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Histological Evaluation Of The Stomach In Individuals With Gastric Ulcers And Its Impact On Liver Function

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Abstract:
Gastric ulcer is one of the most common and serious gastrointestinal diseases, occurring as a result of increased secretion of hydrochloric acid and the enzyme pepsin in the stomach. Infection with Helicobacter pylori is considered one of the most common causes of gastric ulcer. Excessive use of non-steroidal anti-inflammatory drugs (NSAIDs) is the second most common cause. Studies have shown that the prevalence of gastric ulcers increases with age, and smoking has been found to increase the risk of developing gastric ulcers.
This study aims: *Evaluation of histological changes in the stomach of individuals with gastric ulcer and some biochemical variables.*
Materials and working methods: *This study was conducted on gastric ulcers patients, aged between 20-70 years. Sample collection took place from September 19,2024 to February 22,2025, during which 90 blood samples were collected. The samples were divided into two groups: The first group included 60 blood samples from individuals diagnosed with gastric ulcer, confirmed by a specialist physician using gastrointestinal endoscopy. The second group consisted of 30 blood samples from healthy individuals (Control group). For both groups, levels of interleukin-37, total white blood cells, neutrophils, monocyte, lymphocyte, and liver enzyme were measured.*
Results: *The results of the study showed a significant increase in the level of interleukin-37 in individuals with gastric ulcers compared to the control group at a significance level of P≤0.05. The study also revealed significant differences in the levels of monocytes and liver enzymes (ALT, ALP).*
However, no significant differences were observed in the levels of total white blood cells (WBC), neutrophils, lymphocytes, or the AST enzyme.
Conclusion: *Our result indicates an increase in the level of IL-37 which is an anti-inflammatory cytokine with potent suppressive effect on innate and adaptive immune responses. The result also showed an increased level of monocyte and liver enzyme which may affected by NSAIDs taken by patients. And also showed non-significant differences in levels of WBC, neutrophils, lymphocytes, or the AST enzyme.*
Key words: *Gastric ulcer, Interleukin-37, liver enzyme.*

INTRODUCTION:

Gastric ulcer is defined as a deep lesion in the stomach wall caused by complete damage to the mucosal lining. [1] This damage occurs as a result of the penetration of hydrochloric acid and the enzyme pepsin into the layers of the stomach [2,3]. Gastric ulcer disease is one of the most common gastrointestinal disorders and is widespread globally [4].

There are many causes that can lead to the development of gastric ulcers, including infection with ***Helicobacter pylori***, which is considered the most common cause. This bacterium colonizes approximately 45%–50% of the gastric mucosa and triggers an inflammatory response in the body [4].

The second most common cause is the excessive and long-term use of non-steroidal anti-inflammatory drugs (NSAIDs) [5]. Many other less common causes that may lead to the development of gastric ulcers, including psychological stress, excessive acid production, free radicals, and alcohol consumption [6]. Additionally, conditions such as hypergastrinemia (Zollinger-Ellison syndrome), viral infections, chemotherapy and radiotherapy, gastric outlet obstruction, and infiltrative gastric

disorders such as malignancies and Crohn's disease are considered less common causes of gastric ulcer [7].

The symptoms of gastric ulcer are sometimes similar to those of indigestion. The main clinical feature is chronic, intermittent pain in the upper abdominal area, which typically subsides after eating [8], Bleeding is considered the most common and severe complication, occurring more frequently in individuals over the age of 60 [9], Since the symptoms of gastric ulcers are often similar to those of indigestion, diagnosis should involve taking a detailed medical history and performing a physical examination. Medical testing is also essential, especially laboratory tests for any patient presenting with anemia, black stools, hematemesis (vomiting blood), or weight loss, as these symptoms may indicate complications of gastric ulcers, particularly bleeding, perforation, or cancer [10], Since ***Helicobacter pylori*** is the most common cause of gastric ulcers, non-invasive tests are recommended for its detection, such as (the stool antigen test or the urea breath test), In general, esophagogastroduodenoscopy (EGD) is considered the gold standard for diagnosis [11], Given that the immune system plays a major role in all diseases—as it serves as the body's defense mechanism and is composed of a network of cells, tissues, and organs that respond to foreign bodies [12]—several immune parameters were examined in this study. The level of interleukin-37, an anti-inflammatory cytokine discovered in recent years, was measured. It has been found to play a key regulatory role in the development of various inflammatory diseases, autoimmune disorders, and cancers, Additionally, total white blood cell count and the levels of lymphocytes, neutrophils, and monocytes were measured, as they are important components of the immune system. Liver enzyme levels were also studied to assess the impact of non-steroidal anti-inflammatory drug (NSAID) use on liver function [13].

MATERIALS AND METHODS:

This study was conducted on individuals diagnosed with gastric ulcers, aged between 20 and 70 years. Blood sample collection took place over a period from September 19, 2024, to February 22, 2025, during which 90 blood samples were collected from both male and female patients, the samples were divided into two groups: the first group included 60 blood samples from individuals with gastric ulcers, confirmed by a specialist physician using upper gastrointestinal endoscopy. The second group, serving as the control group, consisted of 30 blood samples from healthy individuals, for both groups, levels of interleukin-37, total white blood cells, neutrophils, monocytes, lymphocytes, and liver enzymes were measured.

Blood Sample Collection:

Blood samples were collected using 5 mL medical syringes, with 5 mL of venous blood drawn from each patient, ensuring proper sterilization procedures during the collection process, each sample was then divided into two parts: the first part was placed in a tube containing EDTA to prevent coagulation and was used for complete blood count (CBC) analysis. The second part was placed in a tube containing a gel separator and left at room temperature for 10 minutes, then centrifuged at 6000 rpm for 5 minutes to obtain the serum, after centrifugation, the serum was carefully aspirated using a micropipette and transferred into 2 mL Eppendorf tubes. The samples were then labeled and the patient's name was documented using adhesive labels. Finally, the tubes were stored in a freezer at -20°C until the required laboratory analyses were performed.

Interleukin-37 Concentration:

The concentration of interleukin-37 was measured using a kit produced by ELK Biotechnology, China. The analysis was performed using the ELISA technique, following the manufacturer's instructions and operational principles.

White Blood Cell Count:

The white blood cell count was measured using a CBC analyzer from SYSMEX, Japan.

Liver Enzyme Concentration:

Liver enzyme levels were measured using a kit produced by BIOLABO, France, following the manufacturer's instructions and operational principles.

Histological Sections:

The study included 100 histopathological reports of gastric wall biopsies obtained from the Gastroenterology Unit at Tikrit Teaching Hospital, under official authorization letter No. 7/40/2497 dated September 8, 2024.

Statistical Analysis:

The current results were analyzed using the T-test at a significance level of P≥0.05, utilizing SPSS software, version 20 [14].

RESULTS AND DISCUSSION:

The statistical analysis of the current study showed a significant increase in the concentration level of interleukin-37 in individuals with gastric ulcers, with a mean value of (60.0±15.9), compared to healthy individuals (control group), whose mean value was (7.34±2.66), at a significance level of (P≤ 0.05), The elevation in interleukin-37 levels may be explained by its role as part of the immune system's mechanisms in defending the body against inflammation. In recent years, it has been found to play an important regulatory role in the development of a variety of inflammatory diseases, autoimmune disorders, and tumors [13, 15], The results of our current study are consistent with the findings of Davarpanah et al. (2020), which also confirmed elevated interleukin-37 levels in individuals with gastric ulcers [16], Asignificant difference was also observed in the percentage of monocytes at a significance level of P≤0.05, with a mean of (5.30±2.79) in gastric ulcer patients compared to (6.69±1.94) in the control group, As for the levels of total white blood cells, neutrophils, and lymphocytes, no significant differences were observed in individuals with gastric ulcers, as shown in the following table:

Table 1: Levels of immune variables in serum of patient and control group.

Parameters	Interleukin-37	Monocyte	WBC	Neutrophil	Lymphocyte
Patients	60.0±15.9*	5.30±2.79*	8.10±1.79$^{n.s}$	67.71±8.07$^{n.s}$	29.21±7.13$^{n.s}$
Control	7.34±2.66	6.69±1.94	7.64±1.82	64.29±9.14	29.20±8.59

* asignificant difference at P≤0.05 level. n.s significant differences.

The results of the current study regarding white blood cells did not agree with the findings of Jiao and Zhang (2021), who reported an increased white blood cell count in patients with gastric ulcers [17].

Liver function values were also studied and measured to determine the impact of long-term use of non-steroidal anti-inflammatory drugs (NSAIDs) on liver enzyme levels and liver cells. Based on the results of statistical analysis, significant differences were found in the levels of the following liver enzymes (Alanine aminotransferase, Alkaline phosphatase) in patients with gastric ulcers compared to the control group, at a significance level of P≤0.05. However, no significant difference was observed in the level of the enzyme Aspartate aminotransferase, as shown in the following table:

Table 2: Levels of liver enzyme in serum of patient and control group.

Parameters	ALT	AST	ALP
Patients	22.60±6.46*	27.75±8.02[n.s]	159.2±53.2*
Control	19.11±6.60	25.51±8.71	196.8±71.0

* asignificant difference at P≤0.05 level. n.s significant differences.

The results of our current study regarding liver function are consistent with the study by Jiao and Zhang (2021), which indicated impaired liver function and an elevated level of alkaline phosphatase (ALP) in patients with gastric ulcers. However, the same study differed from our findings concerning the enzyme Aspartate aminotransferase (AST), as no significant difference was observed in its level [17], As for the histological examination results, 100 reports of tissue biopsies taken from the stomach wall were reviewed and analyzed. The findings revealed the following: Edema in the stomach wall was observed in 98% of the samples, indicating its widespread presence among patients with gastric ulcers, Inflammation appeared in 93% of the samples, ranging from acute to chronic, reflecting the common occurrence of inflammatory responses in ulcer patients, Helicobacter pylori was detected in 66% of the samples, confirming its major role as a causative factor in many cases of gastric ulcer, Subepithelial hemorrhage was recorded in only 3% of the samples, which may indicate irritation or acute injury to the gastric mucosa, Fibrosis of the lamina propria was found in 20% of the samples, suggesting chronic tissue changes due to ongoing inflammation, These findings are presented more clearly in the following table:

Table 3: Histological examination results of the stomach wall.

Result	Percentage
Oedema	**98%**
Inflammation	**93%**
H.pylori	**66%**
Sub epithelial hemorrhage	**3%**
Fibrosis of lamina propria	**20%**

The histological examination results of the current study are in agreement with the findings of Toktay and Selli (2022), which emphasize the widespread presence of inflammation in nearly all affected individuals. Their study also confirms that 80% of duodenal ulcers are caused by Helicobacter pylori, and 60% of gastric ulcers are associated with this bacterium [18], Histological sections were taken from patients with gastric ulcers and examined under a microscope. The results are shown in the images below:

Figure 1: Histological section of the stomach of patient with a peptic ulcer, ulcer shows atrophied gastric mucosa on both sides (A), extending into a deep ulcer whose base contains inflamed and necrotic remnants (B), Stained with H&E, X400.

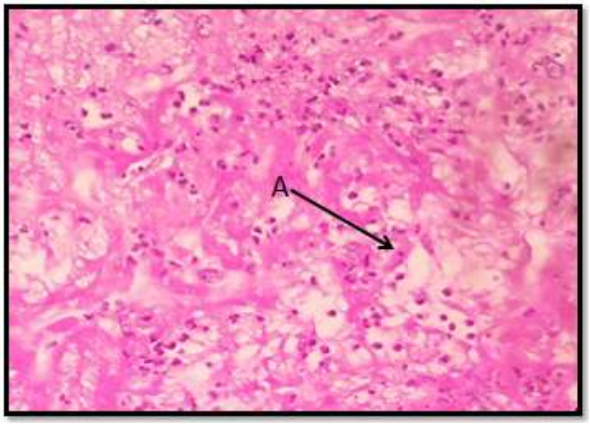

Figure 2: Histological section of the stomach of patient with a peptic ulcer, showed a deep ulcer whose base contain inflamed and necrotic debris (A), Stained with H&E, X400.

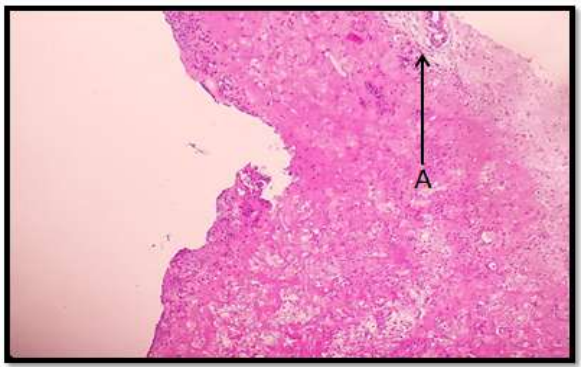

Figure 3: Histological section of the stomach of patient with a peptic ulcer, showed a fibrinoid necrosis at the base and margins, granulation tissue with chronic inflammatory cells (A), Stained with H&E, X400.

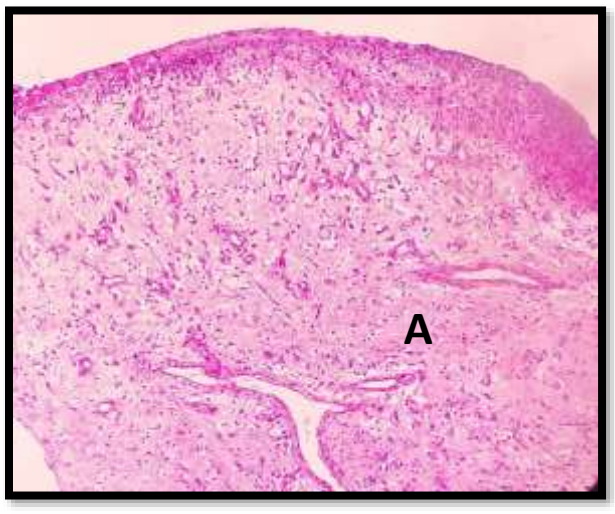

Figure 4: Histological section of the stomach of patient with a peptic ulcer, showed a fibrous or collagenous scars in muscularis propria with thickened blood vessels showing endarteritis obliterans, (A), Stained with H&E, X400.

The histological sections reveal the presence of gastric ulcers with well-defined margins, accompanied by atrophy of the gastric mucosa. This indicates erosion of the stomach's inner lining as a result of chronic inflammation or ongoing ulceration. The ulcer extends into the submucosal layers, suggesting that it is a deep ulcer affecting the deeper structures of the gastric wall.

The findings of the histological sections in this study were consistent with those of Wang et al., (2022) indicating the presence of mucosal atrophy in the stomach during infection. This atrophy can be classified into five stages, including: glandular atrophy in the lamina propria, compensatory proliferative atrophy, intestinal metaplasia-related atrophy, smooth muscle proliferative atrophy, and atrophy of the proliferative zone.[19]

Necrotic tissue debris is observed at the base of the ulcer, serving as clear evidence of an active inflammatory response within the stomach. This tissue necrosis reflects complete cellular death and may indicate the potential for serious complications such as gastrointestinal bleeding. Some sections also show irregularly shaped dead cells along with a significant number of inflammatory cells, particularly neutrophils, which point to the presence of an acute and active inflammation.

In addition, some sections display fibrinoid necrosis, a form of cell death characterized microscopically by bright pink, irregular material due to the deposition of proteins such as fibrin in the tissues. This type of necrosis is typically a marker of severe tissue injury, often resulting from chronic immune responses or persistent damage.

The penetration of the gastric mucosal barrier further indicates that the ulcerative and inflammatory process has reached the deeper layers of the stomach wall, thereby increasing the severity of the condition and necessitating precise medical intervention.

CONCLUSION:

1. The elevated levels of interleukin-37 (IL-37) observed in patients with gastric ulcers suggest a potential role of this cytokine in the inflammatory response associated with the disease, indicating an active immune reaction to mucosal injury.
2. The study showed a noticeable increase in liver function markers in patients with gastric ulcers, which may reflect a possible link between gastric ulceration and liver function, either through direct inflammatory pathways or shared immunological mechanisms.
3. Among the assessed white blood cell types, a statistically significant difference was found only in monocytes, whereas neutrophils and lymphocytes did not show significant changes. This may imply a more specific involvement of monocytes in the immune response to gastric ulceration.
4. Histopathological examination of gastric tissue biopsies revealed a high prevalence of chronic inflammation, confirming the persistent inflammatory nature of gastric ulcers and highlighting the importance of early diagnosis and targeted therapy.
5. A high rate of infection with ***Helicobacter pylori*** was detected in more than half of the cases, reinforcing the critical role of this bacterium in the pathogenesis of gastric inflammation and ulceration, consistent with previous findings.

Recommendations:

1- All individuals should pay attention to their dietary patterns by avoiding contaminated foods or those containing high levels of spices, as these may potentially contribute to the development of stomach ulcers.
2- Refrain from smoking and limit alcohol consumption due to their harmful effects on the stomach's mucous membrane and their role in the progression of gastric ulcers.
3- It is advised to avoid prolonged exposure to stress and to reduce the use of nonsteroidal anti-inflammatory drugs (NSAIDs), as they are major factors contributing to stomach ulcers.

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