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# Rate Of *Helicobacter pylori* Antigen Detection In Relation To Laboratory Criteria Among Adult Patients With Acute Gastroenteritis.

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**ABSTRACT**

Gastroenteritis are one of the social problems in developing countries. The pathogens commonly associated with Patients are *Salmonella, Clostridium difficile*, *Shigella, Yersinia, Escherichia coli and H.pylori.* The aim of the study was to evaluate the presence of *H.pylori* antigen in acute gastroenteritis in adult patients in relation to other laboratory criteria. The study was performed on freshly collected stool samples among 118 acute gastroenteritis patients admitted to two teaching hospitals from May 2017 to January 2018. A questionnaire was completed for each patient name, age, gender, clinical data like fever, nausea, Vomiting, abdominal pain. The criteria included hemorrhagic fresh stool sample in addition to containing parasites agent. Fresh stool samples were tested by Immunochromatographic assay for antigenic detection of *H.pylori.* a blood samples was taken from each patients as well as other(30)healthy control matching in age and gender. The study included measurement the concentration of Interleukin-8, serum amylase activity in sera of patients and control. H.pylori antigen identified in 35 stool samples 16 for females and 19 samples for males. most patients show fever , vomiting and abdominal pain ,stool samples show 100 % without blood,84.74 % with pus ,10.16 % with mucous. presence of *Entamoeba histolytica* and *Giardia lamblia* cyst. The percent was 15.25% and 7.63% respectively .also, The result indicated. The concentration of IL-8,increased significantly while the serum amylase activity decreased significantly in both interval ages in patients sera in comparison with healthy control. H.pylori Antigen present in 35 stool samples out of 118 cases most the patients show vomiting ,fever , abdominal pain , all the cases without blood ,100 cases with pus.16 cases with mucous , 9 cases with *G.lamblia* and 18 cases with cyst of *E.histolytica* . The concentration of IL-8increased significantly while the serum amylase activity decreased significantly in both interval ages in patients sera in comparison with healthy control.

**Keywords:** *Helicobacter pylori*, Interleukin- 8, amylase

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## INTRODUCTION

***Helicobacter pylori***, is a gram-negative, microaerophilic bacterium usually found in the stomach. It was identified in 1982 by Australian scientists Barry Marshall and Robin Warren, who found that it was present in a person with chronic gastritis and gastric ulcers, conditions not previously believed to have a microbial cause.(1`)At least half the world's population is infected by the bacterium, making it the most widespread infection in the world. Actual infection rates vary from nation to nation; the developing world has much higher infection rates than the West, where rates are estimated to be around 25%(2) bacterium seems to influence the pathologic outcome of the infection. People infected at an early age are likely to develop more intense inflammation that may be followed by atrophic gastritis with a higher subsequent risk of gastric ulcer, gastric cancer, or both. Acquisition at an older age brings different gastric changes more likely to lead to duodenal ulcer(3). Infections are usually acquired in early childhood in all countries but the percentage of infected people increases with age, with about 50% infected for those over the age of 60 compared with around 10% between 18 and 30 years. The higher prevalence among the elderly reflects higher infection rates in the past when the individuals were children rather than more recent infection at a later age of the individual. most likely due to socioeconomic factors(4,5) *H. pylori* is contagious, although the exact route of transmission is not known.

Person-to-person transmission by either the oral–oral or fecal–oral route is most likely. Consistent with these transmission routes, the bacteria have been isolated from feces, saliva, and dental plaque of some infected people. Findings suggest *H. pylori* is more easily transmitted by gastric mucus than saliva. Transmission occurs mainly within families in developed nations, yet can also be acquired from the community in developing countries. *H. pylori* may also be transmitted orally by means of fecal matter through the ingestion of waste-tainted water, so a hygienic environment could help decrease the risk of *H. pylori* infection(6,7,8). To avoid the acidic environment of the interior of the stomach (lumen), *H. pylori* uses its flagella to burrow into the mucus lining of the stomach to reach the epithelial cells underneath, where it is less acidic(9). *H. pylori* is able to sense the pH gradient in the mucus and move towards the less acidic region (chemotaxis). This also keeps the bacteria from being swept away into the lumen with the bacteria's mucus environment, which is constantly moving from its site of creation at the epithelium to its dissolution at the lumen interface(10) It adheres to the epithelial cells by producing adhesins, which bind to lipids and carbohydrates in the epithelial cell membrane.

One such adhesin, BabA, binds to the Lewis b antigen displayed on the surface of stomach epithelial cells(11) *H. pylori* adherence via BabA is acid sensitive and can be fully reversed by increased pH. It has been proposed that BabA's acid responsiveness enables adherence while also allowing an effective escape from unfavorable environment at pH that is harmful to the organism(12) Another such adhesin, SabA, binds to increased levels of sialyl-Lewis x antigen expressed on gastric mucosa(13) Following attachment of *H. pylori* to stomach epithelial cells, the type IV secretion system expressed by the *cag* PAI "injects" the inflammation-inducing agent, peptidoglycan, from their own cell walls into the epithelial cells. The injected peptidoglycan is recognized by the cytoplasmic pattern recognition receptor (immune sensor) Nod1, which then stimulates expression of cytokines that promote inflammation(14) *H. pylori* harms the stomach and duodenal linings by several mechanisms. The ammonia produced to regulate pH is toxic to epithelial cells, as are biochemical's produced by *H. pylori* such as proteases, vacuolating cytotoxin A (VacA) (this damages epithelial cells, disrupts tight junctions and causes apoptosis), and certain phospholipases.

Cytotoxin associated gene *CagA* can also cause inflammation and is potentially a carcinogen (14). Colonization of the stomach by *H. pylori* can result in chronic gastritis, an inflammation of the stomach lining, at the site of infection. *Helicobacter* cysteine-rich proteins (Hcp), particularly HcpA (hp0211), are known to trigger an immune response, causing inflammation (15). Ulcers in the stomach and duodenum result when the consequences of inflammation allow stomach acid and the digestive enzyme pepsin to overwhelm the mechanisms that protect the stomach and duodenal mucous membranes. The location of colonization of *H. pylori*, which affects the location of the ulcer, depends on the acidity of the stomach(16) he inflammatory response caused by bacteria colonizing near the pyloric antrum induces G cells in the antrum to secrete the hormone gastrin, which travels through the bloodstream to parietal cells in the fundus(17).

Gastrin stimulates the parietal cells to secrete more acid into the stomach lumen, and over time increases the number of parietal cells, as well(18). The increased acid load damages the duodenum, which may

eventually result in ulcers forming in the duodenum. When *H. pylori* colonizes other areas of the stomach, the inflammatory response can result in atrophy of the stomach lining and eventually ulcers in the stomach. This also may increase the risk of stomach cancer (19).

## MATERIALS AND METHODS

### Study population

During a period of eight months from May 2017 to January 2018, a study was conducted at two teaching hospitals in Baghdad on freshly collected stool samples from a total number of 118 cases of gastroenteritis among adult patients. A questionnaire was completed for each patients containing the following information: name, age, gender, clinical data (fever, nausea, vomiting, abdominal pain, and diarrhea), macroscopic and microscopic laboratory examinations of stool samples.

The inclusion criteria was to include in this study watery stool samples (at macroscopic examination) and a parasite –free stool samples at microscopic examination (using saline and iodine preparations) from the diarrheal cases that were not lasting more than seven days after the onset of illness. The criteria was also, to include reported hemorrhagic fresh stool samples containing parasitic agents (*Giardia lamblia or Entamoeba histolytica*) in their stools. Stool samples were collected in a labeled screw cap clean container. Stool samples were tested by Immunochromatographic assay (purchased from CerTest Biotech, Spain) for antigenic detection of *H.pylori* and were done according to instructions of the manufacturers. Allowing the card –device, test reagents and stool samples to reach to room temperature prior to testing. A separate stool collection tube and device were used for each sample and the assay was done right after collection. To detect *H.pylori*, approximately 100mg or 100 microtiter of stool sample was put and shaken in collection tube containing the diluents. Four drops or 100µl was dispensed in the circular window of the card. The results (appearance of the colored bands) were read after 10 minutes. This CerTest-*H.pylori* KIT is qualitative Immunochromatographic assay for determination of H.pylori in fecal samples.

The membrane on the test band region is pre coated with mouse monoclonal antibodies against *H.pylori* antigens . During testing, the sample is allowed to react with the colored conjugates (anti-H.pylori mouse monoclonal antibodies-red microspheres) which were pre-dried on the test. The mixture then moves upward on the membrane by capillary action. As the sample flows through the test membrane, the colored particles migrate. In the case of positive result, the specific antibodies present on the membrane will capture the colored particles and a red colored line becomes visible. The mixture captures the colored particles and a red colored line becomes visible. The mixture continues to move across the membrane to the immobilized antibody placed in the control band region, a green-colored band always appear. The presence of this green band serves as 1-verification that sufficient volume is added, 2-that proper flow is obtained and 3-as an internal control for the reagents. Insufficient specimen volume, incorrect procedural or deterioration of the reagents are the most likely reasons for control line failure. Negative results were indicated by only one green band (control line).

For positive result, in addition to the green control band, a red band also appear on the site of result line. A total absence of the control colored band (green) regardless the appearance or not of the result line (red) was evaluated as an invalid result.

### Blood samples

Three mL of Venous blood was obtained from each patients and collected in sterilized screw cap plastic tube, blood samples were left for 30 min. at room temperature, then centrifuge at 3000 rpm for five minute, then the serum for each sample was collected in eppendorf tubes and stored in deep freeze at -20c°until the time for using. The current study included Immunological & Clinical biochemical aspects. the level of interleukin -8(IL-8) estimated by ELISA according to manual procedure of cusabio Biotech(Germany). serum amylase activity determined according to manufactures instructions of Biosystem(Spain).

### Statistical Analysis

The results were analyzed using statistical system SPSS version -18 (T-testing).

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## RESULT

### Gender

Distribution of *H. pylori* patients according to their gender, were studied, among them 19 were males and 16 were females. H. pylori antigen was revealed in 118 of fecal samples. Among that studied who has antigen H. pylori positive fecal samples only 35.

**Table 1: Distribution of *H. pylori* patients according to their gender**

| *H. pylori* antigen | Females (No.)% | Males (No.)% | Total (No.)% |
|---|---|---|---|
| *H. pylori* +ve Ag | (16) 45.71 % | (19) 54.29 % | (35) 100% |
| *H. pylori* -ve Ag | (31) 37.34 % | (52) 62.66 % | (83) 100% |
| Total | (47) | (71) | (118) 100% |

### Fever

Patients with whom fecal specimens were positive to *H. pylori* antigen or negative develops fever more than those without fever (72.88% versus 27.12%). The result revealed statistically significant difference ($p<0.01$).

**Table 2: Distribution of *H. pylori* patients according to fever**

| *H. pylori* antigen | Fever positive(No.)% | Fever negative(No.)% | Total (No.)% |
|---|---|---|---|
| *H. pylori* +ve Ag | (32) 91.42 % | (3) 8.58 % | (35) 100% |
| *H. pylori* -ve Ag | (54) 65.04 % | (29) 34.96 % | (83) 100% |
| Total | (86) 72.88 % | (32) 27.12% | (118) 100% |

### Abdominal pain

Patients whom fecal specimens were H. pylori positive antigen and negative antigen develops Abdominal pain more than those without abdominal pain (77.11% versus 22.89%).The result revealed significant difference ($p<0.01$).

**Table 3: Distribution of *H. pylori* patients according to abdominal pain**

| *H. pylori* antigen | With Abdominal pain (No.)% | Without Abdominal pain (No.)% | Total (No.)% |
|---|---|---|---|
| *H. pylori* +ve Ag | (30) 85.71 % | (5) 14.29% | (35) 100% |
| *H. pylori* -ve Ag | (61) 73.49 % | (22) 26.51 % | (83) 100% |
| Total | (91) 77.11 % | (27) 22.89% | (118) 100% |

### Vomiting

Patients whom fecal specimens were *H. pylori* positive antigen and negative antigen develops vomiting less than those without abdominal pain (43.22% versus 56.78%).The result revealed significant difference ($p<0.01$).

**Table 4: Distribution of *H. pylori* patients according to vomiting**

| *H. pylori* antigen | With vomiting (No.)% | Without vomiting (No.)% | Total (No.)% |
|---|---|---|---|
| *H. pylori* +ve Ag | (22) 62.85 % | (13) 37.15% | (35) 100% |
| *H. pylori* -ve Ag | (29) 34.39 % | (54) 65.61 % | (83) 100% |
| Total | (51) 43.22 % | (67) 56.78% | (118) 100% |

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**Headache**

All patients whom fecal specimens were positive to *H. pylori* antigen or negative develops headache (100%).

**Table 5: Distribution of *H. pylori* patients according to headache**

| *H. pylori* antigen | With headache (No.)% | Without headache (No.)% | Total (No.)% |
|---|---|---|---|
| *H. pylori* +ve Ag | Zero | (35) 100 % | (35) 100% |
| *H. pylori* -ve Ag | Zero | (83) 100% | (83) 100% |
| Total | Zero | (118) 100% | (118) 100% |

**Blood**

The patients whom fecal specimens were *H. pylori* positive antigen and negative antigen show (100%) negative bloody stool. The results indicated significant difference ($p<0.01$) between groups.

**Table 6: Distribution of *H. pylori* patients according to presence of blood in their stool**

| *H. pylori* antigen | With blood (No.)% | Without blood (No.)% | Total (No.)% |
|---|---|---|---|
| *H. pylori* +ve Ag | Zero | (35) 100 % | (35) 100% |
| *H. pylori* -ve Ag | Zero | (83) 100% | (83) 100% |
| Total | Zero | (118) 100% | (118) 100% |

**Diarrhea**

A Patients whom fecal specimens were *H. pylori* positive antigen and negative antigen show diarrhea ($p<0.01$) in comparison with other groups (9.32% versus 90.68%).

**Table7: Distribution of *H. pylori* patients according to diarrhea.**

| *H. pylori* antigen | With diarrhea. (No.)% | Without diarrhea. (No.)% | Total (No.)% |
|---|---|---|---|
| *H. pylori* +ve Ag | (4) 11.42 % | (31) 88.58 % | (35) 100% |
| *H. pylori* -ve Ag | (7) 8. 43% | (76) 91.57% | (83) 100% |
| Total | (11) 9.32 % | (107) 90.68% | (118) 100% |

**Nausea**

A Patients whom fecal specimens were *H. pylori* positive antigen and negative antigen show Nausea ($p<0.01$) in comparison with other groups (3.38% versus 96.62%).

**Table 8: Distribution of *H. pylori* patients according to Nausea**

| *H. pylori* antigen | Nausea positive (No.)% | Nausea negative (No.)% | Total (No.)% |
|---|---|---|---|
| *H. pylori* +ve Ag | (1) 2.85 % | (34) 97.15 % | (35) 100% |
| *H. pylori* -ve Ag | (3) 3.61% | (80) 96.39% | (83) 100% |
| Total | (4) 3.38 % | (114) 96.62% | (118) 100% |

**Mucous**

A Patients whom fecal specimens were *H. pylori* positive antigen a negative antigen show mucous in their stool ($p<0.01$) in comparison with other groups (10.16% versus 89.84%).

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**Table 9: Distribution of *H. pylori* patients according to presence of mucous in their stool**

| *H. pylori* antigen | With mucous (No.)% | Without mucous (No.)% | Total (No.)% |
|---|---|---|---|
| *H. pylori* +ve Ag | (2) 5.71 % | (33) 94.29 % | (35) 100% |
| *H. pylori* -ve Ag | (10) 12.04% | (73) 87.96% | (83) 100% |
| Total | (12) 10.16 % | (106) 89.84% | (118) 100% |

**Pus cells**

A patients whom fecal specimens were ***H. pylori*** positive antigen and negative antigen show 84.74% pus cells in their stool versus 15.26%.

**Table 10: Distribution of *H. pylori* patients according to presence of pus cells in their stool**

| *H. pylori* antigen | With pus (No.)% | Without pus (No.)% | Total (No.)% |
|---|---|---|---|
| *H. pylori* +ve Ag | (32) 91.42 % | (3) 8.58 % | (35) 100% |
| *H. pylori* -ve Ag | (68) 81.19% | (15) 18.81% | (83) 100% |
| Total | (100) 84.74 % | (18) 15.26% | (118) 100% |

**Cysts**

A patients whom fecal specimens were ***H. pylori*** negative antigen and positive antigen show presence of *Entamoeba histolytica* and *Giardia lamblia* cyst. The percent was 15.25% and 7.63% respectively versus 77.12% without cyst.

**Table 11: Distribution of *H. pylori* patients according to presence of cyst in their stool**

| *H. pylori* antigen | With cyst (No.)% | | Without cyst (No.)% | Total (No.)% |
|---|---|---|---|---|
| | *E.histolytica*(No.)% | *G.lamblia*(No.)% | | |
| *H. pylori* +ve Ag | (10) 28.57 % | (6) 17.13 % | (19) 54.20 % | (35) 100% |
| *H. pylori* -ve Ag | (8) 9.63% | (3) 3.61 % | (72) 86.76 % | (83) 100% |
| Total | (18) 15.25 % | (9) 7.63 % | (91) 77.12 % | (118) 100% |

**Amylase activity**

The activity of amylase decreased significantly (p≤0.05) in both interval ages of patients in comparison with healthy control.

**Table 12: Serum amylase activity in patients with *H. pylori* and healthy control**

| Interval age (years) | Amylase IU/ml | |
|---|---|---|
| 17-35 | Patients | 28.20 ±2.0 * |
| | Control | 74.34 ± 1.20 |
| 36-70 | Patients | 34.0 ± 0.8 * |
| | Control | 69 ± 2.0 |

** p < 0.01 statistically significant*

**Interleukin-8**

The level of IL-8 Increased siginifigantly(p≤0.05) in patients with *H. pylori* in comparison with healthy control in both interval ages the value126.2,138.6 pg ml for patients and56.3,68.6 pgmlfor healthy control respectively.

**Table 13: concentration of IL-8 in patients with *H. pylori* and healthy control**

| Interval age (years) | | IL-8 Pg/ml |
|---|---|---|
| 17-35 | Patients | 126.2 ± 0.3 * |
| | Control | 56.3 ± 0.7 |
| 36-70 | Patients | 138.6 ± 0.4 * |
| | Control | 68.6 ± 0.3 |

** p < 0.01 statistically significant*

**DISCUSSION**

*H.pylori* was identified in 35 stool samples of patient out of 118 samples. (Table 1). The infections may be due to lack of sanitary facilities and poor living condition among the major causes of infection . The result was consistent with that reported in Kirkuk (20), in Diyala by Hasan *et al*. (21), in Basrah by Al-Hamdi and Khashan (22). But the variation in the rate of infection between different studies may be due to the type of the sample (blood, stool and tissue), size of the sample, place and period of the study and techniques used for detection of the bacteria.

The rate of infection in males was higher than females. The result indicated that H. Pylori infection in males 54.29% was higher than 45.71% in female the results in line with other results were reported in Diyala by Al-Ezzy (23). The clinical symptom with the highest rate was 77.11% abdominal pain followed by Fever, Vomiting, diarrhea, Nausea and headache with a highly significant difference ($p<0.01$). The result in line with Agar *et al*. (24), demon-started that the main gastrointestinal symptoms observed were heartburn (60.6%) followed by vomiting (28.3%) and abdominal distention (24%). While in Sulaimanya, Sheikhani *et al*. (25) revealed that there was no relationship between patient symptoms and *H. pylori* ($p> 0.05$) except vomiting, loss of appetite and weight loss ($p< 0.05$).Also, the result indicated the presence of pus cells in patients stool (Table-10) till to 92.42% versus 8.58% may be due to Infection by *Helicobacter pylori* can cause gastritis and is also highly associated with gastric ulcers, and mucosa-associated lymphoid tissue lymphomas (26).Upon *H. pylori* infection, gastric epithelial cells respond to *H. pylori* by activating many signaling cascades. These lead to cytokine and chemokine secretion, which recruit innate and adaptive immune cells to the site of infection and induce inflammatory response but functionally ineffective. In a general, patients with H. pylori and other pathogenic bacteria is often containing mucous, pus specially when the diarrhea is sever. Some patients show presence of *Entamoeba histolytica* cyst and *Giardia lamblia* cyst in their stools (Table 11).

In a general, the Entamoebiasis represented the most common parasites which are transmitted via the ingested un healthy food (27). However, There is no specific vaccination to prevent neither spread nor infection of the disease(28) Amoebiasis is more risky infectious disease than other while the cyst of Entamoeba can survive for up to a month in a soil or for up to 45 min under fingernails .Invasion of the intestinal lining causes amoebic bloody diarrhea or amoebic colitis. The result show statically decreasing in serum amylase activity in patients with H pylori in comparison with healthy control (Table-12) may be due to the patients presenting like infectious diarrhea and upper abdominal pain associated with pancreatitis or with loss of appetite (29).

The result indicated statistically elevation of interleukin-8 in patients in comparison with healthy control in all interval age (Table-13). the reasons due to Interleukin-8 (IL-8) is an important chemokine in mediating the inflammatory response to *H. pylori*. may be mediated by NF-_B and activating protein 1 (AP-1)DNA binding sites within the IL-8 promoter are required for optimal transcription in response to infection of gastric epithelial cells by *H. pylori* (30). During *H. pylori* infections, both NF-_B and members of the mitogen-activated protein kinase (MAPK) family become activated (31). Activated MAPKs then phosphorylate AP-1 complexes, which results in increased AP-1-dependent transcription. As such, signaling pathways that activate NF-_B and/or AP-1 could result in increased IL-8 secretion. Conclusion: H.pylori Antigen present in 35 stool samples out of 118 cases most the patients show vomiting ,fever , abdominal pain , all the cases without blood ,100 cases with pus.16 cases with mucous , 9 cases with *G.lamblia* and 18 cases with cyst of *E.histolytica* . The concentration of IL-8 increased significantly while the serum amylase activity decreased significantly in both interval ages in patients sera in comparison with healthy control.

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