

Study the Role of Helicobacter Pylori Infection in a Group of Iraqi Patients with Colorectal Cancer

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Abstract

Background Increased developed of colorectal tumor may be linked with Helicobacter pylori. However, the underlying mechanisms were still uncertain.

objective: Helicobacter pylori infection in the world, in particular in developing countries, is one of most common chronic bacterial infections, This bacterium is responsible for many diseases such as gastritis, peptic ulcer, lymphoma and in some patients may lead to gastric cancer, it is in the world has known 2nd major cause of death from cancer. *H.pylori* infection may likely raise the risk of colorectal cancer, according to recently published studies. The aimed of this study to detected the role of *H. pylori* in colorectal cancer.

Methods: Serum of 50 colorectal cancer and colorectal normal with positive *H. pylori* infection patients were estimated by 14Urea breath test and 25 subjects with no any inflammatory disease as the control group. from each patient were collected Blood samples to investigated of *H. pylori* specific immunoglobulin G (IgG) and CagA IgG antibodies by using enzyme-linked immunosorbent assay (ELISA).

Results: A total of 50 patients in this study 25 had colorectal cancer and 25 had colorectal normal with *H. pylori* infection (immunoglobulin G (IgG) $P < 0.01$ and CagA IgG antibodies $P < 0.01$) were significantly more prevalent in the patients with colorectal_ cancer and colorectal normal with *Helicobacter pylori* _infection compared with the healthy controls ($P= 0.00019$, $P= 0.00022$ respectively) The relation was statistically non-significant between the antibody seropositivity and gender but Highly significant with age.

Conclusion: The findings indicate that *Helicobacter pylori*_ infection can be regarded as a contributing influence for progressive tumor in colorectal.

Key Words: colorectal cancer, Helicobacter pylori-Infection, Serum, Immunoglobulins

Introduction

Colorectal cancer (CRC): One of the world's most common cancers and the third-largest cause of death from cancer. As shown in 2018 accordingly to epidemiological survey, 1,800,977 new cases with colorectal cancer and 861,663 mortality related to colorectal cancer were registered ⁽¹⁾. The International Cancer Research Agency has listed *H.pylori* as Group I carcinogenic in gastric cancer ⁽²⁾. It's generally exists in the stomach and

that is microaerophilic gram negative (-ve) bacterium ⁽³⁾. Warren and Marshall first cultivated it in 1981 ⁽⁴⁾. than half of the population are infected with this pathogens and It was most common infection in the world ⁽⁵⁾. *H.pylori* transmitted by contaminated water and food It acquired mainly in early childhood and may remain untreated for life, but it also can be acquired in adults ⁽⁶⁾. Infection prevalence varies in worldwide depending on socioeconomic factors and hygiene rates ⁽⁷⁾. Most people will not have any problems with the infection but in some *H.pylori* long-lasting inflammation in the stomach may cause with peptic ulcer disease and mucosa associated lymphoma ⁽⁸⁾. A major risk for stomach adenocarcinoma occurrences is Helicobacter pylori ⁽⁹⁾.

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The cytotoxin-associated gene (*CagA*) may also contribute to cause inflammation and carcinogenic effect ⁽¹⁰⁾. The region of CagPAI approximately 40-kb of *H. pylori* chromosome. The disease of *H. pylori* can be enhanced by *cagA* pathogenicity genes in West countries, around 50–70% of *H. pylori* strains carry it ⁽¹¹⁾. Persons with *H. pylori* CagA-positive strains infection produce CagA protein circulating antibodies, which are used as diagnostic markers ⁽¹²⁾. In extra gastric diseases has been also proposed that play an important role, the colorectal was the major extra-gastric organ with *H. pylori* that expressed of *CagA* tumor formation and increase developing of colorectal cancer ⁽¹³⁾.

Colorectal tissue infection with *H. pylori* may doesn't contribute in order to elevated the threat of colorectal _cancer directly ⁽¹⁴⁾. One hypothesis is that gastric ;Cytotoxin-linked gene A Protein in *Helicobacter pylori* infection triggers a rise in serum gastrin levels by overproduction of IL8 that high level of gastrin may lead to hypergastrinemia; ⁽¹⁵⁾. That is expected to be Intestinal mucosal proliferative consequence carcinogenesis involves cell inflammation and deregulation cycle ⁽¹⁶⁾. *H.pylori* carcinogenesis involves inflammation and the deregulation of the cell cycle by means of the Cytotoxin-associated gene A (CagA) *H.pylori* protein, binding SHP2 (a human), and acting on it the oncoprotein-based phosphatase which can produce tumor cell growth ⁽¹⁷⁾ . Links between *H.pylori* and colorectal tumor either indirect such as correlating increased CagA+ levels and these lesions ⁽¹⁸⁾ or increased gastrin levels ⁽¹⁹⁾.

The aim of present study to examine the correlation between *H. pylori* and progressive tumor in colorectal.

Material and Method

The present study included 50 patients which

divided in to (25 were colorectal cancer, 25 were colorectal normal with *H. pylori* infection) and 25 subjects without any pathological findings as A healthy control group. The current case-control study was attending the gastroenterology & hepatology teaching Hospital/medical city, the endoscopy unit of Ramadi teaching Hospital, and endoscopy unit of Fallujah general Hospital unit from a period September 2019 to February 2020. Arabian patients of Iraq in the Middle East. Patients were chosen ;with the assistance of surgeons in hospitals. Information has been registered for every patient. Used H2 antagonist or ;proton-pump inhibitors treatment, former stomach operation and malignancy at another site was exclusion from current study criteria. There are various *H. pylori* diagnostic tests including invasive tests (endoscopy, biopsy, histopathology, rapid urease, and PCR) and noninvasive tests (respiratory urease, ELISA and stool antigen). Due to their high sensitivity, specificity and simplicity, the current research used the ELISA system. To detected the presence of anti -*Helicobacter pylori* antibodies. Five ml blood was obtained, from 75 for each group subjects their sera has been tested for *Anti-Helicobacter pylori* IgG, IgG (*CagA*) by using enzyme-linked immunosorbent assay (ELISA). Chi-square analyses were conducted for statistical analysis. P values below 0.05 were statistically significant and greater than 0.05 were non-significant..

Results and Discussion

The distribution of patients according to gender was higher in the male patients with colorectal_ cancer and colorectal normal with *Helicobacter pylori_* infection than female but no significant differences (**P= 0.64**), In Table (1)

Table (1) Distribution of patients according to gander.

Gender	Colorectal cancer		Colorectal normal and H. pylori +ve		Healthy control		Total	
	No.	%	No.	%	No.	%	NO.	%
Female	8	32.0	9	36	6	24	23	30.66
Male	17	68.0	16	64	19	76	52	69.34
Total	25	100	25	100	25	100	75	100

C2 = 0.878 P= 0.64 P > 0.05 Non-significant

Our study agreement with Teimoorian F,et al. ⁽²⁰⁾ which conducted The rate of colorectal cancer was (64%) in males and (35%) in females. whereas Fujimori S,et al ⁽²¹⁾ colorectal adenocarcinoma incidence was higher incidence in women than men. High risk for development of colorectal cancer with *H. pylori* infection may due to Adult females typically have better innate and adaptive immune responses than males.

In Table (2) The study that has been conducted the highest incidence of colorectal cancer infection was shown (56%) who belonged to the age group (59-69) years, while the other patients were within the age groups (48-58) and (37-47) years in rate (28%) and (12%) respectively. The highest rate of infection in colorectal normal patients were found in (36%) with age group (48-58) year followed by those within the age group (59-69) and (37-47) years in rate (28%) and (16%) respectively. the results highly significant *P. value* = 0.0005.

Table (2) distribution of patients according to age

Age groups (Years)	Colorectal cancer	Colorectal normal and <i>H. pylori</i> +ve	Colorectal normal and <i>H. pylori</i> -ve	Total	
				No	%
15-25	0(0%)	2(8%)	10(40%)	12	16
26-36	1(4%)	3(12%)	7(28%)	11	14.67
37-47	3(12%)	4(16%)	4(16%)	11	14.67
48-58	7(28%)	9(36%)	2(8%)	18	24
59-69	14(56%)	7(28%)	2(8%)	23	30.66
Total	25	25	25	75	100
C2 = 33.084 P. value = 0.0005 Highly Signifiant (HS)					

Colorectal cancer that combine with *H. pylori* infection in our study appeared significantly higher in the old age people that agrees with previous studies like Zhao Y,et al ⁽²²⁾. In colorectal normal with *H. pylori* positive patients this study in agreement with Al-Jubori et al, ⁽²³⁾ which demonstrated the same range of *H. pylori* infection at age between (48-58) in Duhok province

while not match with study⁽²⁴⁾, who recorded the highest infected group ranged between (20 - 39) years old .Highest rate of infection in old age may be due to low in immunity state . In Table (3). The *anti-helicobacter pylori* IgG antibodies was highly significantly higher in patients with colorectal _cancer and colorectal normal with *Helicobacter pylori*_ infection compared with the healthy controls (*P* = **0.00019**).

Table (3) Detection of *Anti-Helicobacter pylori*-IgG in patients and control.

Seroprevalence of IgG Antibodies	Colorectal cancer		Colorectal normal and H. pylori +ve		Colorectal normal and H. pylori - ve		Total	
	No.	%	No.	%	No.	%	NO.	%
IgG +ve	16	64.0	19	76.0	2	8.0	37	49.33
IgG -ve	9	36.0	6	24.0	23	92.0	38	50.64
Total	25	100	25	100	25	100	75	100
C2 = 26.351 P= 0.00019 P < 0.01 Highly Significant								

Our study in agreement with study by (Fireman et al., 2000), that's reported the highest rate of anti-helicobacter pylori IgG in the colorectal cancer than in healthy control, but different with Buso et al. ⁽²⁵⁾, which reported H. pylori IgG antibodies was (71%) in the colorectal_ cancer group and patients in the control group (65%), the difference having non-statistical significance.

H. pylori have been found in the whole world repeatedly most people diagnosed with *H. pylori* are asymptomatic, the infection acquired for lifespan⁽²⁶⁾. It is rarely spontaneously eradicated with any therapy. According to Table (4) CagA IgG antibodies was significantly higher in the patients with colorectal _cancer and colorectal normal with *Helicobacter pylori* _infection compared with the healthy controls (P= 0.00022).

Table (4) Detection the levels of (CagA) IgG antibodies among patient groups and control group.

CagA-IgG Antibodies	Colon cancer and		Colon normal and H. pylori +ve		Colon normal and H. pylori - ve		Total	
	No.	%	No.	%	No.	%	NO.	%
Positive	17	68.0	8	32.0	0	0	25	33.33
Negative	8	32.0	17	68.0	25	100	50	66.67
Total	25	100	25	100	25	100	75	100
C2 =26.04 P= 0.00022 P < 0.01 highly Significant								

Current study agrees with Shmueli et al, ⁽²⁷⁾, which showed that in patients with colorectal cancer, seropositive CagA rate was about twice higher than in control and statistically significant, but different study with Zumkeller

et al.⁽²⁸⁾ who has been investigated no link between *Helicobacter pylori* CagA seropositivity and incident colorectal_ adenocarcinoma .

There is still little understanding of the mechanism by which *H. pylori* elevated the risk of colorectal cancer. CagA has a pathogenic function in increased risk of gastric cancer ⁽²⁹⁾. *CagA toxin* induces serum gastrin secretion, which can serve as a growth hormone in colonic cells ⁽³⁰⁾ . can cause hypergastrinemia, suggesting an appropriate mechanism for the carcinogenicity of that organism. Moreover, infected with CagA-positive *Helicobacter pylori* strains are correlated with the increased risk of atrophic gastritis developing ⁽³¹⁾. Secondary a tropical gastritis to *Helicobacter pylori*_ infection is associated with decreased acid production which makes the intestinal tract more common to a large number and variety of microbial species. which are associated with tumor in colonic growth ^{(32),(33)}. A number of observational studies have investigated the correlation between *H.pylori* serum positive and colorectal cancer risk ^{(21),(34)} and other found no relationships at all between this infection and the cancer ⁽³⁵⁾.

Another study by PCR The incidence of *Helicobacter pylori* in colorectal_ adenocarcinoma tissue was significantly higher in contrast with the normal colorectal tissue ⁽³⁶⁾ in particular CagA positive strains the gastric colonized mucus trigger D gastric antrum cell deficiencies. Lead to elevated of gastrin that act as mitogen proliferative of tumor in colorectal tissue⁽³⁷⁾.

Conclusion

The research indicated that a significant link between CagA-positive *Helicobacter pylori* and colorectal _cancer; development by different mechanism. Nevertheless, Much farther studies with larger samples are required to accurately evaluate the role of *H. pylori* in these pathologies. Shed further bright on their probable role in colorectal_ carcinogenesis with *Helicobacter pylori*_ infection by study other virulence factor VacA cytotoxin and BabA adhesion.

ETHICAL CLEARANCE

The Research Ethical Committee at scientific research by ethical approval of both MOH and MOHSER in Iraq

Conflict of Interest: None

Funding: Self-funding

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