD

The design of this study used a quantitative analytical observational method with a cross sectional approach by observing the relationship between *Helicobacter pylori* to the spread of inflammatory cells and gastric mucosal atrophy at one time in gastritis patients who underwent histopathological examinations in Banjarmasin in 2019.

The population of the study were 88 patients who had been diagnosed with gastritis in Banjarmasin in the 2019 period. The samples in this study were gastritis patients who underwent histopathological examination at the anatomical pathology laboratory at Sari Mulia Hospital, Banjarmasin, which were taken using a non-probability technique with a purposive sampling approach. Sampling was carried out on a population determined based on inclusion criteria, that is gastric histopathology slides from gastritis patients who did not have physical disabilities or in the manufacturing process, had parts in the corpus and antrum, then had immunohistochemistry (IHC) and hematoxylin-eosin (HE) staining. The final sample results obtained were 87 samples.

This study used *H. pylori* infection as the independent variable, while the inflammatory cells and gastric mucosa atrophy as the dependent variables. The research instrument was histopathological slides that met the criteria and were examined using a light microscope. Positive or negative examination of *H. pylori* using IHC staining with 400 times magnification in all visual fields and inflamma-

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tory cells using HE staining with 400 times magnification in 5 fields of view in the corpus and antrum was measured using the Sydney system. Gastric mucosal atrophy using staining HE with 100 times magnification in all visual fields in the corpus and antrum was measured based on the severity and stage of the OLGA staging system. The identification results were then analyzed between *H. pylori* and inflammatory cells or *H. pylori* with gastric mucosal atrophy, using Statistikal Package for the Social Sciens (SPSS) version 21 application through the Kolmogorov-Smirnov statistical test with 95% confidence intervals.

Assessment of the level of spread of inflammatory cells in gastritis using one of the parameters of chronic inflammation based totally on visual analogue scales from the revised Sydney system. This parameter assesses the intensity of inflammatory cells such as lymphocytes and plasma cells inside the lamina propria which is assessed into four levels. The degree of spread of inflammatory cell infiltration is determined by the aggregate of the degree of inflammatory lesions within the antrum and corpus mucosa.[13]

Table 1. Grading of chronic inflammation from Revised Sydney System.[13]

Type of feature	Density of the histological feature	Grade
Chronic inflammation (lymphocytes and plasma cells)	2-3 chronic inflammatory cells scattered randomly in the biopsy	0
	10-15 chronic inflammatory cells/hpf (high power field)	1
	Some areas with dense chronic inflammatory cells	2
	Diffuse infiltration with dense chronic inflammatory cells	3

The definition of gastric mucosal atrophy is the lack of appropriate glands without or with metaplasia, resulting in a mismatch of location and function of the glands.[2] The focal point of atrophy is located within the gastric mucosa of the corpus and antrum which increases with time. A gastritis report is proposed in a single staging, namely the Operative Link for Gastritis Assessment (OLGA). OLGA compiled a histological spectrum based on the change from gastric mucosal atrophy to a formal classification along with its severity (Table 2) and then related to the stage of atrophy (Table 3). This stage regulates the histological phenotype of gastritis from non-atrophic (stage 0) to mild to severe atrophy (stages I–IV). The degree of atrophic changes in the gastric mucosa has a positive correlation with the incidence of gastric cancer.[14,15]

Table 2. Grading of gastric mucosal atrophy.[16]

Histological Type	Location		Grading
	Antrum	Corpus	
Non-metaplasic	Gland disappearance (shrinking) Fibrosis of the lamina propria		Non-atrofi: 0%
			Mild: 1-30%
			Moderate: 31-60%
			Severe: >60%
Metaplastic	Metaplasia: Intestinal	Metaplasia: Pseudopilorus Intestinal	Non-atrofi: 0%
			Mild: 1-30%
			Moderate: 31-60%
			Severe: >60%

Table 3. OLGA Staging System[16]

Atrophy Score	Corpus			
	Non-atrofi	Mild	Moderate	Severe
Antrum				
Non-atrofi	Stage 0	Stage I	Stage II	Stage II
Mild	Stage I	Stage I	Stage II	Stage III
Moderate	Stage II	Stage II	Stage III	Stage IV
Severe	Stage III	Stage III	Stage IV	Stage IV

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RESULTS

Research has been carried out on the relationship between *Helicobacter pylori* bacteria and the spread of inflammatory cells and gastric mucosa atrophy in Banjarmasin. The research was carried out in the anatomical pathology laboratory of Sari Mulia Hospital, Banjarmasin in September–November 2021.

Table 4. General characteristics of gastritis patients.

Characteristics	*Helicobacter pylori*		Total (n=87) (%)
	Positive (n=40) (%)	Negative (n=47) (%)	
Sex			
Male	19 (47.50)	23 (48.94)	42 (48.28)
Female	21 (52.50)	24 (41.06)	45 (51.72)
Age (years)			
11-20	3 (7.50)	1 (2.13)	4 (4.60)
21-30	6 (15.00)	2 (4.26)	8 (9.20)
31-40	5 (12.50)	9 (19.15)	14 (16.09)
41-50	10 (25.00)	10 (21.28)	20 (22.99)
51-60	7 (17.50)	11 (23.40)	18 (20.69)
61-70	3 (7.50)	9 (19.15)	12 (13.79)
71-80	5 (12.50)	4 (8.51)	9 (10.34)
81-90	1 (2.50)	1 (2.13)	2 (2.30)

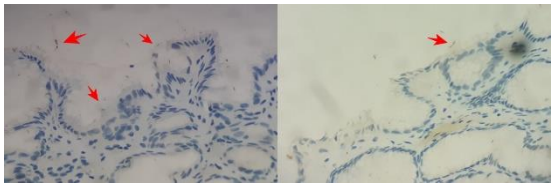

Figure 1. Immunohistochemical staining to see the bacteria *Helicobacter pylori* with 400 times magnification.

During the study period, 88 populations were obtained and 87 samples that met the inclusion criteria were taken from slides of gastric histopathology preparations in gastritis patients for the 2019 period. One sample did not meet the requirements. it is a slide preparation that does not contain any part of the body of the stomach in it. Samples were obtained from gastritis patients aged 15 to 87 years old with all genders. Based on the data obtained, the characteristics of gastritis patients are more common at the age of 41 to 60 years old as shown in Table 4. An explanation of these characteristics is not discussed in more detail in this study because the study only looked at the results of laboratory tests and did not make direct contact with patients.

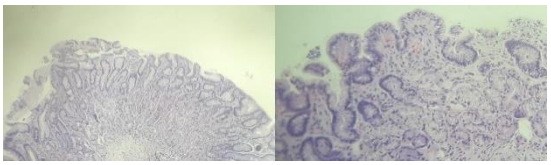

Figure 2. Hematoxylin-eosin staining to see inflammatory cell infiltration and gastric mucosa atrophy with 100 times and 400 times magnification.

According to the results of the analytical tests that have been carried out, there were significant results between *H. pylori* infection with inflammatory cell infiltration ($p<0.001$) and *H. pylori* infection with gastric mucosal atrophy ($p<0.001$).

Table 5. Analysis of *Helicobacter pylori* with inflammatory cell infiltration and gastric mucosal atrophy.

	H. pylori (+) (n=40) (45.98)	*H. pylori* (-) (n=47) (54.02)	Total (n=87) (%)	p-value
Sydney System				<0.001
Grade 0	0 (0)	0 (0)	0 (0)	
Grade 1	7 (17.50)	28 (59.57)	35 (40.23)	
Grade 2	9 (22.50)	5 (10.64)	14 (16.09)	
Grade 3	24 (60.00)	14 (29.79)	38 (43.68)	
OLGA Staging System				< 0.001
Stage 0	11 (27.50)	35 (74.47)	46 (52.87)	
Stage I	18 (45.00)	4 (8.51)	22 (25.29)	
Stage II	10 (25.00)	3 (6.38)	13 (14.94)	
Stage III	1 (2.50)	4 (8.51)	5 (5.75)	
Stage IV	0 (0)	1 (2.13)		

DISCUSSION

H. pylori is a bacterium belonging to the genus Bacillus, spiral-shaped, gram-negative, with microaerophilic behavior.[16] WHO has classified this bacterium as a group 1 carcinogen in 1994.[17] This bacterium is capable of causing gastric infections in approximately 50% of the global popu-

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lation.[10,16] Transmission occurs between mothers and their children, between siblings, and person-to-person contact through oral-oral, fecal-oral, or gastric-oral mechanisms.[18]

The results of the identification of gastritis patients in Banjarmasin who were *H. pylori*-positive did not reach half of the total sample studied, which was only 45.98%. Other studies that also show the prevalence value of *H. pylori*-positive which is below half of the total sample are the study of Hussain et al in 2021 in Timergara with a value of 22.10% and the study of Dhakwa et al in 2012 with a value of 44%.[19,20] The prevalence data in this study and the two studies that have been mentioned are lower than the statement from Hanafy et al in 2019 which said that *H. pylori* is capable of causing infection in about 50% of the world's populace.[10,16] Several studies showing *H. pylori*-positive patient data is more than half of the total sample, as in the study of Leja et al in 2012 in Latvia with a score of 79.21% and the study of Nam et al in 2014 in Korea with a score of 59.02%.

Individuals who are positive for *H. pylori* infection start when flagellin, lipoprotein and lipopolysaccharide belonging to the bacteria are detected by the toll-like receptor (TLR) by dendritic cells and macrophages in the gastric epithelium. This *H. pylori* contamination then ends in a complex immune response that is influenced by various factors and causes inflammation.[21]

Based on table 5, it was found that the distribution of the most grade 3 inflammatory cells was 43.68%. As for the spread of grade 0 inflammatory cells, the results were non-existent. This shows that there are lymphocytic inflammatory cells in all histopathological slides of gastritis patients, that is 87 samples (100%) with 38 samples (43.68%) having a description of the spread of severe inflammatory cell infiltration. This result is in step with the studies performed through Ariefiany et al 2014 which obtained 100% of samples with chronic inflammation.[22] This is not far from the research conducted by Qamar et al in 2010 which stated that chronic inflammation occurred in 92% of the sample.[23] Description of the spread of inflammatory cells Lymphocytes, macrophages and plasma are signs of chronic inflammation in a disease.[24]

The *H. pylori*-positive sample found the most spread of inflammatory cells in grade 3, as many as 24 samples (27.59%). As for the *H. pylori*-negative sample, the most spread of inflammatory cell infiltration was in grade 1, as many as 28 samples (32.18%). These facts are in keeping with the studies through Yulida et al in 2013 which showed that 69% of *H. pylori*-positive gastritis sufferers had severe spread of chronic inflammatory cell infiltration.[4]

Incineration of cells occurs due to inflammatory mechanisms inclusive of IL-1, IL-1β, IL-8 and IL-10 that are prompted with the aid of *H. pylori*. Pathogenic factors associated with *H. pylori* include motility of flagella, chemotaxis by urease and neutralization of gastric pH, antidote to the manufacture of antimicrobial nitric oxide using RocF arginase and binding of bacteria to epithelial cells using several outer membrane proteins, the final adhesive consisting of blood group antigen-binding adhesin (BabA/B), sialic acid binding (SabA), adherence-associated lipoprotein (AlpA/B), Outer inflammatory protein A (OipA), and others.[16]

The host reaction to *H. pylori* participates within the induction of gastric epithelial harm and consequently has an important function in pathogenesis. For the duration of the early phase of contamination, binding of *H. pylori* to epithelial cells, particularly via BabA and through strains harboring the pathogenicity of cagA, consequences within the production of IL-8 and chemokines. Epithelial cells secrete chemokines that bind to a proteoglycan scaffold which eventually produces polymorphonuclear cells (PMNs). At some point of the chronic phase of gastritis, *H. pylori* reasons an adaptive lymphocyte response to arise in the early innate response. Expression of chemokines facilitates lymphocyte extravasation through a vascular mediated pathway of vascular cell adhesion molecule-1 (VCAM-1) and intercellular adhesion molecule-1 (ICAM-1). Macrophages produce IL-8 which aims to produce proinflammatory cytokines which will later be involved in cell activation, especially helper T cells, and a bias response of Th1 to *H. pylori* occurs.[25]

In simple terms, inflammatory cells are regulated by members of the chemokine supergene such as the CC (beta chemoxine)

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and CXC (alpha chemoxine) subfamilies. The chemokines CXC growth related oncogene-alpha (GRO-alpha) and IL-8 are neutrophil chemotaxis agents, while interferon gamma IP-10 and monokines induce T-lymphocytes selectively to the site of inflammation so that there is an infiltration of lymphocyte inflammatory cells in the lamina propria.[26] occurs through one or two processes, such as following an acute inflammatory process or the initial response is chronic. Acute inflammation can turn chronic if the cause of inflammation persists or the normal healing process is disrupted.[24] Chronic inflammation in the absence of neutrophils has cytotoxic T-lymphocyte activity that damages the mucosa and glands in some types of gastritis. This is why chronic inflammation is almost always found in the histopathological picture of gastritis patients.[20]

Based on statistical tests using the Kolmogorov-Smirnov test, a p-value of <0.001 was obtained, which indicates significant outcomes or a courting among *H. pylori* and the spread of inflammatory cells in gastritis patients in Banjarmasin periode 2019. According to Carrasco's research in 2013 said the incidence of gastritis with chronic inflammatory cell proliferation caused by *H. pylori* infection is the first step of gastric cancer. The sequence of gastric cancer incidence includes chronic gastritis, multifocal atrophic gastritis, intestinal metaplasia, mild dysplasia, severe dysplasia, to invasive adenocarcinoma.[27]

The data in table 5 shows that 41 samples (47.13%) of gastritis patients experienced gastric mucosal atrophy with or without metaplasia at various stages (I–IV). Based on another study by Zhang et al in 2020 showed almost the same prevalence value for gastritis patients with gastric mucosal atrophy using gastroscopy with a value of 46.60%.[28] Consistent with a new observe by way of Shah et al in 2021, the estimated occurrence of gastric mucosal atrophy reaches up to 15% of the populace inside the America and can be more in certain areas or populations with a higher incidence of *H. pylori* infection or the presence of gastric cancer.[29]

The results showed that 29 (72.50%) of the 40 *H. pylori*-positive samples had gastric mucosal atrophy. This value showed a higher value compared to atrophic *H. pylori*-negative which was only 12 (25.53%) of the 47 samples. According to Leja et al in 2012, the incidence of atrophy occurs in about 40–50% of a person infected with *H. pylori*.[12] Primarily based on a meta-analysis, the 2010 observe by Adamu et al additionally said that ratio of the prevalence rate of gastric mucosal atrophy amongst positive and negative sufferers with *H. pylori* contamination turned into 5.0 (95% CI, 3.1-8.3), and the occurrence of atrophy may be very low (<1% per year) in *H. pylori*-negative patients.[30]

The data show that patients with *H. pylori*-positive are mostly at stages I-II and relatively few for stages III-IV. Then, for patients with *H. pylori*- negative, although only a quarter of the sample had gastric mucosal atrophy, the scores in all stages were evenly distributed. This may be due to other chance factors that still cause atrophy apart from *H. pylori* which on this observe could not be decided.[2,14,29]

The affiliation of *H. pylori* with gastric mucosal atrophy as assessed by the OLGA staging system turned into analyzed the usage of the Kolmogorov-Smirnov statistical test with p-value <0.001. These values show evidence that there may be a significant courting among *H. pylori* and gastric mucosal atrophy in gastritis patients.

The process by which H. pylori causes atrophy of the gastric mucosa in individuals is not clear how long it takes, but this tends to occur when there is prolonged infection[10] The pathogenesis of gastric mucosal atrophy involves interactions between environmental and genetic determinants of gastric mucosal atrophy. The degrees are vary depending at the primary trigger, *H. pylori* infection and autoimmunity. The impact of infection from bacteria varies from host to host depending on several factors, which include a person's genetics, the presence or absence of different environmental hazard factors that can affect the gastric mucosal barrier (eg bad eating regimen, drinking alcohol, drug use, and smoking), bacterial strain, virulence factors, and duration of infection.[29,31,32] However, based on the research of Wen et al in 2021 who conducted experiments using Sprague-Dawley rats in their research, a model of

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chronic atrophic gastritis was obtained after 8 weeks of being infected with the bacterium *H. pylori*.[33]

Using various types of screening tests, it has been proven that H. pylori infection can cause DNA damage. However, the buildup and pathogenic mechanisms underlying such DNA damage remain in large part unknown.

According to Sayed et al in 2020, *H. pylori* contamination triggers accumulation of mutations via dysregulation of Nei-like DNA glycosylase 2 (NEIL2). NEIL2 is one of the anti-inflammatory proteins that has a function in repairing damaged DNA. The study confirmed that NEIL2 degrees had been reduced in *H. pylori* infection increase accumulation of DNA damage and an inflammatory response.[34]

In preferred, inflammation induced by *H. pylori* allows oxidative stress and a continuous increase in the range of oxygen free radicals, especially reactive oxygen species (ROS), which leads to impaired DNA damage repair (DDR). [21,31] Toller et al (2011) study additionally confirmed the presence of DNA double-strand breaks (DSBs) in *H. pylori*-positive samples, which is one of the most severe types of DNA damage. Chromosomal aberrations can occur as a result of those DSBs, which include deletions, insertions, and translocations which might be the main reasons of loss of heterozygosity.[21,35]

H. pylori infection causes DSBs through direct interactions between bacteria and hosts. The DSBs process triggers DDR through activation of ATM and ATR, resulting in H2AX phosphorylation of Ser139 (γH2AX). H2AX turns on Chk1 and Chk2 transducers which then activate p53 and cause cell cycle arrest to repair damaged DNA. If the damage cannot be repaired, then the alternative is apoptosis or premature aging. All of these p53-induced responses are tumor suppressors. Oxidative stress cause stress on DNA replication which then results in genome instability as well as selective stress for p53 which causes abrogation of tumor suppressor action.[36]

Chronic inflammation is associated with systemic effects and local changes in the gastric mucosa. Changes that occur in the form of morphogenic epithelial cells, loss of cell contact, and interactions with the stromal compartment cause the transition of epithelial-mesenchymal cells to the transformation of the gastric mucosa. This situation allows the occurrence of gastric mucosal atrophy, metaplasia, dysplasia, to gastric cancer.[31] Data from the WHO shows that gastric cancer is the fourth most common cancer worldwide and according to the American Cancer Society (ACS) gastric cancer is the third leading cause of death in the America.[37]

CONCLUSION

Based on histopathological examination the usage of IHC and HE staining, it become determined that *H. pylori* contamination can reason chronic gastritis that is characterized by an increase in inflammatory cell infiltration compared to usual. In addition, *H. pylori* also increases the occurrence of gastric mucosal atrophy from mild to severe without or with metaplasia. Suggestions from this study are the need for other studies using cohort or experimental research methods to determine the possibility of how long *H. pylori* infection can affect inflammatory cell infiltration and gastric mucosal atrophy without the influence of other risk factors.

REFERENCES

1. Setiati S, Alwi I, Sudoyo AW, Et al. Buku ajar ilmu penyakit dalam. 6th ed. Ilmu Penyakit Dalam FK UI (PPIP FK UI). Jakarta: Interna Publising; 2014. 1768–71.
2. Rugge M, Pennelli G, Pilozzi E, et al. Gastritis: The histology report. Digestive and Liver Disease. 2011;43(SUPPL. 4).
3. Sipponen P, Maaroos HI. Chronic gastritis. Scandinavian Journal of Gastroenterology. 2015;50(6):657–67.
4. Yulida E, Oktaviyanti IK, Rosida L. Gambaran derajat infiltrasi sel radang dan infeksi *Helicobacter pylori* pada biopsi lambung pasien gastritis di RSUD Ulin Banjarmasin tahun 2009-2011. Berkala Kedokteran Unlam. 2013;9(1):51–65.
5. Sjomina O, Pavlova J, Niv Y, Leja M. Epidemiology of *Helicobacter pylori* infection. Helicobacter. 2018;23:6–11.
6. Liu Q, Zeng X, Wang W, et al. Awareness of risk factors and warning symptoms and

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e-ISSN 25279106
Accredited by KEMENRISTEKDIKTI/Sinta-3

attitude towards gastric cancer screening among the general public in China: a cross-sectional study. BMJ open. 2019;9(7):e029638.
7. Kemenkes RI. Profil kesehatan Indonesia tahun 2010. Kementerian Kesehatan Republik Indonesia. 2011.
8. Irianty H, Hayati R, Suryanto D. Kejadian gastritis berdasarkan aspek promosi kesehatan dan pola makan. Window of Health : Jurnal Kesehatan. 2020;3(3):251–8.
9. Prashar A, Lozano-Ruf A, Jones NL. *Helicobacter pylori* infection (including pediatric). 2nd ed. Encyclopedia of Gastroenterology. Elsevier Inc.; 2019. 1–8.
10. Hanafy AS, Seleem WM. Refractory *Helicobacter pylori* gastritis: The hidden predictors of resistance. Journal of Global Antimicrobial Resistance. 2019;19:194–200.
11. Correa P, Piazuelo MB. The gastric precancerous cascade. Journal of Digestive Diseases. 2012;13(1):2–9.
12. Leja M, Cine E, Rudzite D, et al. Prevalence of *Helicobacter pylori* infection and atrophic gastritis in Latvia. European Journal of Gastroenterology and Hepatology. 2012;24(12):1410–7.
13. Garg B, Sandhu V, Sood N, Sood A, Malhotra V. Histopathological analysis of chronic gastritis and correlation of pathological features with each other and with endoscopic findings. Polish Journal of Pathology. 2012;3:172–8.
14. Crafa P, Russo M, Miraglia C, et al. From sidney to OLGA: An overview of atrophic gastritis. Acta Biomedica. 2018;89(3):93–9.
15. Corvalán AH, Carrasco G, Olivares W. Molecular pathology of gastritis. Gastritis and Gastric Cancer - New Insights in Gastroprotection, Diagnosis and Treatments. 2011;115.
16. Sachs G, Marcus EA, Wen Y, Scott DR. Basis of gastric infection by *Helicobacter pylori*. Third Edit. Reference Module in Biomedical Sciences. Elsevier; 2014. 1–11.
17. Lee HS. Histopathologic diagnosis of *H. pylori* infection and associated gastric diseases. *Helicobacter pylori*. 2016. 119–127.
18. Bastos J, Carreira H, La Vecchia C, Lunet N. Childcare attendance and *Helicobacter pylori* infection: Systematic review and meta-analysis. European Journal of Cancer Prevention. 2013;22(4):311–9.
19. Hussain Shah SR, Almugadam BS, Hussain A, Ahmad T, Ahmed S, Sadiqui S. Epidemiology and risk factors of *Helicobacter pylori* infection in Timergara city of Pakistan: A cross-sectional study. Clinical Epidemiology and Global Health. 2021 Oct;12:100909.
20. Dhakhwa R, Acharya IL, Shrestha HG, Joshi DM, Lama S, Lakhey M. Histopathologic study of chronic antral gastritis. Journal of Nepal Health Research Council. 2012 Jan;10(1):57–60.
21. Lee WP, Hou MC, Lan KH, Li CP, Chao Y, Lin HC, et al. *Helicobacter pylori*-induced chronic inflammation causes telomere shortening of gastric mucosa by promoting PARP-1-mediated non-homologous end joining of DNA. Archives of Biochemistry and Biophysics. 2016 Sep;606:90–8.
22. Ariefiany D, Hassan AH, Dewayani BM, Yantisetiasti A. Analisis gambaran histopatologi gastritis kronik dengan dan tanpa bakteri *Helicobacter pylori* menurut sistem Sydney. Majalah Patologi. 2014;23(2):20–6.
23. Qamar S, Bukhari M, Asrar A, Sarwar S, Niazi S. Evaluation of antral gastric biopsies. A study of 50 patients at Mayo hospital. Vol. 16, SPECIAL EDITION ANNALS.
24. SV Stankov. Definition of Inflammation, Causes of Inflammation and Possible Anti-inflammatory Strategies. The Open Inflammation Journal. 2012 Jul 27;5(1):1–9.
25. Suerbaum S, Michetti P. *Helicobacter pylori* Infection. Hunter's Tropical Medicine and Emerging Infectious Disease: Ninth Edition. 2012;347(15):437–41.

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26. Yeh LY, Raj M, Hassan S, Aziz SA, Othman NH, Mutum SS, et al. Chronic atrophic antral gastritis and risk of metaplasia and dysplasia in an area with low prevalence of *Helicobacter pylori*. Indian Journal of Gastroenterology. 2009;28(2):49–52.
27. Carrasco G, Corvalan AH. *Helicobacter pylori* -induced chronic gastritis and assessing risks for gastric cancer. Gastroenterology Research and Practice. 2013;2013:1–8.
28. Zhang Y, Li F, Yuan F, Zhang K, Huo L, Dong Z, et al. Diagnosing chronic atrophic gastritis by gastroscopy using artificial intelligence. Digestive and Liver Disease [Internet]. 2020;52(5):566–72. Available from: https://doi.org/10.1016/j.dld.2019.12.146
29. Shah SC, Piazuelo MB, Kuipers EJ, Li D. AGA clinical practice update on the diagnosis and management of atrophic gastritis: Expert review. Gastroenterology. 2021 Oct;161(4):1325-1332.e7.
30. Adamu MA, Weck MN, Gao L, Brenner H. Incidence of chronic atrophic gastritis: systematic review and meta-analysis of follow-up studies. European Journal of Epidemiology. 2010 Jul 29;25(7):439–48.
31. Bornschein J, Quante M, Fassan M. Gastric cancer; epidemiology and diagnosis. In: Encyclopedia of Gastroenterology. Elsevier; 2020. p. 553–64.
32. Wroblewski LE, Peek RM. *Helicobacter pylori*: A stealth assassin. Trends in Cancer. 2021 Sep;7(9):807–8.
33. Wen J, Wu S, Ma X, Zhao Y. Zuojin Pill attenuates *Helicobacter pylori*-induced chronic atrophic gastritis in rats and improves gastric epithelial cells function in GES-1 cells. Journal of Ethnopharmacology. 2021 Nov;114855.
34. Sayed IM, Sahan AZ, Venkova T, Chakraborty A, Mukhopadhyay D, Bimczok D, et al. *Helicobacter pylori* infection downregulates the DNA glycosylase NEIL2, resulting in increased genome damage and inflammation in gastric epithelial cells. Journal of Biological Chemistry. 2020 Aug;295(32):11082–98.
35. Hanada K, Uchida T, Tsukamoto Y, Watada M, Yamaguchi N, Yamamoto K, et al. *Helicobacter pylori* Infection Introduces DNA Double-Strand Breaks in Host Cells. Infection and Immunity. 2014 Oct;82(10):4182–9.
36. Kalisperati P, Spanou E, Pateras IS, Korkolopoulou P, Varvarigou A, Karavokyros I, et al. Inflammation, DNA damage, *Helicobacter pylori* and gastric tumorigenesis. Frontiers in Genetics. 2017 Feb 27;8.
37. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: A Cancer Journal for Clinicians. 2018 Nov;68(6):394–424.

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