Zagazig University Medical Journal
www.zumj.journals.ekb.eg
https://doi.org/10.21608/zumj.2024.289169.3394 Volume 30, Issue 4, July 2024
Manuscript ID ZUMJ-2405-3394 (R2)
DOI 10.21608/ZUMJ.2024.289169.3394
ORIGINAL ARTICLE

Helicobacter Pylori Status and Serum Gastrin Level as Risk Factors for Hepatocellular Carcinoma in Patients with HCV-Related Liver Cirrhosis

Monkez Yousif [1] , Shaimaa Morsy Mohamed Salah[1], Osama Abd EL-Aziz Gaber[2], Fayrouz Othman Selim[1], Ahmed I. El-Agrody[1*]
[1]Department of Internal Medicine, Faculty of Medicine, Zagazig University, Egypt.
[2] Medical Biochemistry Department, Faculty of Medicine, Zagazig University, Egypt.

***corresponding author:**
Ahmed I. El-Agrody

Submit Date 2024-05-16
Revise Date 2024-05-29
Accept Date 2024-05-30

ABSTRACT

Introduction: Assessment of H. pylori infection and related alteration of serum gastrin levels with the risk of hepatocellular carcinoma in HCV-related liver cirrhosis is still debated.

Aims: Our study aims to assess H. Pylori status in HCV-related liver cirrhosis and to find out its impact on the development of HCC in these patients from our community.

Patients & Methods: The current study included 60 subjects. They were divided into two groups, thirty patients with HCV-related cirrhotic patients with HCC (Case group) Group (1) and thirty patients with HCV-related cirrhotic patients without HCC (Control group) Group (2). Clinical, laboratory, and radiologic assessment between the 2 groups for comparison and detection is there is a role of H. pylori, Gastrin hormone level, or Cag A toxin antigen in pathogenesis or development of HCC in patients with HCV-related cirrhosis.

Results: There was a statistically significant increase in gastrin level among H pylori +ve cases compared to –ve cases. With no statistically significant difference between HCC and non-HCC H. pylori +ve cases (P value=0.17). Patients complicated with HCC had a higher frequency of H. pylori seropositivity than patients without HCC (76.7% Vs 60%, respectively), There was an increase in Cag A toxin level among the HCC group compared to the Non-HCC group but it was statistically insignificant (P value= 0.07).

Conclusions: H. Pylori infection is common in patients with HCV-related liver cirrhosis with no impact on the development of hepatocellular carcinoma.

Keywords: H. pylori; Gastrin hormone Cag toxin antigen; HCC; HCV.

INTRODUCTION

Hepatocellular Carcinoma (HCC) is a multifactorial disease that has been linked to both viral and chemical carcinogens. Established causal risk factors include hepatitis B (HBV) infection, dietary aflatoxin exposure, chronic alcohol consumption, and cirrhosis of the liver [1]

Helicobacter pylori is a gastrointestinal pathogen that affects over 50% of the global population. Infection with H. pylori promotes chronic inflammation and increases the chance of developing stomach ulcers and cancer. Infection with H. pylori is the strongest known risk factor for gastric cancer, which is the second leading cause of cancer-related deaths worldwide[2]

However, long-term carriage of H. pylori represents a significant possibility of gathering site-specific illness.

Among infected individuals, approximately 10% develop peptic ulcer disease, 1 to 3% develop gastric adenocarcinoma and < 0.1% develop Mucosa-Associated Lymphoid Tissue (MALT) lymphoma.[3]

Gastrin is a trophic factor within the normal GI tract and is also a mitogen for several GI and non-GI tumors.[4]

Information about the association of H. pylori infection and related alteration of serum gastrin levels with the risk of hepatocellular carcinoma in HCV-related liver cirrhosis among Egyptians is scarce in the literature.

Our study aims to assess H. Pylori status in HCV-related liver cirrhosis and to find out its impact on the development of HCC in these patients from our community.

PATIENTS AND METHODS

This is an observational analytical case-control study. Was carried out in the Internal Medicine and Biochemistry departments, at Zagazig University Hospitals Between December 2020 and December 2021. Approval for performing the study was obtained from internal medicine, the medical ICU unit, and clinical pathology departments, at Zagazig University Hospitals after obtaining Institutional Review Board (IRB) approval (4312/2-4-2018). The study was done according to the Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Patients:

This study was performed on (60) patients divided into (2) groups:

•Group I: Included (30) HCV-related cirrhotic patients with HCC (Case group).

• GroupII: Included (30) HCV-relatedcirrhotic patients without HCC (Control group).

Inclusion criteria:

•Age: Subjects >18 years.

•Patients of both sexes.

•Cirrhotic patients secondary to HCV infection some with HCC and some without HCC.

•Patients with child A and child B.

Exclusion criteria:

•Patients with liver Cirrhosis secondary to other etiologies than HCV.

•Thosethat had undergone or werecurrently undergoing H. pylori eradication.

•Those receiving anti-ulcer treatment in the last three months.

•Patients with child C.

Methods:

All patients of the study were subjected to Full history taking (personal data) and questioning about symptoms of chronic liver disease and decompensation. Thorough Physical examination: looking for physical signs of chronic liver disease (jaundice, bleeding manifestations, fetor hepaticus, spider angiomatous, palmar erythema, parotid enlargement, gynecomastia or hepatic encephalopathy). Local abdominal examination: looking for ascites and organomegaly.

Investigations including:

A-Routine laboratory investigations: Complete blood count (CBC), Liver function tests, Kidney function tests, Bleeding profile, (INR, Prothrombin time), Blood glucose level, Alphafeto protein (AFP).

B-Radiological investigations: Including, pelvi-abdominal ultrasound, triphasic CT abdomen, and/or dynamic MRI as required to diagnose HCC and to check for signs of portal HTN, ascites, and organomegally).

C- Diagnosis of HCV infection: Patients with positive HCV antibody were confirmed by plasma HCV RNA testing using Roche COBAS Taq Man HCV PCR test version 2 (Roche Diagnosis).

I -Specific investigations:

•Serology for H.pylori (IgG).

•Measurement of serum Cag A toxin antigen titer.

•Measurement of serum gastrin level.

1-H. pylori antibody (IgG) in serum by Rapid Test Cassette. The advanced Quality rapid anti-H pylori test is a simple and visual qualitative test to detect antibodies in human whole blood, serum, or plasma. The test is based on the immunochromatography technique.

Principle of the test: The sample is applied to the sample well followed by adding the diluents application to the diluents well. The mouse anti-human IgG colloidal gold conjugate embedded in the sample pad reacts with the H. pylori antibody in the sample and is allowed to migrate by the effect of the diluents. The conjugate H. Pylori antibody complex is captured by H. Pylori antigen immobilized on a membrane forming a colored test band in the test region. A negative sample does not create a test line.

Test procedure: One drop of serum (10 ul) was added to the sample pad of the test strip. About 100 ul of sample diluents was added to the sample diluents well of the test strip.

Results were interpreted at 15-20 minutes.

2-Serum Gastrin :

Principle of the test: The kit uses a double-antibody sandwich enzyme-linked immunosorbent assay (ELISA) to assay the level of Human Gastrin (GAS) in samples. Blood sample containing Gastrin (GAS) is added to the well in the ELISA plate, these wells are pre-coated with Human Gastrin (GAS) monoclonal antibody. After incubation, another Gastrin (GAS) antibody labeled with biotin, and combined with Streptavidin-HRP is added to the well to form an immune complex. Another incubation is done followed by washing to remove the uncombined enzyme. Then the enzyme-substrate (Chromogen) is added for color development. Finally, the stop solution is added to get the final color ready for reading on the ELISA reader. The concentration of the Gastrin levels of samples was calculated using the standard curve.

Materials supplied in the Test Kit:

According to standards' concentration and the corresponding OD values, each sample well gastrin level was calculated.
the normal range for gastrin levels is: 0-180 pg/mL (picograms per milliliter of blood) for adults

3- CagA toxin antigen:

• This kit is used to assay the Cytotoxin-associated protein (CagA) in the sample of human serum, blood plasma, and other related tissue Liquid.

Test principle: The kit uses a double-antibody sandwich enzyme-linked immunosorbent assay (ELISA) to assay the level of cytotoxin-associated protein (CagA) in samples. Pre-coated well with Human Cytotoxin-associated protein (CagA) monoclonal antibody will bind to Cytotoxin-associated protein (CagA) in the samples. After incubation, another Cytotoxin-associated protein (CagA) antibody labeled with biotin, and combined with Streptavidin-HRP is added to form an immune complex followed by washing to remove the uncombined enzyme. Then the enzyme substrate (Chromogen Solution A, B) is added the color of the liquid changes to blue after incubation. And by the effect of acid (stop solution), the color finally becomes yellow. The intensity of the color and the concentration of the Cytotoxin-associated protein (CagA) of the sample can be calculated.

cagA, a gene that codes for an immunodominant antigen, is present only in *Helicobacter pylori* strains that are associated with severe forms of gastroduodenal disease (type I strains).

Statistical analysis

The collected data were computerized and statistically analyzed using the SPSS program (Statistical Package for Social Science) version 27.0 (IBM, 2020) (SPSS Inc., Chicago, IL, USA) & MedCalc 13 for Windows (MedCalc Software, Ostend, Belgium). The Shapiro Walk test was used to determine whether the data followed a normal distribution. Qualitative data was provided as frequencies and relative percentages. The qualitative variables were compared using the chi-square test ($\chi 2$) and Fisher exact test, as stated. Parametric data were expressed as mean ± S.D. (Standard deviation), whereas non-parametric data were expressed as median or range. The Independent T-test and Mann-Whitney test were used to compare quantitative variables in two groups for parametric and non-parametric variables, respectively. All statistical comparisons were two-tailed with a significance level of P-value < 0.05.[5]

RESULTS:

Table (1):
This table shows that there was a statistically significant increase in Albumin, protein, ALT, AST, Hb, and platelets count among HCC cases compared to non-HCC cases and a decrease in urea and PT among HCC cases compared to non-HCC cases.

Table (2):
This table shows that there were no statistically significant differences between the studied groups at the Gastrin level, in frequency of +ve H pylori infection or CAg toxin.

Table (3):
- This table shows that there was a statistically significant +ve correlation between Gastrin and age and Cag toxin level among the studied groups.

Table (4):
There was a statistically significant increase in gastrin level among H pylori +ve cases compared to –ve cases.

Table (5):
There was a statistically significant increase in gastrin level among H pylori CagA +ve cases compared to –ve cases.

Table (6):
This table shows that Gastrin had a significant validity in the prediction of H pylori infection with an accuracy of 71.7%.

Table (1): Laboratory findings of the studied groups:

Variable		All case (n=60)	Group I (HCC) (n=30)	Group II (Control) (n=30)	MW/ t*	P
S.Albumin (g/dl)	Mean ± SD Range	3.03±0.60 2.03-5.2	3.30±0.63 2.2-5.2	2.76±0.44 2.03-3.6	3.81*	<0.001 **
Total Protein (g/dl)	Mean ± SD Range	6.28±0.97 4.02-9.2	6.69±0.81 5.13-9.2	5.87±0.96 4.02-8.2	3.61*	0.001*
Direct bilirubin: (mg/dl)	Mean ± SD Median (IQR) Range	2.19±3.76 1.41(0.9-2.08) 0.1-26	2.93±5.18 1.48(0.99-2) 0.45-26	1.45±0.89 1.3(0.76-2.23) 0.1-4	0.90	0.37 NS

Variable		All case (n=60)	Group I (HCC) (n=30)	Group II (Control) (n=30)	MW/ t*	P
Total bilirubin: (mg/dl)	Mean ± SD Median (IQR) Range	1.32±2.9 0.6(0.3-1.25) 0.05-18	1.78±4.03 0.62(0.3-1.13) 0.1-18	0.85±0.71 0.59(0.26-1.3) 0.05-2.8	0.07	0.94 NS
ALP: (U/L)	Mean ± SD Median (IQR) Range	150.67±130.6 109.5(81.75-177.5) 37-714	186.47±168.9 118(95-191) 70-714	114.87±59.28 100.5(69.25-149.75) 37-268	1.94	0.053 NS
AST (U/L)	Mean ± SD Median (IQR) Range	58.14±38.56 46.5(32.48-74) 10-170	68.75±43.19 56(38.4-86.7) 10-170	47.53±30.44 39.4(27-53.9) 16.4-158	2.21	0.03*
ALT (U/L)	Mean ± SD Median (IQR) Range	36.58±24.87 30.1(19.6-48.5) 8.3-132	42.02±27.76 36.2(23.1-53) 8.3-132	31.14±20.66 23.4(17.93-42) 17.93-42	1.99	0.04*
Creatinine: (mg/dl)	Mean ± SD Median (IQR) Range	1.28±0.80 1.08(0.76-1.48) 0.46-4.3	1.15±0.63 1.01(0.71-1.29) 0.46-3.3	1.41±0.93 1.16(0.8-1.65) 0.46-4.3	1.10	0.28 NS
Urea: (mg/dl)	Mean ± SD Median (IQR) Range	44.91±36.23 34.5(25-48) 15-220	31.05±13.95 27.6(21.05-39.3) 15-83	58.77±45.58 42(32-69.25) 20-220	3.78	<0.001 **
Hb (gm/dl)	Mean ± SD Range	10.5±2.31 6-16.3	11.41±2.36 6-16.3	9.59±1.89 7-13.4	3.30*	0.002*
Platelets ($x10^9$/L)	Mean ± SD Median (IQR) Range	116.27±71.54 106(63.25-138.25) 14-410	138.47±77.24 128(84.5-171) 50-410	94.07±58.54 90(52.5-122.25) 14-277	2.58	0.01*
WBCs ($x10^9$/L)	Mean ± SD Median (IQR) Range	7.72±4.19 7.1(4.83-9.5) 1.9-24	7.29±3.12 7.15(5.13-9.35) 3-16.6	8.14±5.06 7.05(4.58-9.63) 1.9-24	0.15	0.88 NS
INR:	Mean ± SD Range	1.27±0.24 0.9-2.3	1.25±0.24 1-2.03	1.30±0.24 0.9-2.3	0.72*	0.47 NS

SD: Standard deviation, IQR: Inter quartile range MW: Mann Whitney test t: Independent t-test*.
ALP : Alkaline Phosphatase. ALT: Alanine Transaminase. AST: Aspartate Transaminase. Hb: Haemoglobin. WBCs: white blood cells. INR: The international normalised ratio.

Table (2): Gastrin level, H.Pylori Ab and Cag A Toxin among the studied groups:

Variable		All case (n=60)		Group I (HCC) (n=30)		Group II (Control) (n=30)		MW	P
Gastrin: (ng/ml)	**Mean ± SD**	100.51±55.14		98.71±59.18		102.32±51.73			0.61 NS
	Median	78.85		77.15		84.55		0.51	
	Range	18.6-211.7		25.7-211.7		18.6-196.4			
	IQR	56.73-155.95		48.28-168.45		61.98-148.4			
		No	**%**	**No**	**%**	**No**	**%**	χ^2	
H. pylori:	**-ve** **+ve**	19 41	31.7 68.3	7 23	23.3 76.7	12 18	40 60	1.93	0.17 NS
Ca g A toxin:	**-ve** **+ve**	29 31	48.3 51.7	11 19	36.7 63.3	18 12	60 40	3.27	0.07 NS

SD: Stander deviation, MW: Mann Whitney test NS: $\chi 2$: Chai square test. NS: Non significant

H. pylori: Helicobacter pylori. Cag A toxin: Cytotoxin-associated gene A

Table (3): Correlation between Gastrin level and age, clinical scores & Laboratory parameters among the studied groups:

Variable	Gastrin (n=60)		Gastrin Group I (n=30)		Gastrin Group II (n=30)	
	Rs	P	rs	P	rs	P
Age (years)	0.35	0.006*	0.28	0.13 NS	0.30	0.11 NS
FIB4:	-0.09	0.49 NS	-0.17	0.37 NS	-0.03	0.87 NS
APRI:	-0.22	0.09 NS	-0.28	0.14 NS	-0.22	0.25 NS
MELD:	-0.02	0.88 NS	-0.08	0.67 NS	0.07	0.71 NS
CTP:	-0.11	0.41 NS	-0.19	0.33 NS	-0.06	0.72 NS
S.Albumin (g/dl)	0.05	0.71 NS	0.10	0.61 NS	0.08	0.66 NS
Total Protein (g/dl)	0.07	0.61 NS	0.16	0.39 NS	0.19	0.32 NS
Direct bilirubin: (mg/dl)	0.01	0.96 NS	0.10	0.59 NS	0.11	0.56 NS
Total bilirubin: (mg/dl)	0.01	0.92 NS	0.13	0.48 NS	0.18	0.35 NS
ALP: (U/L)	0.03	0.81 NS	0.20	0.28 NS	0.16	0.41 NS
AST (U/L)	0.15	0.26 NS	0.01	0.99 NS	-0.34	0.07 NS
ALT (U/L)	0.18	0.18 NS	0.14	0.46 NS	-0.24	0.22 NS
Creatinine: (mg/dl)	0.01	0.99 NS	-0.06	0.75 NS	0.06	0.74 NS
Urea: (mg/dl)	0.09	0.48 NS	0.25	0.18 NS	-0.10	0.60 NS
Hb (gm/dl)	0.12	0.38 NS	0.28	0.13 NS	-0.03	0.89 NS
Platelets ($x10^9$/L)	0.14	0.30 NS	0.31	0.10 NS	0.01	0.99 NS
WBCs ($x10^9$/L)	0.05	0.73 NS	-0.12	0.53 NS	0.10	0.62 NS
PT: (sec)	-0.01	0.93 NS	0.07	0.72 NS	-0.08	0.66 NS
INR:	-0.14	0.30 NS	0.06	0.74 NS	0.24	0.20 NS
CA g toxin:	0.60	<0.001**	0.70	<0.001**	0.52	0.003*

r: Spearman's correlation coefficient. NS: Non significant (P>0.05)

FIB4: Fibrosis-4 score. APRI: AST to Platelet Ratio Index (APRI) Calculator. MELD: Model for End-Stage Liver Disease. CTP: The Child-Turcotte-Pugh. ALP: Alkaline Phosphatase. ALT: Alanine Transaminase. AST: Aspartate Transaminase. Hb: Haemoglobin. WBCs: white blood cells. INR: The international normalised ratio. Cag A toxin: Cytotoxin-associated gene A. PT: prothrombin time.

Table (4): Gastrin level according to H pylori infection:

Variable		H pylori -ve (n=19)		H pylori +ve (n=41)		χ^2	P
		No	%	No	%		
Gastrin:	Mean ± SD	63.15±31.99		117.83±55.26		3.51	<0.001**
	Median	56.9		114.6			
	Range	18.6-145.7		29.6-211.7			
	IQR	38.7-76.4		66.6-176.45			

SD: Stander deviation, IQR: Inter quartile range, MW: Mann Whitney test . $\chi 2$: Chai square test

Table (5): Gastrin level in H pylori +ve cases according to CAg A Toxin:

Variable		CagA -ve (n=10)	CagA +ve (n=31)	MW	p
Gastrin:	**Mean ± SD**	74.5±26.78	131.8±55.02		0.008 *
	Median	71.9	154.3	2.67	
	Range	45.6-134.3	29.6-211.7		
	IQR	48.25-89	78.3-176.9		

SD: Stander deviation, IQR: Inter quartile range MW: Mann Whitney test.
H. pylori: Helicobacter pylori. Cag A toxin: Cytotoxin-associated gene A.

Table (6) : Validity of Gastrin in the prediction of HCC and H pylori infection among the studied groups:

Variable	Cut off	AUC (95%CI)	Sensitivity	Specificity	PPV	NPV	Accuracy	P
HCC	>83.35	0.46 (0.31-0.61)	46.7%	50%	48.2%	48.4%	48.3%	0.61 NS
H pylori	>73.7	0.78 (0.67-0.90)	70.7%	73.7%	85.3%	53.8%	71.7%	<0.001 **

HCC: Hepatocellular Carcinoma. H. pylori: Helicobacter pylori.

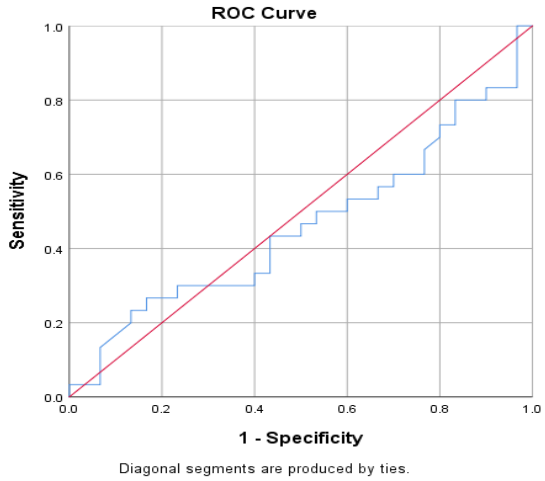

Figure 1:- Roc curve for validity of gastrin in prediction of HCC among the studied groups.

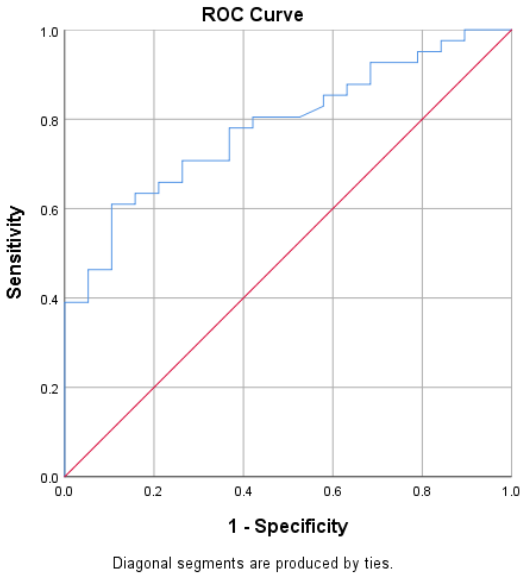

Figure 2:- Roc curve for validity of gastrin in prediction of H pylori infection among the studied groups.

DISCUSSION

HCC is a significant medical issue, particularly in some nations. In Egypt, HCC is the fourth most frequent malignancy and the second leading cause of cancer death in both sexes. [6] HCV is an important risk factor for HCC in Egypt where 71% of HCC cases were positive for anti-HCV antibodies.[7]

In 1994, H. pylori was recognized as a type I carcinogen and now it is considered the most common etiologic agent of infection-related cancers, which represent 5.5% of the global cancer burden.[8]

One of the most studied virulence factors encoded within the pathogenicity island is the Cag A gene the protein it codes for, Cag A.[9]

Our study aims to shed light on H. Pylori status in HCV-related liver cirrhosis and to find out its impact on the development of HCC in these patients from our community.

The obtained results showed that the frequency distribution of H. Pylori seropositivity (current or past infection) in all patients included in this study using H. Pylori serum antibody (IgG) was 41 patients with a percentage of 68.3%.

In this study, H. pylori infection was encountered in more than two-thirds (68.3%) of patients with HCV-related liver cirrhosis. This is agreed with the research conducted by Hanafy et al., (2016),[10] who have demonstrated H. pylori infection in 70% (281/400) of patients chronically infected with HCV. Also, our results go in agreement with that obtained by Suto et al., (2001)[11] Who stated that the prevalence of H. pylori infection in cirrhosis is 45.5-89%, which is much greater than in non-cirrhosis.

Also, in this study, patients complicated with HCC had a higher frequency of H. pylori seropositivity than patients without HCC (76.7% vs.60%, respectively), However, this finding showed no significant statistical difference between the two studied groups (P-value = 0.17).

The results of our study proved that the H. pylori infection has no impact as a risk factor for HCC in HCV-related liver cirrhosis with adjusted OR 0.953 (0.122 -7.433, 95%Cl). Our finding is consistent with Nicola et al., (2003)[12]study which suggested that Helicobacter species were not involved in the pathogenesis of virus-related HCC, chronic hepatitis, or liver carcinoma metastasis.

Also, the study of Pellicano, et al (2004)[13] demonstrated that H. pylori were identified in 23.3% of the healthy control group and 61.7% of patients with HCC. Also, Meloni et al., (2017)[14] mentioned that Seropositivity to H. pylori was found in 183 out of 220 patients with HCC (83.1%) and in 220 of 409 controls (53.7%) ($p < 0.0001$) (OR 3.97; 95% CI 2.60-6.06). also, this is in line with another study which found that high H. pylori seropositivity was associated with HCV infected group with HCC among both male and female Egyptian Patients compared to HCV infected group without HCC and the difference between were statistically significant. [15]

In this study, we found that the CagA producing strains were encountered in 75.6% of patients with seropositive H. pylori, and this is consistent with a study reported by Cover et al., (1995)[16] which found that about 60-70% of the H. pylori isolates are shown to be CagA positive. Our results were higher than other Egyptian studies (66.6%, 62.2%) by El-Fakhry et al. (2012),[17] and Zaki et al., (2016)[18] respectively.

Several other studies reported that Cag A was more prevalent in peptic ulcer and gastric carcinoma than gastritis. [19]

The results of our study found that the serum gastrin level was higher in patients infected with H. pylori compared to those who were H. pylori-negative ($p>0.001$), and also was higher in CagA+ve Vs Cag A-ve strains ($p= 0.008$). This is in line with a study conducted by Nujumi et al., (1991)[20] who found that serum gastrin concentrations were significantly higher in H. pylori-positive patients with a mean of 108.3 ±35.0 pg/ml than H. pylori negatives with a mean of 55.1± 17.6 pg/ml.

Also, our results are in agreement with a study conducted by Zhou et al., (2011)[21] who reported a relationship between gastrin and H. pylori infections and showed that gastrin mRNA was upregulated by Helicobacter pylori-cytotoxin-associated protein A (CagA).

In our study serum gastrin was comparable in patients with and without HCC with no statistically significant difference between both groups ($p=0.61$). So serum gastrin is not a reliable test for the diagnosis of HCC with low sensitivity and specificity.

The current study found serum CagA toxin level, and age was positively correlated with Gastrin level among the studied groups, $r= 0.60 (p<0.001)$ suggesting that gastrin levels increase as CagA toxin level, possibly may be related to antral D-cell deficiency, which is caused by H. pylori infection with the expression of CagA, which agrees with results of Jung et al., (1999)[22]who found that gastrin concentrations in CagA +ve patients were significantly increased compared to CagA –ve patients with (111.7± 108.3 vs 33.5± 8.7 pg/ml : $p< 0.05$).

Limitations, and recommendations for future research The study design as a case control one which could not reflect the temporal association

between H. pylori infection and development of HCC in this group of HCV- related liver cirrhosis. A cohort long term prospective study is warranted. We relied on using H. pylori antibodies which cannot tell whether the infection was current or past, further work using more sensitive diagnostic tools is recommended like stool antigen test or urea breath test. Lastly our sample size is relatively small and further work using larger sample is to be considered in future.

Conclusions: H. Pylori infection is common in patients with HCV-related liver cirrhosis with no impact on the development of hepatocellular carcinoma. Serum gastrin level is elevated in presence of H. pylori infection and becomes more elevated in CagA-producing strains, However , is not a reliable test for the presence of hepatocellular carcinoma.

REFRENCES:

1- Farazi PA. and DePinho RA, (2006) Hepatocellular carcinoma pathogenesis: From genes to environment. Nat. Rev. Cancer, 6: 674-7.
2- Wroblewski LE, Peek RMJ, Wilson KT, (2010). Helicobacter pylori and gastric cancer: Factors that modulate disease risk. Clin. Microbiol. Rev., 23: 713-9.
3- Peek RMJ, Crabtree JE, (2006). Helicobacter infection and gastric neoplasia. J. Pathol., 208: 233-8.
4- Caplin M, Khan K, Savage K, Rode J, Varro A, Michaeli D, et al (1999) Expression and processing of gastrin in hepatocellular carcinoma, fibrolamellar carcinoma and cholangiocarcinoma. J Hepatol 30(3): 519-6.
5- Kirkwood Betty R. & Jonathan A. C. Sterne (2003). essential medical statistics. Blackwell Science, Inc., 350 Main Street, Malden, Massachusetts 02148–5020, USA: Blackwell. ISBN 978-0-86542-871-3.
6- Akinyemiju T, Wiener H, Pisu M, (2017). Cancer-related factors and incidence of major cancers by race gender and region; analysis of the NIH-AARP diet and health study. BMC Cancer;17(1):597.
7- Rahman El-Zayadi A, Abaza H, Shawky S, Mohamed MK, Selim OE, Badran HM. (2001) Prevalence and epidemiological features of hepatocellular carcinoma in Egypt-a single center experience. Hepatol Res;19:170-9.
8- Parkin DM, (2001). Global cancer statistics in the year 2000. Lancet Oncol.;2(9): 533-3.
9- Michael H, Peter H (2003). Helicobacter pylori virulence factors— one part of a big picture. Lancet; 362: 1231-3.
10- Hanafy AS, El-Hawary AT, Hamed EF, Hassaneen AM. (2016) Impact of Helicobacter pylori eradication on refractory thrombocytopenia in patients with chronic HCV awaiting antiviral therapy. Eur J Clin Microbiol Infect Dis;35 (7):1171–6.
11- Suto H, Azuma T, Ito S, Ohtani M, Dojo M, Ito Y, et al.(2001) Helicobacter pylori infection induces hyperammonaemia in Mongolian gerbils with liver cirrhosis. Gut; 48(5): 605–8.
12- Nicola Coppola, Giorgio de Stefano, Cecilia Marrocco, Ferdinando Scarano, Carlo Scolastico, Luciano Tarantino, et al. (2003). Helicobacter spp. and liver diseases., Le Infezioni in Medicina,11 (4) 201-7.
13- Pellicano R, Mazzaferro V, Grigioni WF, Cutufia MA, Fagoonee S, Silengo L, et al. (2004). Helicobacter species sequences in liver samples from patients with and without hepatocellular carcinoma. World J Gastroenterol;10(4):598–1.
14- Meloni MF, Ponzetto A, Livraghi T, Moretti E, Stroffolini T. (2017) Pathogenic Strains of Helicobacter pylori in Patients with Hepatocellular Carcinoma. J Oncol Res Ther: JONT-128
15- Waleed M S. (2015). The relation between helicobacter pylori infection and hepatocellular carcinoma in liver cirrhosis, Amer J Biochem, Biotechnol:11(2);110-3.
16- Cover TL, Glupczynski Y, Lage AP, Burette A, Tummuru MKR, Perez-Perez GI, et al (1995) Serologic detection of infection with CagA +ve Helicobacter pylori strains. J Clin Microbiol;33(6):1496-0.
17- El-Fakhry AA, El-Daker MA, Badr RI, El-Nady GM, Mesbah MR, Youssef T, et al. (2012) Association of the cagA gene positive H. pylori and tissue levels of interleukin 17 and interleukin 8 in gastric ulcer patients. Egypt J Immunol;19 (1):51–2.
18- Zaki ME, Elewa A, Ali MA, Shehta A. (2016): a study of Virulence Genes Cag A and Vac A in Helicobacter pylori isolated from Mansoura University Hospital patients by multiplex PCR. Int J Curr Microbiol App Sci;5(2):154– 0.
19- Wei GC, Chen J, Liu AY, Zhang M, Liu XJ, Liu D, et al. (2012). Prevalence of Helicobacter pylori vacA, cagA and iceA genotypes and correlation with clinical outcome, Exp Ther Med; 4(6): 1039–4.
20- Nujumi AME, Dorrian CA, Chittajallu WD, Neither-cut WD, McColl KEL. (1991): Effect of inhibition of Helicobacter pylori urease activity by acetohydroxamic acid on serum gastrin in duodenal ulcer subjects, Gut 32:6.
21- Zhou J, Xie Y, Zhao Y, Wang S, Li Y. (2011) Human gastrin mRNA expression up-regulated by Helicobacter pylori CagA through MEK/ERK and JAK2-signaling pathways in gastric cancer cells. Gastric Cancer;14(4):322-1.

22- Jung HK, Park HJ, Cho JS, Lee KS, Lee SI, Park IS, et al. (1999). Relationship of CagA to Serum Gastrin Concentrations and Antral G, D Cell Densities in Helicobacter pylori Infection. Yonsei Med J, 40(4), 301- 6.

To Cite:

Yousif, M., Mohamed Salah, S., mahmoud, O., Selim, F., Agrody, A. Assessment of Helicobacter Pylori Status and Serum Gastrin Level as Risk Factors for Hepatocellular Carcinoma in Patients with HCV-Related Liver Cirrhosis. Zagazig University Medical Journal, 2024; (1412-1420): -. doi: 10.21608/zumj.2024.289169.3394