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# Relationship between H.pylori and Gastric cancer cases. A: bacteriological study

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***Abstract :***

*The term cancer is a general term that covers over 200 types of diseases that occur in different tissues. The characteristics related to the incidence, spread and survival rates of each of the diseases expressed by the term cancer are specific to the disease. However, uncontrolled cell division from a single first region appears to be a common feature for all types of cancer. Convincing evidence links some species to carcinogenesis while others appear promising in the diagnosis, prevention or treatment of cancers. Thus bacterial species and their roles in particular cancers appear to differ among different individuals. Many species, however, share an important characteristic: highly site-specific colonization. This critical factor may lead to the development of non-invasive diagnostic tests, innovative treatments and cancer vaccines , The classic examples are gastric adenocarcinoma induced by Helicobacter pylori, the association of streptococcal bacteremia of the bovis group and colon cancer and lymphomas of lymphoid tissue associated with mucous membranes (MALT) in connection with Helicobacter species (gastric MALT) and with Chlamydophila spp. (MALT eyepieces). The isolation of any of these pathogens should be a wake-up call to induce the study of a malignant disease.*

***Keywords :*** *Cancer , Bacteria Helicobacter pylori , Gastric cancer .*

## I. Introduction :

Cancer is commonly defined as the uncontrolled growth of abnormal cells that have accumulated enough DNA damage to be freed from the normal restraints of the cell cycle. Several pathogenic bacteria(Boleij, 2011), particularly those that can establish a persistent, infection, can promote or initiate abnormal cell growth by evading the immune system or suppressing apoptosis. Intracellular pathogens survive by evading the ability of the host to identify them as foreign (Hussein , 2008). Gram positive bacteria cause 45-70% of documented infections. However, this only refers to patients with bacteremia, and it is an incomplete fact, since only 15-25% of febrile neutropenic patients have positive blood cultures. It should be considered that the most common infection sites are the respiratory, urinary and gastrointestinal tract, in addition to skin and soft tissue, where the microorganisms mostly responsible for these infections are gram negative bacilli (33%) and the polymicrobialmicrobiota, among which gram negative bacilli is documented in 80% of cases (Huten , 2005). The most frequently isolated microorganisms are from the patient's endogenous microbiota, such as *Escherichia*

*coli,Klebsiella spp., Enterobacter spp. and P. aeruginosa. In a study on bacteremia in febrile*neutropenics, Klastersky et al. show the higher mortality in complicated bacteraemias (those with an infectious focus) and in those produced by gram negative bacilli 12 compared to bacteraemias due to gram positive cocci (18% vs. 5%, respectively) (Hussein , 2008). These data reveal the importance of covering these microorganisms in the initial empirical treatment, not only because of their virulence, but because they continue to be the most responsible for infections at different sites in the blood. Research has found that certain bacteria are associated with human cancers. The recovery of some sporadic isolation microorganisms in the clinical microbiology laboratory could mean the existence of a special immune defect in the patient. For example, an important correlation between *Clostridium septicum* and colon carcinoma has been described, and species that almost always appear as contaminants (Bacillus spp., *Corynebacterium* spp.) (Saribasak , 2004) And others rarely isolated in other contexts have been related to leukemia and lymphoma. (*Capnocytophaga* spp.). There are bacteria that are almost exclusively isolated from patients with AIDS (*Rhodococcusequi*). A higher frequency of infections by *Campylobacter* spp., *Aeromonas* spp. and group G *streptococci* and mitis group in individuals with some type of cancer than in the rest of the patients. There are also bacteria that are markers of some undetected cancer or that affect neutropenic patients more than normoimmune individuals (Nimri , 2006). The alteration of the inflammatory reaction, the bacterial antigen-mediated lymphoproliferation and the induction of hormones that increase the proliferation of epithelial cells could be causes of bacterial oncogenesis.

## II. Material and Methods :

An observational, descriptive, correlational and retrospective study on patients who were diagnosed with various type of cancers at the Al-Karama Teaching Hospital. During the 4 months study more than 170 endoscopies of patients , 20 controls were diagnosed by this procedure, which constitutes the sampling unit.

Inclusion criteria: patients who were diagnosed with single or multiple cancer , by endoscopic study. Patients of both sexes, 19 years and older. Exclusion criteria: patients with a history of surgical interventions on the stomach, cholecystectomy or who were treated with antibiotics, proton pump blocking drugs (omeprazole, pantoprazole, lanzoprazole), non-steroidal anti-inflammatory drugs, simethicone or bismuth-type cytoprotectors in the latter month before endoscopy. Active or recent high digestive bleeding endoscopically demonstrated at the time of diagnosis , After applying the inclusion and exclusion criteria, the sample with which the study was conducted was constituted by nearly 50 patients of both sexes, aged 19 years and older. The following variables were considered: age, sex, diagnosis of different bacterias, histological diagnoses (chronic gastritis, cancer, acute chronic gastritis, normal histology, acute gastritis etc) (Hooi et al , 2017). For the endoscopic diagnosis in each patient, an Olympus Type E gastroduodenoscope was used. Two biopsies of the gastric antrum and two of the body were taken for the diagnosis of Hp infection and gastric ulcer samples for histological study. The samples were immediately immersed in bottles containing 10% formalin and were conveniently labeled according to the biopsy site, patient name and medical history number. They were transferred to the pathology department of the hospital, where hematoxylin-eosin and giemsa stains were processed and used in each sample for structural diagnosis and Helicobacter pylori. At the end of each endoscopy, the mechanical cleaning of the gastroduodenoscope was performed, as well as the chemistry with 2% glutaraldehyde. The biopsy forceps was

washed with water, detergent and brushed, immersed in 2% glutaraldehyde solution for 30 minutes, just like the endoscope and before being used it was rinsed with sterile water.

The records of endoscopic and biopsy reports of the gastroenterology department, the biopsy registry of the pathology department, the medical records as well as the reports of gastric biopsies of each patient were reviewed in order to obtain the necessary information that was collected on a data collection form. The absolute frequency and the percentage were used to determine the magnitude of the qualitative variables. The general frequency of Hp infection was estimated by obtaining the ratio between the number of patients with positive Hp and the total number of patients studied, multiplied by one hundred. The arithmetic mean and the standard deviation for the age variable were calculated as well as the odds ratio and its confidence interval for the risk estimation. The Chi-square test was used to estimate the relationship between Hp infection and histological diagnoses. The Epiinfo version 6.02 program was used for statistical calculations. The results are presented in a graph and tables. Limitations of the study: the retrospective design of this research has forced us to depend on a single diagnostic method of bacterial infection, histological, and within it the coloration of giemsa which can influence the results. In a prospective design, the use of another method that complements the histological one can be planned, which improves the sensitivity and specificity of the diagnosis (Floch et al , 2017).

**Serum Anti–Helicobacter pylori Antibody Titer :**

Helicobacter pylori contamination is a danger factor for stomach malignancy. Stomach malignancy is uncommon in patients without H.pylori contamination, particularly in :

Thusly, the appraisal of H. pylori contamination or the presence of a persistent infection gastritis brought about by Helicobacter pylori is the most significant danger factor for stomach disease (Itoh , 2015) . Turkey Ministry of Health and Welfare has endorsed six test techniques for H.pylori contamination including neutralizer testing. From these techniques, The blood counter acting agent test against H. pylori is the most well-known in clinical practice.

Additionally a populace based thorough stomach malignant growth overview in Turkey. Particularly, A particular sort of protein connected immunosorbent examine called plate E (Eiken) . The antigen utilized in this gathering was removed from the standard H. pylori strain got from a turkey patient .The cutoff level utilized in this electronic board is 10 units/ml, however ongoing investigations have indicated that most of genuine patients not contaminated with H.pylori have a titre of under 3 units/ml (Miki , 2007) .

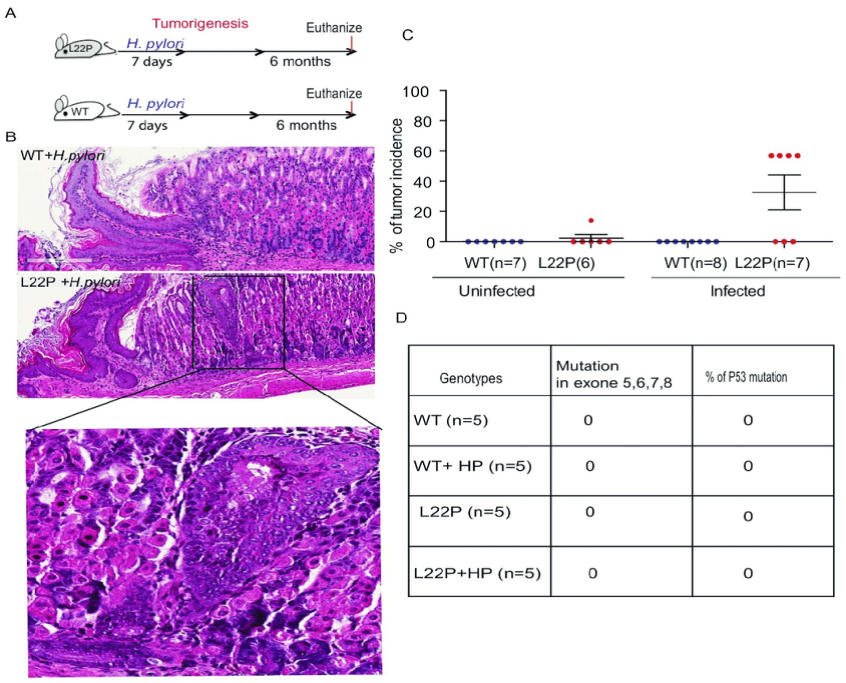
This demonstrates that many have been tainted with H.pylori (the vast majority of them ought to have had a past contamination) patients had a negative titre of 3.0 to 9.9 units/ml (called high titer negative) . the startling or incidental annihilation of H.pylori by anti-microbials might be the principle reason that a few patients with past contamination have a negative high titre against H.pylori (Naito et al , 2005).

## III. Results and Discussion

**Results :**

This investigation was led on 100 men and 90 ladies, between the ages of 22 and 62 years (normal: 49 years). The conveyance of biopsy examples as per histopathology in each gastric zone is summed up in170

patients (90%) indicated proof of MALT in at any rate one gastric biopsy example and 45 cases (45%) had no proof of MALT.




| Genotypes | Mutation in exone 5,6,7,8 | % of P53 mutation |
|---|---|---|
| WT (n=5) | 0 | 0 |
| WT+ HP (n=5) | 0 | 0 |
| L22P (n=5) | 0 | 0 |
| L22P+HP (n=5) | 0 | 0 |

**Figure (1) : H.pylori infection increases tumor incidence and latency in POLB mutated mouse model**

Generally, H. pylori was distinguished in 74 (74%) patients. The connection between mucosa-related lymphoid tissue and H. pylori contamination is appeared, demonstrating that 71% of patients with mucosal lymphoid tissue related with H.pylori had H.pylori disease rather than 8% of them without (P <0.001). Furthermore, lymphoid follicles were recognized all the more often in patients contaminated with H.pylori (59%) contrasted with negative H.pylori cases (3%).

**Number controls :**

**CON 1**

Pancreas, duodenum, stomach, omentum, "Whipple" operation;

ADENOCARCINOMA (well differentiated) in the ampulla vater region

The tumor is approximately 2.5x2x1.5 cm. in size

Pancreas: There is tumor infiltration

Resection borders (pancreas, common bile duct, stomach, duodenum); no tumor

Periduodenal - Peripancreatic lymph nodes (12 pcs.); no tumor

Blood and lymph vessel invasion: not observed

Perineural invasion: not monitored

Gallbladder, cholecystectomy: no tumor

lymph node, gallbladder: no tumor

**CON 2**

Pancreas, duodenum, stomach, "Whipple" operation;

ADENOCARCINOMA (poorly differentiated)

The tumor is 2.8 cm long

Duodenum: no tumor

Peripancreatic invasion: Yes

Pancreatic resection margin; no tumor

Lymph node (10 pieces); 1 has tumor metastasis

Blood and lymph vessel invasion; not watched

Perineural invasion; There is

Gallbladder, cholecystectomy; no tumor

Lymph node, hepatic artery, 8 units; no tumor

Lymph node, portal vein, 4 pcs; There is 1 tumor nodule

Lymph node, celiac, 2 pcs.; no tumor

Hepatic artery, surgical margin; <0.1 cm from the tumor

Portal vein; Have tumor infiltration

**CON 3**

Pancreas, duodenum, stomach, "Whipple" operation;

Ductal Adenocarcinoma (moderately differentiated) in the pancreatic head

Tumor largest size: 3 cm

Peripancreatic invasion: Yes

Duodenum; no tumor

Omentum; no tumor

Resection borders (pancreas, common bile duct, stomach, duodenum); no tumor

Perineural invasion: Yes

Blood and lymph vessel invasion; not watched

Lymph nodes, peripancreatic (7 units); no tumor

Gallbladder: no tumor (chronic cholecystitis)

**CON 4**

Pancreas, duodenum, stomach, omentum, "Whipple" operation;

located in the head of the pancreas, advanced to the duodenum

Ductal Adenocarcinoma (moderately differentiated)

Tumor largest size: 4.5 cm

Duodenum; Have tumor invasion

Peripancreatic invasion: Yes

Resection borders (pancreas, common bile duct, stomach, duodenum); no tumor

Perineural invasion: Yes

Blood and lymph vessel invasion; not watched

Lymph nodes, peripancreatic (2 units); no tumor

**CON 5**

Pancreas, duodenum, stomach, omentum, "Whipple" operation;

located in the head of the pancreas, advanced to the duodenum

Ductal Adenocarcinoma (moderately differentiated)

Tumor largest size: 4.5 cm

Duodenum; Have tumor invasion

Peripancreatic invasion: Yes

Resection borders (pancreas, common bile duct, stomach, duodenum); no tumor

Perineural invasion: Yes

Blood and lymph vessel invasion; not watched

Lymph nodes, peripancreatic (2 units); no tumor

**Number patients :**

P1

In the large number of sections examined: There is a tumor in stomach samples. Tumor cells oval round with hyperchromatic nuclei, They have medium-sized cytoplasm and form structures similar to gland. Histochemical Staining: "Helicobacter pylori" was observed with "Modified Giemsa".

P2

In the examined sections; There is a tumor in stomach samples. Tumor cells oval round hyperchromatic They have nuclei, medium-width cytoplasm and form structures similar to the gland. Histochemical Staining: "Modified Giemsa" and "Helicobacter pylori" were observed.

P3

In many sections examined; There are stone ring cell tumors that are distributed one by one in the samples belonging to the stomach.

Histochemical Staining: Intestinal Metaplasia with "Modified Giemsa" and "Helicobacter pylori" (+) "PAS-Alcian Blue" (+)

P4

In the analyzed sections; There is a tumor in stomach samples. Tumor cells oval round hyperchromatic

They have nuclei, medium-width cytoplasm and form structures similar to the gland.

Histochemical Staining: Intestinal Metaplasia with "Modified Giemsa" and "Helicobacter pylori" (+) "PAS-Alcian Blue" (+)

P5

In the examined sections; There is a tumor in stomach samples. Tumor cells oval round hyperchromatic

They have nuclei, medium-width cytoplasm and form structures similar to the gland.

Histochemical Staining: "Modified Giemsa" and "Helicobacter pylori" were observed.

P6

In many sections examined; There are stone ring cell tumors that are distributed one by one in the samples belonging to the stomach.

Histochemical Staining: Intestinal with "Modified Giemsa" and "Helicobacter pylori" (+) "PAS-Alcian Blue"

Metaplasia (+)

P7

In the sections examined; Tumors are seen in stomach samples. Tumor cells rounded hyperchromatic

nucleated medium-sized cytoplasm, dispersed one by one or gland-like structures

they form.

Histochemical Staining: Intestinal Metaplasia with "Modified Giemsa" and "Helicobacter pylori" (+) "PAS-Alcian Blue" (+)

P8

Tumor originating from the mucosa is observed in the sections examined. Tumor cells prominent with oval rounded hyperchromatic nuclei

They have nucleoli, vacuole cytoplasm and form gland-like structures.

Histochemical Staining: Intestinal Metaplasia with "Modified Giemsa" and "Helicobacter pylori" (+) "PAS-Alcian Blue" (+)

P9

In the analyzed sections; There is a tumor that can be observed in the mucosa in stomach samples. Tumor cells oval

medium-width cytoplasm with rounded hyperchromatic nucleus and gland-like structures

they form.

Histochemical Staining: Intestinal Metaplasia with "Modified Giemsa" and "Helicobacter pylori" (+) "PAS-Alcian Blue" (+)

P10

In the analyzed sections; There is tumor in stomach samples. Tumor cells oval round hyperchromatic They have nuclei, medium-width cytoplasm and form structures similar to the gland. Histochemical Staining: "Modified Giemsa" and "Helicobacter pylori" were observed.

P11

1,2; In the examined sections; There is a tumor that can be observed in the mucosa in stomach samples. Tumor cells medium-width cytoplasm with oval-rounded hyperchromatic nuclei and gland-like structures they form. Histochemical Staining: "Modified Giemsa" and "Helicobacter pylori" were observed.

P12

1-2: In the sections examined; tumor is seen. Tumor cells medium with rounded hyperchromatic nucleus large cytoplasm and dispersed one by one in mucin lakes or gland-like structures they form. Histochemical Staining: Intestinal Metaplasia with "Modified Giemsa" and "Helicobacter pylori" (+) "PAS-Alcian Blue" (+)

P13

In the sections examined; There is a tumor in stomach samples. Tumor cells oval round hyperchromatic They have nuclei, medium-sized cytoplasm and form structures similar to the gland.Histochemical Staining: Intestinal Metaplasia with "Modified Giemsa" and "Helicobacter pylori" (+) "PAS-Alcian Blue" (+)

P14

In the examined sections; There is a tumor in stomach samples. Tumor cells oval round hyperchromatic They have nuclei, medium-width cytoplasm and form structures similar to the gland. Histochemical Staining: "Modified Giemsa" and "Helicobacter pylori" were observed.

P15

In the sections examined; There is a tumor in stomach samples. Tumor cells oval round hyperchromatic They have nuclei, medium-sized cytoplasm and form structures similar to the gland. Histochemical Staining: Intestinal Metaplasia with "Modified Giemsa" and "Helicobacter pylori" (+) "PAS-Alcian Blue" (+)

P16

In the sections examined, a tumor that starts from the mucosa and progresses to the serosa, going beyond the muscular layer is observed. Tumor cells oval They have distinct nucleoli with round nuclei, vacuole cytoplasm and generally form gland-like structures. Histochemical Staining: "Modified Giemsa" and "Helicobacter pylori" were monitored.

P17

In the examined sections; There is a tumor in stomach samples. Tumor cells oval round hyperchromatic They have nuclei, medium-width cytoplasm and form structures similar to the gland. Histochemical Staining: Intestinal Metaplasia with "Modified Giemsa" and "Helicobacter pylori" (+) "PAS-Alcian Blue" (+)

P18

In the examined sections, a tumor starting from the mucosa and progressing to the serosa is observed.Tumor cells are oval round nuclei with distinct nucleoli and large vacuole cytoplasm and stone ring cells. they are distributed irregularly. Helicobacter pylori ", modified giemsa (+).

P19

In the sections examined; There is a tumor in stomach samples. Tumor cells oval round hyperchromatic They have nuclei, medium-sized cytoplasm and form structures similar to the gland. Histochemical Staining: Intestinal Metaplasia with "Modified Giemsa" and "Helicobacter pylori" (+) "PAS-Alcian Blue" (+)

P20

In the analyzed sections; There is a tumor in stomach samples. Tumor cells oval round hyperchromatic They have nuclei, medium-width cytoplasm and form structures similar to the gland. Histochemical Staining: "Modified Giemsa" and "Helicobacter pylori" were observed.

## IV. Discussion :

This examination assessed the commonness of follicles and lymphocytes (forerunners to MALT lymphomas) in gastric mucosal biopsies and connected them to H.pylori disease. MALT lymphomas are non-Hodgkin's B-cell tumors that are gotten from lymphoid totals in the lamina propria. Antigenic drive that can animate the resistant framework and quicken the expansion of lymphoid follicles in the gastric mucosa (Kuo , 2013).

In this examination, the commonness of H.pylori disease was 74%. H. pylori predominance goes from 15.1% to 87.7% in past distributions relying upon financial status, cleanliness and ailments (Zullo , 2010). Improvements in these components lead to a lower predominance of H. pylori and subsequently in peptic ulcer

malady. The host's insusceptible reaction, and particularly the capacity of cytotoxic T cells (executioner T cells), assumes a significant function in the result of H.pylori infection. Although half of the total populace is contaminated with this bacterium, just about 3% surprisingly tainted with H.pylori Those with gastric adenocarcinoma. Some reports have depicted that positive H. pylori cagA strains have improved pathogenicity by invigorating cell change.

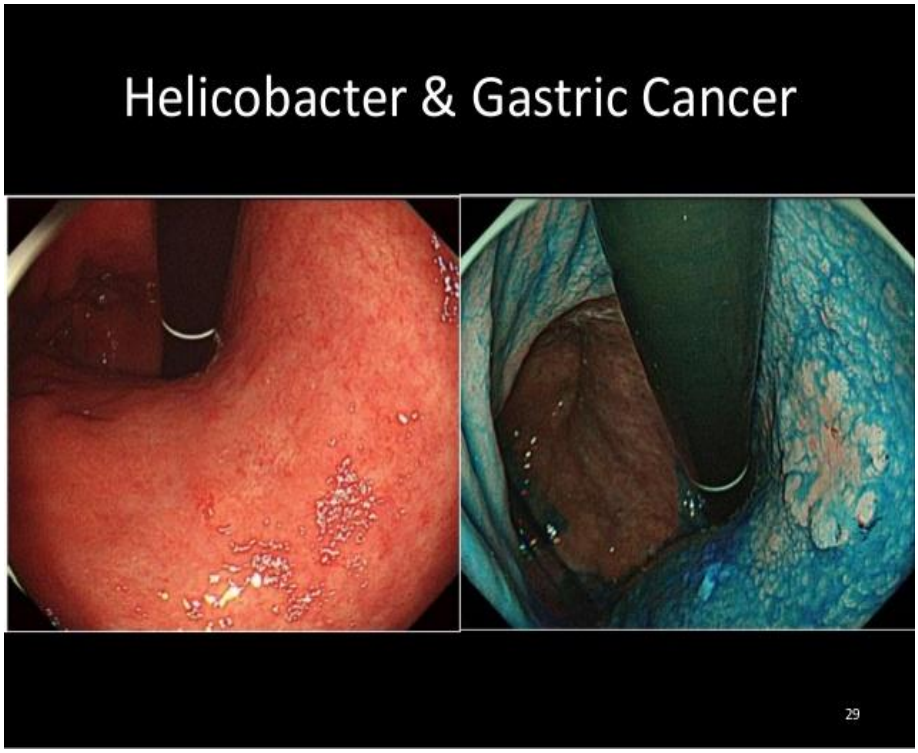



**Figure (2) : Helicobacter pylori gastric cancer an evidence based approach for primary care**

## V. Conclusion :

In this study it was pointed out that there are bacteria frankly associated with malignant diseases, some as a consequence of these conditions and others generating them through various mechanisms. Although in some cases the evidence is not conclusive, the frequency of the associations should be a wake-up call to rule out any malignant disease or to try to prevent it, if possible, when a certain uncommon pathogen is isolated.

The variety explicit variety has been recommended to share the capacity of H. cause different sicknesses. The cagA quality item, CagA, has been demonstrated to be they were infused into the host's cytoplasm through a sort IV emission framework, and phosphorylated by the host cell kinases (Asahi et al. 2000; Covacci et al. 1999; Odenbreit et al. 2000). Moreover, CagA structures a physical compound utilizing SHP-2, which is known to have a significant positive function in communicating mitotic signals, and initiates phosphatase movement (Higashi et al. 2002b). In Japan, almost 100% of the strains have practical cag PAI (Azuma et al. 2002; Ito et al. 1997), and the rate of atrophic gastritis and stomach malignancy is high contrasted with Western nations .

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