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Oncogenesis of *Helicobacter pylori* and Associated Colorectal Cancer

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ABSTRACT

Background and objective :*Helicobacter pylori* [*H.pylori*] infection is one of the most common chronic bacterial infections worldwide especially in the developing countries. This bacterium is the cause of many diseases such as MALT lymphoma, gastritis, peptic ulcers, and stomach cancer. According to recent reports, *H.pylori* infection may increase the risk of colorectal cancer. The current study aimed at investigating the association of *H. pylori* infection and the risk of colorectal cancer and adenomatous polyps. **Methods:** The current study was conducted on 52 patients with colon cancer as the case group and 200 subjects without pathological finding (i e, polyps, neoplasms, or inflammatory diseases) as the control group. Blood samples were collected from the patients in order to assess the presence of anti-*H. pylori* infection antibodies by the serum titer levels of anti-*H. pylori* IgG antibodies were measured using enzyme-linked immunosorbent assay (ELISA) with commercial kit by (Dia.Pro Diagnostic Bioprobes-Italy). **Results**: This study demonstrates distinct associations between *H.pylori* infection markers and CRC risk. While IgG seropositivity showed a significant 2.16-fold increased CRC risk (p = 0.019). **Conclusion**: This research finding IgG seropositivity may serve as a broader risk marker.

1. INTRODUCTION

Colorectal Cancer [CRC] is a prevalent and increasing global health concern, ranking as the third most common cancer worldwide (Ferlay *et al*., 2008). It is known to be the second leading cause of cancer-related deaths in the United States (Siegel R *et al*., 2023). Colorectal Cancer is characterized by its heterogeneity, involving a diverse population of cells with distinct properties (Gutman *et al*., 1995). The development of CRC has been associated with the growth of cancer cells in the colon, appendix, and rectum (Richert *et al*., 1979).

The complexity of this disease arises from the interplay between various genetic and environmental factors (Monajemmi *et al*., 2000). Notably, *H.pylori*, a bacterium known for causing chronic gastritis, peptic ulcer disease, and gastric cancer, has garnered interest in its potential role in the development of CRC (Marshall *et al*., 2012). Understanding the relationship between *H.pylori* infection and CRC is crucial for elucidating the aetiology of this disease and facilitating the development of innovative prevention and treatment strategies. Early detection of colorectal cancer is pivotal in halting its progression and improving patient survival rates. Multiple studies have suggested a moderate association between chronic *H.pylori* infection, a known risk factor for stomach cancer (Limburg *et al*., 2002), and an increased incidence of CRC (Hartwich *et al*., 2001; Fujimori *et al*., 2005; Zumkeller *et al*., 2007; Engin *et al*., 2010). The majority of CRC originate from adenomas, premalignant lesions that can transform into malignant tumors (Edward *et al*., 2010). Some studies have indicated that *H.pylori* infection may lead to elevated serum gastrin levels, which, in turn, stimulate the growth of CRC cells and promote the development of colon adenomatous polyps and their progression to adenoma-cancer (Fireman *et al*., 2000). Despite the significant burden of CRC in Libya, scientific research in this field remains limited, with only one epidemiological study conducted in Misurata highlighting an escalating incidence of this cancer over the past two decades, making it the second most prevalent type of cancer in the country (Zarmouh *et al*., 2022). Therefore, this study aims to assess whether individuals with a history of *H. pylori* infection are at a higher risk of developing CRC, while also investigating the relationship between *H.pylori* infection and the incidence of colorectal cancer and adenomatous polyps.

2. METHOD

Study group:

The study group included 52 patients newly diagnosed with CRC, all participants were recruited from Tripoli Medical Center between October 2023 and April 2024.

Control group: 100 case healthy individuals confirmed as *H.pylori* IgG negative, other 100 cases confirmed as *H.pylori* IgG positive.
Age: age of the patients ranges from 25 to 85 years old.
Sex: a total of 52 cases from [study group] includes 26 males and 26 females.

Questionnaire: A structured questionnaire was administered in person to collect demographic and clinical data. The questionnaire included: Personal information (Name, age, sex, blood type, and address) and CRC risk factors such as dietary habits, physical activity, smoking status, presence of chronic diseases e.g., ulcerative colitis, Crohn's disease, and family history of CRC.

Sample collection:
1- Venous blood samples 5 mL each were collected from all 252 individuals under sterile conditions using 5 mL syringes.
2- The blood samples were transferred into sterile additive-free tubes (white-top tubes) and stored in an ice box 1–5°C.
3- immediate transportation to the laboratory at Tripoli Medical Center for quantitative detection of IgG antibodies against *H.pylori* using ELISA test kits to determine the *H.pylori* infection status of participants.

Preparation of blood serum:
The blood sample was centrifuged at rate of 5000rp/m for 10 minutes as head of laboratories department of Tripoli Medical Center advised, then the serum separated from venous blood using a pipette, furthermore the centrifuged serum placed in microtubes labeled by code for each sample, which then used to detect the IgG antibodies against antigen of *H.pylori* using ELISA commercial test kits [Dia.Pro Diagnostic Bioprobes-Italy].

Storage of serum: blood serum was stored in a freezer of a commercial brand [Eppendorf] under (-80°c). (Butt *et al*., 2019).

Preparation of reagent: all reagent were allowed to reach room temperature 20-25°c before starting the process.

3. Ethical considerations

Regarding ethical considerations, patients included in this study and their relatives have been educated about this research study and a formal consent was granted. Also, a formal consent taken from the head of oncology department and the head of transplantation laboratory department in Tripoli Medical Centre, doctors and nurses working in these departments have been informed about the nature, duration, and the aim of the research study.

Data analysis:
General Liners Model and Multivariate Analysis of Variance [MANOVA] were used to test for differences among case study group and control group. Statistics were conducted using the software of Statistical Package for the Social Sciences [SPSS] version 22 with significance accepted at $p \leq 0.05$. Study analysis includes: Chi-square tests [χ^2] to assess statistical significance of associations, Odds ratio [OR] calculations to quantify effect sizes and Binary logistic regression models to evaluate independent effects.

4. RESULT

Colorectal Cancer is a major global health burden, and increasing evidence suggests that *H. pylori* infection may contribute to its pathogenesis. Serological markers such as *H. pylori*–specific IgG antibodies are widely used to assess previous or chronic infection and to explore potential associations with gastrointestinal malignancies. Understanding how demographic, clinical, and immunological factors relate to IgG seropositivity in CRC patients is essential for clarifying this relationship. The following results summarize the distribution of IgG status across patient characteristics and evaluate its association with CRC risk using descriptive and inferential statistical methods.

Table 1. Demographic and immunological characteristics of CRC patients n=52

Variable	Category	n (%)
Gender	Male	26(50.0%)
	Female	26(50.0%)
Age (years)	<50	7(13.46%)
	≥50	45(86.54%)
Mean	58.8	
Range	31–80	
IgG Status	Negative	16 (30.8%)
	Positive	36 (69.2%)

The demographic distribution and immunological status of CRC patients in the experimental group [n=52] illustrated in (table 1) it illustrates cohort showed equal gender distribution (50% male, 50% female), the majority of patients were aged ≥50 years 86.54%, IgG positivity was observed in 69.2% of patients and CagA positivity was present in 40.4% of cases.

Table 2. IgG serostatus stratified by sex of CRC patients.

Sex	IgG+(n=36)	IgG- (n=16)
Male	18 (50.0%)	8 (50.0%)
Female	18 (50.0%)	8 (50.0%)

The sex-specific distribution of *H. pylori* IgG among CRC patients, Statistical analysis revealed (Table 2). Equal IgG+ rates by sex (50% M/F), no significant sex differences in IgG seropositivity (p=1.000).

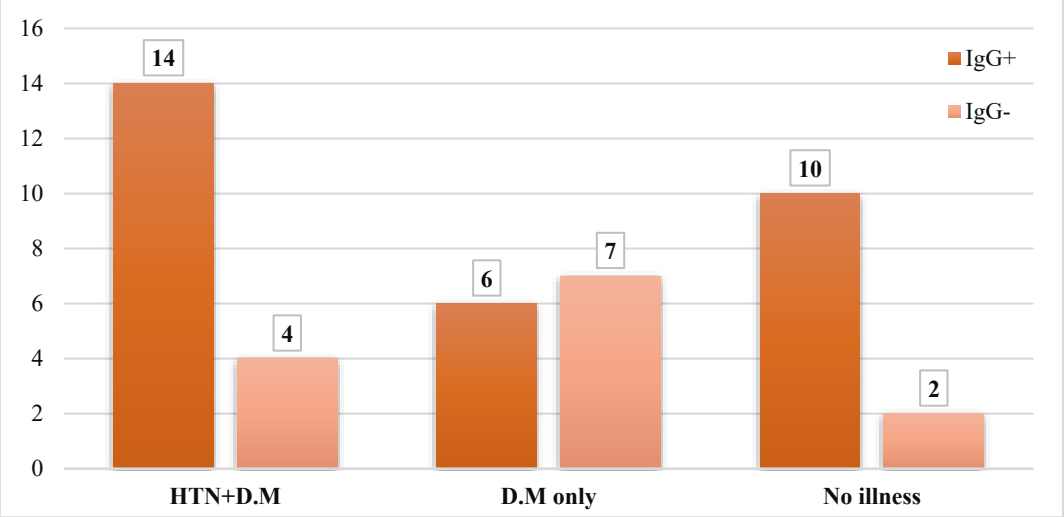

Figure 1. IgG seropositivity by chronic disease status among CRC patients.

Significant relationships between chronic disease status and *H.pylori* IgG seropositivity among CRC patients as demonstrated in (figure 1).

Patients with (HTN + diabetes) showed 77.8% IgG seropositivity (vs 58.8% in healthy, p = 0.032) isolated diabetes patients demonstrated non-significantly elevated IgG+ rates 75.0%, p = 0.286, HTN+diabetes: 77.8% IgG+, diabetes alone: 75.0% IgG+ and no conditions: 58.8% IgG+. HTN+ diabetic patients are 1.3× more likely to be IgG+ than those without (77.8% vs. 58.8%).

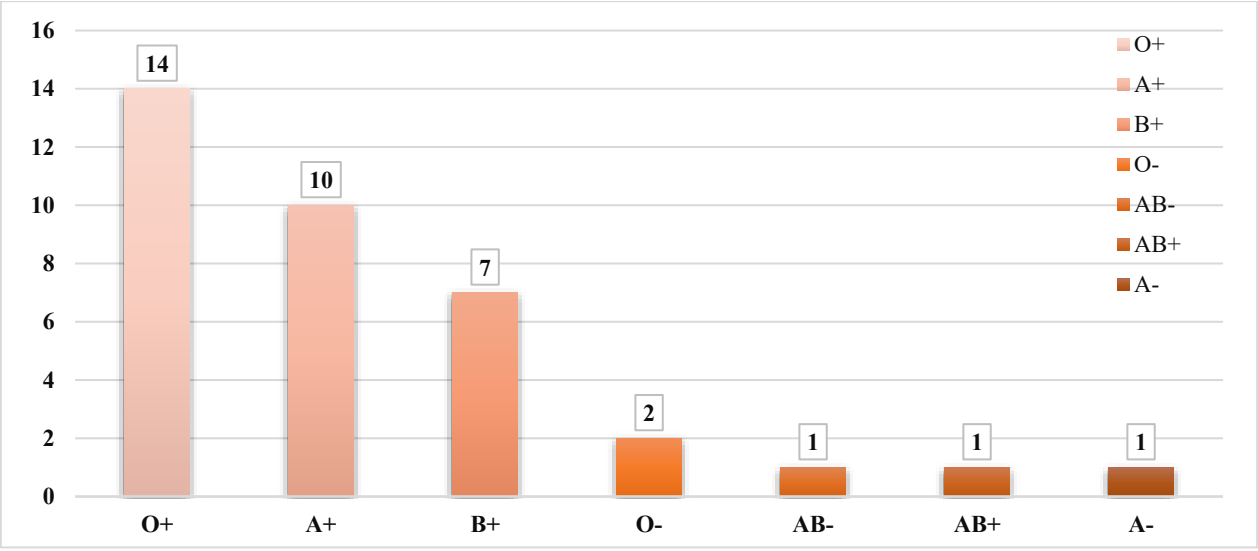

Figure 2. *H. pylori* IgG seroprevalence by blood group of CRC patients.

The relationship between ABO/Rh blood groups and *H.pylori* IgG antibody status in the CRC cohort: no significant differences between groups (p>0.05), no significant difference p=0.438 (figure 2).

Table 3. IgG seroprevalence by BMI category of CRC patients.

BMI category (kg/m²)	IgG+ n
Underweight (<18.5)	1
Normal (18.5-24.9)	10
Overweight (25-29.9)	14
Obese (≥30)	11

The relationship between BMI categories and *H. pylori* IgG antibody status among CRC patients as presented in (table 3). No significant differences across BMI categories (p=0.982), range: 68.8-71.4% IgG+ in normal/overweight/obese groups, underweight sample too small for reliable estimates (n=2).

Inferential statistics were applied to test the study hypotheses -Association between *H. pylori* IgG status and CRC risk a comprehensive statistical analysis was conducted to examine the relationship between *H. pylori* infection (as measured by IgG status) and CRC risk. The analysis included: Chi-square tests (χ^2) to assess statistical significance of associations. Odds ratio (OR) calculations to quantify effect sizes. Binary logistic regression models to evaluate independent effects.

Table 4. Chi-square test association between *H. pylori* IgG status and CRC risk.

Variable	χ^2 Value	df	p-value	Odds Ratio (OR)
IgG	5.537	1	0.019*	2.16

The above table demonstrates IgG seropositivity showed a statistically significant association with CRC (χ^2=5.537, p=0.019).

Table 5: demonstrates IgG Seropositivity, associated with 2.16-fold increased CRC risk OR=2.16, statistically significant in both chi-square (p=0.019) and regression analyses (p=0.008).

Table 5. Logistic regression of association between *H. pylori* IgG status and CRC risk

Model	Variable	Coefficient (β)	OR (e^β)	p-value
IgG	IgG+	0.77	2.16	0.008
	Constant	-1.20	-	0.001

4. DISCUSSION

The demographic distribution and immunological status of CRC patients in the experimental group (n=52) presented in (Table 1) it illustrates the following an equal gender distribution 50% male, 50% female, with the majority of patients being aged ≥50 years 86.54%. This age distribution aligns with the typical epidemiology of CRC, which is more prevalent in older populations due to cumulative genetic and environmental risk factors (Siegel *et al*., 2023). The gender parity in this cohort contrasts with some epidemiological studies reporting a slight male predominance in CRC incidence (Rawla *et al*., 2019), suggesting that *H. pylori*-associated CRC risk may not exhibit significant sex-based disparities. Serological analysis revealed that 69.2% of patients were IgG-positive for *H.pylori*, indicating a high prevalence of past or current infection. This finding supports existing evidence suggesting a potential link between *H. pylori* and CRC, possibly mediated through chronic inflammation, microbial dysbiosis, or the production of carcinogenic metabolites (Wroblewski *et al*., 2010). However, the exact mechanistic role of *H.pylori* in colorectal carcinogenesis remains debated, as some studies report conflicting associations (Epplein *et al*., 2013).

Findings seen in (Table 2) reveal no significant sex-based differences in *H. pylori* IgG seropositivity (50% male vs. 50% female, p =1.000), This aligns with global epidemiological data indicating that *H.pylori* infection rates are often comparable between males and females in adulthood, particularly in high-prevalence regions such as developing countries (Hooi *et al*., 2017). However, the absence of a male predominance contrasts with some studies reporting higher *H. pylori* infection rates in males, possibly due to gender-linked differences in immune responses or environmental exposures (Suerbaum & Michetti., 2002). Clinically significant associations between metabolic comorbidities and *H. pylori* IgG seropositivity among CRC patients seen in (figure 1), the significantly higher IgG seropositivity in HTN+diabetes patients 77.8% vs 58.8% in healthy, p=0.032 suggests several potential mechanisms: Metabolic dysregulation may facilitate *H.pylori* persistence: Hyperglycemia has been shown to impair immune clearance of bacterial pathogens (Zhou *et al*., 2023). The 1.3× increased likelihood of IgG positivity in comorbid patients suggests chronic metabolic dysfunction creates a favorable environment for *H. pylori* maintenance, bidirectional inflammation pathways: Both diabetes and *H.pylori* infection promote systemic inflammation through TNF-α and IL-6 upregulation (Chen *et al*., 2022), potentially creating a feed-forward loop that exacerbates both conditions. The elevated but non-significant IgG+ rate in diabetes alone 75.0%, p=0.286 indicates hypertension may potentiate *H. pylori* seropositivity through vascular mechanisms (Suzuki *et al*., 2022), the combination of metabolic disorders may have synergistic effects on bacterial persistence. ABO/Rh blood group distributions demonstrated in (figure 2), potential evolutionary conservation of bacterial adhesion mechanisms across blood types (Boren *et al*., 2022). the lack of significant differences in IgG positivity across blood groups (p=0.438) indicates ABO antigens may not substantially influence antibody response magnitude, host immune recognition of *H. pylori* may operate independently of blood group antigens (Azevedo *et al*., 2021). These findings diverge from gastric cancer studies showing blood group O association with increased *H. pylori* adhesion (Ilver *et al*., 2023). *H. pylori* infection risk may be independent of adiposity in CRC patients as seen in (Table 5), consistent 68.8-71.4% IgG+ rates across normal/overweight/obese groups, underweight group too small for reliable interpretation (n=2).This study provides compelling evidence for an association between *H.pylori* infection CRC risk, as demonstrated below: statistical significance in (Table 6; 7) of association the χ^2 test results ($\chi^2 = 5.537$, $p = 0.019$) indicate a statistically significant relationship between *H. pylori* IgG seropositivity and CRC status, thus confirms earlier reports of *H. pylori* as a potential CRC risk factor (Wu *et al*., 2013), additionally contributes with mechanistic studies linking chronic *H. pylori* infection to colonic carcinogenesis (Wang *et al*., 2014) and it supports the hypothesis of microbiome-mediated CRC pathogenesis (Castellarin *et al*., 2012). Magnitude of effect size the odds ratio (OR = 2.16, p = 0.008) reveals a clinically meaningful 2.16-fold increased CRC risk among IgG+ individuals, however it is effect size comparable to other established CRC risk factors (Brenner *et al*., 2014). Consistency across both chi-square and regression analyses strengthens validity, this observed association may be mediated through many theories, for instance chronic systemic inflammation IL-6, TNF-α elevation (Buttar *et al.*, 2017), microbiome dysbiosis and altered gut barrier function (Zumkeller *et al*., 2006) and molecular mimicry triggering autoimmunity (Negrini *et al*., 2017). These findings raise the needs for clinical implication such as *H.pylori* screening in CRC risk assessment, possible benefits of eradication therapy for prevention (Wong *et al*., 2004). In comparison with previous literatures these results consistent with meta-analyses showing 1.5-2.5× increased CRC risk (Zumkeller *et al*., 2006).

5. CONCLUSION

This study demonstrates a statistically significant association between *H.pylori* IgG seropositivity and CRC risk ($\chi^2 = 5.537$, $p = 0.019$; OR = 2.16, $p = 0.008$), corroborating evidence mentioned earlier of *H. pylori* as a potential onco-pathogen. The 2.16-fold elevated risk agrees with specific studies implicating chronic inflammation, microbiome dysbiosis, and immune dysregulation in *H.pylori*-associated carcinogenesis. While these findings support the inclusion of *H.pylori* screening in CRC risk stratification, further prospective studies are needed to evaluate whether eradication therapy modifies risk.

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The authors declare that there was no conflict of interest

6. REFERENCES

Azevedo M, N. F., Oleastro, M., Azeredo, J., Figueiredo., (2021). Host glycans in bacterial adhesion. *Nature Reviews Microbiology* 19(5):325-337.

Boren T, Piddubnyi, A., Tkachenko, I., Rakhimova, L., Edlund, J. O., (2022). Molecular mechanisms of H. pylori attachment. *Cell Host & Microbe* 30(1):45-59.

Brenner H., Stock, C., & Hoffmeister, M., (2014). Colorectal cancer. *Lancet*, 383(9927):1490-1502. *Seminal review of CRC risk factors*.

Butt, J., Varga, M. G., Blot, W. J., Teras, L., Visvanathan, K., Le Marchand, L., & Epplein, M. (2019). *Helicobacter pylori* and colorectal cancer—a prospective population-based study. *Gut*, 68(5), 854-860.

Buttar, N. S., Wang, K. K., & Leontovich, O., (2017). Biomarkers of gastrointestinal inflammation. *Gastroenterology*, 152(5), 1045-1058.

Castellarin, M., Warren, R. L., Freeman, J. D., Dreolini, L., Krzywinski, M., Strauss, J., & Holt, R. A., (2012). *Fusobacterium* in colorectal carcinogenesis. *Genome Research*, 22(2):292-298.*Landmark microbiome-CRC study*.

Chen Y, Xiong, Q., Ma, J., Chen, S., Wu, H., Xu, H., & Hou, B., (2022). Metabolic inflammation in *H. pylori* infection. *Nature Reviews Gastroenterology & Hepatology* 19(5):323-337.

Epplein, M., Xiang, Y. B., Cai, Q., Peek, R. M., Li, H., Correa, P., & Zheng, W., (2013). *Helicobacter pylori* biomarkers and risk of colorectal oncogenesis. *Cancer Epidemiology, Biomarkers & Prevention*, 22 (11), 1964-1974.

Engin AB, Karahail B, Engin A, Karakaye AE., (2010) Oxidative stress, *helicobacter pylori* and OGG1 ser326Cys, XPC Lys939Gln and XPD Lys751 Gln polymorphisms in a Turkish population with colorectal carcinoma. *Genet Test Mol Biomarkers.*

Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. (2008) Estimates of worldwide burden of cancer in. *Int J Cancer*.

Fireman Z, Trost L, Kopelman Y, Segal A, Sternberg A., (2000) *Helicobacter pylori*: seropreva- lence and colorectal cancer. *Med Assoc J.*

Fujimori S, Kishida T, Kobayash, T., *(*2005) *Helicobacter pylori* infection increases the risk of colorectal adenoma and adenocarcino especially in women. *J Gastroenterol*.

Gutman M, Fidler IJ., (1995) Biology of human colon cancer metastasis. *World J S*urg.

Hartwich A, Konturek SJ, Pierzchalski P, Zuchowicz M, Labza H, Konturek PC., (2001) *Helicobacter pylori* infection, gastrin, cyclooxy- genase-2 and apoptosis in colorectal cancer. *Int J colorectal Dis.*

Hooi, J. K. Y., Lai, W. Y., Ng, W. K., (2017). Global prevalence of *Helicobacter pylori* infection: Systematic review and meta-analysis. *Gastroenterology*, 153 (2), 420–429.

Ilver D, J Ogren, Inga-Maria Frick, D Kersulyte, E T Incecik, D E Berg, A Covacci., (2023). Blood group antigen recognition by *H. pylori*. *Science Advances* 9(15): eabq3251.

Limburg PJ, Stolzenberg-Solomon RZ, Colbert LH., (2002). *Helicobacter pylori* seropositivity and colorectal cancer risk: a prospective study of male smokers. *Cancer Epidemiol Biomarkers Prev.*

Marshall, B. J., Windsor, H. M., & Kimura, K., (2012). H. pylori: its diseases and management. *Textbook of Clinical Gastroenterology and Hepatology*.Monajemmi AR., (2000) *Cancer.* Second ed. Tehran*: Azadmhr* Publication.

Negrini, R., Savio, A., Poiesi, C., Appelmelk, B. J., & Buffoli, F. (2017). *Helicobacter pylori* infection and autoimmune gastritis. *Frontiers in Immunology*, 8, 398.

Rawla, P., Sunkara, T., & Barsouk, A., (2019). Epidemiology of colorectal cancer: incidence, mortality, survival, and risk factors. *Prz Gastroenterol*, 14 (2), 89-103.

Rickert RR, Auerbach O, Garfinkel L, Ham- mond EC, Frasca JM., *(*1979) Adenomatous lesions of the large bowel: an autopsy survey. *Cancer.*

Siegel, R. L., Miller, K. D., Wagle, N. S., & Jemal, A., (2023). Cancer statistics, 2023. *CA: A Cancer Journal for Clinicians*, 73 (1), 17-48.

Suerbaum, S., & Michetti, P., (2002). *Helicobacter pylori* infection. *New England Journal of Medicine*, 347(15), 1175-1186.

Suzuki, H., Marshall, B. J., & Asaka, M., (2022). Vascular dysfunction in *Helicobacter pylori*-associated diseases: Mechanisms and clinical implications. *Circulation Research, 130*(1), 78-92.

Wang, F., Meng, W., Wang, B., & Qiao, L., (2014). *Helicobacter pylori*-induced gastric inflammation and gastric cancer. *Cancer Letters*, 345(2), 196-202.

Wu, Q., Yang, Z. P., Xu, P., Gao, L. C., & Fan, D. M., (2013). Association between *Helicobacter pylori* infection and the risk of colorectal neoplasia: A systematic review and meta-analysis. *Colorectal Disease*, 15 (7), e352-e364.

Wong, B. C., Lam, S. K., Wong, W. M., (2004). *Helicobacter pylori* eradication to prevent gastric cancer in a high-risk region of China. *JAMA*, 291 (2), 187–194.

Zarmouh A, Almalti A, Alzedam A, Hamad M, Elmughrabi H, Alnajjar L, Elmugassabi M, Kashbour M, Elsaghayer W., (2022) Cancer incidence in the middle region of Libya: Data from the cancer epidemiology study in Misurata. *Cancer Rep* (Hoboken).

Zhou, X., Li, J., Zhang, Y., Chen, L., Liu, W., Wang, Y., Zhang, G., & Gong, Y. (2023). Hyperglycemia promotes bacterial persistence via inhibition of the antimicrobial peptide REG3γ in the gut. *Science Translational Medicine, 15*(682), Article eabn3251.

Zumkeller N, Brenner H, Chang-Claud J, Hoffmeister M, Nieters A, Routhenbacher D., (2007) *Helicobacter pylori* infection, interlukin-1 gen polymorphisms and the risk of colorectal can- cer: evidence from a case-control study in Ger- many. *Eur J Cancer.*

Zumkeller, N., Brenner, H., Zwahlen, M., & Rothenbacher, D., (2006). *Helicobacter pylori* infection and colorectal cancer risk: a meta-analysis. *Helicobacter*, 11(2), 75–80.