Relation between Helicobacter pylori infection and non-alcoholic fatty liver Disease

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Abstract

Background: Around the world, non-alcoholic fatty liver disease is the main cause of liver diseases. A substantial relationship between NAFLD and H.pylori infection has been discovered recently.

Objectives: We aimed to explore the relationship between H.pylori infection and NAFLD in Egyptians.

Patients and methods: A case-control study involved 200 patients who underwent Oesophagogastroduodenoscopy. We divided Participants into 2 groups: Group A: contained 100 patients with confirmed H Pylori infection, Group B: contained 100 patients without H.Pylori infection. We diagnosed Fatty liver by ultrasonography.

Results: Our study results showed that prevalence of non-alcoholic fatty liver disease (NAFLD) was similar in patients with H.pylori infection in comparison to control group (16% Vs 12% in GroupA and B, respectively). We found that the prevalence of dyslipidemia was higher in patients with H.pylori infection in comparison to control group.

Conclusion: There is no significant relationship between H.pylori infection and non-alcoholic fatty liver disease (NAFLD). Dyslipidemia was higher in patients with H.pylori infection than in healthy persons.

Key words: H pylori, Dyslipidemia, NAFLD

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Introduction

H.pylori infection isone of the most common causes of upper GI diseases, such as gastroesophageal reflux disease, heartburn, peptic ulcer disease, dyspepsia, and even malignancy(**Rana et al., 2017).** H.pyloriis a highly prevalent infectious disease, that infect more than half of the population (inchildren about 30 %, in adults about 60 %), and is linked to 70% of benign ulcers of stomach and 90% of ulcers of the duodenum (Choi, 2016). In an H.Pylori-positive group, the relative risk of stomach cancer is higher than in H.Pylori-negative group by 1.7-5.3 times **(Vtor and Vale, 2011).**

It presents in the developing countries more than in the developed countries, implying that socioeconomics and standards of living play a significant influence in spread of illness. However, current data show that the prevalence of H.Pylori infection in the adults (those over the age of 40) is decreasing **(Rana et al., 2017).**

Non-alcoholic fatty liver disease is a hepatic presentation of insulin resistance. It is defined as buildup of hepatic fat >5% per hepatic mass with alcohol consumption by a 10grams daily. (**Loria et al., 2010**).Examples of NAFLD include cirrhosis, non-alcoholic steatohepatitis, simple steatosis, and hepatocellular cancer(**Yilmaz et al., 2012).** Based on the following points, a possible association between H.pylori and NAFLD emerges: (1) H.pylori and NAFLD primarily tend to prevail among the world's elderly population; (2) Non-alcoholic fatty liver diseaseis a hepatic presentation of metabolic syndrome, and insulin resistance is considered as its main pathogenetic factor; (3) NAFLD patients have an increase in GIT permeability, which is positively linked to hepatic lipid accumulation (**Miele et al., 2009**); (4) In some non-digestive diseases, H.pylori infection has been involved **(Abenavoli et al., 2013).**

We aimed to find the relationship between H.pylori infection and NAFLD in Egyptians.

Patients and methods

We included a total number of 200 patients who underwent oesophagogastroduodenoscopy in this case-control study. Patients were chosen at random from the gastrointestinal outpatient clinic and endoscopic units of the Tropical Medicine Department, Qena University Hospital, throughout a six-month period from August, 2020, to January, 2021.

We divided participants into 2 groups (arms):

- Group A:100 patients were included with gastric biopsy proven H Pylori infection
- Group B: 100 healthy subjects without H Pylori infection.

The inclusion criteria included: Patients with ages between eighteen and sixty years old who were undergo endoscopic examination and abdominal ultrasound.

Exclusion criteria included patients with alcoholism, diabetic patients, and patients with history of intake of proton pump inhibitors, histamine type 2 receptor antagonists, or H. pylori eradication therapy in the past month. Patients suffered from acute/chronic hepatic disease, and patients who had undergone gastric surgery were excluded.

A written consent has been obtained from all patients have before being included in our study that has been approved by the institutional ethical committee of the Faculty of Medicine, South Valley university.

All patients underwent the following

I. History and Clinical Examination

1- Complete history taking, which included history of other chronic

illnesses such as CKD, DM, and Cardiac diseases and. Also, drug history was taken.

2- Full Clinical Examination: which include manifestations of chronic liver diseases (such as jaundice, lower limb edema, organomegaly, ascites). Anthropometric measures of patients were assessed which include BMI, height, and weight. BMI is calculated using the followingformula: Weight (kg) /Height (m²).

II. Laboratory Investigations:-The following laboratory tests were done:

1- CBC.
2- Liver function tests: ALT, AST,total & direct bilirubin, albumin, INR and prothrombin time.
3- Serum triglyceride, cholesterol,low-density lipoprotein cholesterol, high-density lipoprotein cholesterol,and fasting blood glucose.
4- Viral markers (HCV-Ab, Hbs-Ag).
5- Kidney functions: serum urea and creatinine.

III. Imaging study: Abdominal ultrasonography was done and Scanning process will include the following:-

- We detected NAFLD usingultrasonography utilizing B-mode (Toshiba Aplio xv ultrasound, Japan)by experienced ultrasound specialists, who measured the liver's size in the midline and mid-clavicular lines, as well as its surface and echogenicity. Fatty liverdisease was diagnosed if a patient had two of the three criteria – will be mentioned - according to recommendations for diagnosis and therapy of non-alcoholic fatty liver disease;(updates in 2010): (i) The liver's near-field echo is diffusely enhanced, more so than two kidney's; (ii) unclear intra-hepatic duct structure; (iii) the echo of liver's far-fieldis gradually decreasing.
- Asses the diameter and patency of portal vein
- Presence of splenomegaly and ascites will be also recorded.

IV. Oesophagogastroduodenoscopy

After thorough preparation of the patient, Oesophagogastroduodenoscopy was done utilizing a sterile upper gastrointestinal video scope. After an overnight fast, an endoscopic examination was done. Under local xylocain spray of the throat, all endoscopies were performed with an Olympus GIFQ- 40. For each patient, the results of the gastrointestinal inspection were documented. Two biopsies were collected from the anterior and posterior antrums, two from the anterior and posterior bodies, and two from any other abnormalities. Specimens for histological investigation were routinely treated after being immersed in a 10% formalin solution. For identification of H. pylori, serial sections of 4m thickness were cut and stained with Modified Giemsa stain, which was stained blue to purple.

V. Statistical analysis

We studied the data using SPSS computer application, version 18.0.We expressedquantitative data as: mean ± standard deviation. But qualitative data were expressed as frequency with percentage number (%), and we compared them by Student's t-test. We used Chi-square testfor comparison non-parametric data. $P < 0.05$ was considered significant.

Results

Baseline characteristics

As regard description of demographic and laboratory data, Among Group A, 84% were males, The mean of age and BMI were 41 years and 27.9 kg/m² respectively,16patients were diabetics (16%), 14 patients were hypertensive (14%). Relating laboratory tests, results revealed that the mean value of ALT, AST, platelets count, WBCs, HB, and fasting blood glucose were 22 U/L, 22.5 U/L,

255.2(x 10 log3/ul), 6.5 (x 10 log3/ul), 14.5 g/dl, 90 mg/dl, respectively. Relating lipid profile tests, results revealed that the median ofTotal cholesterol, HDL, LDL,and triglycerides were 195.5 mg/dL, 45 mg/dL, 113.5 mg/dL and 113 mg/dL, respectively.

Among Group B, 86 % were males, mean age was 43.2 years, and mean BMI was 23.9 ± 1.7 kg/m².Two patient were diabetic (2%), two patients were hypertensive (2%). Relating laboratory tests, results revealed that the mean values of ALT, AST, platelets count, WBCs, HB, and fasting blood glucose were 26 U/L, 23 U/L, 244.7(x 10 log3/ul), 6.6 (x 10 log3/ul), 14.8 g/dl, 88 mg/dl, respectively. Relating lipid profile tests, the results revealed that the mean values oftotal cholesterol, HDL, LDLand Triglyceride were 173 mg/dL, 44.5 mg/dL, 95 mg/dL and 112 mg/dL, respectively.

Our study results revealedno significant difference between subjects with and without H pylori infection regarding NAFLD prevalence (16 percent Vs 12 percent in Group A and B, respectively).

Our study revealed that dyslipidemia prevalence was higher in H.pylori - infected patients compared with healthy persons.

Table 1. Demographic data of studied groups

Variables		Group A(N = 100)		Group B(N = 100)		P-value
Age (years)	Mean	41		42.2		0.514 NS
	±SD	10.4		7.4		
Sex	Male	84	84%	72	72%	0.148 NS
	Female	16	16%	28	28%	
BMI(kg/m²)	Median	27.9		25.2		0.052 NS
	IQR	24 - 29.8		24.1 - 27.9		
DM	No	84	84%	86	86%	0.779 NS
	Yes	16	16%	14	14%	
HTN	No	86	86%	86	86%	1.0 NS
	Yes	14	14%	14	14%	

This table shows a statisticallynon-significant differences(p-value > 0.05) between the two groups regarding demographic data (age, sex, BMI, DM and HTN)

Table 2. Lipogram data in studied groups

Variables		Group A (N = 100)	Group B (N = 100)	P-value
Cholesterol(mg/dl)	Median	195.5	173	0.172 NS
	IQR	120 - 223.5	145.5 – 190	
LDL(mg/dl)	Median	113.5	95	**0.031 S**
	IQR	81.8 - 141.3	83.8 - 113.8	
TG(mg/dl)	Median	113	112	**0.039 S**
	IQR	90 - 183.5	76.3 - 132.5	
HDL(mg/dl)	Median	45	44.5	0.898 NS
	IQR	36.8 – 50	34.8 - 53.3	

This table shows a statistically significant differences (Mann Whitney test; p-value =0.001) between both groups regarding LDL and TG.

Table 3. Laboratory data in studied groups

Variables		Group A (N = 100)	Group B (N = 100)	P-value
ALT(U/L)	**Median**	22	26	0.094 NS
	IQR	17.7 - 28.3	19.8 - 33.5	
AST(U/L)	**Median**	22.5	23	0.358 NS
	IQR	17 – 27	19 - 26.5	
Hb(g/dl)	**Mean**	14.5	14.8	0.366 NS
	±SD	1.5	1.3	
RBCs(million/mm³)	**Mean**	5.5	5.6	0.259 NS
	±SD	0.4	0.6	
PLTs(x10³/mm³)	**Mean**	255.2	244.7	0.307 NS
	±SD	54.5	47.0	
WBCs(x10³/mm³)	**Mean**	6.5	6.6	0.677 NS
	±SD	1.7	1.6	
FBS(mg/dl)	**Median**	90	88	0.498 NS
	IQR	84.8 - 95.5	85 – 95	

This table shows statistically non-significant differences (p-value > 0.05) between both groups regardinghematological indices and liver enzymes.

Table 4. Imaging results in studied groups

Variables		Group A(N = 100)		Group B(N = 100)		P-value
U/S	**Normal**	84	84%	88	88%	0.185NS
	Fatty liver	16	16%	12	12%	
Fatty liver grade	**Grade I**	8	50%	6	50%	0.138 NS
	Grade II	4	25%	6	50%	
	Grade III	4	25%	0	0%	

Discussion:

In the present study, no significant difference was found between subjects with and without H.pylori infection regarding prevalence of NAFLD(16 percent Vs 12 percent in Group A and Group B, respectively).

The findings of the current study were consistent with those of Cai and colleagues who conducted a cross-sectional study on 2051 asymptomatic Chinese people who were subjected to a 13C urea breath test & abdominal ultrasound. The link between NAFLD and H.pylori infection has been investigated. Regression analysis (P = 0 70) revealed no statistically significant link between NAFLD and H. pylori infection. In group with the risk of NAFLD (P = 0 47) or group without the risk of NAFLD (P = 0 59), there was no statistically significant difference in the rates of H.pylori infection between those with and without NAFLD (P = 0 47) **(Cai et al., 2018).**

In agreement with this finding, in South Korea, Baeg et al. performed retrospective

study that focused on 3663 patients to find risk variables for NAFLD. We divided participants into H. pylori +ve or -ve depending on 13C urea breath tests. We usedNAFLD liver fat score and hepatic steatosis index (HSI) to define NAFLD (NAFLD-LFS). They stated that infection with H. pylori wasn't a risk factor for NAFLD **(Baeg et al., 2016)**.

Okushin et al. assessed the relationship between H.Pylori infection and fatty liver disease in a cross-sectional study of 13,737 patients in Japan using logistic regression analysis. While other factors such as BMI were found to be linked to NAFLD, HP infection (as measured by IgG seropositivity) was not **(Okushin et al., 2015).**

Several additional clinical trials, in contrast to our findings, have found link between HP infection and NAFLD.

Xu et al. conducted a retrospective analysis using a large sample size and a health record database to evaluate the relationship between H. pylori infection and NAFLD. and A total of 17971 people took part in the study. They observed a link between NAFLD and infection with H.pylori (OR = 1:664; 95 percent CI: 1.549-1.787; P 0:001) **(Xu et al., 2020).**

Similarly, a study of 174 patients with functional dyspepsia categorized as either HP positive or HP negative found that those who were HP positive had a greater prevalence of fatty liver (p=0.02) **(Dogan et al., 2013).**

Abdel-Razik et al. conducted a cohort multicenteric research of 369 persons without using NAFLD at baseline, which is similar to the current study. The presence of Helicobacter pylori (46.3%) was linked to an increase in NAFLD-liver fat score.According to NAFLD-LFS multivariate analysis, the presence of H. pylori infection was an independent risk factor for the presence of NAFLD **(Abdel-Razik et al., 2018).**

Esam-Eldin evaluated 646 patients in another recent study from our area. Infection with H. pylori was discovered in 538 patients (83.3%), with females having a greater prevalence than males. The prevalence of NAFLD (as measured by U/S and Fibroscan) was substantially greater in the group which is H. pylori positive than in the group that is H. pylori negative **(Esam-Eldin et al., 2020).**

In our study, the prevalence of dyslipidemia was higher in patients with H. pylori infection than in healthy people.

In accordance with our results, Kim et al. noted that patients with H. pylori seropositivity were more likely to have higher total cholesterol, BMI,LDL-C, HOMA-IR, and triglycerides, and lower HDL-C levels than those without seropositivity**(Kim et al. 2017).**

Conclusion:

Depending on the results of our study, we can conclude that there is no relationship between NAFLD and H.pylori infection. When compared to healthy people, H.pylori infected patients had higher prevalence of dyslipidemia.

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