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Original article

The prevalence of *Helicobacter pylori* infection in Egyptian patients with metabolic associated fatty liver disease

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Abstract:

Background: *Helicobacter pylori* is a common bacteria that is present in about half of all population. *H pylori infection* causes atrophic and even metaplastic changes in the stomach; this infection is also linked to peptic ulcer disease and systemic inflammation that alters metabolism. **Objective:** To investigate the prevelance of *H- pylori infection* among Egyptian adults its association with Metabolic dysfunction associated fatty liver disease (MAFLD) **Methods:** The study will involve 200 patients 100 cases and 100 control . Height and weight were measured and calculation of BMI (BMI = kg/m2), waist & hip circumference were measured, Blood pressure was assessed by mechanical monitor (systolic& diastolic). Degree of fibrosis (FIB4, APRI) was measured . *H pylori* antigen in stool was done. Ultrasonography & Fibroscan of the liver was performed .**Results:** Our results showed there is a significant difference between both groups (P-value 0.001) regarding the following: The *H. pylori* were positive in 79% of the case group, while only 33% of the control group were

positive. The bright Hepatomegaly was positive in 93% of the case group, and the whole control group was negative (normal). The Fibroscan, the control group had F0 (45%) and F1 (55%) while the distribution among the case group was significantly different F0 (2%), F1 (44%), F2 (38%) and F3 (16%). **Conclusion:** *H.pylori* infection is a risk factor for developing MAFLD in Egyptian patients.

1. Introduction :

Around half of all people on the planet are afflicted by the common bacteria Helicobacter pylori. An H pylori infection that persists is known to cause atrophic and even metaplastic alterations in the stomach and is linked to peptic ulcer illness. Oral or fecal-oral contact is the most common way for H. pylori to infect someone. (1)

Numerous stomach disorders, including chronic gastritis, peptic ulcer disease, gastric cancer, and gastric mucosa-associated lymphoid tissue (MALT) lymphoma, are brought on by H. pylori infection (2)

Numerous studies have noted the significance of H. pylori infection in the onset of autoimmune illnesses affecting the liver and biliary tract, liver fibrosis, cirrhosis, non-alcoholic fatty liver disease, and insulin resistance. (3)

A number of extragastric disorders, such as vitamin B12 deficiency, insulin resistance, metabolic syndrome, diabetes, nonalcoholic fatty liver disease (NAFLD), cardiovascular, neurological, dermatological, and ophthalmic diseases, may also be determined or affected by the disruption of several biological processes caused by H. pylori infection.(4)

The novel idea of metabolic dysfunction associated fatty liver disease (MAFLD), which was put forth in 2020, will take the place of the term nonalcoholic fatty liver disease (NAFLD). Unlike NAFLD, MAFLD does not need the exclusion of other liver disease aetiologies, such as excessive alcohol intake or viral hepatitis. MAFLD is diagnosed in patients who have hepatic steatosis along with one of the three metabolic illnesses (overweight or obesity, diabetes mellitus, or indications of metabolic dysregulation (MD) in lean persons). Thanks to this creative idea and set of standards, clinicians may now identify a greater number of patients in clinical practice who are at risk of unfavourable outcomes (5)

Patients with a range of liver diseases have had H. pylori detected in their liver specimens, and some research has suggested a connection between H. pylori infection and nonalcoholic fatty liver disease (NAFLD). Conversely, some asserted that there was no relationship between them. Since knowing potential risk factors is essential for managing non-alcoholic fatty liver disease (NAFLD), we have conducted research to examine the connection between H. pylori infection and NAFLD (7)..

2. Subjects and Methods :

2.1. subjects: This case-control study was conducted on 200 subjects , 100 *H Pylori* infected patients and 100 healthy controls . Between January 2023 and November 2023, patients were selected from the Beni-Suef University Hospitals in upper Egypt's outpatient clinics. Patients who gave their consent to be included in the study were adult male and female patients over the age of 18 who were attending Beni-Suef University Hospital's outpatient clinics. Individuals with a history of diabetes, hypertension, dyslipidemia, a BMI of greater than 18.5, and those who were overweight or obese (BMI ≥25 kg/m2) were also included. Participants with a history of alcohol use, viral or autoimmune hepatitis, or any other type of chronic liver disease were not allowed to participate in the study. Every patient underwent a comprehensive history taking process, with particular emphasis placed on the history of any coexisting conditions. Patients' height, weight, and waist circumference were measured. BMI (BMI = kg/m2) was also calculated. A mechanical monitor was used to measure the blood pressure (systolic and diastolic). Blood sample was taken for performing CBC , FBS , HbA1C , lipid profile , cholesterol , TG , LDL , HDL , ALT , AST , bilirubin , albumin , INR , HOMA-IR , creatinine . Degree of fibrosis and steatosis (FIB4 , APRI) was measured . *H pylori* antigen in stool was done . Ultrasonography & Fibro scan of the liver was performed.

Ethical considerations

Giving patients comprehensive information about the study. The Beni-Suef University ethical committee's approval, bearing approval number FMBSUREC/06122022/Mohamed, was obtained.

2.2 Statistical Analysis:

Data collected and coded to facilitate data manipulation and double entered into Microsoft Access and data analysis performed using the Statistical Package of Social Science (SPSS) software version 22 in windows 7 (SPSS Inc., Chicago, IL, USA).

The significance of the results was assessed in the form of P-value that was differentiated into: Non-significant when P-value > 0.05, Significant when P-value ≤ 0.05 and Highly significant when P-value ≤ 0.001.

3. Results :

Table (1): Age of the studied cases and control:

	Group				P-value
	Cases		Control		
	Mean	SD	Mean	SD	
Age	46	15	38	10	.0001

There is a significant difference between the two groups' age means (P-value =0.0001)

Table (2): Baseline characteristic of both groups:

		Group				P-value
		Cases		Control		
		Count	%	Count	%	
Residency	Urban	41	50.6%	40	49.4%	0.86
	Rural	59	49.6%	60	50.4%	
Sex	Male	41	43.6%	53	56.4%	0.089
	Female	59	55.7%	47	44.3%	
Smoking	Yes	21	100.0%	0	0.0%	0.001
	NO	79	44.1%	100	55.9%	
Alcohol	Yes	0	0.0%	0	0.0%	-----
	NO	100	50.0%	100	50.0%	

The difference between the two groups in residency, sex, and alcohol consumption was not significant.

There is a significant difference between the control and case study groups regarding smoking, 21% of the case group are smokers while no smokers were found in the control group. (P-value = 0.001)

Table (3): Measurement of blood pressure among both groups:

	Group				p-value
	Cases		Control		
	Mean	Standard Deviation	Mean	Standard Deviation	
Systolic	136.40	19.15	115.60	8.33	0.001
Diastolic	84	9	74	6	0.001

Systolic and diastolic blood pressure were significantly higher among cases than control. (P-value 0.001)

Table (4): Anthropometric measurements of the participants:

	Group				p-value
	Cases		Control		
	Mean	SD	Mean	SD	
Height	1.64	.06	1.61	.06	0.001
Weight	77	9	61	5	0.001
BMI	28.7	2.13	23.66	1.03	0.001
Waist circumference	105	10	81	4	0.001

There is a significant difference (P-value =0.001) between the heights of the two groups. The height of the case group is (1.64) and the height of the control group is (1.61).

There is a significant difference (P-value= 0.001) between the weights of the two groups. The weight of the case group is (77) and the weight of the control group is (61).

There is a significant difference (P-value= 0.001) between the BMIs of the two groups. The BMI of the case group is (28.7) and the weight of the control group is (23.66).

There is a significant difference (P-value= 0.001) between the Waist circumferences of the two groups. The Waist circumference of the case group is (105) and the weight of the control group is (81).

Table (5): Blood glucose measurements for the studied participants:

	Group				P-value
	Cases		**Control**		
	Mean	**SD**	**Mean**	**SD**	
Fasting glucose	105	30	91	16	0.001
HPP	144	36	130	11	0.001
HBAIC	6.19	0.82	5.58	0.32	0.001
Insulin level	10.09	8.65	10.01	9.19	0.947
HOMA-IR	2.63	2.31	2.42	2.80	0.565

As shown in the table above there is a significant difference between the mean of the cases group and the control group regarding the fasting glucose, 2HPP and HBAIC (P-value = 0.001).
There is no significant difference between the mean of the insulin level and the HOMA-IR within the 2 groups (P value above 0.005)

Table (6): Kidney, liver and platelets count among studied participants:

	Group				p-value
	Cases		Control		
	Mean	SD	Mean	SD	
Albumin	4.1	0.4	4.2	0.4	0.129
Creat	0.7	0.1	0.7	0.1	-----
ALT	69	15	29	8	0.001
ASt	67	16	27	8	0.001
Bilirubin	1	0	1	0	----
INR	1	0	1	0	--
HB	13.1	1.5	13.8	1.5	0.001
Platelet	266	54	297	51	0.001

The table above shows that there is a significant difference between the mean of ALT, ASt, HB, and Platelet between the group of cases and the group of control (P-value = 0.001).

The difference between the mean of Albuim in both groups is insignificant (P-value= 0.129).

There is no difference between the mean of the cases group and the control group regarding the Creat, Bilirubin, and INR at all.

Table (7): H. pylori and liver imaging among the studied participants:

		Group				P- value
		Cases		Control		
		Count	%	Count	%	
H. Pylori	Positive	79	79.0%	33	33.0%	0.001
	Negative	21	21.0%	67	67.0%	
US	Bright hepatomegaly	93	93.0%	0	0.0%	0.001
	Normal	7	7.0%	100	100.0%	
Fibro scan	F0	2	2.0%	55	55.0%	0.001
	F1	44	44.0%	45	45.0%	
	F2	38	38.0%	0	0.0%	
	F3	16	16.0%	0	0.0%	

From the figures and table above, there is a significant difference between both groups (P-value 0.001) regarding the following:

-The *H. pylori* were positive in 79% of the case group, while only 33% of the control group were positive.

-The bright Hepatomegaly was positive in 93% of the case group, and the whole control group was negative (normal).

-The Fibroscan, the control group had F0 (45%) and F1 (55%) while the distribution among the case group was significantly different F0 (2%), F1 (44%), F2 (38%) and F3 (16%).

Table (8): Distribution of steatosis grades among cases and controls:

		Group				P-value
		Cases		Control		
		Count	Column N %	Count	Column N %	
Steatosis grade	s0	0	0.0%	70	70.0%	0.001
	s1	13	13.0%	24	24.0%	
	s2	38	38.0%	6	6.0%	
	s3	49	49.0%	0	0.0%	

The distribution of steatosis grades distribution was statistically significant among different groups.

Table (9): cap score among both studied groups:

	Group				p-value
	Cases		Control		
	Mean	Standard Deviation	Mean	Standard Deviation	
Cap Score	292.99	33.71	234.81	21.04	0.001

The cap score was significantly higher among cases than control.

4. Discussion :

The hallmark of metabolic dysfunction associated fatty liver disease (MAFLD), a significant form of chronic liver disease, is hepatic steatosis without alcohol consumption or other liver disease causes. The fact that MAFLD can induce extrahepatic symptoms like obesity, dyslipidemia, diabetes, insulin resistance, chronic kidney disease, and extrahepatic malignancies in addition to liver disease is becoming more widely recognised. The previously heavy clinical and economical burden is increased by the current, rapid rise in MAFLD prevalence. Therefore, it is essential to understand the risk factors and the burden associated with them in order to prevent and treat MAFLD. (8).

There are several theories linking the intestinal microbiome to various types of multiple sclerosis (MAFLD), including its effects on the innate immune system, the function of the intestinal endothelial barrier, the production of metabolites in the gut, and the fermentation of indigestible carbohydrates. According to research on animals, intestinal dysbiosis or Helicobacter pylori (H. pylori) infection may be the root cause of the development and symptoms of MAFLD.A gram-negative bacterium called H. pylori colonises the stomach epithelium.

There are several theories linking the intestinal microbiome to various types of multiple sclerosis (MAFLD), including its effects on the innate immune system, the function of the intestinal endothelial barrier, the production of metabolites in the gut, and the fermentation of indigestible carbohydrates. According to research on animals, intestinal dysbiosis or Helicobacter pylori (H. pylori) infection may be the root cause of the development and symptoms of MAFLD. H. pylori infection has been connected to extra-digestive tract problems, such as cutaneous, neurological, ocular, cardiovascular, pulmonary, and metabolic diseases, as well as gastrointestinal malignancies, albeit the evidence is still preliminary. (9)

In light of this information, the purpose of this study was to determine the prevalence of *H. pylori* in a cohort of patients with MAFLD, highlighting the potential involvement of this infection as a risk factor for the development of MAFLD in the Egyptian community.

This study included 100 patients with MAFLD through one-year duration. In the present study, FPG , 2HrPP , and HbA1c were done .

Our results showed there is a significant difference between both groups (P-value 0.001) regarding the following:

-The *H. pylori* were positive in 79% of the case group, while only 33% of the control group were positive.

-The bright Hepatomegaly was positive in 93% of the case group, and the whole control group was negative (normal).

-The Fibroscan, the control group had F0 (45%) and F1 (55%) while the distribution among the case group was significantly different F0 (2%), F1 (44%), F2 (38%) and F3 (16%).

Also, The distribution of steatosis grades distribution was statistically significant among different groups in our study.

Our findings were consistent with those of several case-control studies that examined the prevalence of *H. Pylori* in MAFLD patients.

A study conducted in Egypt had 300 participants who were selected from the Diabetes & Endocrinology Unit and Obesity Clinic at the Specialized Medical Hospital of Mansoura University. Two groups of 200 patients with metabolic syndrome were created, one for those with non-alcoholic fatty liver disease (MAFLD) and the other for those without the condition, who served as the control group. It's crucial to remember that *H Pylori* infection increases the risk of MAFLD development in MET S patients. According to our data, *H Pylori* infection is more common in MET S patients with MAFLD (73%) than in MET S patients without MAFLD (47%), with a significant difference (P value < 0.001).(10)

With an overall predictive value of 75%, the study found a high (P value < 0.001) association between *H Pylori* infection and increased degree of fibrosis leading to noticeable fibrosis, which may exacerbate NASH, especially in those with hyperglycemia. (10)

A second Egyptian study plan was authorized by the clinical research and ethics committee of Tanta University Faculty of Medicine and carried out in compliance with the Helsinki Declaration's ethical principles. During the period of June to October 2019, this cross-sectional study included all outpatient clinic attendees who were over the age of 18, from four major university hospitals and two research and clinical institutes in a developing country, and who gave their consent to be included in the study. Patients were evaluated for the diagnosis of MAFLD using CAP, fibroscan, and ultrasound; they were also evaluated for the diagnosis of *H.*

pylori infection as indicated by *H. pylori* antigen in stool.(11)

Of the 646 patients that were part of the trial, 538 (83.3%) had an *H. pylori* infection. The MAFLD (found by both U/S and Fibroscan with CAP) +ve group exhibited significantly higher levels of ALT, AST, hepatomegaly, hypertension, and fasting blood sugar than the *H. pylori* −ve group. After determining whether *Helicobacter pylori* was involved or not using linear regression, the following independent risk factors for MAFLD were found: diastolic blood pressure, *H. pylori* positive, total cholesterol, ultrasonography-detected degree of fatty liver, and fasting blood sugar.(11)

Weijun Wang et al. studied the Chinese patients at Wuhan Union Hospital between January 2015 and December 2019. There were 71,633 healthy individuals in this cross-sectional study. Compared to the *H. pylori* -ve group (31.3%), the MAFLD prevalence in the *H. pylori* +ve group (34.8%) was significantly higher. Additional sex-specific analyses revealed that the prevalence of MAFLD with *H. pylori* +ve in men was 44.4%, higher than that in the *H. pylori* -ve group 41.1%. Furthermore, the frequency of MAFLD in females with *H. pylori* +ve was significantly higher at 21.1% compared to the *H. pylori* -ve group's 17.9%. (12)

The association between *H. pylori* infection and the prevalence of MAFLD was investigated using logistic regression analysis. The risk of MAFLD was found to be elevated by *H. pylori* infection, according to univariate analysis of all the samples. Then, we performed a multicollinearity analysis using the significant variables and found that there was multicollinearity between LDL-C and total cholesterol. In contrast, there was no multicollinearity among the other variables. Then, total cholesterol was eliminated from the multivariate regression model. The multivariate analysis's findings showed no link between *H. pylori* infection and MAFLD. (12)

Additionally, at the Tianjin Medical University General Hospital in Tianjin, China, another cross-sectional investigation was carried out. Between January and December 2018, 91 patients (nonsmokers and nondrinkers, 56 men and 35 women, mean age 52.8 ± 14.7 years, range 18–83 years) who had abdominal B-mode ultrasonography diagnoses of MAFLD were included. *H. pylori* infection risk was considerably higher in patients with severe MAFLD ($P<0.01$). Furthermore, the striograph of abdominal B-mode ultrasonography revealed a consistent

outcome in patients with mild, moderate, and severe MAFLD, with a comparable rate of *H. pylori* infection. (13).

A noteworthy cross-sectional study was conducted in Iran. The findings of the abdomen ultrasonography examination, the lack of a history of drug use that could have caused hepatic injury, and abstaining from alcohol were used to diagnose MAFLD, in accordance with the guidelines of the American College of Gastroenterology. For convenience, a random selection of the patients was made. Based on the results of a previous study, a sample size of 64 patients per group was established. An ultrasound scan revealed that 65 patients in one group had MAFLD and 65 individuals in the other group were controls who did not have MAFLD. The controls were matched in terms of age and gender. 38 patients in the MAFLD group (58.5%) and 37 people in the control group (56.9%) had positive serum levels of anti-*H. pylori* IgG; p = 0.86. The MAFLD group's anti-*H. pylori* IgG mean (±SD) was 78.1 ± 9.9 IU/mL, which was higher than that of the control group (51.7± 7.2 IU/mL); p = 0.03. Additionally, the MAFLD group had a higher frequency of positive fecal *H. pylori* antigen tests than the control group (26 patients, or 40% vs. 18 subjects, or 27.7%), but the difference was not statistically significant. (14).

In contrast to these findings, a study conducted in China between May 2013 and June 2014 at the Shanghai First People's Hospital branch in Songjiang involved 28,171 participants. The study included 28,171 participants, of which 13,782 were women and 14,389 were males. The mean (±SD) age of the participants was 48.3 ± 15.0 years. 10,848 (38.5%) of the individuals overall had *H. pylori* infection. The MAFLD prevalence rate was 34.3% overall. Men were substantially more likely than women to have MAFLD (45.9% vs. 22.2%, P < 0.05). When compared to the uninfected controls, those with *H. pylori* infection exhibited a slightly but statistically substantially higher prevalence of MAFLD (36.0% vs. 33.3%, P < 0.05). Subsequent sex-stratified analyses revealed that the prevalence of MAFLD in women with *H. pylori* infection was higher than that in persons without *H. pylori* infection (23.6% vs. 21.5%, P < 0.05). On the other hand, there was no discernible difference in the prevalence of MAFLD in men between the two groups (46.5% vs. 45.5%, P > 0.05). (15).

An additional logistic regression analysis was run to ascertain the independent relationship between *H. pylori* infection and MAFLD

risk. According to univariate analysis, *H. pylori* infection was linked to a greater incidence of MAFLD ($P < 0.001$). When age and sex were taken into account, the OR for MAFLD was still significant ($P < 0.004$). But after further controlling for FPG, HbA1c, TG, TC, HDL-C, LDL-C, and Scr in addition to BMI, SBP, and DBP, the incidence of MAFLD was no longer linked to H. pylori infection. (16).

5. Conclusion :

For a year, 100 MAFLD patients were included in this study. The current investigation included FPG, 2HrPP, and HbA1c. According to our findings, there is a noteworthy distinction between the two groups. Only 33% of the control group had positive H. pylori tests, compared to 79% of the case group denoting that H.Pylori infection is a risk factor for MAFLD .

6. References:

1-Alavinejad, P., Hajiani, E., Parsi, A. et al. Effect of *Helicobacter pylori* eradication on metabolic profile: an international, multicenter, case-control study. BMC Gastroenterol 22, 507 (2022). https://doi.org/10.1186/s12876-022-02604-3

2- Aumpan, N., Mahachai, V. and Vilaichone, R.-k. Management of *Helicobacter pylori* infection. JGH Open, 7: 3-15 (2023),. https://doi.org/10.1002/jgh3.12843.

3- Franceschi F, Annalisa T, Teresa DR, Giovanna D, Ianiro G, Franco S, Viviana G, Valentina T, Riccardo LL, Antonio G. Role of *Helicobacter pylori* infection on nutrition and metabolism. World J Gastroenterol. 2014 Sep 28;20(36):12809-17. doi: 10.3748/wjg.v20.i36.12809.

4. Razuka-Ebela D., Giupponi B., Franceschi F. *Helicobacter pylori* and extragastric diseases. *Helicobacter* . 2018;23(1) doi: 10.1111/hel.12520.

5- Eslam M, Newsome PN, Sarin SK, Anstee QM, Targher G, Romero-Gomez M, et al.,. A new definition for metabolic dysfunction-associated fatty liver disease: An international expert consensus statement. J Hepatol. 2020 Jul;73(1):202-209. doi: 10.1016/j.jhep.2020.03.039.

6- Xu G, Ma S, Dong L, Mendez-Sanchez N, Li H, Qi X. Relationship of *Helicobacter pylori* Infection with Nonalcoholic Fatty Liver Disease: A Meta-Analysis. Can J Gastroenterol Hepatol. 2023 Jan 25;2023:5521239. doi: 10.1155/2023/5521239.

7- Wang W., Fan M., Gong R., et al. *Helicobacter pylori* infection is not an independent risk factor of non-alcoholic fatty liver disease in China. BMC

Gastroenterology . 2022;22(1):p. 81. doi: 10.1186/s12876-022-02148-6.

8- Stefan N, Häring HU, Cusi K. Non-alcoholic fatty liver disease: causes, diagnosis, cardiometabolic consequences, and treatment strategies. Lancet Diabetes Endocrinol. 2019 Apr;7(4):313-324. doi: 10.1016/S2213-8587(18)30154-2.

9- Li W, Zhang J, Ma J, Li Z, Zhang L, Zhang Y et al. Effects of *Helicobacter pylori* treatment and vitamin and garlic supplementation on gastric cancer incidence and mortality: follow-up of a randomized intervention trial BMJ 2019; 366 :l5016 doi:10.1136/bmj.l5016.

10- Rakha, M., Saleh, O., Abdelgawad, M.S. et al. *Helicobacter pylori* infection in patients with metabolic syndrome, with or without nonalcoholic fatty liver disease. Egypt Liver Journal 11, 7 (2021). https://doi.org/10.1186/s43066-020-00071-7.

11- Abo-Amer YE, Sabal A, Ahmed R, Hasan NFE, Refaie R, Mostafa SM, Mohamed AA, Khalil M, Elagawy W, Abd-Elsalam S. Relationship Between *Helicobacter pylori* Infection and Nonalcoholic Fatty Liver Disease (NAFLD) in a Developing Country: A Cross-Sectional Study. Diabetes Metab Syndr Obes. 2020 Mar 2;13:619-625. doi: 10.2147/DMSO.S237866.

12- Wang W, Fan M, Gong R, Zhang Y, Zeng J, Xu S, Lin R. *Helicobacter pylori* infection is not an independent risk factor of non-alcoholic fatty liver disease in China. BMC Gastroenterol. 2022 Feb 24;22(1):81. doi: 10.1186/s12876-022-02148-6.

13- Chen J, Xing Y, Zhao L, Ma H. The Association between *Helicobacter pylori* Infection and Glycated Hemoglobin A in Diabetes: A Meta-Analysis. J Diabetes Res. 2019 Sep 9;2019:3705264. doi: 10.1155/2019/3705264. PMID: 31583248; PMCID: PMC6754895.

14- Mohammadifard M, Saremi Z, Rastgoo M, Akbari E. Relevance between *Helicobacter pylori* Infection and Non-Alcoholic Fatty Liver Disease in Birjand, Iran. J Med Life. 2019 Apr-Jun;12(2):168-172. doi: 10.25122/jml-2019-0012.

15- Fan N, Peng L, Xia Z, Zhang L, Wang Y, Peng Y. *Helicobacter pylori* Infection Is Not Associated with Non-alcoholic Fatty Liver Disease: A Cross-Sectional Study in China. Front Microbiol. 2018 Jan 31;9:73. doi: 10.3389/fmicb.2018.00073.

16- Ning L, Liu R, Lou X, Du H, Chen W, Zhang F, Li S, Chen X, Xu G. Association between *Helicobacter pylori* infection and

nonalcoholic fatty liver disease: a systemic review and meta-analysis. Eur J Gastroenterol Hepatol. 2019 Jul;31(7):735-742. doi: 10.1097/MEG.0000000000001398.