Incidence of *Helicobacter Pylori* Infections in a group of patients in Erbil City, Kurdistan Region, Iraq and Its Association with Gastritis and Adenocarcinoma

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Abstract

Background: Adenocarcinoma is one of the most common causes of Gastric cancer related deaths worldwide. *Helicobacter pylori* is the causative agent of most cases of gastritis, it can cause chronic active gastritis and known as a risk factor for the development of gastric cancer. This study aimed to assess the prevalence of *H. pylori* among patients with symptoms of dyspepsia and other gastritis related symptoms and its association with adenocarcinoma.

Methods: This study was carried out during the period of January 2018 to October 2019 with a total of 227 patients with gastritis related symptoms. The presence of *H. pylori* was detected by Rapid Urease Test (RUT) and histo-pathological tests using biopsy specimens. Statistical Analysis was done by using Chi-square test. $P < 0.05$ was considered to be statistically significant.

Results: From the total of 227 patients with gastritis related symptoms, 26 cases (13.61%) were diagnosed with adenocarcinoma. Their ages were between 13 and 90 years with mean of 47.81 ± 18.23 . The result showed that low severity prevalence of *H. pylori* was highest (111 cases) compared to 17 and 63 cases for high and moderate severity, respectively. Comparison between positive low, moderate, and high *H. pylori* cases for rapid urease test was highly significant ($P < 0.000$). The results showed no association between *H. pylori* severity across various age groups and gender. Moreover, goodness of fit test for metaplasia, activity, glandular atrophy, and endoscopic finding across severity status of *H. pylori* showed highly significant. Four composite categorized groups were initiated based on positive/negative prevalence of *H. pylori* and adenocarcinoma status. Results revealed statistical significance between combination of *H. pylori* and adenocarcinoma with inflammation, lymphoid aggregate, metaplasia, activity of neutrophils, glandular atrophy, rapid urease test, and endoscopic findings.

Conclusion: Histopathology tests are reliable diagnostic tools for the detection of *H. pylori*. Data showed that *H. pylori* was seen more in middle age patients with mucosal lymphoid follicle formation and more than one third of patients with adenocarcinoma. Therefore, screening of these infections is an important strategy for preventing gastric adenocarcinoma.

Background

The discovery of *Helicobacter pylori* (*H. pylori*) in 1982 was the starting point of a revolution concerning the concepts and management of gastroduodenal diseases.^{1,2} *H. pylori* represents one of the most common and medically important infections worldwide.³ Chronic infection due to this pathogen is now believed to account for the majority of cases of chronic gastritis.⁴ In addition, *H. pylori* is the major cause of gastric carcinogenesis and other gastric diseases, such as duodenal and gastric non-ulcer dyspepsia, gastroduodenal ulcers, and gastric mucosa-associated lymphoid tissue lymphoma.^{1,5} In recent years, a variety of extra digestive disorders, including cardiovascular diseases, liver diseases and autoimmune disorders have also been associated with infections caused by *H. pylori*.⁶ Gastric cancer is the third most common cause of death caused and related to cancer worldwide. *H. pylori* infection is the most known

risk factor for the development of gastric cancer. The pathogen can cause chronic active gastritis and atrophic gastritis by producing persistent acute-on-chronic inflammation.⁷ The high association of *H. pylori* infections with precancerous gastric lesions led to the pathogen being recognized as a class I carcinogen by the WHO in 1994.⁸ It has also been reported that in a meta-analysis infections, caused by *H. pylori*, results in a 2- to 3-fold increase in the risk of gastric cancer.⁹ It is estimated that approximately 75% of the gastric cancer burden in the world is attributed to *H. pylori*-induced inflammation.¹⁰

This study aimed to assess the prevalence of *H. pylori* among patients with symptoms of dyspepsia and other gastritis related symptoms. It also aimed to investigate the association between *H. pylori* with adenocarcinoma.

Methods

This study was conducted in the Histopathology laboratory of PAR Private Hospital, Erbil, Iraq, within the period of January 2018 to October 2019. A total of 227 Patients were included of any age and gender with symptoms of gastritis. A questionnaire regarding the age, gender and whether they were taking any dyspepsia related medications was included. The urea breath test was used first to detect *H. pylori*, in which the principle of the test is the pathogen can produce an enzyme called urease, which breaks urea down into ammonia and carbon dioxide. During the test, a tablet containing urea is swallowed and the amount of exhaled carbon dioxide is measured. This indicates the presence of *H. pylori* in the stomach (BreathTek® UBT for *H. pylori* kit was used). Three biopsy specimens from the antrum and the corpus were taken and sent for histopathologic study. In the histopathological unit, the biopsy specimens of patients were fixed in 10% buffered formalin for at least 12 hrs, and then embedded in paraffin wax. Hematoxylin and Eosin (H and E) staining was performed on tissue sections of each case. Three sections for each specimen were de-paraffinized and hydrated in descending grades of alcohol, cut in sequential 4-µm sections. The sections were then stained with H and E stain to determine the presence of *H. pylori* and gastritis. The *H. pylori* were clearly detected as curved bacilli on the surface of the gastric epithelial cells. The slides were evaluated by histopathologist and assigned to each morphological variable. The histopathology was used to confirm gastritis and neoplastic conditions found during endoscopy.

A total of 191 Patients with *H. pylori* gastritis were divided into three groups according to the *H. pylori* severity status of infections (high, moderate and low). Data were categorized as follows: Age years: ≤ 35, 35–60, > 60; Gender: male, female; Inflammation: mild, moderate, severe; lymphoid aggregate: positive, negative; metaplasia: positive, negative; activity: presence, absence of neutrophils; glandular atrophy: positive, negative; rapid urease test: positive, negative; endoscopic finding: nodular, granular, and erosive; clinical manifestation: pain, IDA (Iron deficiency anemia), dyspepsia, and others (chronic non bloody diarrhea and dysphagia).

The positive and negative results of *H. pylori* infection were categorized together with poor and moderate grades adenocarcinoma status according to the age group, gender and different diagnosis variables {positive *H. pylori*/ moderate grade differentiated adenocarcinoma (positive / moderate), positive *H.*

pylori/ poor grade differentiated adenocarcinoma (positive/ poor), negative *H. pylori*/ moderate grade differentiated adenocarcinoma (negative/ moderate) and negative *H. pylori* / poor grade differentiated adenocarcinoma (negative / poor)}.

Statistical Analysis

All variables of the patients were entered into Excel worksheet and data analysis was performed using Chi-square independence test, via contingency tables (Statistical Package for the Social Sciences software, SPSS Inc., Chicago, IL, USA). As Chi-square test for 2×3 , 3×3 or 3×4 contingency tables did not support calculation when zero exists as a cell value. Therefore, a goodness of fit (differences between observed and expected cases) was performed using GraphPad Software.¹¹ The *P* value less than 0.05 was considered to be statistically significant.

Results

The minimum age of the 227 patients was 13 years, maximum age was 90 years and mean age was 47.81 ± 18.23 . Furthermore, the minimum, maximum and mean age of the 191 infected patients with *H. pylori* based on the categorized severity of the *H. pylori* into high, moderate and low is presented in Table 1. The low state prevalence of *H. pylori* was highest (111 cases) compared to 17 and 63 cases for high and moderate severity of *H. pylori*, respectively. This result showed that cases with no detectable infection were 36 (15.86%) out of the 227 patients.

Table 1
Age distribution across severity status of *H. pylori*.

severity of <i>H. pylori</i> (Number of cases), (%)	High (17), (8.9%)	Moderate (63), (32.98%)	Low (111), (58.12%)
Age (yrs): min.	16	13	18
Max.	57	86	90
Average	38.59 ± 13.13	45.56 ± 18.26	47.72 ± 18.03

Results revealed that all patients had positive rapid urease test and no association between *H. pylori* severity across various age groups ($P = 0.245$), and gender ($P < 0.961$). It was noticed that high prevalence of *H. pylori* was most likely to occur in patients of 35–60 years old (43.98%) compared to younger or older ages (30.89, 25.13%), respectively (Table 2). The prevalence of *H. pylori* infection was 50.26% in males 49.74% in females showing similar distribution of *H. pylori* among the gender. The result showed a statistical significant association between *H. pylori* severity across various Inflammation ($P < 0.001$), and Lymphoid aggregate ($P < 0.001$). Chi square for diagnosis variables of metaplasia, activity which represented by presence or absence of neutrophils, glandular atrophy, rapid urease test, endoscopic finding, and clinical manifestation were highly significant ($P < 0.001$) across low, moderate, and high *H. pylori* severity (Fig. 1).

The moderate Inflammation was recorded the highest (71.2%) compared to mild (25.66%) and severe (3.14%). The finding of the positive lymphoid aggregate showed 82.72% compared to 17.28% of the negative tests (Fig. 2).

On the other hand, positive metaplasia was found in 11.52%; neutrophils in 17.8% and positive tests for glandular atrophy in 9.95% of cases.

The distribution of the endoscopic findings showed 64.92% nodular, whereas 35.08% were erosive. Clinical manifestation of most patients (56.02%) had pain, 10.47% had IDA, 16.75% had dyspepsia, and 16.75% had other clinical manifestations.

Table 2
Distribution of H. pylori according to the variables studied.

H. pylori (Number of cases)	No. (%)	High (17)	Moderate (63)	Low (111)	P Value
Age years: ≤ 35	59 (30.89)	6	22	31	0.245*
35–60	84 (43.98)	10	24	50	
>60	48 (25.13)	1	17	30	
Gender:	96 (50.26)	8	32	56	0.961*
Male	95 (49.74)	9	31	55	
Female					
Inflammation:	49 (25.66)	1	8	40	0.001*
mild	136 (71.20)	15	51	70	
moderate		1	4	1	
severe	6 (03.14)				
Lymphoid aggregate: positive	158 (82.72)	17	60	81	0.001
negative	33 (17.28)	0	3	30	
Metaplasia : positive	22 (11.52)	4	4	14	0.001
Negative	169 (88.48)	13	59	97	
Activity:	157 (82.20)	17	57	83	0.001
presence of neutrophils		0	6	28	
absence of neutrophils	34 (17.80)				
Glandular atrophy: positive	19 (09.95)	0	3	16	0.001
Negative	172 (90.05)	17	60	95	
Rapid Urease Test: positive	191 (100)	17	63	111	0.001
Negative	0 (0)	0	0	0	
Endoscopic finding: nodular granular erosive	28 (14.66)	2	12	14	0.001
	96 (50.26)	7	25	64	
	67 (35.08)	8	24	35	

*Chi-square test was calculated as a contingency table.

H. pylori (Number of cases)	No. (%)	High (17)	Moderate (63)	Low (111)	P Value
Clinical manifestation: pain IDA dyspepsia	107	10	41	56	0.012
others	(56.02)	3	4	13	
	20 (10.47)	3	13	16	
	32 (16.75)	1	5	26	
	32 (16.75)				
*Chi-square test was calculated as a contingency table.					

A total of 26 patients out of the total 227 were diagnosed as gastric adenocarcinoma. The 26 cases were categorized based on poor or moderate adenocarcinoma together with positive or negative for the presence *H. pylori*. Four composite groups were initiated: positive *H. pylori* / moderate grade adenocarcinoma (positive / moderate), positive *H. pylori* / poor grade adenocarcinoma (positive / poor), negative *H. pylori* / moderate grade adenocarcinoma (negative / moderate) and negative *H. pylori* / poor grade adenocarcinoma (negative / poor) with 4, 6, 5 and 11 cases, respectively (Table 3, Fig. 3).

Results presented in Table 3 revealed highly statistically significant ($P < 0.001$) difference in the number of cases in each category (combinations) of *H. pylori* and adenocarcinoma with Inflammation, lymphoid aggregate, metaplasia, activity of neutrophils, glandular atrophy, and endoscopic, and rapid urease test. On the other hands, age, gender, and clinical manifestation presence or absent showed no significant associations.

Table 3

Distribution of combination of *H. pylori* and adenocarcinoma according to the variables studied.

<i>H. pylori</i> /adenocarcinoma (Number of cases)	positive/ moderate (4)	positive / poor (6)	negative/ moderate (5)	negative / poor (11)	<i>P</i> <i>value</i>
Age years: ≤ 35**	0	0	0	2	0.333*
35–60	3	1	2	4	
>60	1	5	3	5	
Gender: Male	3	5	4	7	0.814*
Female	1	1	1	4	
Inflammation: negative	0	0	2	10	0.001
mild	4	4	0	0	
moderate	0	2	0	0	
severe	0	0	3	1	
Lymphoid aggregate:	0	2	0	0	0.001
positive	4	4	5	11	
negative					
Metaplasia :	0	2	0	0	0.001
positive	4	4	5	11	
Negative					
Neutrophils: presence	2	2	0	0	0.001
Absence	2	4	5	11	
Glandular atrophy:	3	4	0	0	0.010
positive	1	2	5	11	
Negative					
Rapid Urease Test: positive	4	6	0	0	0.001
Negative	0	0	5	11	
Endoscopic finding: nodule (mass)	1	2	3	8	0.001*
erosive lesion	3	4	2	3	
Clinical signs:	3	4	2	4	0.443*
pain with melena Others	1	2	3	7	
*Chi-square test was calculated as a contingency table.					
**Excluded from chi square test due to zeros exist in cell values.					

Similarly, it can be seen that lymphoid aggregate status (positive vs. negative tests) has similar trends across *H. pylori* severity status (Fig. 5). Both positive and negative lymphoid aggregate showed lowest values (17 and 0, respectively) for high *H. pylori* and both diagnostic tests increased to 60 and 3 cases for the moderate *H. pylori* status, then both attained the peak cases of their lines when *H. pylori* status was low (81 and 30, respectively). Such similar trend plots indicate a high significant statistical positive association.

Table 3, Figs. 6 and 7 illustrate highly statistically significant ($P < 0.001$) findings between a combination of positive and negative *H. pylori* and poor or moderate adenocarcinoma with rapid urease test, and glandular atrophy. Figure 6 shows fluctuations in number of cases among categorization (combination) of *H. pylori* and adenocarcinoma with rapid urease test, which represent an inverse association, as the trend of the positive rapid urease test line has opposite direction and magnitude of the negative rapid urease test line. The positive rapid urease test line increased from 4 to 6 then declined to 0, 0 for (positive / moderate), (positive / poor), (negative / moderate) and (negative / poor), respectively. Whereas, negative rapid urease test line increased from 0, 0 to 5 then to 11 for (positive / moderate), (positive / poor), (negative / moderate) and (negative / poor), respectively.

Similarly, Fig. 7 shows fluctuations in number of cases among categorization (combination) of *H. pylori* and adenocarcinoma with positive and negative glandular atrophy, which represent inverse association, as the trend of the positive glandular atrophy line has opposite direction and magnitude of the negative glandular atrophy line. The negative glandular atrophy line increased from 1 to 2 then to 5 and 11 for (positive / moderate), (positive / poor), (negative / moderate) and (negative / poor), respectively. Whereas, positive glandular atrophy line increased from 3, to 4 then declined to 0, 0 for (positive / moderate), (positive / poor), (negative / moderate) and (negative / poor), respectively.

Discussion

The prevalence of *H. pylori* differs both between and within countries, with high rates of infection being associated with low socioeconomic status and high densities of living.¹² When endoscopy is clinically indicated, the test of first choice is the urease test on an antral-biopsy specimen.¹³ In the current study, the minimum age of the 227 patients was 13 years and the maximum age was 90 years, with mean age of 47.81 ± 18.23 . High prevalence of *H. pylori* was most likely to occur in patients of 35–60 years old (43.98%) compared to younger or older ages (30.89, 25.13%), respectively. The result of this study shows that the prevalence of *H. pylori* infection found in male was 50.26% and in females was 49.74%, this is similar to the distribution of *H. pylori* among the gender in patients studied in Nepal. Where among 2820 eligible patients, males were 54.2% and females were 45.8% with the mean age of 46.3 years ± 17.6 ranging from 8 to 94 years.¹⁴ On the other hand, in a large French cross-sectional study, a significantly lower prevalence of *H. pylori* infection was observed in females as compared with males.¹⁵

Several studies were conducted in Kurdistan dealing with prevalence of *H. pylori* and gastritis. Research result indicated that the prevalence of *H. pylori* in total of 310 samples (170 male and 140 female) were

39.4%. The prevalence of *H. pylori* in the age between 41–50 years were (51.2%), followed by patients with age > 61 years (46.5%). The rate of infection among females were (40.7%), compared with males infection rate of (38.2%). That study concluded that the prevalence of *H. pylori* in Erbil city was high and the infection occurred at different stages of life.¹⁶ Other report found that the prevalence of *H. pylori* infection among 311 students (57.8% female and 42.2% male) increased with age and a higher frequency found in students from low income social status. They also observed that *H. pylori* were highly prevalent among university students in Erbil, being 55.8% of the 311 students.¹⁷ Recently, in a study carried out to investigate the seroprevalence of *H. pylori* infection among Cihan University students, Erbil. A total of 197 blood samples were collected from the students (53 females and 144 males), and tested for anti-*H. pylori* antibodies, using a rapid immunochromatography assay. The prevalence of anti-*H. pylori* antibodies is relatively high among students, with no significant differences between male and female in respect to having *H. pylori* infection. It was concluded that both university and public communities should be aware of infections caused by the pathogen such as gastritis, peptic ulcer, and about its potential association with malignant transformation.¹⁸ Furthermore, investigation of *H. pylori* infection among 190 patients diagnosed with gastric cancer in Sulaimani city indicated that a history of *H. pylori* infection was observed in 63.2% of the patients and that prevalence of gastric cancer was higher among females (61.5%), and patients aged over 50 years (73.6%).¹⁹ Interestingly a study carried out on 50 patients suffering from stomach cancer in Erbil city and 25 healthy individuals, as a control group showed that the highest number of chromosomal aberrations (Dicentric chromosome) occurred in the fifth age group (65–74). It also shown that most patients are males in the age group (45–64), most of whom smoked and drank alcohol and were infected with *H. pylori*.²⁰

The present study also revealed statistically significant associations between *H. pylori* and adenocarcinoma with inflammation, glandular atrophy, and rapid urease test. Furthermore, results revealed highly statistically significant ($P < 0.001$) differences among categorization (combination) of *H. pylori* and adenocarcinoma with inflammation, lymphoid aggregate, metaplasia, activity of neutrophils, glandular atrophy, endoscopic, and rapid urease test. The result also indicated that 26 cases out of 227 cases (13.61%) were diagnosed to have adenocarcinoma, and that 10 out of 26 adenocarcinoma cases (about 38.5%) showed positive rate of *H. pylori* infection. Similar result of low rate of gastric cancer incidence was noted with high prevalence of *H. pylori* infection in India, Philippines, or Thailand; on the other hand, the high rate of gastric cancer incidence was observed in Japan and Korea with variable prevalence of *H. pylori*.^{21–23} It was suggested that *H. pylori* infection is not the only factor related to gastric cancer risk.^{24,25} Furthermore, Individuals with chronic *H. pylori* infection have an increased risk of acquiring a adenocarcinoma,^{26,27,28} as the pathogen indicated as a carcinogen associated with gastric adenocarcinoma.²⁹ Colonization of stomach by *H. pylori* can result in gastritis, and may have a risk of developing peptic ulcers (Kusters et al., 2006), it is notable that in this study 35.08% of the *H. pylori* gastritis revealed erosion. The National Institutes of Health consensus conference in the United States declared an association between *H. pylori* and peptic ulcer disease.^{30,31}

Data produced from this study showed that low density of *H. pylori* was highest (111 cases) compared to 17 and 63 cases for high and moderate density infections, respectively. *H. pylori* caused chronic gastritis in all colonized subjects. This can lead to peptic ulcer disease, atrophic gastritis, gastric adenocarcinoma, and MALT (mucosa-associated lymphoid tissue) lymphoma.³² Patients with current *H. pylori* infection have a higher risk of developing gastric cancer compared with patients with past infection or eradication history of *H. pylori* because the eradication of *H. pylori* reduces the risk of gastric cancer. It was reported that the successful treatment of *H. pylori* decreases the risk of developing gastric cancer by approximately 3 fold.³³ Therefore, screening and treatment of *H. pylori* is an important strategy for preventing gastric cancer in high-risk populations, particularly among societies.

This study has a number of limitations. The generalizability of the findings is limited as samples were collected only from one city (Erbil), this suggests that the study population might not be representative of the general *H. pylori* infections in Kurdistan region. The sample size of this study is relatively small for a region with a high burden of the disease as the diagnosed patients are only from one city of the region in Iraq.

Conclusion

The histopathology and RUT tests are reliable invasive diagnosis for *H. pylori*. It was noticed that *H. pylori* seen more in middle age group patients living in Erbil ,Kurdistan with mucosal lymphoid follicle formation, moderate active inflammatory changes as well as *H. pylori* seen in more than one third of patients with adenocarcinoma cases. So screening, follow up and treatment of *H. pylori* is an important strategy for preventing gastric adenocarcinoma in Erbil, Kurdistan.

List Of Abbreviations

H. pylori: *Helicobacter pylori*, RUT: Rapid Urease Test, WHO: World Health Organization, H and E: Hematoxylin and Eosin, IDA: Iron deficiency anemia, SPSS: Social Sciences software,

Declarations

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Authors'contributions:

TS participated in made substantial contributions to the conception and design of the study.

SB have made substantial contributions to the design of the study and submitting the draft.

RA have drafted the work and substantively revised it.

SA have made his contribution to the analysis and interpretation of data.

AM have made her contribution to the design of the study and analysis of data.

NJ have made substantial contributions to the acquisition of data.

All authors have read and approved the submitted version.

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References

1. Rajan A, Ganguli P, Pathak N, Ranjan A, Thapa R, Tripathi S. Correlation of serology with morphological changes in gastric biopsy of *pylori* infection. International Journal of Research in Medical Sciences. 2017; 26;5 (5):1851-7.
2. Abu-Sbeih RS, Hawari AD, Hassawi DS, Al-Daghistani HI. Isolation and detection of *Helicobacter pylori* from patients suffering from peptic ulcer using biochemical tests and molecular techniques. American Journal of Biochemistry & Biotechnology. 2014; 1:10 (1):58.
3. Akanda MR, Rahman AN. Comparative Study of different methods for detection of *Helicobacter pylori* in gastric biopsies. Dinajpur Med Col J. 2011; 4(1):1-6.
4. 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; 1:63(3):172-8.
5. Lee JY, Kim N. Diagnosis of *Helicobacter pylori* by invasive test: histology. Annals of translational medicine. 2015; 3(1).

6. Choi YJ, Kim N, Lim J, Jo SY, Shin CM, Lee HS, Lee SH, Park YS, Hwang JH, Kim JW, Jeong SH. Accuracy of diagnostic tests for *Helicobacter pylori* in patients with peptic ulcer bleeding. *Helicobacter*. 2012; 17(2):77-85.
7. Kurt O, Ozturk K, Altun B. Association between *Helicobacter pylori* and Gastric Cancers. *Gut and liver*. 2017; 11(2):312-3.
8. Parkin DM, Bray F, Ferlay J, Pisani P. Global cancer statistics, 2002. *CA Cancer J Clin*. 2005; 55(2):74-108.
9. Huang JQ, Sridhar S, Chen Y, Hunt RH. Meta-analysis of the relationship between *Helicobacter pylori* seropositivity and gastric cancer. *Gastroenterology*. 1998; 114(6): 1169-1179.
10. Amieva M, Peek RM Jr. Pathobiology of *Helicobacter pylori*-induced gastric cancer. *Gastroenterology*. 2016; 150(1):64-78.
11. GraphPad Software, Inc. 2018. 7825 Fay Avenue, Suite 230, La Jolla, CA 92037 USA. (Accessed 2018. at <https://www.graphpad.com/scientific-software/prism/>).
12. Hazel, M. and M. Francis, 2002. Epidemiology and diagnosis of *H. pylori* infection. *Helicobacter*, 7: 8-16. DOI: 10.1046/j.1523-5378.7.s1.10.x
13. Ruba SA, Azmi DH, Dhia SH, and Hala IA. Isolation and detection of *helicobacter pylori* from patients suffering from peptic ulcer using biochemical tests and molecular techniques. *American Journal of Biochemistry and Biotechnology* 10 (1): 58-68, 2014. ISSN: 1553-3468.
14. Umid KS, Arnab G, Vijay MA, Suresh CK. Prevalence of *Helicobacter pylori* infection, its correlation with gastroduodenal diseases and the incidence of gastric cancer in Nepal. *JAIM* 2013; 2: 02(04):54. <https://www.researchgate.net/publication/258998213>. DOI:10.3126/jaim.v2i2.8777.
15. Broutet, N, Sarasqueta AM, Sakarovitch C, Cantet CF, and Lethuaire D, *et al.*, 2001. *Helicobacter pylori* infection in patients consulting gastroenterologists in France: Prevalence is linked to gender and region of residence. *Eur. J. Gastroenterol. Hepatol.*, 13: 677-684. DOI: 10.1097/00042737-200106000-0.
16. AL-Mashhadany DA, Layla QI, Ahmed MZ. Seroprevalence of *helicobacter pylori* among human in Erbil governorate, Kurdistan region, Iraq. 2018; *RJLBPCS* 4(2). 268-280.
17. Hussen BM, Saleem SQ, Halgurd FA and Suha HA. The Prevalence of *Helicobacter pylori* among University Students in Iraq. *Indian Journal of Science and Technology*. 2013; 6 (8):5019 -5023.
18. Alsakee HM, Sarah HM, Gulistan HM, Asia SM, Ilaf AR, Naza khan TS. Prevalence of Anti-*Helicobacter pylori* Antibodies among Students of Cihan University, Erbil. *Cihan University-Erbil Scientific Journal*. 2019; 3(1):66-70. <http://journals.cihanuniversity.edu.iq/index.php/cuesj>
19. Mohialdeen FA, Mohammed IMG, Khalid AH, Ahmad RA, Chrakhan JA, Nuha AM, Amir AS, Renwarr RH, Bashdar KA. Distribution of *Helicobacter pylori* Infection among Gastric Cancer in Hiwa Hospital, Sulaimani City. 2019; *Journal of Research in Medical and Dental Science* 7(2): 194-196.
20. Sulaiman KM. Cytogenetic study of stomach cancer in Erbil City. *ZANCO Journal of Pure and Applied Sciences*. 2016; 28 (4): 56-65. <http://doi.org/10.21271/ZJPAS.28.4.9>

21. Miwa H, Go MF, Sato N. H. pylori and Gastric Cancer: TheAsian Enigma. Am J Gastroenterol 2002; **97**:1106-1112.
22. Yamagata H, Kiyohara Y, Aoyagi K, et al. Impact of *Helicobacter pylori* infection on gastric cancer incidence in a general Japanese population: the Hisayama study. Arch Intern Med 2000;**160**:1962-1968.
23. Malaty HM, Kim JG, Kim SD, et al. Prevalence of *Helicobacter pylori* infection in Korean children: inverse relation to socioeconomic status despite a uniformly high prevalence in adults. Am J Epidemiol 1996;143:257-262.
24. Nomura A, Stemmermann GN, Chyou PH et al. *Helicobacter pylori* infection and gastric carcinoma among Japanese-Americans in Hawaii. N Engl J Med 1991; **325**:1132–1136.
25. Kikuchi S, Wada O, Nakajima T et al. Serum anti-*Helicobacter pylori* antibody and gastric carcinoma among young adults. Cancer 1995; 75:2789–2793.
26. Nocturne G, Pontarini E, Bombardieri M, Mariette X. Lymphomas complicating primary Sjögren's syndrome: from autoimmunity to lymphoma. Rheumatology 2019; (Oxford, England).doi:1093/rheumatology/kez052.
27. Abbas H, Niazi M, Makker J. Mucosa-Associated Lymphoid Tissue (MALT) Lymphoma of the Colon: A Case Report and a Literature Review. The American Journal of Case Reports 2017; **18**: 491–97.doi:12659/AJCR.902843. PMC 5424574. PMID 28469125.
28. Paydas S. *Helicobacter pylori* eradication in gastric diffuse large B cell lymphoma. World Journal of Gastroenterology 2015; 21(13): 3773–3776.doi: 3748/wjg.v21.i13.3773.
29. IARC Monographs on the evaluation of carcinogenic risks to humans. In: International Agency for Research on Cancer Monograph 61. Lyon: IARC; 1994. Schistosomes, liver flukes and *Helicobacter pylori*; pp. 177–240.
30. Marshall BJ, Warren JR. Unidentified curved bacilli in the stomach of patients with gastritis and peptic ulceration. Lancet. 1984; 1:1311–1315.
31. NIH Consensus Conference. *Helicobacter pylori* in peptic ulcer disease. NIH Consensus Development Panel on *Helicobacter pylori* in Peptic Ulcer Disease. JAMA. 1994; 272:65–69.
32. Malfertheiner P, F Megraud F, O'Morain CA, Gisbert JP, Kuipers EJ, Axon AT, et al. On behalf of the European Helicobacter and Microbiota Study Group and Consensus panel. Management of *Helicobacter pylori* infection—the Maastricht V/Florence Consensus Report. Online First, published on October 5, 2016 as 10.1136/gutjnl-2016-312288. Copyright Article author (or their employer) 2016. Produced by BMJ Publishing Group Ltd (& BSG) under licence. http://gut.bmj.com/ on November 17, 2016.
33. Omer K, Kadir O, Battal A. Association between *Helicobacter pylori* and Gastric Cancers. Gut and Liver 2017; 11: 2 312-313.

Figures

Figure 1

Chronic gastritis with low density of *H. pylori*. (H&E stain 400x).

Figure 2

Chronic gastritis with lymphoid follicle formation. (H&E stain 400x).

Figure 3

Gastritis adenocarcinoma with low density of *H. pylori*. (H&E stain 100x).

Figure 4

Positive association among severity of *H. pylori* status with diagnostic inflammation

Figure 5

Positive association among severity of H. pylori status with lymphoid aggregate status.

Figure 6

Inverse association among severity of H. pylori status with rapid urease test.

Figure 7

Inverse association among severity of *H. pylori* status with glandular atrophy test.