Prevalence, clinical manifestations of *Helicobacter Pylori*, and its relation to hematological findings of symptomatic patients who conducted gastroscopy at King Abdulaziz University Hospital, Jeddah

## **ABSTRACT:**

**Aim:** To determine the prevalence & symptoms of *Helicobacter pylori* (*H. pylori*), and its relation to the haematological parameters of symptomatic patients who conducted upper gastrointestinal (GIT) endoscopy at King Abdulaziz University Hospital (KAUH), Jeddah, Saudi Arabia.

**Methods:** A retrospective study was done at KAUH, during the academic year 2016/2017. All symptomatic eligible cases (through medical records) who complained from GIT manifestations, conducted upper GIT endoscopy, with sampling taken from the gastric mucosa, and examined by the Rapid Urease Test (RUT) during 2015 were included. Results of two sets of Complete Blood Count (CBC) before and 6 months after treatment of H. pylori were take. Cases were interviewed at 2017 for follow-up.

**Results:** Two-thousand patients' files were reviewed. The prevalence of *H. Pylori* was 29.5%. The most frequent clinical presentation of *H. pylori* was epigastric pain (54.3%). Males had a significantly higher infection rate compared to females. *H. Pylori* was associated with gastritis (OR= 2.15, 95% CI: 1.27-3.66), and gastric ulcer (OR= 4.14, 95% CI: 1.95-8.81). There is no association between *H. Pylori* and counts of either platelets, RBCs or other haematological parameters. Treatment of *H. Pylori* caused little non-significant increase in RBCs and haemoglobin (P > .05).

**Conclusions:** Nearly thirty percent of the symptomatic patients who conducted upper gastroendoscopy at KAUH had *H. Pylori*. Infection was associated with gastritis and gastric ulcer. There is no association between *H. Pylori* and haematological parameters. Screening and management of *H. Pylori* is recommended.

**KEYWORDS:** *Helicobacter pylori*, Prevalence, Symptoms, Endoscopy, Haematological parameters.

## 1. Introduction

The discovery of *Helicobacter pylori* (*H. pylori*) in 1983 is considered one of the most important breakthroughs in the modern gastroenterology. <sup>1,2</sup> *H. pylori* is one of the most important public health problem. <sup>3</sup> Globally, it was estimated during 2015 that 4.4 billion persons were infected with *H. pylori* <sup>1</sup> and such prevalence of over 50% of the world's population makes it the commonest global chronic infection. There is a noticeable discrepancy between the prevalence or infection in the developed and developing countries.<sup>4</sup>

*H. pylori* bacterium is one of the commonest microbiological agents in Saudi Arabia. A recent study revealed that it was highly prevalent among Saudi children from both Jeddah and Riyadh. <sup>5</sup> Although most of individuals infected with *H. pylori* are asymptomatic, it colonizes in the gastric mucosa and implicated in causing gastritis,<sup>6</sup> peptic ulcer disease and gastric malignancy (carcinoma and gastric mucosa-associated lymphoid tissue lymphoma).<sup>7</sup> Hence, *H. pylori* is classified as a carcinogen of class I <sup>4,8</sup> and it is the commonest causative microbe of cancer-related infections. Consequently, screening and management of *H. pylori* is a recommended approach for risk reduction of cancer.<sup>9</sup> *H. Pylori* was suggested to be associated with extra-gastrointestinal conditions, including those from dermatologic, cardiopulmonary, metabolic and neurologic disorders. Some literature found that *H. pylori* may be associated also with haematological manifestations as iron deficiency, vitamin B12 deficiency.<sup>4,10,11</sup> Furthermore, Idiopathic Thrombocytopenic Purpura (ITP) is the commonest autoimmune hematologic disease that affecting individuals of different ages. *H. Pylori* was suggested to be associated with ITP.<sup>12</sup>

There are no recent studies done to illustrate the current prevalence and the associated factors of *H pylori* among patients conducted upper GIT endoscopy at King Abdulaziz University Hospital. Furthermore, the relationship between *H pylori* infection and different haematological parameters was not adequately assessed among Saudi patients, especially in Jeddah. So, such study is needed.

The current study was conducted to determine the prevalence, symptoms, associated factors of *H. Pylori*, and its relation to the haematological parameters between symptomatic patients who conducted upper gastrointestinal (GIT) endoscopy at King Abdulaziz University

Hospital (KAUH), Jeddah.

#### 2. Material and methods

A retrospective cohort study was conducted at KAUH, during the academic year 2016/2017. All symptomatic eligible cases (through reviewing the medical records files) who complained from GIT manifestations, conducted upper GIT endoscopy, with sampling taken from the gastric mucosa, and examined by the Rapid Urease Test (RUT) during 2015 were included. The exclusion criteria were patients with malignancy, GIT bleeding, portal hypertension, liver or kidney diseases, and those on non-steroidal anti-inflammatory drugs, proton pump inhibitors (PPI), cytotoxic drugs or steroids. Furthermore, patients below 18 years or patients with immune thrombocytopenia due to any other causes were also excluded.

Data was collected through reviewing the medical records and then by telphone interviews at 2017 (for the accepted patients). A data collection sheet was constructed (through hospital data extraction sheet and patient's interviewing questionnaire). The sheet collected personal & socio-demographic data, history of chronic medical condition, indications of conduction of endoscopy, findings of endoscopy weere taken. Results of RUT were taken, as one biopsy was placed immediately in the RUT and examined at 10-minute intervals for the next six hours. If positive result was recorded a second biopsy with histopathological examination using Giemsa stain was done. Patients were classified as *H. pylori*-positive if any of these assays were positive.<sup>13</sup> Results of two sets of CBC were take; before and after 6 months of treatment of *H. pylori*.

SPSS version 20 was used for the analysis. Descriptive and inferential statistics were conducted. Chi-square and Fisher's exact test were used for categorical data. Student's t-test. Paired-t test was used to compare between the means of haemtological parameters before and after treatment of *H. pylori*. Odds Ratio (OR) and 95% Confidence Intervals (CI) were calculated. Statistical significance was considered at *P* value < 0.05.

Ethical statement: The study followed the ethical standards of "Helsinki declaration". Approval was obtained from the Institutional Review Board (IRB) of KAUH, with a Reference Number of 99-16. All information is confidential. An oral consent was taken from each participant who accepted to participate in telephone interview.

## 3. Results

Figure (1) illustrates the flow-diagram of the work done for selection of the eligible cases. The files of a total of 2000 symptomatic persons who conducted upper GIT endoscopy during the year 2015 were reviewed. From these file, 312 of them fulfilled the eligibility criteria. Out of the 312 eligible patients, 92 (29.5%) had *H. pylori* positive results, while 220 (70.5%) had negative results by the RUT.

Table (1) shows that males had a higher prevalence of *H. pylori* infection (36.6%) compared to females (24.3%), with a statistical significant difference (P < .05). The prevalence was also higher (36.6%) among those aged  $\geq$ 30 years compared to the younger patients (22.8%). However, there is no statistical difference (P > .05). Similarly, the rate of *H. Pylori* was also higher among smokers, married, diabetics, and hypertensive patients, but without statistical significant differences (P > 0.05).

Table (2) demonstrates that the most frequent clinical presentation of *H. pylori* was epigastric pain (54.3%), followed by each of heartburn and feeling of fullness (26.1% for each), then bloating (21.7%). Vomiting (6.5%), nausea (5.4%), melena (4.3%) and hematemesis (4.3%) were the following complaints.

In the context of endoscopic findings, table (3) shows presence of significant associations between *H. Pylori* with each of gastritis (OR= 2.15, 95% CI: 1.27-3.66) and gastric ulcer (OR= 4.14, 95% CI: 1.95-8.81). On the other hand, there is no significant association between *H. pylori* and duodenitis, gastric cancer, gastric polyp, hiatal hernia, esophagitis, Barrett's esophagus, or esophageal varices.

Table (4) reveals comparisons between different hematological parameters among patients diagnosed with *H pylori* and those without infection. The mean count of the Red Blood Cells (RBCs) was slightly lower among patients who had positive H. pylori ( $4.70\pm .73$  million) compared to the mean between persons obtained negative results ( $4.74\pm .96$ ). However, there is no statistical significant difference (P > .05). Similar findings were also seen regarding the hemoglobin and hematocrit levels. No statistical significant associations were found between the platelets counts, White Blood Cell counts (WBCs) and the presence of H. Pylori (P > 0.05). Regarding the changes of the haemtological parameters after the treatment of *H. pylori*, the

results showed that the mean haemologin level of the cases with *H. Pylori* was slightly increased from  $12.58\pm2.54$  mg/dl before the treatment to reach  $12.78\pm2.33$  mg/dl after it, but without statistical significant difference (Paired t= 0.8, P > .05). Similar findingds were observed concerning RBCs count and hemtocrite level. The number of platelets didn't change after treatment of H Pylori (P > .05).

### 4. Discussion

Our results revealed that the prevalence of *H. Pylori* among the symptomatic patients who underwent upper GIT endoscopy at KAUH in 2015 was 29.5%. Similar prevalence was reported from a recent study done among school students complained from abdominal pain in Makkah city, Saudi Arabia.<sup>14</sup> On the other hand, a much higher rate (59.0%) of *H. Pylori* was reported among patients who conducted endoscopy at the same university hospital during 2005.<sup>13</sup>. This discrepancy between our and the previous results may be due to differences between the time of conduction of both studies. Decline of *H. pylori* prevalence overtime can be due to improvements of sanitation and personal hygiene,<sup>15</sup> during the period of 10-years. Similarly, another study from Ethiopia showed some decrease in the prevalence of *H. pylori* overtime.<sup>16</sup> On the other hand, a recent study from Turkey revealed that *H. pylori* prevalence between patients who conducted upper GIT endoscopy, with sampling from duodenal biopsy, was higher than our rate (47.9%).<sup>17</sup> This discrepancy may be due to the differences between countries, or due to type of diagnostic test, type patients or the sample size taken. However, a lower sero-prevalence (about 15%) of *H. pylori* was reported from two studies done among normal adults from Australia<sup>18</sup> and Indonesia.<sup>19</sup> The cause of such discrepancy between our study and the two previous studies may be because our study was a hospital-based study done among symptomatic patients who complained from GIT symptoms and conducted a diagnostic endoscopy, while the earlier studies were community-based studies that done among normal persons. This may be also due to differences between countries.

There is a debate regarding the role of gender in *infection with H. pylori*. <sup>16</sup> In the present study, males had a significantly higher rate of infection with *H. pylori* compared to females, which agrees with a 5-year trend of the agent from Ethiopia <sup>16</sup> and with a study from India <sup>20</sup>. on the other hand, a recent study, 2018, reported that the prevalence of H. Pylori was higher among females. <sup>6</sup> These gender differences in rate of infection may be attributed to the variations between countries, rates of exposure, and the susceptibility to infection among both genders, samples, and the diagnostic method.

In our study, older patients had a higher prevalence of *H. pylori* than the younger (P > 0.05),

5

which coincides with results from Indonesia<sup>19</sup> and the USA.<sup>21</sup> Furthermore, results of the current study reported absence of significant association between smoking and *H. Pylori*, which coincides with result from a Pakistani study.<sup>3</sup>

In the current study, the commonest complaints of patients with *H. pylori* infection was Epigastric pain (54.3%) which is in line with results of a study from Uganda. <sup>22</sup> Similarly, findings from another recent Ethiopian study, 2018, revealed that *H. pylori* was associated with upper GIT complaints such as Epigastric burning/pain.<sup>23</sup>

In the present study, associations were found between *H. pylori* and each of gastritis and gastric ulcer, which agree with the results from Uganda. <sup>22</sup> *These findings occurred because* infection *with H. pylori* can increase the "pro-inflammatory cytokine gene expressions in gastric epithelial cells by stimulation of NF-kB signalling" which may be implicated in causing gastritis and other gastric complications. <sup>7</sup> However, our results didn't find an association between H. *pylori* and gastric carcinoma, which may be attributed to small number of cases. It was estimated that only 1 - 3% of *H pylori* infected persons can cause gastric carcinoma. <sup>9</sup>

The current study demonstrated absence of statistical association between *H. pylori* and each of thrombocytopenia, anaemia or other haematological parameters. Similarly, a study done among pregnant women from Khartoum, Sudan, also reported absence of associations between H. pylor infection and anaemia and thrombocytopenia.<sup>24</sup> Similar finding was obtained from another study from Mexico.<sup>25</sup> The USA study<sup>21</sup> also concluded that *H. pylori* was not implicated in the pathogenesis of ITP. On the other hand, a study done among 30 patients with ITP and equal number of controls found presence of association between it and *H. pvlori*.<sup>26</sup> This discrepancy between studies may be attributed to differences between sample sizes, or study populations. The current study showed that treatment of *H. pylori* infection was not associated with significant increase in the platelets count. Emilia et al., reported that platelets count improved in some cases after treatment of *H. pylori* and not on the others.<sup>27</sup> However, a meta-analysis done for seventeen studies, 2007, revealed that platelet counts increased in patients with ITP with successful eradication of *H. pylori* infection compared to their control groups.<sup>28</sup> Similar results were reported from Korea<sup>29</sup> and Pakistan.<sup>30</sup> The cause of such discrepancy between the current and previous studies may be attributed to differences between populations, sample size or the received treatment.

#### 5. Conclusion

The prevalence of *H. Pylori* among symptomatic patients who conducted upper GIT endoscopy at KAUH was about thirty percent. Males had a significantly higher prevalence of infection than females. The commonest clinical presentation of *H. pylori* was Epigastric pain (54.3%), followed by each of heartburn and each of feeling of fullness, and bloating. *H. Pylori* positive patients were about 4 times more prone to gastric ulcer and about twice more prone to gastritis. There is no statistical association between *H. Pylori* and platelets, RBCs counts or other haematological parameters. Treatment of *H. Pylori* caused some increase in RBCs and haemoglobin levels but without statistical significance (P > .05). Screening and management for *H. Pylori* infection is recommended.



Figure (1): Flow-diagram for selection of *Helicobacter Pylori* cases among symptomatic patients who conducted upper gastrointestinal endoscopy, King Abdulaziz University, 2015

Table 1: Relationship between *Helicobacter pylori*& characteristics of patients who conducted upper gastrointestinal endoscopy at King Abdulaziz University Hospital

H. pylori	+Ve (92)	-Ve (220)	$X^2$	OR
Variables	No. (%)	No. (%)	( <i>p</i> )	95% CI
Gender				
Male	48 (36.6)	83(63.4)	5.56	1.80
Female	44 (24.3)	137(75.7)	(.01)	(1.1094)
Age				
< 30 years	18 (22.8)	61 (77.2)	2.29	0.63
$\geq$ 30 years	74 (31.8)	159 (68.2)	(.13)	(0.35-1.15)
Marital status				
Married	61(30.8)	137(69.2)	.46	1.19
Single	31(27.2)	83 (72.8)	(.5)	(0.72-1.99)
Smoking				
Yes	10(38.5)	16 (61.5)	1.10	1.56
No	82(28.7)	204(71.3)	(.29)	(0.68-3.57)
Diabetes				
Yes	30 (38.0)	49 (62.0)	3.665	1.69
No	62(26.6)	171(73.4)	(.056)	(0.99-2.89)
Hypertension				
Yes	24(37.5)	40(62.5)	2.49	1.59
No	68(27.4)	180(72.6)	(.115)	(0.89-2.83)

Table (2): Presenting symptoms of cases diagnosed as having Helicobacter pyloriinfection among patients who conducted upper gastro-endoscopy at KingAbdulaziz University Hospital

Symptoms	No. (%) N= 92
Epigastric pain	50 (54.3)
Heartburn	24 (26.1)
Fullness	24 (26.1)
Bloating	20 (21.7)
Vomiting	6 (6.5)
Nausea	5 (5.4)
Melena	4 (4.3)
Hematemesis	4 (4.3)
Fatigue	2 (2.2)
Dysphagia	2 (2.2)
Loss of appetite	2 (2.2)
Haematochezia	2 (2.2)
Diarrhoea	1 (1.1)

N.B. Each symptom was separately collected from the file

 Table (3): Endoscopic findings of patients diagnosed with or without Helicobacter pylori at King Abdulaziz University Hospital

H. pylori	+Ve	-Ve	$X^2$	OR
	(No=92)	(No =120)	( <b>P</b> )	(CI)
Endoscopic	No. (%)	No. (%)		
findings				
Normal				0.55
Yes	12 (20.3)	47 (79.7)	2.92	0.55
No	80 (31.6)	173 (68.4)	(.09)	(0.28-1.10)
Gastritis		100 ((1 ()	0.00	0.15
Yes	67 (25.4)	122 (64.6)	8.20	2.15
No	25 (20.3)	98 (79.7)	(.004)	(1.27-3.66)
Gastric ulcer				
Yes	19 (59.4)	13 (40.6)	15.32	4.14
No	73 (26.1)	207 (73.9)	(.000)	(1.95-8.81)
Duodenal ulcer			-	
Yes	4 (26.7)	11 (73.3)	.060	.86
No	88 (29.6)	209 (70.4)	(.806)	(.27-2.79)
Peptic ulcer				
Yes	21 (23.1)	21 (9.7)	9.775	2.8
No	70 (76.9)	196 (90.3)	(.002)	(1.44-5.43)
Gastric cancer				
Yes	1 (25.0)	3 (75.0)	.039	.80
No	91 (29.5)	217 (70.5)	(.84)	(.08-7.74)
Duodenitis	15 (41.7)	<b>01</b> (50 <b>0</b> )	2 00	1.05
Yes	15 (41.7)	21 (58.3)	2.90	1.85
No	77 (27.9)	199 (72.1)	(.08)	(0.09-3.77)
Hiatal hernia				
Yes	30 (23.8)	96 (76 2)	3 28	63
No	62 (33 3)	124 (66 7)	(.07)	(0.49-1.04)
	- (55.5)		(,)	
Esophagitis				
Yes	10 (28.6)	25 (71.4)	.01	0.95
No	82 (29.6)	195 (70.4)	(.90)	(.44-2.07)

\* Fisher's exact test

5

H. pylori	+Ve	-Ve	Student's t-test	
Blood parameters	Mean ± SD	Mean ± SD		P- value
WBCs (thousands)	$7.50 \pm 3.41$	7.60±3.37	-0.21	.84
RBCs (million)	4.70 ±.73	4.74±.69	-0.356	.72
Haemoglobin (g/dl)	12.58±2.54	12.78±2.33	-0.581	.56
Haematocrit (%)	38.08±6.439	38.75±5.60	-0.805	.42
Platelets (thousands)	300.17±113.97	297.71±97.89	0.169	.86
Neutrophil (thousands)	4.53±3.239	4.49±4.90	0.049	.96
Lymphocytes (%)	22.7±8.72	27.7±2.71	-1.46	.14
Monocytes (%)	6.0±2.4	6.1±3.7	-1.46	.94
Eosinophil (%)	2.19±1.9	2.24± 2.8	-0.14	.88
Basophile (%)	0.8±0.24	0.7±0.40	0.16	.87

# Table 4: Comparisons between the means of different blood parameters among patients diagnosed with *Helicobacter pylori* and those with negative results

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