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Interleukin-13 level accompanying with *Helicobacter pylori* gastric infection in Kirkuk city

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ABSTRACT

Background: Helicobacter pylori recognized as the most common cause of chronic gastritis and an important pathogenic factor in peptic ulcer, after colonization and stomach mucus layers caused increase in the levels of anti-inflammatory cytokine such as IL-13 .

The aims of this study is compare of IL-13 levels among treated patients with H. Pylori gastric infection, patients with H. Pylori gastric infection without treatment and healthy person

Materials and Methods: The study was conducted in Kirkuk city from the September 2020 to March 2020, ELISA test used for interleukin -13 with peptic ulcer diseases (PUD).

Results: Elevated levels of IL-13 reported in patients with acute and chronic H. pylori gastric infection compared to control group (44.74+8.18). A moderate significant in IL-13 level determined in infected patients without treatment, previously treated patients (140.12+45.36 vs 105+22.71). While, there was a high significant difference when these two groups and compared with the control group (44.74+8.18)).

Conclusion: IL-13 levels is highest in patients with H. pylori gastric infection in compare healthy person.

Introduction

Helicobacter pylori is a Gram negative bacterium caused chronic gastritis and peptic ulcer disease. In the development of distal gastric adenocarcinoma and gastric mucosa associated lymphoid tissue (MALT) lymphoma, H. pylori play a critical pathogenic role. [1]. Gastritis is a term used to describe an inflammation of the stomach, such as nausea or dyspepsia, in which no real clinical symptoms or radiological anomalies appear [2]. It can be diagnosed histologically, endoscopically, or symptomatically. [3].

Peptic ulcer disease (PUD) is a chronic illness that affects up to 10% of the population of the world. The existence of stomach acid secretion or pepsin, as well as a reduction in mucosal defenses, is required for the development of peptic ulcers. [4]. Interleukins (ILs) are a class of cytokines that were produced in leucocytes and interplay between immune system cells. Interleukins can help cells grow, differentiate, and activate their functions. [5]. Interleukin (IL)-13 is a cytokine that plays a key function in the T helper (Th2) immune response and has been linked to a variety of intestinal diseases [6]. Th2 cells generate IL-13, which has pleiotropic effects, acting as either a pathogen or a protector depending from the experimental circumstances. Because it can be produced by stimuli from an infected or inflamed epithelium of special relevance to the gut, IL-13 may play a key role in a new innate immune response [7].

Materials and Methods

A cross sectional study conducted in Kirkuk city from the September 2020 to March 2021. The study included 112 individuals with upper gastrointestinal problems, whose ages were between 20 to 59 years old Table1.

Table 1: Distribution of patients with *H. pylori* gastric infection according to the age groups

Age groups (years)	Total	%
20-29	22	19.6
30-39	34	30.4
40-49	45	40.2
50-59	11	9.8
Total	**112**	**100**

Blood samples were collected from 112 patients (patients whom positive *H. pylori* antigen in stool). By vein puncture about 5 ml of blood collected using sterile syringe. Blood sample was placed in a plain tube and allowed to clot at 20-25 C° in a water bath for 15 minutes. After that, blood samples were centrifuged at 3000 rpm for 5 minutes to separate the serum was pipetted and labelled Eppendorf tube. Serum in Eppendorf tubes stored at -20°C (deep freeze) for serological and immunological tests. From 112 samples, 88 samples were selected for ELISA examinations IL-13.

Table 2: Collection of Samples

Samples	patients
Stool	**112**
Blood	**112**
Serum	**88**

Estimation of serum IL-13

The concentration of serum IL-17 in the sera was quantitatively measured using sandwich ELISA format. Interleukin-13 standard range 62.5-4000 pg/ml.

This kit is an Enzyme-Linked Immunosorbent Assay. The plate has been pre-coated with human interleukins antibody. Interleukins present in the sample is added and binds to antibodies coated on the wells. And then biotinylated human interleukins antibody is added and binds to interleukins in the sample. Then Streptavidin-HRP added and binds to the Biotinylated interleukins antibody. After incubation unbound Streptavidin-HRP washed away during a washing step. Substrate solution added and the color develops in proportion to the amount of human interleukin. The reaction terminated by the addition of acidic stop solution and the absorbance measured at 450 nm.

Statistical Analysis:

Computerized statistical analysis was performed using ANOVA test at probability P value of less than 0.05 with basic statistical calculations like (mean, standard deviation and F- ratio).

Results

1- Level of IL-13 in patients with *H. pylori* gastric infection and control group

Our study determined that there was a highly significant difference between acute and chronic *H. pylori* gastric infection in study categories concerning IL-13 level (Table 3). There was a high significant difference when compare infected patients in all categories with the control group (44.74±8.18). Whereas, there wasn't a significant difference in acute infection between gastritis and duodenitis when compares IL-13 level (76.54±9.06 *vs* 77.86±7.49). Also, IL-13 level in chronic *H. pylori* gastric infection no significant difference determined when compare among gastritis, duodenitis, gastric ulcer and doudenal ulcer (155.48±41.28, 102±25.28, 114.71±53.79 and 153.92±32.97) respectively.

Table 3: Level of IL-13 in patients with *H. pylori* gastric infection and control group.

IL-13 level (pg/ml)	*H. pylori* gastric infection (NO:88)						control (10)
	Acute *H. pylori* gastric infection (20)		Chronic *H. pylori* gastric infection (58)				
	Gastritis	Duodenitis	Gastritis	Duodenitis	Gastric ulcer	Duodenal ulcer	
No.	13	7	29	9	7	13	10
Mean	76.54	77.86	155.48	102.71	114.71	153.92	44.74
SD.	9.06	7.49	41.28	25.28	53.79	32.97	8.18
F ratio: 2.19 P value: 0.033 Relation: HS ANOVA: P-value ≤ 0.05							

2- Level of IL-13 in patients with *H. pylori* gastric infection without treatment, previously treated patients and control group

The study reported a moderate significant difference between patients with *H. pylori* gastric infection without treatment and previously treated patients concerning IL-13 level (140.12±45.36 *vs* 105±22.71). While, there was a high significant difference when these two groups and compared with the control group (44.74±8.18) Table (4) and Figure (1).

Table 4: Level of IL-13 in patients with *H. pylori* gastric infection without treatment, previously treated patients and control group.

IL-13 level (pg/ml)	*H. pylori* gastric infection		Control
	Without treatment	Previously treated	
No.	50	8	10
Mean	140.12	105	44.74
SD.	45.36	22.71	8.18
F ratio: 1.49 P value: 0.02 Relation: MS ANOVA:P-value<=0.05			

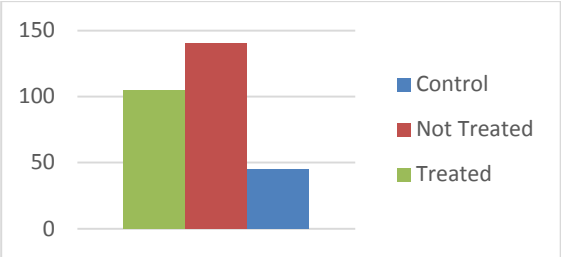

Fig. 1: Histogram of IL-13 in patients with *H. pylori* gastric infection without treatment, previously treated patients and control group

Discussion

1- Level of IL-13 in patients with *H. pylori* gastric infection and control group.

Inflammation, mucus formation, tissue remodeling, and fibrosis are all regulated by IL-13, a Th2 cytokine. Several investigations have found that polarization of the H. pylori-specific T-cell response to Th1 is associated with more severe illness [8].

In agreements with our study, Marotti *et al*. (2008) reported *H. pylori*-positive patients had considerably higher levels of IL-13 than *H. pylori*-negative patients, suggesting that IL-13 may have a role in the varied outcomes of *H. pylori* infection. Yet, Thomson *et al.* (2003) disagreed with our results; they reported that the formation of gastric mucosal ulcers had no influence on IL-13 concentrations in the gastric mucosa.

Th2 cytokines including IL-4, IL-10, and IL-13 are crucial for balancing and eliminating some of the bad effects of polarized Th1 responses. As a result, it appears that an unrestricted Th1 response is linked to stomach inflammation and illness, even though a mixed Th1/Th2 response can suppress the pro-inflammatory Th1 response [11]. Type 1 T helper (Th1) cells produce interferon-gamma, interleukin (IL)-2, and tumor necrosis factor (TNF)-beta, which activate **macrophages** and are responsible for cell-mediated immunity and phagocyte-dependent protective responses [12].

2- IL-13 Level in patients with *H. pylori* gastric infection without treatment, previously treated patients and control group

IL-13 is a cytokine that is becoming more known for its new functions in inflammatory diseases. IL-13, like many other immune response components, has a physiological purpose in combating infection in the gut, but may also have pathological consequences when overproduced [7].

Few studies reporting the reduction of IL-13 in individuals with H. pylori stomach disease after certain treatment, Tanabe *et al*. (2011) confirmed that clarithromycin inhibited IL-13, the immunomodulatory effect of Clarithromycin impacted IL-13 receptor janus kinase signal transducers, activators of transcription 6 and reduced MUC5AC mRNA expression produced by IL-13 in a dose-dependent manner (STAT6). Their effects include modulation of inflammatory cytokine production and blocking bacterial biofilm formation and virulence factor production [14]. PPI treatment has recently been shown to have anti-inflammatory properties. PPIs can either limit IL-4 and IL-13 signaling via STAT67 or prevent Th2 cytokine-stimulated eotaxin-3 production, according to research [15].

Conclusions

IL-13 in patients with *H. pylori* gastric infection in compare with healthy persons

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مستوى انترلوكين −13 المصابة لعدوى الملوية البوابية في مدينة كركوك

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الملخص

تمهيد : تعرف الملوية البوابية بأنها السبب الأكثر شيوعًا لالتهاب المعدة المزمن وعامل ممرضا مهما في مرض القرحة الهضمية ، تقوم هذه البكتريا بغزو والاستعمارالطبقات المخاطية للمعدة مسببة ومؤدية إلى ارتفاع مستويات IL- 13.

المواد وطرائق العمل:أجريت الدراسة في مدينة كركوك في الفترة من أيلول 2020 إلى آذار 2020 تحديد مستوى الإنترلوكين المفترض −13 مع أمراض القرحة الهضمية (PUD) .

النتائج: ظهرت النتائج ارتفاع مستويات مرتفعة من IL-13 في المرضى الذين يعانون من العدوى الحادة والمزمنة بالبكتيريا الحلزونية البوابية مقارنة بمجموعة التحكم (قيمة .(P <0.033 معتدل معتدل في مستوى IL-13 المحدد في المرضى المصابين دون علاج ، والمرضى الذين عولجوا سابقًا والمجموعة الضابطة (قيمةP <0.02).

الاستنتاج: ارتفاع معنوي لمستوى IL-13 عند المرضى الذين يعانون من عدوى المعدة بالبكتيريا الملوية البوابية مقارنة بالأشخاص الاصحاء