To cite this article: Kilic G, Kilic GE Konur S, Ozkahraman A, Kayar Y. Association between Helicobacter pylori infection and non-alcoholic fatty liver disease in older adult patients. Turk J Clin Lab 2024; 1: 23-27

Research Article

Association between eradication success of Helicobacter pylori with presence of non-alcoholic fatty liver disease in older adult patients

Yaşlı erişkin hastalarda Helicobacter pylori eradikasyon başarısı ile non-alkolik yağlı karaciğer hastalığı arasındaki ilişki

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Abstract

Aim: The aim of this study was to show the effect of H. pylori eradication on the eradication of non-alcoholic fatty liver disease (NAFLD) in the older adult population.

Material and Methods: The patients included in the study were separated into two groups as the older adult group aged ≥65 years and the young adult group aged <65 years. Treatment of gemifloxacin 320mg/day, amoxicillin 2 gr/day, and rabeprazole 40 mg/day was administered to all the patients for the eradication of H.pylori. Hepatic steatosis was evaluated with hepatobiliary ultrasonography and was classified as grade 1, 2, or 3.

Results: Evaluation was made of 271 patients who were determined endoscopically and histopathologically with HP infection and treated accordingly. Successful HP eradication was achieved in 54 (79.4%) patients in the older adult group. In the examination of the relationship between fatty liver and HP eradication after treatment in the older age group, no significant relationship was observed between the presence of hepatosteatosis and HP eradication (p>0.05)

Conclusion: The known relationship between NAFLD and HP is of greater importance in patients of advanced age

Keywords: Helicobacter pylori, non-alcoholic fatty liver, older adult

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Doi: 10.18663/tjcl.1317042
Recevied: 20.06.2023 accepted: 26.01.2024

TJCL Volume 15 Number 1 p: 23-27

Öz

Amaç: Bu çalışmanın amacı yaşlı erişkin popülasyonda H. pylori eradikasyonunun non-alkolik yağlı karaciğer hastalığı (NAYKH) eradikasyonu üzerindeki etkisini göstermekti.

Gereç ve Yöntemler: Çalışmaya alınan hastalar 65 yaş ve üstü yaşlı erişkin grubu ve 65 yaş altı genç erişkin grubu olarak iki gruba ayrıldı. H.pylori eradikasyonu için tüm hastalara gemifloksasin 320mg/gün, amoksisilin 2 gr/gün ve rabeprazol 40 mg/gün tedavisi uygulandı. Karaciğer yağlanması hepatobiliyer ultrasonografi ile değerlendirildi ve derece 1, 2 veya 3 olarak sınıflandırıldı.

Bulgular: Endoskopik ve histopatolojik olarak HP enfeksiyonu saptanan ve tedavi edilen 271 hasta değerlendirmeye alındı. Yaşlı erişkin grupta 54 (%79.4) hastada başarılı HP eradikasyonu sağlandı.İleri yaş grubunda karaciğer yağlanması varlığı ile HP eradikasyonu başarısı arasında istatistiki olarak anlamlı bir ilişki gözlenmedi (p>0,05)

Sonuç: NAYKH ve HP arasındaki bilinen ilişki ileri yaştaki hastalarda daha fazla önem taşımaktadır.

Anahtar Kelimeler: Helicobacter pylori, non-alkolik yağlı karaciğer, yaşlı erişkin

Introduction

Non-alcoholic fatty liver disease (NAFLD) is a chronic liver disease that leads to non-alcoholic steatohepatitis, cirrhosis, hepatocellular cancer, and ultimately death, which has shown an increasing prevalence in recent years (1). In Turkey in 2021, the prevalence of NAFLD was found to be 48.3% in a study by Değertekin et al (2). Previous studies have shown the importance of insulin resistance in fatty liver (3). Although not yet accepted as a definitive component, NAFLD is now be accepted as a hepatic manifestation of metabolic syndrome (4).

The prevalence of NAFLD in the general population increases with age. The rate has been shown to be 18% between the ages of 20-40 years, 39% in the 40-50 years age range, and 40% in those aged over 70 years (5, 6). In general, fatty liver is more common in males than females up to the age of 60 years, but following menopause, the prevalence of fatty liver in females shows a sharp increase (7). H. pylori infection is also known to contribute to the development of NAFLD by participating in the regulation of the gastric hormones, leptin and ghrelin, which affect insulin sensitivity and adiposity (8). Recent studies have shown that the insulin resistance and increased intestinal permeability of H. pylori infection could have a potential role in the development of NAFLD (9). The aim of this study was to show whether there is an effect of NAFLD on H. pylori eradication in the old population.

Material and Method

Study Design

This retrospective study included 271 patients aged 18-85 years who presented at the Gastroenterology Polyclinic between May 2021 and October 2021 with dyspeptic complaints and underwent upper gastrointestinal system (GIS) endoscopy in respect of these complaints. Patients were excluded from the study if they were pregnant, had undergone organ transplantation (liver, kidney, bone marrow), had chronic liver or kidney disease, a history of GIS surgery, or had received antibiotic treatment within the last a month. The patients included in the study were separated into two groups as the older adult group aged ≥65 years and the young adult group aged <65 years. For H.pylori eradication, all patients were treated with gemifloxacin 320 mg/day, amoxicillin 2 g/day and rabeprazole 40 mg/day for 7 days. After 1 month of treatment, faeces were examined to determine whether or not H.pylori had been eradicated. A record was made for each patient of demographic characteristics (age, gender), and comorbidities such as diabetes mellitus (DM), hypertension (HT), hyperlipidemia (HL), ischaemic heart disease (IHD), chronic renal failure (CRF), and cerebrovascular events (CVE). Hepatic steatosis was evaluated with hepatobiliary ultrasonography and was classified as grade 1, 2, or 3.

Endoscopic evaluation

The endoscopic findings and histopathological data of the patients were documented. The endoscopy examination was performed using a Fujinon EG530WR endoscopy device in the endoscopy unit of our hospital. After 8 hours fasting, local pharyngeal xylocaine anesthesia was applied then the endoscopy procedure was performed. The stomach and duodenum were examined in detail and biopsies were taken to determine H.pylori infection.

Histopathological evaluation

In the patients who underwent endoscopic evaluations, a punch biopsy was taken from the antrum using biopsy forceps. The biopsy materials taken were sent to the pathology laboratory in 10% formaldehyde. After routine tissue monitoring procedures, the tissue samples were embedded in paraffin blocks, from which 5 micron-thick sections were cut, routinely stained with Giemsa and then evaluated under a light microscope. Samples without tissue competence for evaluation were excluded from the study.

Ethics statement

Approval for this study was obtained from the Ethics Committee of our hospital (decision no:2023/01-01, dated:04.01.2023). All procedures were in accordance with the ethical standards of the Institutional Human Research Committee and the Helsinki Declaration. Written informed consent forms were obtained from all participants in the study.

Statistical analysis

Data obtained in the study were analyzed using SPSS ver. 19.0 software (Statistical Package for the Social Sciences, IBM Corp., Armonk, NY, USA). Continuous variables were given as mean ± standard deviation (SD) values, and categorical data as frequency (n) and percentage (%). The groups were compared using the Student's t-test for continuous parametric data and the Chi-square test for categorical data. A value of $p<0.05$ was considered statistically significant.

Results

Evaluation was made of 271 patients who were determined endoscopically and histopathologically with HP infection and treated accordingly. These patients comprised 164 (60.5%) females and 107 (39.5%) males with a mean age of 44.1±11.7 years (range, 18-76 years). The older adult group included 68 (25.1%) patients and the younger adult group, 203 (74.9%) patients. In the evaluations performed after treatment, HP eradication was achieved in 238 (87.8%) patients, and not in 33 (12.2%) patients. Successful HP eradication was achieved in 54 (79.4%) patients in the older adult group.

In the comparisons between the two age groups, the BMI values of the older adult group were determined to be higher than those of the younger group (29.0±4.2 and 24.9±4.1 respectively, p <0.001). Comorbid diseases were determined at statistically significantly higher rates in the older adult group than in the younger group (78.5% vs. 13.3%); DM: 35.3% vs. 1.5%, HT:44.1% vs. 5.9%, HL:8.8% vs. 1.5%, IHD: 26.5% vs. 3.0%, CRF:14.7% vs.1.5%, CVE: 8.8% vs. 0.0% ($p<0.05$) (Table 1). In the comparisons made in respect of the laboratory analyses, the ALT, ALP, and CRP values were statistically significantly higher in the older adult group and the AST (p:0.171) and GGT (p:0.140) values were higher but not at a statistically significant level compared to those of the younger age group.

In the comparisons made in respect of hepatosteatosis, fatty liver was seen significantly more in the older age group than in the younger patients (73.5% vs. 34.5%). The rates at all grades were significantly higher in the older patients than in the younger group; Grade 1: 38.2% vs. 21.2%, Grade 2: 26.5% vs.13.3%, Grade 3: 8.8% vs. 0.0% (Table 1). In the examination of the relationship between fatty liver and HP eradication after treatment in the older age group, no significant relationship was observed between the presence of hepatosteatosis and HP eradication ($p>0.05$) (Table 2).

Table 1: The demographic and laboratory data, comorbidities, and presence of steatosis of the patients

Variables	Older adult patients (≥65 years) n:68	Patients aged <65 years n:203	Total n:271	P value
Age (years)	66.1±5.6	36.6±10.1	44.1±11.7	<0.001
Gender (female)	50 (73.5%)	114 (56.2%)	164 (60.5%)	0.011
BMI	29.0±4.2	24.9±4.1	26.0±4.5	<0.001
Presence of comorbid disease				
-DM	52 (76.5%)	27 (13.3%)	79 (29.2%)	<0.001
-HT	24 (35.3%)	3(1.5%)	27 (10.1%)	<0.001
-HL	30 (44.1%)	12 (5.9%)	42 (15.5%)	<0.001
-IHD	6 (8.8%)	3 (1.5%)	9 (3.3%)	0.003
-CRF	18 (26.5%)	6 (3.0%)	24 (8.9%)	<0.001
-CVE	10 (14.7%)	3 (1.5%)	13 (4.8%)	<0.001
	6 (8.8%)	0 (0.0%)	6 (2.2%)	<0.001
AST	18.6±5.9	17.5±3.3	18.3±5.4	0.171
ALT	18.8±10.3	13.7±4.8	17.5±8.4	<0.001
ALP	87.4±25.2	68.6±24.6	73.1±26.1	<0.001
GGT	22.7±14.9	19.7±15.6	20.5±15.4	0.140
CRP	3.8±1.7	2.4±1.6	2.8±1.6	0.002
HP eradication	54 (79.4%)	184 (90.6%)	238 (87.8%)	0.014
Steatosis (present)	50 (73.5%)	70 (34.5%)	120 (44.3%)	<0.001
Grade 1	26 (38.2%)	43 (21.2%)	69 (25.0%)	0.005
Grade 2	18 (26.5%)	27 (13.3%)	45 (16.6%)	0.012
Grade 3	6 (8.8%)	0 (0.0%)	6 (2.2%)	<0.001

Table 2: The relationship between hepatosteatosis and H.Pylori eradication in the older age group patients

Variables	Patients with HP eradication n: 54	Patients without HP eradication n:14	Total N:68	P value
Presence of hepatosteatosis	38 (70.4%)	12 (85.7%)	50 (73.5%)	0.246
Grade 1 fatty liver	16 (29.6%)	10 (71.4%)	26 (38.2%)	0.004
Grade 2 fatty liver	16 (29.6%)	2 (14.3%)	18 (26.5%)	0.246
Grade 3 fatty liver	6 (11.1%)	0 (0.0%)	6 (8.8%)	0.191

Discussion

It has long been known that there is an increase in diseases such as DM, HT, HL, IHD, and CRF as age increases. Non-alcoholic fatty liver disease (NAFLD) is also seen more often in the older adult population, associated with an age-related increase in DM, HT, and HL, which are components of metabolic syndrome. Hepatic steatosis at all grades was determined to be seen more often in the older population than in the younger age group in the current study.

For many years the relationship between NAFLD and H.pylori (HP) has been a subject of interest on which various studies have been conducted. Polyzos et al. first reported significantly higher anti-HP IgG levels in patients with NAFLD confirmed by liver biopsy. This showed that HP infection could contribute to NAFLD directly or indirectly through insulin resistance (10). In patients with HP infection, there has been shown to be an increase in the expression of inflammatory factors such as IL-1, IL-6, and TNF-α, which decrease insulin sensitivity (11). NAFLD can also lead to damage in the liver as result of bacteria and toxins reaching the liver through the portal vein in patients with increased intestinal permeability. Thus, it can be assumed that these pro-inflammatory cytokines induced by HP can enter the liver through the portal vein and contribute to the pathogenesis of NAFLD (12).

The eradication of HP is more difficult in the geriatric population in particular compared to other populations. In the current study, eradication was obtained in 79.4% of the older age group and in 90.6% of the younger population. In a study by Tanaka et al. comparing HP eradication in older and younger populations, eradication was reported at the rate of 64.5% in the older population and at 75.6% in the younger population. The addition of clarithromycin, metronidazole, and sitafloxacin at low doses to amoxicillin (750mg bid) in the treatment protocol of that study could have been the reason for the low eradication rates (13). The treatments of gemifloxacin, amoxicillin and rabeprazole used in the current study can be safely used in older patients with few side-effects and high eradication rates. In a meta-analysis compiled by Heydari et al., it was thought that it would be reasonable to expect a better eradication rate in patients with NAFLD receiving H. pylori treatment, but current evidence does not support this theory (14).

The accumulation of liver fat in hepatocytes caused by insulin resistance makes the liver more vulnerable to oxidative stress and subsequent lipid peroxidation. These factors lead to the development of NAFLD (15). H. pylori infection plays a role in the pathogenesis of insulin resistance through several mechanisms. HP has been shown to have an effect on the pathogenesis of NAFLD, for which there is no effective treatment other than losing weight, and it is thought that the eradication of HP will reduce fatty liver. The combination of NAFLD and HP, which increases with age, is common, and an increase in the frequencies of comorbidities such as DM, HT, and HL, which are components of metabolic syndrome, increases the cardiovascular risk in these patients.

The main limitations of this study were the retrospective design and low number of patients in the older age group. In addition, Per Protocol (PP) and Intention to Treat (ITT) results are lacking in this study. However, the strong aspects of the study can be considered to be that the diagnosis of HP infection was made histopathologically, the risks which could affect NAFLD were documented, and that a new HP eradication protocol was used, which has been shown to be extremely effective.

In conclusion, although the relationship between H.pylori eradication and NAFLD in elderly patients has been reported in the literature, no relationship was found in our study due to the small number of elderly patients, further studies with a larger sample size are needed.

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