

## DEMOGRAPHICAL FACTORS ESTIMATION IN GASTRODUODENAL DISORDER PATIENTS INFECTED WITH *HELICOBACTER PYLORI* IN BASRAH PROVINCE

Ahmed W. Al-Hilfi<sup>1</sup>, Ihsan E. Alsaimary<sup>1, \*</sup>, Ali D. Al-Hilfi<sup>2</sup>

<sup>1</sup>Department of Microbiology, College of Medicine, University of Basrah

[ahmedwadi45@gmail.com](mailto:ahmedwadi45@gmail.com)

<sup>2</sup>Consultant GIT, HBP, Laparo-Endoscopic & Bariatric Surgeon Al-Sader Teaching Hospital

\*Corresponding author: Prof. Dr. Ihsan E. Alsaimary, Email: [ihsanalsaimary@gmail.com](mailto:ihsanalsaimary@gmail.com)

### Summary

The aim of this study was to investigate the demographical factors of gastroduodenal disorder patients infected with *H. pylori* in Basrah province. A case-control study included 112 confirmed gastroduodenal patients and 112 individuals as a control group. Data about age, gender, smoking, alcohol abuse, residence, and clinical findings for all study populations were collected. This study shows the effect of demographical factors (age, gender, smoking, alcohol abuse, and residence) in patients with GIT disorders and the control group. The study shows a significant effect of these factors with an increased risk of gastroduodenal disorder.

**Keywords:** Demographical factors (age, sex, residence, marital status), gastroduodenal disorder, *Helicobacter pylori*, smoking, and alcohol abuse.

### Introduction: -

*Helicobacter pylori* (*Hp*) is a Gram-negative microaerophilic bacteria that is highly adapted to colonize and survive in the gastric mucus membrane of infected individuals (Adinortey, *et al.*, 2018). *Hp* is associated with a formidable array of gastroduodenal and intestinal disorders including gastritis, peptic ulcer diseases (PUDs), duodenal ulcers (DUs), and low-grade B-cell mucosa-associated lymphoid tissue (MALT) gastric lymphoma (Fan, *et al.*, 2018). *H. pylori* move toward the thick mucus layer of the stomach by the mean of 2-6 multiple tuft unipolar sheathed flagella measuring 3 µm in length located at its distal end which promote swift motility through the gastric epithelium (Kumar, 2016).

*H. pylori* is the most common transmissible human gastric pathogen worldwide, infecting an estimated 50% of the global population (Yong, *et al.*, 2015, and AL-Abdul, 2014), equivalent to approximately 4.4 billion people (Hooi, *et al.*, 2017), with most cases being asymptomatic (Reshetnyak, *et al.*, 2021).

*Helicobacter pylori* are urease positive, urease breaks down urea to ammonia and CO<sub>2</sub> (Yang, *et al.*, 2014). Urease regulates *H. pylori*-macrophage interaction, *H. pylori* activate the infiltration of T lymphocytes, plasma cells, polymorphonuclear lymphocyte, dendritic cells, neutrophils, and accelerate proinflammatory cytokines production, such as interferon-gamma (IFN), interleukin-4 (IL-4) and interleukin-8 (Atherton, 2006). Urease is a chemotactic agent that recruits macrophages to the infected stomach, this enzyme can modulate phagosome-megasome formation, such a mechanism is important for microorganisms especially *H. pylori* for escaping host defence (Schwartz, 2006). *H. pylori* was successfully isolated from water (tap and R.O.) by culture methods and PCR techniques (Al-Sulami, *et al.*, 2012). Several studies have shown that the prevalence of

*H. pylori* is relatively high in most countries. In Iraq, Erbil, Kurdistan region, the prevalence of *H. pylori* infection was 39.4% (Al-Hilfi, *et al.*, 2021), and up to (58%) in people who suffer from abdominal pain and stomach discomfort in Basrah (Alatbee, 2019).

## Materials and methods

A Case-control study was conducted between November 2021 to November 2022 carried for patients with gastroduodenal disorder according to a minimum sampling size equation that depends on the disease ratio, A total of 224 individuals were enrolled in this present study, out of 112 individuals with age around (13-90) years selected as the patients' group and out of 112 individuals with age around (13-82) years observed as the control group suffering from various gastrointestinal symptoms underwent upper endoscopic examination at the Endoscopic Unit in Al-Sadder Teaching Hospital in Basrah province. During the collection process, data about each individual were reported in a questionnaire paper for each one, which included age, gender, family history, smoking, alcohol drinking, occupation, residence, and clinical findings of the disease which we have highlighted in the current study. The endoscopic examinations were done and recorded under the supervision of a gastroenterologist. Each patient and control individuals were subjected to a biopsy urease test and urea breath test for a definitive diagnosis of *H. pylori* infection.

### Exclusion criteria

1. Patients on recent antibiotics.
2. Proton pump inhibitors (PPIs) consuming patients, two weeks before endoscopy.
3. Immunocompromised patients.
4. Pregnant women

were excluded from this case-control study.

### Inclusion criteria

Any patient suffering from gastroduodenal disorder (epigastric pain, dyspepsia, abdominal pain, and heartburn) associated with *H. pylori* infection which is diagnosed by urea breath test and biopsy urease test and under the supervision of a specialist GIT physician was included in this case-control study.

### Statistical analysis: -

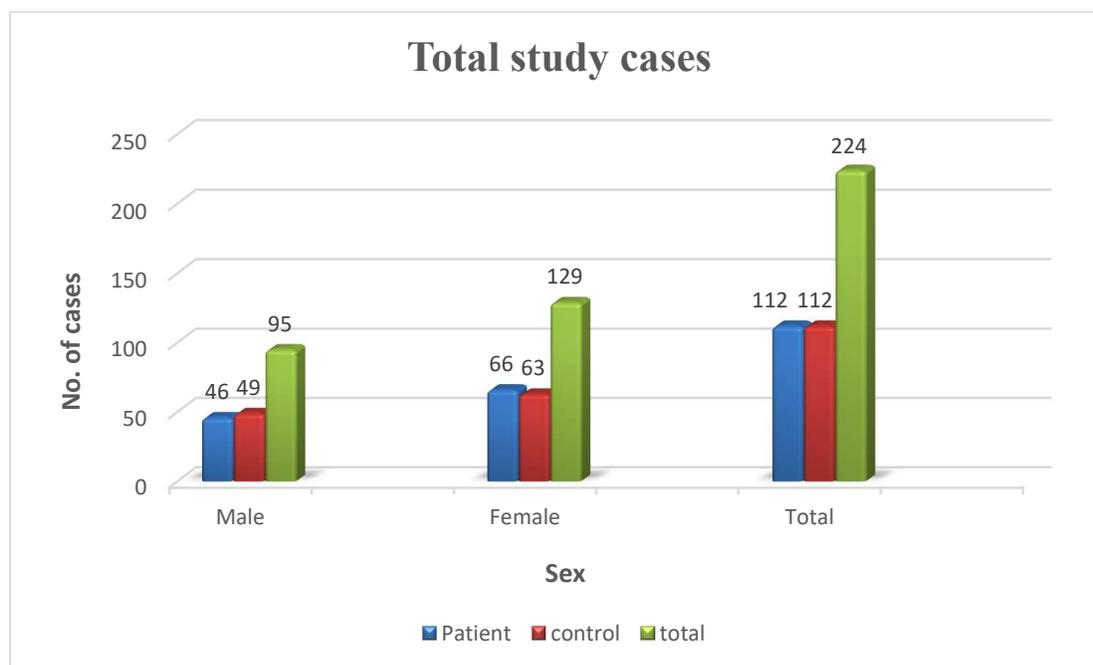
Statistical analysis was performed with SPSS statistical program version 23 and Microsoft Excel 2021. Numerical data were defined according to the mean, and standard deviation of the mean, for comparison between different groups, logistic regression was used. The lowest accepted difference in statistical importance is 0.05 or less.

## Results

### The distribution of the study population based on sex

All study populations are illustrated in figure (1-1) observed with a total of 112 (100%) individuals (46 (41.1%) males and 66 (58.9%) females) in the patient group and a total of 112

(100%) individuals (49 (43.8%) males and 63 (56.3%) females) in the control group from the total study cases 224 (100.0%).



**Figure (1-1): The distribution of the study population based on sex.**

**The distribution of the study population according to age groups (Years).**

Results shown in table (1-1) document that the highest age group of patients with the gastroduodenal disorder was the second to the third decade (21-30 years), which were 9 (39.1%) males and 14 (60.9%) females from patients group and 13 (40.6%) males and 19 (59.4%) females from the control group from the total study population 224 (100%), followed by the third to the fourth decade (31-40 years) were 12 (46.2%) males and 14 (53.8%) females from the patient group and 11 (45.8%) males and 13 (54.2%) females from the control group closely with the fourth to the fifth decade (41-50 years) were 7 (31.8%) males and 15 (68.2%) females from the patient group and 7 (30.4%) and 16 (69.6%) from the control group. The age group less than or equal to twenty years ( $\leq 20$ ) were 6 (54.5%) males and 5 (45.5%) females from the patient group and 6 (60.0%) males and 4 (40.0%) females from the control group were relatively close to age group greater than or equal to sixty years ( $\geq 60$ ) were 6 (46.2%) males and 7 (53.8%) females from the patient group and 4 (44.4%) males and 5 (55.6%) females from the control group, while the age group from fifty one to sixty years (51-60) which were 6 (35.3%) males and 11 (64.7%) females from the patient group and 8 (57.1%) males and 6 (42.9%) females from the control group from the total study population 224 (100%). Statistically, this difference was non-significant. The distribution of the study population according to age groups was statistically non-significant (p-value= 0.755).

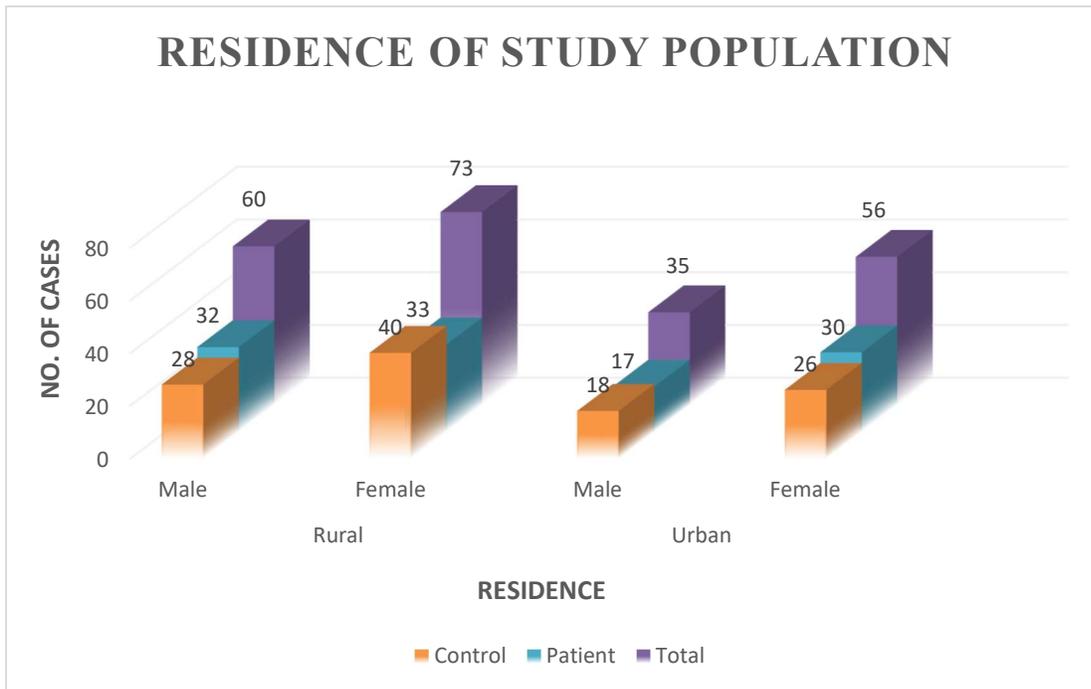
**Table (1-1): The distribution of the study population according to age groups (Years)**

Age groups (Years)	Sex		Category		Total	p-value
			Patient	Control		
≤ 20	Male	No.	6	6	12	0.801
		%	54.5%	60.0%	57.1%	
	Female	No.	5	4	9	
		%	45.5%	40.0%	42.9%	
(21 to 30)	Male	No.	9	13	22	0.911
		%	39.1%	40.6%	40.0%	
	Female	No.	14	19	33	
		%	60.9%	59.4%	60.0%	
(31 to 40)	Male	No.	12	11	23	0.982
		%	46.2%	45.8%	46.0%	
	Female	No.	14	13	27	
		%	53.8%	54.2%	54.0%	
(41 to 50)	Male	No.	7	7	14	0.920
		%	31.8%	30.4%	31.1%	
	Female	No.	15	16	31	
		%	68.2%	69.6%	68.9%	
(51 to 60)	Male	No.	6	8	14	0.224
		%	35.3%	57.1%	45.2%	
	Female	No.	11	6	17	
		%	64.7%	42.9%	54.8%	
≥ 60	Male	No.	6	4	10	0.937
		%	46.2%	44.4%	45.5%	
	Female	No.	7	5	12	
		%	53.8%	55.6%	54.5%	
Total	Male	No.	46	49	95	0.685
		%	41.1%	43.8%	42.4%	
	Female	No.	66	63	129	
		%	58.9%	56.3%	57.6%	
	Total	No.	112	112	224	
		%	100.0%	100.0%	100.0%	
Chi-square	2.64					
P-value	0.755					

\* Chi-Square

The distribution of the study population according to the residence.

Figure (1-2) illustrate that the greatest number of cases associated with gastroduodenal disorders were in rural areas with a total of 60 (100.0%) individuals of 28 (41.2%) males from the control group and 32 (49.2%) males from the patient group and a total of 73 (100.0%) individuals of 40 (58.8%) females from the control group and 33 (50.8%) females from the patients' group. Statistically, this difference was non-significant (P-value=0.351). The total cases from urban areas were relatively fewer with a total of 35 (100.0%) individuals of 18 (40.9%) males from the control group 17 (36.2%) males from the patients' group and a total of 56 (100.0%) individuals of 26 (59.1%) females from the control group and 30 (63.8%) females from the patients' group. Statistically, this difference was non-significant ( P-value=0.642).



**Figure (1-2): The distribution of the study population according to the residence. The distribution of the study population according to marital status.**

Table (1-2) documents that the greatest number of gastroduodenal disorders are found among married individuals with a total of 158 (100.0%) cases with 79 (100%) individuals of 34 (43.0%) males and 45 (57.0%) females in the patients' group and 79 (100.0%) individuals of 33 (41.8%) males and 46 (58.2%) females in the control group. Statistically, this difference was non-significant (P-value=0.872). A total of 27 (100%) cases in the single group with 12 (100%) individuals of 7 (58.3%) males and 5 (41.7%) females in the patients' group and 15 (100%) individuals of 11 (73.3%) males and 4 (26.7%) females in the control group. Widow individuals comprise a total of 20 (100%) cases of 9 (100%) individuals of 3 (33.3%) males and 6 (66.7%) females in the patients' group and 11 (100%) individuals of 4 (36.4%) males and 7 (63.3%) females in the control group, the difference was statistically non-significant (P-value=0.888). A total of 19 (100%) individuals in the divorced group, 12 (100%) individuals of 2 (16.7%) males

and 10 (83.3%) females from the patients group and 7 individuals of 1 (14.3%) male and 6 (85.7%) females from the control group. Statistically, this difference was non-significant (P-value=0.891).

**Table (1-2): The distribution of the study population according to marital status.**

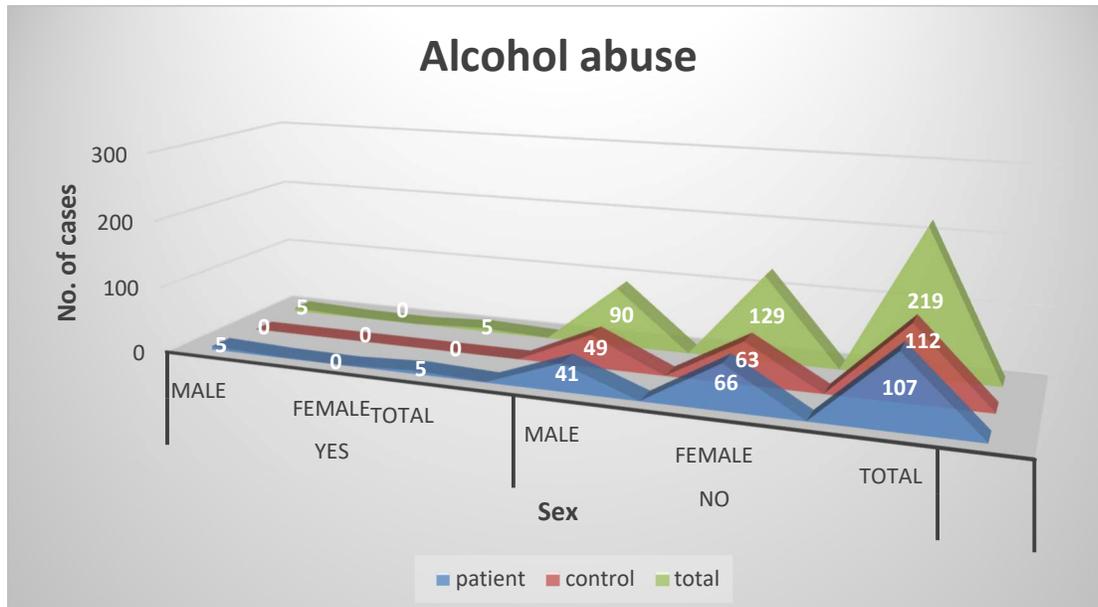
Marital status	Sex		Category		Total	Sig.*
			Patient	Control		
Single	Male	No.	7	11	18	0.411
		%	58.3%	73.3%	66.7%	
	Female	No.	5	4	9	
		%	41.7%	26.7%	33.3%	
	Total	No.	12	15	27	
		%	100.0%	100.0%	100.0%	
Married	Male	No.	34	33	67	0.872
		%	43.0%	41.8%	42.4%	
	Female	No.	45	46	91	
		%	57.0%	58.2%	57.6%	
	Total	No.	79	79	158	
		%	100.0%	100.0%	100.0%	
Widow	Male	No.	3	4	7	0.888
		%	33.3%	36.4%	35.0%	
	Female	No.	6	7	13	
		%	66.7%	63.6%	65.0%	
	Total	No.	9	11	20	
		%	100.0%	100.0%	100.0%	
Divorced	Male	No.	2	1	3	0.891
		%	16.7%	14.3%	15.8%	
	Female	No.	10	6	16	
		%	83.3%	85.7%	84.2%	
	Total	No.	12	7	19	
		%	100.0%	100.0%	100.0%	
<b>Chi-square</b>	1.849					
<b>P-value</b>	0.604					

\*Chi-Square Test

**The distribution of the study population according to alcohol abuse.**

The total cases of alcohol abuse in the study population are illustrated in figure (1-3). A total of 5 (100%) individuals of 5 (100%) males and 0 (0.0%) females from the patients' group are drinking alcohol. A total of 107 individuals of 41 (38.3%) males and 66 (61.7%) females are not drinking. The control group were a total of 112 (100%) individuals of 49 (43.8%) males and 63

(56.3%) females are not alcohol drinking. Statistically, this difference was significant (P-value=0.024).



**Figure (1-3): The distribution of the study population according to alcohol abuse. The distribution of the study population according to smoking.**

Table (1-3) documents that most patients suffering from gastroduodenal disorders are heavy smokers, with a total of 33 (100%) individuals of 25 (75.8%) males and 8 (24.2%) females. A total of 191 (100%) cases of 79 (100%) individuals (21 (26.6%) males and 58 (73.4%) females) from the patients' group and a total of 112 (100%) individuals of 49 (43.8%) males and 63 (56.3%) females in the control group are non-smokers. Statistically, this difference was highly significant (P-value=0.001).

**Table (1-3): The distribution of the study population according to smoking.**

Smoking	Sex		Category		Total	P-value
			Patient	Control		
Yes	Male	No.	25	0	25	0.015
		%	75.8%	0.0%	75.8%	
	Female	No.	8	0	8	
		%	24.2%	0.0%	24.2%	
	Total	No.	33	0	33	
		%	100.0%	0.0%	100.0%	
No	Male	No.	21	49	70	
		%	26.6%	43.8%	36.6%	
	Female	No.	58	63	121	
		%	73.4%	56.3%	63.4%	
	Total	No.	79	112	191	

		%	100.0%	100.0%	100.0%	
<b>Chi-square</b>	38.702					
<b>P-value</b>	0.001					

\*The control group was selected as non-smoker cases.

## Discussion

All individuals in the current study were subjected to a thorough examination procedure for an accurate diagnosis of *H. pylori* infection. *H. pylori* can be diagnosed by endoscopic and non-endoscopic techniques. In the current study, both urea breath test (non-endoscopic test) and biopsy urease test (endoscopic test) were used as diagnostic tool.

In this investigation, we found that most cases of GIT disorders were recorded among females with 66 (58.9%) cases from the patients' group and 63 (56.3%) females from the control group versus 46 (41.1%) males in the patients' group and 49 (43.8) males in the control group, according to these findings our results were similar to (Ferroni, *et al.*, 2022, Almario, *et al.*, 2018 and Perona, *et al.*, 2005). Based on feedback from the online survey by (Sperber *et al.*, 2021), they reported that FGIDs were more prevalent among women than men.

Cain *et al.*, (2009) reported that GIT symptoms were more strongly in postmenopausal women. We suggest that hormonal dysregulation in women during pregnancy, lactation, and pre and/or post-menopausal represent a risk factor for serious chronic complaints and severe, moderate to self-limited recurring GI symptoms. Many physiological changes occur during women lifetime, which makes them prone to bacterial infections and immunological threats than men, gastrointestinal diseases in females characterized by a variety of physiological changes that might result in a variety of symptoms, often gastrointestinal issues such as heartburn, nausea, vomiting, constipation, and chronic digestive disorders were reported by (Gomes *et al.*, 2018)

Responding to the present study, the highest age group of individuals with GIT disorders was the second to the third decade (21-30) years with a total of 14 (60.9%) females and 9 (39.1%) males from the patients' group versus a total of 19 (59.4%) females and 13 (40.6%) males from the control group. While the lowest cases of GIT disorders were recorded in the age group under or equal to twenty years ( $\leq 20$ ) with 5 (45.5%) females and 6 (54.5%) males from the patients' group versus a total of 4 (40.0%) females and 6 (60.0%) males from the control group, our results were agreed with Dumic *et al.*, (2019) who recommended that the prevalence of GIT disorders associated with *H. pylori* infection is highest among children in developing nations, while it rises with age in developed countries and elderly people appear to experience more severe upper gastrointestinal symptoms related to *H. pylori* infection. The study by Aitila *et al.*, (2019) concluded that the prevalence of *H. pylori* among children aged 1-15 years presenting with gastrointestinal complaints was high and increases with age, overcrowding school attendance, unsafe source of school drinking water, and the inadequate sanitary facility at school represent the major risk factors for *H. pylori* infection.

According to resident of our study population the greatest number of cases associated with GIT disorder were recorded in the rural areas with 28 (41.2%) males and 40 (58.8%) females from the

control group versus 32 (49.2%) males and 33 (50.8%) females from the patients' group, these results were similar to Gizaw *et al.*, (2020). Another study done by Chuah & Mahadeva, (2018) revealed great differences in the prevalence of GIT disorders between urban and rural populations in different countries.

These Urban-Rural GI disorders communities' variations may be attributed to Multiculturalism, physiological sensitivity, Diet, environmental and socio-demographic factors, and increasing industrialization.

Regarding marital status, married individuals have the highest rate of GIT disorders with 34 (43.0%) males and 45 (57.0%) females in the patients' group and 33 (41.8%) males and 46 (58.2%) females in the control group. The present study supposed that more frequent disorders among married individuals mainly newly married couples may be due to uncontrolled or fatty diet, frequent restaurant dining, unhealthy fast food, and sources of marriage issues resulting in anxiety and stress. In response to our current results, the lowest cases suffering from GI disorder were the divorced group with 2 (16.7%) males and 10 (83.3%) females in the patients' group and 11 (14.3%) males and 6 (85.7%) females in the control group. Based on these findings we declare that the brain has direct effects on the digestive system, confused mutual signals between the gut-brain milieu might cause gastric upset since the gastrointestinal is sensitive to emotional stress.

In the present study, the effects of alcohol consumption manifest a significant relationship with the occurrence of GIT disorders relatively associated with *H. pylori* infection, these results were in agreement with (Zhang, *et al.*, 2009) how reported that alcohol consumption appears to be statistically associated with *H. pylori* infection. Alcohol intake and persistent *H. pylori* infection are a major risk factor for gastric tumorigenesis. Together, they contribute to increase cancer cell proliferation and survival (Aziz, *et al.*, 2022). Related to gender, a relationship was reported in a study conducted in Japan between the frequency of alcohol drinking habits and failure of first line eradication therapy of *H. pylori* in women than men (Ozeki, *et al.*, 2019).

Smoking habits which considered a major risk factor affecting GIT and lead to many GIT disorders. In this study, a total of 33 individuals of 25 (75.8%) males and 8 (24.2) females from the patients' group were smokers. These results agree with many previous studies (Gui *et al.*, 2021, Berkowitz *et al.*, 2018, Shanahan *et al.*, 2018, and Loretan, *et al.*, 2022), but Zhang, *et al.*, (2009) reported "there is no significant association between development of *H. pylori* infection and smoking". Smoking represents a source of toxic chemical exposures to humans and the adverse consequences of cigarette smoking are mediated by its effect on both neuronal and neuro-inflammatory systems (Gui *et al.*, 2021).

Smoking is associated with a significantly lower bacterial diversity in the upper small intestine mucosa compared to people who had never smoked (Shanahan *et al.*, 2018). Cigarette smoking also alters the risks associated with GI infections, most notably *Helicobacter pylori* infection (Parasher and Eastwood, 2000). Nicotine may impact the gastrointestinal epithelial blood flow, mucus secretion, and epidermal growth factor efflux, which may help the worthy organism colonization after exposure. According to WHO smokers will develop serious smoking-related

diseases, such as chronic obstructive pulmonary disease (COPD), cardiovascular disease, and cancers (WHO, 2022)

Smoking generates potential free radicals that cause harmful damage to the biomolecules including lipids, DNA, and proteins leading to oxidative stress and mischievous human diseases such as Diabetes mellitus, lung cancer, gastric cancer and acceleration of aging process (Phaniendra *et al.*, 2015).

## References

1. Adinortey, M. B.; Ansah, C.; Adinortey, C. A.; Bockarie, A. S.; Morna, M. T.; and Amewovor, D. H. (2018). Isolation of *Helicobacter pylori* from gastric biopsy of dyspeptic patients in Ghana and in vitro preliminary assessment of the effect of *Dioscorea rotundifolia* extract on its growth., *J. Trop. Med.* 2018:1-6.
2. Fan, L.; Li, R.; Li, H.; Zhang, J.; and Wang, L. (2018). genes in *Helicobacter pylori* isolated from gastric ulcer patients. 42(4):155-62.
3. Kumar S. (2016). *Essentials of Microbiology*. 1<sup>st</sup> ed., 299-300.
4. Yong, X.; Tang, B.; Li, B.; Xie, R.; Hu, C.; Luo, G.; Qin, Y.; Dong, H.; and Yanget, S. (2015). *Helicobacter pylori* virulence factor CagA promotes tumorigenesis of gastric cancer via multiple signaling pathways. *Cell Commun. Signal.*, 13(30):1-13.
5. AL-Abdul. A. A. (2014). Detection of *Helicobacter pylori* IgG in diabetic patients and non-diabetic. *University of Thi-Qar, J. Sci.*, 4(3):53-57.
6. Hooi, JKY.; Lai, WY.; Ng, WK.; Suen, MMY.; Underwood, FE.; Tanyingoh, D.; Malfertheiner, P.; Graham, Y. D.; Vincent W.S.; Wong, W.S.; Justin, C.Y.; Wu, C.Y.; Francis K.L.; Chan, K.L.; Joseph, J.Y.; Sung, J.Y.; Gilead, G.; Kaplan, G.G.; and Ng, C. (2017). The global prevalence of *Helicobacter pylori* infection: systematic review and meta-analysis. *gastroenterol.*, 153(2):420-429.
7. Reshetnyak, VI.; Burmistrov, AI.; and Maev, IV. (2021). *Helicobacter pylori*: Commensal, symbiont, or pathogen?. *World J. Gastroenterol.*, 27(7):545-560.
8. Yang, X.; Li, H.; Cheng, T.; Xia, W.; Lai, Y. T.; and Sun, H. (2014). Nickel translocation between metallochaperones HypA and UreE in *Helicobacter pylori*. *Metallomics*, 6(9):1731-1736.
9. Atherton, J. C. (2006). The pathogenesis of *Helicobacter pylori* induced gastro-duodenal diseases. *Annu. Rev. Pathol.*, (1):63-96.
10. Schwartz, J. T. (2006). Role of urease in megasome formation and *Helicobacter pylori* survival in macrophages. *J. Leuk. Biol.* 79(6):1214-1225.
11. Al-Sulami, A. A., Al-Edani, T. A. A., and Al-Abdula, A. A. (2012). Culture method and PCR for the detection of *Helicobacter pylori* in drinking water in Basrah governorate Iraq. *Gastroenterol. Resea. Pract.*, 2012, 1-6.
12. AL-Hilfi N.; Mohameed, K.; Al-Hilfi, D.; and Ali, N. (2021). Accuracy of serological and stool antigen tests (non-invasive) for detection of *H. pylori*, *J. Uni. Duhok*, 24(1):54-59.
13. Alatbee, A. H. D. (2019). High prevalence of *Helicobacter pylori* in Basra city Southern of Iraq, *J. Phys.*, 1279 (2019):1-7.

14. Ferroni, E.; Denas, G.; Gennaro, N.; Fedeli, U.; and Pengo, V. (2022). Gender related differences in Gastrointestinal bleeding with oral anticoagulation in atrial fibrillation., *J. Cardiovasc. Pharmacol. Therap.*, 27:1-6.
15. Almario, C.; Ballal, M.; Chey, W.; Nordstrom, C.; Khanna, D.; and Spiegel, B. (2018). Burden of Gastrointestinal symptoms in the United States: results of a nationally representative survey of over 71,000 Americans. *Am. J. Gastroenterol.*, 113(11):1701-1710.
16. Perona, M.; Benasayag, R.; Perello, A.; Santos, J.; Zarate, N.; Zarate, P.; and Mearin, F. (2005). Prevalence of functional gastrointestinal disorders in women who report domestic violence to the police. *Clin. Gastroenterol. Hepatol.*, 3(5):436-441.
17. Sperber, A. D.; Bangdiwala, S. I.; Drossman, D. A.; Ghoshal, U. C.; Simren, M.; Tack, J.; Whitehead, W. E.; Dumitrascu, D. L.; Fang, X.; Fukudo, S.; Kellow, J.; Okeke, E.; Quigley, E. M. M.; Schmulson, M.; Whorwell, P.; Archampong, T.; Adibi, P.; Andresen, V.; Benninga, M. A.; and Palsson, O. S. (2021). Worldwide prevalence and burden of functional gastrointestinal disorders, results of Rome Foundation Global study. *Gastroenterol.*, 160(1):99-114.
18. Cain, K.; Jarrett, M.; Burr, R.; Rosen, S.; Hertig, V.; Heitkemper, M. (2009). Gender Differences in Gastrointestinal, Psychological, and Somatic Symptoms in Irritable Bowel Syndrome. *Dig. Dis. Sci.*, 54(7):1542-1549.
19. Gomes, C. F.; Sousa, M.; Lourenco, I.; Martins, D.; and Torres, J. (2018). Gastrointestinal diseases during pregnancy: What does the gastroenterologist need to know. *Ann. Gastroenterol.*, 31(4):385-394.
20. Dunic, I.; Nordin, T.; Jecmenica, M.; Stojkovic Lalosevic, M.; Milosavljevic, T.; and Milovanovic, T. (2019). Gastrointestinal tract disorders in older age. *Canad. J. Gastroenterol. Hepatol.*, 2019:1-19.
21. Aitila, P.; Mutyaba, M.; Okeny, S.; Ndawula Kasule, M.; Kasule, R.; Ssedyabane, F.; Okongo, B.; Onyuthi Apecu, R.; Muwanguzi, E.; and Oyet, C. (2019). Prevalence and risk factors of *Helicobacter pylori* infection among children aged 1 to 15 years at Holy Innocents Children's Hospital, Mbarara, South Western Uganda. *J. Trop. Med.*, 2019:1-6.
22. Gizaw, Z.; Addisu, A.; and Guadie, D. (2020). Common gastrointestinal symptoms and associated factors among under-5 children in Rural Dembiya, Northwest Ethiopia: A community-based cross-sectional study. *Environmental Health Insights*, 14:1-7.
23. Chuah, K. H.; and Mahadeva, S. (2018). Cultural factors influencing functional gastrointestinal disorders in the east. *J. Neurogastroenterol. Motil.*, 24(4):536-543.
24. Zhang, L.; Eslick, G. D.; Xia, H. H. X.; Wu, C.; Phung, N.; and Talley, N. J. (2009). Relationship between alcohol consumption and active *Helicobacter pylori* infection. *Alcohol and Alcoholism*, 45(1):89-94.
25. Aziz, F.; Chakraborty, A.; Liu, K.; Zhang, T.; Li, X.; Du, R.; Monts, J.; Xu, G. Li, Y.; Bai, R.; and Dong, Z. (2022). Gastric tumorigenesis induced by combining *Helicobacter pylori* infection and chronic alcohol through IL-10 inhibition. *Carcinogenesis*. 43(2):126-139.

26. Ozeki, K; Asano, M; Furuta, T; and Ojima, T, (2019). Relationship between primary eradication of *Helicobacter pylori* and drinking habits in women: collaborative research between a pharmacy and a clinic. *Epidemiology and Infection*, 147:1-5.
27. Gui, X.; Yang, Z.; and Li, M. D. (2021). Effect of cigarette smoke on gut microbiota. *Front. Physiol.*, 12(June);1-14.
28. Berkowitz, L.; Schultz, B. M.; Salazar, G. A.; Pardo-Roa, C.; Sebastian, V. P.; Alvarez-Lobos, M. M.; and Bueno, S. M. (2018). Impact of cigarette smoking on the gastrointestinal tract inflammation: Opposing effects in Crohn's disease and ulcerative colitis. *Front. Immunol.*, 9(JAN):1-10.
29. Shanahan, E. R.; Shah, A.; Koloski, N.; Walker, M. M.; Talley, N. J.; Morrison, M.; and Holtmann, G. J. (2018). Influence of cigarette smoking on the human duodenal mucosa-associated microbiota. *Microbiome*, 6(1):1-12.
30. Loretan, C.; Cornelius, M.; Jamal, A.; Cheng, Y.; and Homa, D, 2022. Cigarette Smoking Among US Adults with Selected Chronic Diseases Associated with Smoking, 2010–2019, *Prev. Chronic Dis.*, 19:1-6.
31. Zhang, L.; Eslick, G. D.; Xia, H. H. X.; Wu, C.; Phung, N.; and Talley, N. J. (2009). Relationship between alcohol consumption and active *Helicobacter pylori* infection. *Alcohol and Alcoholism*, 45(1):89-94.
32. Parasher, G.; and Eastwood, GL. (2000). Smoking and peptic ulcer in the *Helicobacter pylori*, era. *Eur. J. Gastroenterol. Hepatol.*, 12(8):843-53.
33. WHO, (20 May) 2022, Chronic obstructive pulmonary disease (COPD).
34. Phaniendra, A., Jestadi, D. B., and Periyasamy, L. (2015). Free Radicals: Properties, Sources, Targets, and Their Implication in Various Diseases. *Ind. J. Clin. Biochem.*, 30(1):11-26.