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THE IMMUNOLOGICAL ROLE OF ANTI-H. PYLORI ANTIBODIES LEVEL, INF-Γ, AND TNF-A IN A NUMBER OF PATIENTS WITH A TUMOR IN THE DIGESTIVE SYSTEM IN BABYLON GOVERNORATE

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Abstract

General Background: Helicobacter pylori is a well-known bacterium responsible for chronic infections, significantly contributing to gastric and mucosa-associated lymphoid tissue cancers, as well as peptic ulcer disease. **Specific Background**: The link between H. pylori infection and gastrointestinal (GIT) tumors remains under-explored, particularly concerning immunological parameters. **Knowledge Gap:** The role of immune markers, such as anti-H. pylori IgG antibodies, TNF-α, and IFN-γ, in distinguishing between malignant and benign GIT tumors is unclear. **Aims**: This study aimed to assess the relationship between H. pylori infection and immunological factors in patients with malignant and benign GIT tumors, as well as controls, using serum levels of Anti-H. pylori IgG, TNF-α, and IFN-γ. **Results**: The study included 100 serum samples from patients with malignant (n=40) and benign (n=35) GIT tumors, irritable bowel disease (IBD) controls (n=15), and healthy controls (n=10). The results revealed significantly elevated levels of anti-H. pylori IgG in patients with malignant tumors compared to those with benign tumors, IBD controls, and healthy controls. Male patients had higher anti-H. pylori IgG levels than females. Elevated levels of TNF-α and IFN-γ were also observed in patients with malignant tumors, correlating with higher anti-H. pylori IgG levels. **Novelty**: This study highlights the association between elevated H. pylori IgG antibodies and increased TNF-α and IFN-γ levels in malignant GIT tumors, particularly in males, suggesting H. pylori's role in cancer progression. **Implications**: The findings suggest that early detection of elevated anti-H. pylori IgG and inflammatory cytokines could improve the diagnosis and management of GIT malignancies, especially in male populations. Further research on a larger cohort is recommended to explore the mechanisms driving this relationship.

Keywords: H. Pylori Ab, INF-γ, TNF-α, GIT tumors

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Introduction

Gastric cancer occupies the fourth stage in terms of cancer-related deaths and the sixth most frequently diagnosed type of cancer. Helicobacter pylori is one of the most important major risk factors causing this type of tumor. The pathogens of chronic inflammation and virulence factors that are unique to Helicobacter pylori, which may damage the DNA of cells. Gastric epithelial and inducing genomic instability are the two main factors of bacterial carcinogenic processes [1]. To eliminate malignant cancer cells, all components of the immune system cooperate. Cancer cells become clear to the innate immune system and are treated by antigen-presenting cells (APCs). This process takes place as a result of genetic changes and the occurrence of desensitization [2]. Trans membrane TNF-a acts as a bipolar molecule that transmits signals in the form of a ligand and as a receptor in a cell-to-cell communication manner. Its biological functions are performed by binding to tumor necrosis factor receptors (TNF-R1, R2) [3] neoplastic necrosis factor (TNF)-α is intimately associated with the early stages of gastric cancer and has a significant role in viral, neoplastic, and inflammatory processes. It is a pro-inflammatory cytokine that is secreted by lymphocytes, mast cells, neutrophils, keratinocytes, smooth muscle cells, and some tumor cell lines in addition to macrophages and monocytes [4].The development of AG carcinogenesis and gastric mucosal hyperplasia are significantly influenced by inflammation The IFN-γ pathway is one of the pathways that suppresses proinflammatory cytokines and reduces tissue damage to the gastric mucosa caused by H. pylori[5] .Variations in the TNF-α promoter impact the risk of Gastrointestinal cancer it could promote carcinogenesis [6]. Although inflammatory mediators like TNF-α are frequently linked to the metastatic transformation of cells, the precise connection between TNF-α and cell metastatic transformation remains unclear. The process of metastatic transformation involves several factors, and the processes behind the phenotypic alterations mediated by TNF-α are [7]. When infected with Helicobacter pylori bacteria, there is an increase in programmed cell death of epithelial cells in the stomach, and this has a role in the causes of gastritis, peptic ulcers, and tumors. There are recent studies indicating that T cells increase during infection. Cytokines such as interferon gamma(IFN-γ) and tumor necrosis factor (TNF-α.) increase the release of T cells. Proinflammatory cytokines and increased apoptosis resulting from Helicobacter pylori infection[8]. The presence of IgG antibodies in human blood serum is considered indicative of bacterial infection and does not lead to the elimination of bacteria, but it is believed that it contributes to tissue damage. Increased body atrophy is associated with the reaction of antibodies directed against the H + / K + -ATPase of the parietal cells in the stomach in some individuals infected with H. pylori [9].

Methods

After obtaining more than 100 samples from patients from various parts of Babil Governorate who were either undergoing treatment at Marjan Teaching Hospital or were in the process of treatment, a number of immunological parameters were examined and evaluated. The samples taken from them were as follows: 35 samples came from patients with benign tumors in the digestive system, while 40 samples came from

patients with malignant tumors. Digestive system: Ten healthy subjects as a negative control group and fifteen cases of irritable bowel syndrome as a positive control group in the same age group. After endoscopy and biopsy sections were performed to confirm the diagnosis, serum samples were obtained from all patients and controls. Every patient admitted to Babylon's GIT and liver facility at Marjan Medical City between April and December of 2023. INF-g, TNF-a, and the H. Pylori IgG antibody were measured using the Bio-Assay company's ELISA manual process. LSD value and descriptive statistic statistical analysis are performed using SPSS.

Results and Discussion

Anti-H. Pylori -IgG level

The ELISA method was used to select a set of study parameters, and the results are presented in the accompanying figures and tables. Results from anti-H. Pylori -IgG antibody level measurements indicated that patients with malignant gastrointestinal tumors had higher levels than those with benign gastrointestinal tumors, control (+ve) (IBD), or control (-ve), or healthy control at mean ± SD (48.6 ± 8.19, 34.9 ± 5.80, 25.8 ± 4.77, 25.57 ± 5.04), LSD value (2.24), respectively. Figure (1) shows the anti-H. pylori-IgG level result.

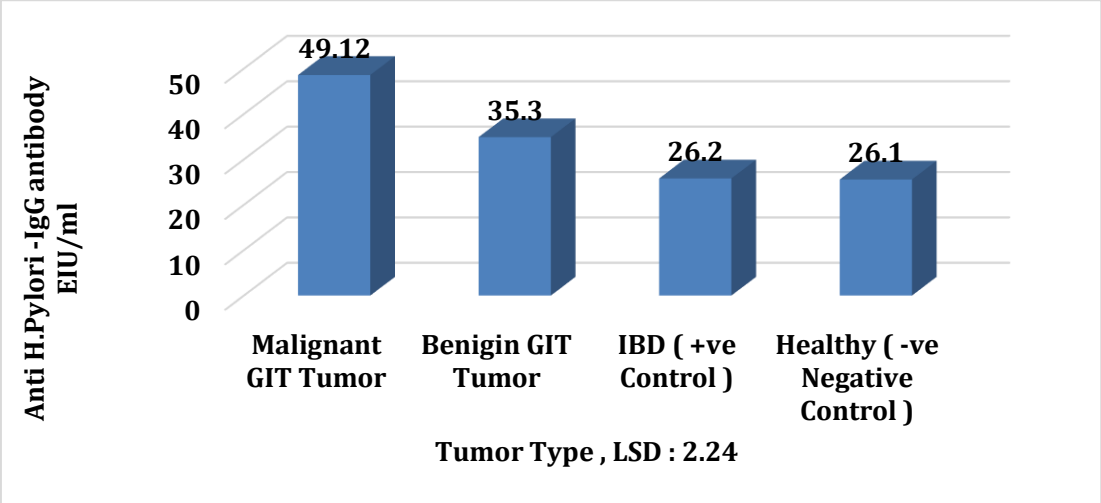

Fig. 1: GIT tumor patients' H. Pylori -IgG levels in relation to Controls.

When compared to both male and female controls, the male patients had greater levels of Anti-H. Pylori –IgG antibodies than the female patients, Table (1) lists the mean ± standard deviation (39.4 ± 6.6, 33.2 ± 7.53, 24.0 ± 5.57, and 21.2 ± 4.81) in corresponding order at LSD value (2.14).

Table 1: Anti-H. Pylori –IgG antibody distribution by gender

Anti-H. Pylori–IgG antibody / Sex		No.	Mean ± SD	L SD value
Infected people	Male	46	39.4 ± 6.61	2.14
	Female	29	33.2 ± 7.53	
Control	Male	13	24 .0 ± 5.57	
	Female	12	21.2 ± 4.81	
Total		100		

INF-γ levels

The findings show that, when mean ± SD (49.56). ±13.5, 42.59±18.1) 49.37±18.6, 57.29±15.1), respectively, with an LSD value of 3.45, patients with malignant gastrointestinal cancer have higher levels of INF-γ than those with benign gastrointestinal tumors, positive controls (IBD), and lower levels than healthy controls (-Ve). Figure 2 displays the INF-γ level result.

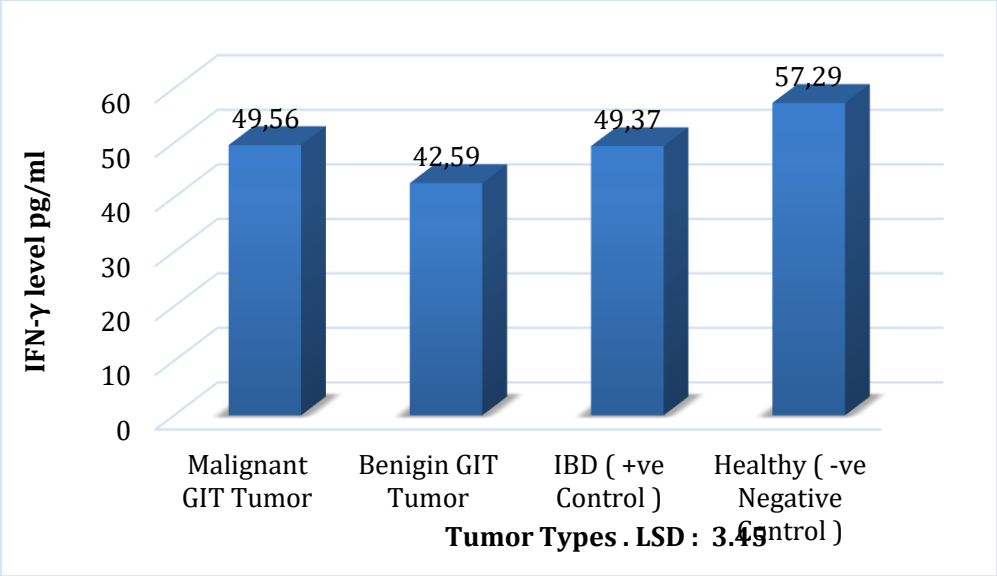

Fig. (2): Interferon gamma levels in GI tumor patients relative to controls.

Compared to the male and female control group, the INF-g levels in the male and female patients were lower. at Mean ± SD (49 .44± 5.99 , 42.51 ± 7.42 , 58.91 ± 8.87 , 52.61 ± 4.52) in at LSD vale (7.12) Table (2)below shows this.

Table (2) Interferon gamma values by gender

Interferon gamma values Sex / Sex		No.	Mean ± SD	L SD value
Infected people	Male	46	49.44 ± 5.99	7.12
	Female	29	42.51 ± 7.42	
Control	Male	13	58 .91 ± 8.87	
	Female	12	52.61 ± 4.52	
Total		100		

The TNF-α level

Figure (3) revealed the result of the level of TNF-α in people suffering from malignant tumors in the digestive system, and the results showed that the level of Interferon gamma in their serum was higher than those suffering from benign tumors in the digestive system, the positive(+ve) control (IBD) and the negative(-ve) control, and Healthy control, at mean ± SD (27.6 ± 6.98, 22.46 ± 5.2, 19.82 ± 4.9, 17.21 ± 4.1), respectively, with an LSD value of 2.54.

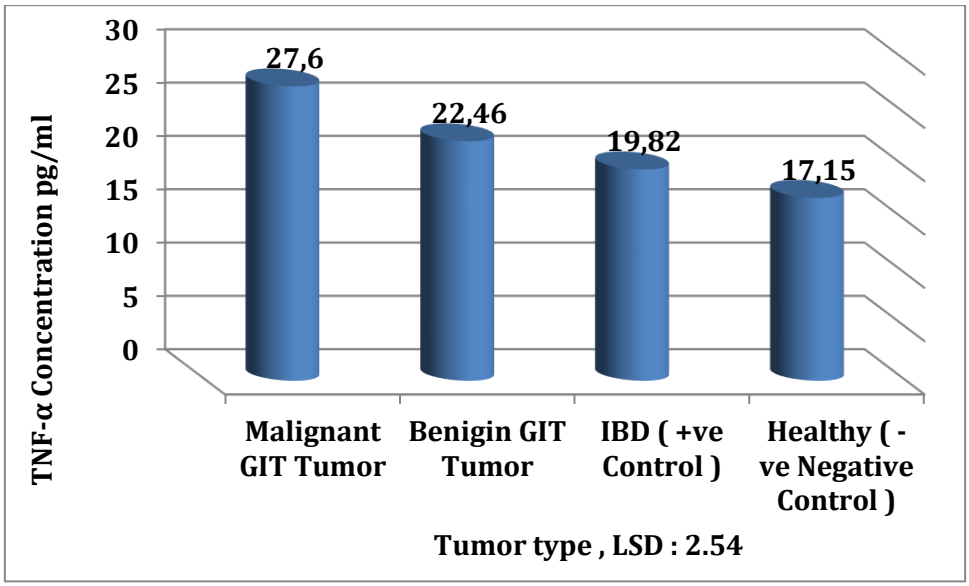

Fig. (3) TNF-α levels in patients and controls

It was found in the current study that the level of TNF- α in male and female patients is higher than in male, female and negative control at mean ± SD (24.79 ±78.9, 18.59 ±2.7,

Table (3): Table (3) shows the patients' and controls'Tumour Necrosis Factor alpha concentration results.

Tumor necrosis factor - Alpha Level / Sex		No.	Mean ± SD	L SD
Infected people	Male	46	18.59±2.7	3.210
	Female	29	24.79 ±78.9	
Control group	Male	13	16.61±2.9	
	Female	12	19.97 ±± 2.4	
Total		100		

Our study found a clear association between levels of antibodies to Helicobacter Pylori and TNF-α and INF-γ. This is a clear indication that patients with gastrointestinal tumor infection may have higher levels of anti-H. Pylori-IgG antibodies, which in turn leads to higher levels of TNF-α and INF-g. The results are shown in Table (4)

Gastrointestinal lymphoma is a fairly uncommon disease with a wide range of clinical presentations. This review focuses on the epidemiology, histological subtypes,

and association between intestinal lymphoma and Helicobacter Pylori infection. Regarding the positive association between H. pylori infection and gastric MALT lymphoma. This association has not been observed in other noninfectious pilonidal lymphomas)[10].

Table (4) : Correlation result between the factors under study

Discussion

Correlations		TNF - α level	IFN- γ Level	H. Pylori Ab
TNF- α level	Pearson Correlation	1		
	Sig. (2-tailed)			
IFN- γ Level	Pearson Correlation	-.013-	1	
	Sig. (2-tailed)	.031		
H. Pylori -Ab	Pearson Correlation	.310**.	0.97	1
	Sig. (2-tailed)	.003	0.369	
**. Correlation is significant at the 0.01 level (2-tailed).				
*. Correlation is significant at the 0.05 level (2-tailed).				

Discussion

Some studies have shown evidence of the synthesis of Helicobacter pylori IgA and IgG in the stomach antrum of people infected with the bacteria in response to Th1 stimuli. This response, in turn, leads to an increase in the synthesis of Interferon gamma and Tumor Necrosis Factor-Alpha. Researchers believe that this response is linked to the formation of peptic ulcers or peptic ulcers and adenocarcinoma. B-cell lymphoma associated with Helicobacter pylori [11]. The emergence of Helicobacter pylori antibodes is considered. H. pylori IgG and IgA antibodies in patients suffering from gastric atrophy, dysplasia, and intestinal metaplasia. A broad immune response. It is an accurate method for detecting the presence of H. pylori bacteria without any surgical intervention [1]. There may be an increase in antibody levels (H. Pylori - IgG and Interferon gamma) in the event of high levels of crosstalk, and an increase in these immune parameters compared to healthy individuals increases the likelihood of contracting the disease. Tumor in the digestive system. Males who are younger have been demonstrated to be more vulnerable to malignant GET illness. It has been shown that antibody levels (H. Pylori - IgG and Interferon gamma) are high in the serum of patients with malignant tumors of the digestive system compared to benign gastrointestinal tumors and healthy people [12]. [13]. [14]. In addition, Each of Innate and adaptive immunity and cytokines such as IFN-γ, TNF-a, ICAM4, and IFN-γ constantly work together to prevent or eliminate the development of inflammatory lesions and tumors, which is called immunomodulation[15].A significant risk factor for the progression of gastric mucosa atrophy, IM, and DYS is H. pylori infection. Serum levels of IgG and IgA are useful markers to assess this advancement within a particular range. Research on the efficient combinations of clinical manifestations might lead to a

deeper comprehension of the etiology, diagnosis, and management of H. pylori infection [16]. Recent studies have shown that the role of IFN-γ in innate and adaptive immune responses is prominent and essential, and that it possesses important anti-infective and anti-tumor properties [17]. The results of high expression of the immune standard interferon-gamma in patients with ovarian cancer are associated with improved health conditions [18] [19]. found that the gastric epithelial cells expressed the neonatal Fc receptor, which has been demonstrated to transfer IgG into the stomach discharge, These findings suggest that the stomach mucosa may be accessible to the systemic anti-H. pylori IgG response, which might then have antibacterial and/or pro-inflammatory effects [20]. H. pylori dominates in this niche because of the stomach's extremely low pH, and it has a higher probability of colonizing the stomach when there is enough gastric transit time. A functional cagPAI in H. pylori strains raised the risk of gastric cancer by a factor of 1.64. The 2020 Taipei global agreement states that in high-risk communities, H. pylori eradication and widespread screening are required to avoid Gastrointestinal cancer [21] .

Conclusion

Fundamental Finding: This study demonstrates that patients with malignant gastrointestinal (GIT) tumors exhibit significantly higher levels of anti-Helicobacter pylori IgG antibodies, TNF-α, and IFN-γ compared to patients with benign GIT tumors, irritable bowel disease controls, and healthy individuals. Male patients, particularly those in their fifth decade of life, were disproportionately affected by malignant GIT tumors associated with H. pylori. **Implication:** These findings suggest that elevated immune markers such as anti-H. pylori IgG, TNF-α, and IFN-γ may serve as potential biomarkers for early detection and differentiation of malignant GIT tumors, particularly in high-risk male populations. This could aid in improving diagnostic accuracy and informing more targeted therapeutic interventions. **Limitation:** The study is limited by its relatively small sample size and the specific geographical focus on Iraqi males, which may not fully represent other populations or genders. Additionally, the cross-sectional nature of the study limits the ability to infer causality between H. pylori infection and tumor progression. **Further Research:** Future studies with larger, more diverse cohorts are necessary to validate these findings and explore the mechanistic pathways linking H. pylori infection to malignant GIT tumors. Longitudinal studies are also recommended to better understand the temporal relationship between immune responses and tumor development.

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