

Is H.Pylori Incriminated as Etiology for Acute Appendicitis or not?

H.R.Moslem, A.S.Ezzat, A.M.Zidan, S.A.Elghazzar and A.N.Zaki

Department of General Surgery Dept., Faculty of Medicine, Benha Univ., Benha, Egypt

E-Mail: amgad.nashat200024@yahoo.com

Abstract

Background: Appendicitis is the most common abdominal surgical emergency. There is an approximately 6% to 8% lifetime risk of appendicitis. Appendicitis is primarily a disease of adolescents and young adults with a peak incidence in the second and third decades of life. H.pylori colonizes mainly stomach and duodenum but also, reported in other sites. **Objective:** This study was proposed for finding out if there is a relation between H.pylori infection and acute appendicitis. **Methods:** The current study was prospectively conducted at Surgical Department of Benha University and Assiut General Hospital. The study conducted two hundreds patients were clinically, laboratory and radiologically diagnosed to have acute appendicitis. **Results:** Many authors studied the relationship between appendicitis and H.pylori but still this relation is controversial. This study was done to study if there is a relation between H.pylori infection and acute appendicitis. Two hundred patients with confirmed acute appendicitis were enrolled. Diagnosis of acute appendicitis was done based on clinical, laboratory and radiological data. Majority (63%) of those patients were males with mean age of all patients were 24.12 ± 9.50 years with range between 8 and 62 years. based on blood tests, 143 (71.5%) patients were seropositive while only 57 (28.5%) patients were seronegative. Also, H.pylori antigen in stool was positive in 88 (44%) patients and histopathology of the specimen revealed that only 10 (5%) patients were positive to H.pylori. Also, in the current study; 48.3% of those with seropositive H.pylori had suppurative appendicitis while 59.6% of those with seronegative H.pylori had catarrhal appendicitis. Based on the current we found that patients with seropositive H.pylori had more severe form of acute appendicitis. Till now, there is controversy about role of H.pylori in the pathogenesis of acute appendicitis. Based on the current study, it's recommended to perform such studies prospectively in multiple centers with large sample size. **Conclusion:** It seems that there is controversy about role of H.pylori in the pathogenesis of acute appendicitis. However seropositive patients are more likely to have perforated and gangrenous appendicitis and have more post-operative SSI.

Keywords: Appendicitis, PCR, H.pylori, proton pump inhibitors.

1. Introduction

Appendicitis is the most common abdominal surgical emergency. There is an approximately 6% to 8% lifetime risk of appendicitis. Appendicitis is primarily a disease of adolescents and young adults with a peak incidence in the second and third decades of life [1].

The inflammatory process in acute appendicitis could be similar to proposed mechanisms of H. pylori induced gastroduodenal epithelial damage [2].

Helicobacter pylori, a spiral-shaped pathogenic bacterium found on the human gastric mucosa, was first isolated by Warren and Marshall in 1982 and soon after was linked with chronic antral gastritis and peptic ulceration. Initially, this bacterium was classified as Campylobacter pylori but in 1989 was included in a new genus, Helicobacter, and renamed Helicobacter pylori [3].

H. pylori are a common bacterium, and approximately 50 percent of the world's population has been estimated to be infected (198). Humans are the principal reservoir. The prevalence of H. pylori infection varies widely by geographic area, age, race, ethnicity, and SES. Rates appear to be higher in developing than in developed countries. H.pylori has been associated with several serious diseases of the gastrointestinal tract, including duodenal ulcer and gastric cancer[4].

It was proved that H. pylori can survive outside the gastroduodenum. It has been detected in 90 per cent of faecal specimens in patients with proven gastric H. pylori and cultured faeces using selective media and

environment proving it is viable at the level of the lower colon [6].

Appendicitis starts with mucosal inflammation which then spreads to the serosal surface resulting in peritonitis. Formation of an abscess or perforation occurs in 25 percent of patients. It was proven that H.pylori infection could cause MALT hypertrophy in the appendix then under certain conditions, luminal obstruction and acute inflammation might occur. It is possible that an inflammatory response could be primed because of the presence of H.pylori or its products by enhanced mucosal macrophage iNOS expression (as occurs in the foregut) [6].

2. Aim of the work

This study was proposed for finding out the relationship between H.pylori and acute appendicitis.

3. Patients and methods

Prospective study non randomized, Non probability, Purposive Sampling from emergency department at Assiut General Hospital and Benha University Hospital. Through one year started from 1st of March 2020 to 31st of February 2021.

200 patients were enrolled in this study with symptoms and signs of acute appendicitis including acute onset abdominal pain mainly in right lower quadrant, nausea, vomiting, anorexia, elevated temperature and right lower quadrant tenderness and rebound tenderness rebound tenderness. Also preoperative consents were discussed and obtained

from all patients according to approved standards of The Ethical committee of Benha University.

Preoperatively a record of their medical history, physical examinations, labs values including H.pylori serum IgG and H.pylori stool antigen (if it was possible) were done, and patients were classified according to their results to be +ve or -ve. Alvarado score was also calculated for all patients with suspected acute appendicitis and was recorded in their files.

Intraoperatively both open and laparoscopic appendectomy operations were used in this study. Each removed appendix was classified according its gross appearance to be catarrhal, suppurative, perforated or gangrenous.

Postoperatively pathological examination of the removed appendix was done (if it was possible) to

determine the presence of H.pylori inside the appendix. Patients were followed up for postoperative complications as vomiting, epigastric pain, ileus, fever, diarrhea and surgical site infection and all results were recorded

Inclusion Criteria were patients at any age, both genders, diagnosed to have acute appendicitis as mentioned before.

Exclusion Criteria were pregnant patients, patients diagnosed as complicated appendicitis, patients below 5 years and above 70 years of age and patients who refused to have appendectomy.

All data was collected, tabulated and statistically analyzed according to type of data obtained from each parameter using Statistical Package For Social Science (SPSS 20).

4. Results

Table (1) Demographic data of enrolled patients.

	N= 200
Age (years)	24.12 ± 9.50
Range	8-62
Sex	
Male	126 (63%)
Female	74 (37%)

Data expressed as frequency (percentage), mean (SD)

Table (2) Alvarado score and type of procedure among enrolled patients.

	N= 200
Alvarado score	7.86 ± 1.32
Range	5-10
Type of procedure	
Open	181 (90.5%)
Laparoscopic	19 (9.5%)

Data expressed as frequency (percentage), mean (SD)

Table (3) Perioperative data among enrolled patients

	N= 200
Hospital stay (hour)	26.64 ± 8.60
Range	24-72
Type of appendicitis	
Suppurative	88 (44%)
Catarrhal	76 (38%)
Gangrenous	26 (13%)
Perforated	10 (5%)
Post-operative epigastric pain	27 (13.5%)
Post-operative vomiting	21 (10.5%)
Post-operative SSI	19 (9.5%)
Post-operative fever	16 (8%)
Post-operative diarrhea	13 (6.5%)
Post-operative ileus	6 (3%)

Data expressed as frequency (percentage), mean (SD)

Table (4) Seropositivity for H.pylori among enrolled patients.

N= 200	
H.pylori serum antibodies	
Positive	143 (71.5%)
Negative	57 (28.5%)
H.pylori antigen in stool	
Positive	88 (44%)
Negative	63 (31.5%)
Not done	49 (24.5%)
Histopathogy for H.pylori	
Positive	10 (5%)
Negative	135 (67.5%)
Not done	55 (27.5%)

Data expressed as frequency (percentage)

Table (5) Characteristic of enrolled patients based on seropositivity for H.pylori.

	Seronegative (n= 57)	Seropositive (n=143)	P value
Age (years)	22.59 ± 9.33	24.72 ± 9.53	0.15
Sex			
Male	39 (68.4%)	87 (60.8%)	0.20
Female	18 (31.6%)	56 (39.2%)	
Alvarado score	7.33 ± 1.35	8.07 ± 1.25	< 0.001
Type of procedure			
Open	48 (84.2%)	133 (93%)	0.05
Laparoscopic	9 (15.8%)	10 (7%)	
Hospital stay (hour)	24.42 ± 3.17	27.52 ± 9.84	0.21
Type of appendicitis			
Suppurative	19 (33.3%)	69 (48.3%)	
Catarrhal	34 (59.6%)	42 (29.4%)	< 0.001
Gangrenous	3 (5.3%)	23 (16.1%)	
Perforated	1 (1.8%)	9 (6.3%)	
Post-operative SSI	1 (1.8%)	18 (12.6%)	0.01
Post-operative epigastric pain	6 (10.5%)	21 (14.7%)	0.29
Post-operative vomiting	4 (7%)	17 (11.9%)	0.22
Post-operative fever	2 (3.5%)	14 (9.8%)	0.11
Post-operative diarrhea	1 (1.8%)	12 (8.4%)	0.07
Post-operative ileus	0	6 (4.2%)	0.13
Histopathogy for H.pylori			
Positive	0	10 (7%)	
Negative	2 (3.5%)	133 (93%)	< 0.001
Not done	55 (96.5%)	0	

Data expressed as mean (SD), frequency (percentage). P value was significant if < 0.05

Table (6) Characteristics of patients with positive stool antigen for H.pylori.

N= 88	
Age (years)	23.59 ± 8.30
Sex	
Male	54 (61.4%)
Female	34 (38.6%)
Alvarado score	8.22 ± 1.27
Type of procedure	
Open	82 (93.2%)
Laparoscopic	6 (6.8%)
Hospital stay (hour)	28.36 ± 11.24
Type of appendicitis	
Suppurative	45 (51.1%)
Catarrhal	20 (22.7%)
Gangrenous	15 (17%)

Perforated	8 (9.1%)
Post-operative SSI	13 (14.8%)
Seropositive	88 (100%)
Post-operative epigastric pain	13 (14.8%)
Post-operative vomiting	14 (15.9%)
Post-operative fever	9 (10.2%)
Post-operative diarrhea	8 (9.1%)
Post-operative ileus	5 (5.7%)
Histopathology for H.pylori	
Positive	9 (10.2%)
Negative	79 (89.8%)

Data expressed as mean (SD), frequency (percentage).

Table (7) Characteristics of patients with positive histopathology for H.pylori.

	N= 10
Age (years)	28.80 ± 8.12
Sex	
Male	4 (40%)
Female	6 (60%)
Alvarado score	8.70 ± 1.25
Type of procedure	
Open	10 (100%)
Laparoscopic	0
Hospital stay (hour)	38.40 ± 20.23
Type of appendicitis	
Suppurative	5 (50%)
Gangrenous	1 (10%)
Perforated	4 (40%)
Post-operative SSI	3 (30%)
Post-operative epigastric pain	5 (50%)
Post-operative vomiting	3 (30%)
Post-operative fever	4 (40%)
Post-operative diarrhea	5 (50%)
Post-operative ileus	2 (20%)
Seropositivity	10 (100%)
Positive stool antigen for H.pylori	
Positive	9 (90%)
Negative	1 (10%)

Data expressed as mean (SD), frequency (percentage).

5. Discussion

Acute appendicitis is considered as the most common acute surgical condition of the abdomen. The lifetime risk of acute appendicitis is about 6%~8% in general population. The cause of acute appendicitis remains not known. Obstruction of the lumen of the appendix is considered an important part of the pathogenesis of acute appendicitis[7].

The obstruction can be multi-factorial, including fecaliths, lymphoid hypertrophy (related to viral illnesses and bacterial and fungal infections), parasites, foreign bodies, Crohn's disease, tuberculosis, tumors, or endometriosis [8].

However, two recent large-scale studies showed that only 6.8% and 10.5% of appendicitis specimens had a mechanical obstruction. Furthermore, previous studies reported that in a certain portion of appendicitis cases, luminal obstruction was caused by spasms or hypertonicity of the neuromuscular tissues at the junction between the cecum and the appendix similar

to the mechanism of pyloric spasms, caused by an autonomic nervous dysfunction [9].

Helicobacter pylori (H. pylori) mainly colonizes the surface of the gastric epithelium and is an essential human pathogen that was discovered in the past century. The prevalence of H. pylori is probably 44.3% of the entire human population. According to the statistics, its prevalence is 34.7% in developed countries and 50.8% in developing countries, and the worldwide annual recurrence rate is 4.3%. Although the global infection rate of H. pylori is high, a large proportion of infected people have no apparent symptoms and only show gastritis under an endoscope [10].

Helicobacter pylori infection has been found in the upper GI tract. It is incriminated as a cause for various pathological conditions. This study was made to determine whether H. pylori infection plays a role as a cause for acute appendicitis. The study conducted two hundreds patients were clinically, laboratory and radiologically diagnosed to have acute appendicitis.

Mean age of enrolled patients 24.12 ± 9.50 years with range between 8 and 62 years. Majority 126 (63%) of the studied was male while 74 (37%) patient was females. In consistent with the current study; it was reported that a total of 772 out of 784 cases of appendicitis documented were confirmed histologically from the hospital records. Fifty-two percent were males and 48% were females with overall mean age was $28.64 \pm SD 10.12$ years with 6% below the age of ten and 1.5% above 60 years [11].

Also, a previous study enrolled 50 patients with acute appendicitis to study helicobacter species and bacterial DNA in those patients. Mean age of those patients was 30 years with range between 9 and 87 years. Also, majority (52%) of those patients was males and 24 (48%) patients were females [12].

Appendicitis is generally a disease of young people. The usual finding of the highest incidence was seen in the second and third decades of life. The mean average age of 25.7 years is in-keeping with that cited by Al Omran. The age distribution is the same in both sexes; this supports that there is no effect of sex or the X chromosome as a predisposing factor to appendicitis [13].

As it is known that appendicitis is relatively rare in the first decade and progressive decrease after the third decade it may be inferred that the peak incidence seems to coincide with the age endowed with the most active lymphoreticular activity in the mucosa-associated lymphoid tissues, which make up most of the appendix [14].

Based on the current study, blood test for antibody against H.pylori was performed among all enrolled patients where 143 (71.5%) patients were seropositive while only 57 (28.5%) patients were seronegative. Also, H.pylori antigen in stool was positive in 88 (44%) patients and all of them were seropositive for H.pylori antibody. Pathological examination of the specimen for the presence of H.pylori was positive in only 10 (5%) patients and those patients were seropositive and had positive H.pylori antigen in stool.

Also, the current study revealed that majority (59.6%) of seronegative patients had catarrhal appendicitis while suppurative appendicitis was frequently present in seropositive patients (88.3%). Frequency of gangrenous and perforated appendicitis was significantly higher among seropositive patients (16.1% and 6.3%) in comparison to seronegative patients (5.3% vs. 1.3%).

In previous study H. pylori was investigated in 46 patients who underwent emergent appendectomy for acute appendicitis. H. pylori serum test was positive in 18 patients (39%), but the microbe was detected in just two appendix specimens (4%) [15]. This discrepancy between that study and the current study may be attributed to difference in sample size and selection bias.

The authors also reported that in all seropositive patients acute appendicitis was confirmed by the pathological study; it was serous in (33%) and purulent or gangrenous in (67%). The latter incidence in the sero-negative patients was 50%. There were found

eight specimens (17%) negative for inflammation dealing all with seronegative patients [15].

In contrast to the current study, previous study showed that there were 3/50 (6%) samples that tested positive for Helicobacter spp., among normal appendixes. All of them showed 98%-99% sequence similarity to H. pylori. However Helicobacter spp. was not found in any samples of acute appendicitis [12].

However, most authors could not demonstrate the presence of H. pylori in case of appendicitis. H. pylori commonly colonizes the gastrointestinal tract. However, some previous studies suggest that Helicobacter is not important as an etiological factor for acute appendicitis.

Furthermore, studies found that appendicitis was significantly related to ulcers of the duodenum, but not with Helicobacter pylori.

Also, seropositivity for H.pylori account for 35% of patients with confirmed appendicitis as reported by RM and Villanueva in comparison to those with control group (15%). Though was noticed difference between both groups, this one was not significant. It seems that H. pylori colonizes the appendix in small proportion and is unlikely to be associated directly with acute appendicitis. However, seropositive patients with acute inflammation are likely to suffer from perforated or gangrenous forms of acute appendicitis [16].

Till our knowledge this the first reported study that stated the effect of positive seropositive H.pylori on outcome in patients with acute appendicitis. It was found that patients with seropositive H.pylori had significantly higher Alvarado score (8.07 ± 1.25 vs. 7.33 ± 1.35 ; $P < 0.001$), also frequency of postoperative SSI was significantly higher among seropositive patients (18 (12.6%) vs. 1 (1.8%); $P = 0.01$).

Also, the current study found no significant differences between those with seropositive and those with seronegative as regard age, sex, type of procedure, and postoperative epigastric pain, vomiting, fever, diarrhea and ileus ($P > 0.05$). Based on these results, patients with seropositive H.pylori had significantly higher Alvarado score, purulent appendicitis and postoperative SSI.

6. Conclusion

Acute abdominal pain resembles 7–10% of all emergency department patient flow. Acute appendicitis is considered one of the most common causes of lower abdominal pain leading patients to attend the emergency department and the most common diagnosis made in young patients admitted to the hospital with an acute abdomen. It seems that there is controversy about role of H.pylori in the pathogenesis of acute appendicitis. However seropositive patients are more likely to have purulent or gangrenous appendicitis, higher Alvarado score and more post-operative SSI.

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