Helicobacter Pylori Infection in Patients with Non Alcholic Fatty Liver Disease

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Abstract

Background: Although there have been conflicting results, several subsequent clinical trials have demonstrated a higher rate of fatty liver and NASH in H. pylori -positive patients compared to HP-negative patients; in addition, small trials examining the effect of H. pylori eradication have shown improvement in markers of NAFLD activity, further supporting a link between these two conditions. **Aim**: This study was conducted to evaluate the relation of H. Pylori infection with Non Alcholic Fatty Liver Disease (NAFLD). **Methods:** This study is a case control study carried out at outpatient's clinics of El Mahalla El Aam Hospital from November 2017 till May 2018, Subjects were classified into two groups: One hundred patients with NAFLD who attended outpatient's clinics of El Mahalla El Aam Hospital, Group (A) (case group): Included 50 patients with NAFLD (diagnosed by ultrasonography). Group (B) (control group): Included 50 subjects (diagnosed by ultrasonography) who will serve as a control group. **Results**: There was a statistical significant difference in Hp results between group I and group II groups, with significant Ag positive-Ab positive to Group I, and there was no statistical significant differences in US grades of NAFLD according to HP Ag or Ab results. **Conclusion**: Our study was display a significant increase in MPVin patients with NAFLD. The burden of H. Pylori infection among NAFLD patients was noticeably high, in comparison with the healthy control group.

Key words: Non Alcoholic Fatty Liver Disease, H. pylori, infection, case control.

Abbreviations; NAFLD= Non Alcholic Fatty Liver Disease, HP= H. Pylori, US= ultrasonography.

Introduction

(NAFLD) requires that there is evidence of hepatic steatosis, either by imaging or by histology and there are no causes for secondary hepatic fat accumulation such as significant alcohol consumption,use of steatogenic medication or hereditary disorders.

Non-alcoholic steatohepatitis (NASH) is the most extreme form of NAFLD. NAFLD is the most common liver disorder in developed countries **[1]**.

Non-alcoholic fatty liver disease (NAFLD) includes a spectrum of diseases that range from simple steatosis to steatohepatitis, advanced fibrosis and cirrhosis. NAFLD is now the most common chronic liver disease in many developed countries and is closely associated with obesity and cardiovascular disease. Furthermore, NAFLD is expected to become an even more serious public health issue because of the increasing prevalence of obesity and aging **[2**].

Helicobacter pylori infection (H. pylori) is closely related to gastric atrophy, intestinal metaplasia, and progression to dysplasia or cancer **[3**].

Given the evidence that H. pylori infection has been associated with effects throughout the gastrointestinal tract, there has been speculation regarding the possible association of H. pylori infection with the development of NAFLD, which is the hepatic component of metabolic syndrome, a condition that is also associated with obesity, diabetes, and cardiovascular disease **[4**].

Accumulating evidence has implicated helicobacter pylori (H. pylori) infection in extragastrointestinal diseases, including obesity, type 2 diabetes mellitus, cardiovascular disease, and liver disease. Recently, there has been a special focus on H. pylori infection as a risk factor for the development of (NAFLD). NAFLD is currently considered to be the most common liver disorder in western countries, and is rapidly becoming a serious threat to public health **[5**].

The findings of possible association between H. pylori infection and NAFLD initially stemmed from the isolation of H. pylori bacteria in the livers of patients with NAFLD. Although there have been conflicting results, several subsequent clinical trials have demonstrated a higher rate of fatty liver and NASH in H. pylori - positive patients compared to HP-negative patients; in addition, small trials examining the effect of H. pylori eradication have shown improvement in markers of NAFLD

activity, further supporting a link between these two conditions. The pathophysiology behind the possible association between H. pylori infection and NAFLD has yet to be fully elucidated; several possible mechanisms include induction of a pro-inflammatory state that shifts the body toward a more lipogenic profile, and a hormonal shift that favors progression toward insulin resistance and fibrosis **[6**].

Materials and methods

This study is a case control study carried out at outpatient's clinics of El Mahalla El Aam Hospital from November 2017 till May 2018 and these procedures ara approved by ethical commitee benha faculty of medecine

Subjects were classified into two groups:

One hundred patients with NAFLD who attended outpatients clinics of El Mahalla El Aam Hospital.

Group (A) (case group): Included 50 patients with NAFLD (diagnosed by ultrasonography). Group (B) (control goup): Included 50 subjects (diagnosed by ultrasonography) who will serve as a control group.

- **Inclusion Criteria:** Adult persons 18 years and Patients with NAFLD diagnosed by ultrasonography
- **Exclusion criteria:** 1. Patients with alcohol consumption or previous alcohol consumption, 2. HBV infected patients; 3. HCV infected patients, 4. History of steatogenic medications, 5. History of metabolic diseases which may cause Fatty liver (e.g Diabetis Mellites) and 6 . drugs cause nafld.

Methodology

1. Clinical assessment:

a) **History taking**: 1. Demographic information: Age and sex, 2. Residental history: Urban or rural type of residence, 3. Special habits: Alcohol intake and Smoking, 4. Steatogenic medications and 5. History suggesting chronic liver disease as autoimmune hepatitis, hemochromatosis and Wilson's disease

b) Clinical examination: 1. General examination; with stress on weight, height and BMI, 2. Cardiovascular examination, 3. Chest examination and 4. Abdominal examination; with stress on: Liver (size, surface, consistency and borders), Spleen if enlarged or not and any stigmata of liver cell failure

2. Laboratory assessment: (routine and general evaluation tests)

- Complete blood count(CBC): Hemoglopin (HB)%(g/dl), White blood cells (wbcs)(c/mm), Platelet count(cmm), Fasting and 2 hours post prandial plasma glucose(mg/dl) and HbA1c.

- Kidney functions: Blood urea (mg/dl) and Serum creatinine(mg/dl).
- Liver profile including: Alanine amino transferase (ALT) (Iu/l), Aspartate amino transferase (AST) (Iu/l), Serum albumin(g/dl) , Total and direct serum bilirubin(mg/dl) and Prothrombin time (P.T) and I.N.R .
- Serum lipids: Cholesterol (mg/dl), Very_low_density_lipoprotein (VLDL) (mg/dl), low-density (LDL) (mg/dl), High-density lipoprotein (HDL) (mg/dl) and Triglycerides(mg/dl).

Imaging:

Real time abdominal ultrasound was done by TOSHIBA-SSA-700A (Apilo 5) for all patients and control included in the study for the evaluation of: 1. liver: size, border, parenchymal echotexture, hepatic veins, biliary radicals, common bile duct and focal lesions. 2. Portal vein: Caleber, patency by color Doppler. 3. Spleen: Size, splenic vein diameter and collaterals. 4.Ascites: Present or not

4. Assessment and grading of steatosis by ultrasound:

Grading of steatosis revealed by ultrasound was done according to Singh et al., 2013 as follows: **Grade I:** when the echogenicity is just increased more than cortex of the kidney . **Grade II:** when the echogenic liver obscures the echogenic walls of portal vein branches. **Grade III:** when the echogenic liver obscures the diaphragmatic outline.

5. H. pylori Ag Rapid Test:

Interpretation:

1. NEGATIVE RESULT: If only the C line develops, the test indicates that no detectable H. pylori antigen is present in the specimen. The result is negative or non-reactive.

2. POSITIVE RESULT: If both C and T lines develop, the test indicates the presence of detectable H. pylori antigen in the specimen. The result is positive or reactive. Fecal specimens with positive results should be interpreted in conjunction with other testing procedures and clinical findings before a diagnosis is made.

3. INVALID: If no C line develops, the assay is invalid regardless of any color development on the T line as indicated below. Repeat the assay with a new test device. Excess fecal specimen can lead to invalid test results; if this is the cause, resample and re-test (see instructions for collection of specimen).

Statistical analysis: The collected data were tabulated and analyzed using SPSS version 16 software (SPSS Inc, Chicago, ILL Company). Categorical data were presented as number and percentages while

quantitative data were expressed as mean± standard deviation (S.D), median, IQR and range. Chi square test (X^2), or Fisher's exact test (FET) were used to analyze categorical variables. Coordinate of correlation was assessed by Cohen Kappa test was used to assess degree of agreement between 2 raters.

Results

There was no statistical significant difference between studied groups as regard age, gender and smoking (p= 0.451, 0.190, 0.161). TG, TC, LDL, VLDL were significantly higher (p=0.049, 0.021, 0.016 and 0.040), while HDL showed significantly lower concentration in group I when compared to group II (p=0.034). Group I had statistically significant higher frequency of HP Ag in stool and H. pylori Ab in blood when compared to group II (p=0.001 and 0.001).

There was a statistical significant difference in Hp results between group I and group II groups, with significant Ag positive-Ab positive to Group I.

No statistical significant differences in US grades of NAFLD according to HP Ag or Ab results.

Ordinal regression analysis was conducted for prediction of severity of studied Group I, using age, gender, BMI, smoking, diet, life style, IR, lipid profile, HP Ag and Ab as covariates. High BMI, IR, TC, TG, LDL, VLDL, low HDL was significantly associated with more severe Group I in univariable analysis. However, after conducting multivariable analysis, using significant covariate in univariable analysis, revealed that only high BMI, IR, TC, TG, LDL, VLDL, low HDL were considered as independent risk factors for higher degree of Group I severity.

Table 1: Socio-demographic characteristics, smoking, lipid profile and H pylori (Hp) fecal Ag test and H pylori specific IgG Ab in blood of studied groups

Variable		Group I (patients) (n=50)		Group II (control) (n=50)		P
Age (years)	**mean±SD**	34.4±10.3		36.2±11.2		0.451[t]
Gender						
Male	**N (%)**	18	(36%)	12	(24%)	0.190[C]
Female	**N (%)**	32	(64%)	38	(76%)	
Smoking	**N (%)**	10	(20%)	5	(10%)	0.161[C]
TG (mg/dL)	**mean±SD**	153.3	±42.4	138.9	±24.7	**0.049[t]**
TC (mg/dL)	**mean±SD**	183.3	±54.7	162.9	±29.4	**0.021[t]**
LDL (mg/dL)	**mean±SD**	116.8	±25.4	95.7	±21.6	**0.016[t]**
HDL (mg/dL)	**mean±SD**	49.2	±12.3	58.8	±13.1	**0.034[t]**
VLDL (mg/dL)	**mean±SD**	37.4	±11.6	21.7	±5.7	**0.040[t]**
H. pylori (H.p)Ag in stool	**N (%)**	37	(74%)	11	(22%)	**<0.001[C]**
H. pylori(H.p) Ab in blood	**N (%)**	46	(92%)	32	(64%)	**0.001[C]**

Table 2: Hp results between studied groups.

Variable	Group I (n=50) N	%	Group II (n=50) N	%	p `
Ag negative-Ab negative	3	(6%)	18	(36%)	
Ag positive-Ab negative	1	(2%)	0	(0%)	
Ag negative-Ab positive	10	(20%)	21	(42%)	**<0.001**[F]
Ag positive-Ab positive	36	(72%)	11	(22%)	
Total	50	(100%)	50	(100%)	

F, Fisher exact.

Table 3: Ultrasonography grades of NAFLD as regard HP Ag or Ab results in studied group I

Variable		NAFLD with HP Ag Negative (n=13)	NAFLD with HP Ag Positive (n=37)	p	NAFLD with HP Ab Negative (n=4)	NAFLD with HP Ab Positive (n=46)	P
Grade I	**N (%)**	10 (76.9%)	16 (43.2%)		3 (75%)	23 (50%)	
Grade II	**N (%)**	2 (15.4%)	12 (32.4%)	0.143[F]	0 (0%)	14 (30.4%)	0.517[F]
Grade III	**N (%)**	1 (7.7%)	9 (24.3%)		1 (25%)	9 (19.6%)	

F, Fisher exact test

Table 4 (a): Prediction of severity of NAFLD

	Multivariable		
	95% CI	OR	p
Age			
Gender			
BMI	1.014-1.886	1.383	**0.041**
Smoking			
Unhealthy diet			
Sedentary life style			
IR	1.826-6.189	3.362	**<0.001**
TG	1.165-1.907	1.333	**0.047**
TC	1.158-1.996	1.525	**0.026**
LDL	1.018-1.857	1.485	**0.021**
HDL	0.188-0.913	0.548	**0.015**
VLDL	1.180-1.874	1.560	**0.031**
HP ab			
HP ag			

Table 4 (b): Prediction of severity of NAFLD

	Univariable		
	95% CI	**OR**	**p**
Age	0.983-1.039	1.010	0.468
Gender	0.692-2.548	1.327	0.395
BMI	1.199-1.687	1.422	**<0.001**
Smoking	0.411-1.961	0.898	0.787
Unhealthy diet	0.383-1.355	0.720	0.309
Sedentary life style	0.451-1.635	0.858	0.642
IR	2.346-5.997	3.750	**<0.001**
TG	1.001-1.014	1.008	**0.015**
TC	1.001-1.012	1.007	**0.027**
LDL	1.003-1.017	1.010	**0.008**
HDL	0.945-.991	0.968	**0.008**
VLDL	1.021-1.111	1.065	**0.004**
HP ab	0.305-2.897	0.941	0.915
HP ag	0.816-3.430	1.673	0.160

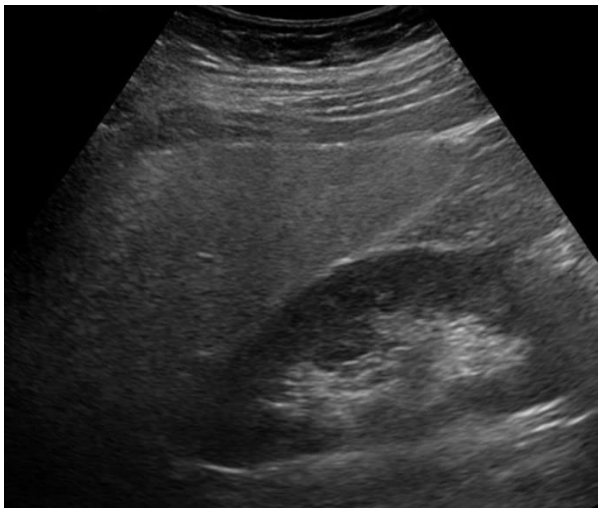

fig. 1

Discussion

Nonalcoholic fatty liver disease (NAFLD) is a type of liver injury induced by metabolic stress and is related to insulin resistance (IR) and hereditary susceptibility **[7].**

It is generally deemed to be the hepatic manifestation of metabolic syndrome **[8].**

Apart from known and common risk factors, such as obesity, type 2 diabetes, hypertension, and dyslipidemia, it has been postulated that helicobacter pylori infection

is involved in the pathogenesis of insulin resistance (IR) and may be associated with NAFLD **[9**].

H. pylori is a Gram-negative bacterium which selectively colonizes the gastric mucosa and is considered to be the main pathogenic bacteria involved in peptic ulcers, chronic active gastritis, mucosa-associated lymphoid tissue lymphoma, and gastric cancer **[10].**

In the present study, the mean age of group I (NAFLD) was (34.4±10.3years) and group II (Non NAFLD) were (36.2±11.2), and the majority of cases were female (64% and 76% in both groups respectively), there were no statistical significant differenc between both groups found in age, gender and smoking as (p= 0.451, 0.190 and 0.161 respectively) .

This was in agreement with Polyzos and his collegues who found that, There were no statistically significant differences as regard gender and age in a study included 28 patients with biopsy-proven NAFLD (and 25 matched healthy controls **[11].**

agreement with this current study is in , **Khalil et al., (2019) [12]**prospective observational case-control study included a total of 60 patients with NAFLD and 20 apparently healthy subjects served as control found no statistical significant difference between both groups as regard age and gender as a mean age of (35.65 ± 10.73 and 39.72 ± 11.14), respectively.

The present study revealed statistical significant differences were found in weight and BMI between group I and group II as (p=0.002, 0.568 and 0.005 respectively).

In agreement with current study, **Kang et al**, **(2018) [13**] found that, body mass index (BMI), waist circumference were higher in subjects with NAFLD than those without NAFLD**.**

Also, **Ozhan et al., (2010)[14]**found NAFLD patients had significantly higher body mass index compared to the control cases**.**

Also, **Almobarak et al**.,**(2014)[15**] reported in their study, the increase in BMI is associated with NAFLD. The mean BMI of individuals with NAFLD was found to be 30.6 and for those without NAFLD was 24.3 (95% CI23.4–25.2) and the difference in BMI in relation to NAFLD was found to be significant using ($p < 0.05$)**.**

Okushin et al., (2015)[16] conducted a large-scale study of 13,737 participants, and authors concluded that BMI was associated with NAFLD**.**

The current study revealed that grade I NAFLD (52%), while grade II and III constituted (28% and 20% respectively).

Similar with **Mohammadifard et al., (2019)[17**] who concluded in his study that grade I NAFLD was predominant which 33 patients (50.8%), 30 were cases (46.2%) grade II, and two cases (3.1%) had grade III disease**.**

In the present study, NAFLD associated with significantly higher insulin level and IR when compared to group II group ($p<0.001$). Subjects with NAFLD demonstrate a blunted inhibition of fatty acid oxidation, reflecting the decreased uptake and use of glucose as a source of fuel. These findings suggest the possibility that insulin resistance may be an intrinsic defect in NAFLD, and that diminished insulin responsiveness at the level of the adipocyte may contribute to hepatic steatosis by excess FFA flux to the liver.

This supported the finding of many studies concluded that, NAFLD is strongly associated with both hepatic and adipose tissue insulin resistance as well as reduced whole-body insulin sensitivity **[18].**

Pacifico et al., (2016)[19]who published a study included268 with NAFLD and 328 without NAFLD, and 130 healthy normal-weight controls. Patients with NAFLD were had higher insulin levels and homeostasis model assessment of insulin resistance (HOMA-IR) values and lower whole-body insulin sensitivity index (WBISI) than those without NAFLD**.**

In the current study TG, TC, LDL, VLDL were significantly higher, while HDL was significantly lower in group I when compared to group II ($p=0.049$, 0.021, 0.016, 0.034 and 0.040 respectively).

This finding was supported by observation of many authors showed that, A pattern of atherogenic dyslipidemia characterized by high concentrations of plasma TG, low HDL cholesterol and small dense LDL particles is frequently observed in NAFLD patients , which is related to increased insulin-induced hepatic lipid synthesis and is associated with disease severity **[20].**

Also **Cai et al., (2018)[21**] found those with NAFLD were more likely to had higher levels of TG, TC, LDL and lower levels of HDL-C($P = 0. 00$) which in accordance with our results**.**

Similarly **Ozhan et al., (2010)[14]**found that triglyceride was significantly higher and high-density lipoprotein was significantly lower in NAFLD group.

This study showed that, group I had statistically significant higher frequency of H. pylori Ag in stool, H. pylori Ab in blood and higher incidence of Ag positive-Ab positive when compared to group II ($p=0.001$).

A study by **Polyzos and his colleagues**study recruiting 28 NAFLD cases and 25 controls, the authors found that a higher percentage of NAFLD patients (23 out of 25, 82.1%) was seropositive for anti-H. pylori IgG than control group (14 out of 25, 56%); p = 0.03, and demonstrated that H. pylori infection might contribute to NAFLD directly or indirectly via IR,. However, their study included a relatively small number of participants (28), and H. pylori seropositivity, which cannot distinguish between current and past infection, was used to detect H. pylori infections**[11].**

Also, **Mohammadifard et al., (2019)[17**] reported that, mean (±SD) of anti-H. Pylori IgG in NAFLD group (78.1 ± 9.9 IU/mL) was more than control group (51.7± 7.2 IU/mL); p = 0.03. Positive fecal H. pylori antigen test was also more frequent in NAFLD group compared to the control group (26 patients (40%) vs. 18 subjects (27.7%)), but the difference was not statistically significant (p = 0.13)**.**

In compliance with the current investigation, another investigation of 130 Japanese participants notified that the burden of NAFLD is noticeably higher in H. pylori-infected patients in comparison with non-infected candidates **[22].**

Data from 2051 participants who collected by **Cai et al., (2018)[21**] In the NAFLD risk group, the H. pylori infection rate among participants with NAFLD (34.16%) was slightly higher than that among participants without NAFLD (32.04%), although the difference was not significant (P = 0. 47) **.**

This study showed that, no statistical significant differences in US grades of NAFLD among H. pylori positive and negative patients.

This was in accordance with **Sumida et al., (2015)[23]**study found no relationship was observed between the levels of H. pylori-IgG status and the grades for steatosis**.**

Also, **Polyzos et al., (2012)[24]** reported there were no significant differences in steatosis grade, fibrosis stage, lobular or portal inflammation, or ballooning, when NAFLD patients were divided according to Hp IgG seropositivity or (13) C urea breath test positivity**.**

Similarly, **Kim et al., (2017)[22]**found that, Participants with H. pylori seropositivity were more likely to had higher total cholesterol, LDL-C, triglycerides, and lower levels of HDL-C than those without seropositivity**.**

Kang et al.,(2018)[13]found that, lipid panels were higher in subjects with positive H. pylori serology than without**.**

In our study showed that, Ordinal regression analysis was conducted for prediction of severity of NAFLD, using age, gender, BMI, smoking, diet, life style, IR, lipid profile, H.pylori Ag and Ab as covariates revealed that High BMI, IR, TC, TG, LDL, VLDL, low HDL was significantly associated with more severe grades of NAFLD in univariable analysis. However, after conducting multivariable analysis, using significant covariate in univariable analysis, revealed that only high BMI, IR, TC,TG, LDL, VLDL, low HDL were considered as independent risk factors for higher degree of NAFLD.

Similarly, a population-based historical cohort study in Japan showed that TG/HDL-C predicted the severity of NAFLD **[25]**

Abangah and his colleagues in their studyshowed that only BMI ($P < 0.001$), cholesterol ($p=0.06$) and TG ($P < 0.011$) among variables had statistically significant associations with severity of NAFLD diagnosed by ultrasonography grade (USG), and ordinal logistic regression model showed that BMI and AST were the best predictors **[26].**

Conclusion

The association between H. pylori infection and NAFLD has been controversial and our research found strong association despite our limitations. Our study was display a significant increase in MPV in patients with NAFLD. The burden of H. Pylori infection among NAFLD patients was noticeably high, in comparison with the healthy control group. Additionally, higher Insulin level and IR, TG, TC, LDL, VLDL, with low levels of HDL-C were more expected to have H. Pylori infection.

References

1. Clark, J. M. & Diehl, A. M. Nonalcoholic fatty liver disease: an underrecognized cause of cryptogenic cirrhosis. Jama. Vol. 289, pp. 3000-4, 2003.
2. Farrell, G. C., Wong, V. W. & Chitturi, S. NAFLD in Asia--as common and important as in the West. Nat Rev Gastroenterol Hepatol. Vol. 10,pp.307-18, 2013.
3. Correa, P. & Houghton, J. Carcinogenesis of Helicobacter pylori. Gastroenterology. Vol. 133, 659-72, 2007.
4. Cindoruk, M., Cirak, M. Y., Unal, S., Karakan, T., Erkan, G., Engin, D., et al. Identification of Helicobacter species by 16S rDNA PCR and sequence analysis in human liver samples from patients with various etiologies of benign liver diseases. Eur J Gastroenterol Hepatol. Vol. 20,pp.33-6, 2008.
5. Li, M., Shen, Z. & Li, Y. M. Potential role of Helicobacter pylori infection in nonalcoholic fatty liver disease. World J Gastroenterol. Vol. 19,pp.7024-31, 2013.
6. Tang, D. M. & Kumar, S. The Association Between Helicobacter pylori Infection and Nonalcoholic Fatty Liver Disease. Curr Gastroenterol Rep. Vol. 19,pp.5, 2017.
7. Fan, J. G., Jia, J. D., Li, Y. M., Wang, B. Y., Lu, L. G., Shi, J. P., et al. Guidelines for the diagnosis and management of nonalcoholic fatty liver disease: Update 2010: (Published in

Chinese on Chinese Journal of Hepatology 2010; 18: 163–166). Journal of digestive diseases. Vol. 12,pp.38-44, 2011.

8. Yilmaz, Y. NAFLD in the absence of metabolic syndrome: different epidemiology, pathogenetic mechanisms, risk factors for disease progression? Seminars in liver disease, Thieme Medical Publishers,pp. 014-021, 2012.

9. Younossi, Z. M., Koenig, A. B., Abdelatif, D., Fazel, Y., Henry, L. & Wymer, M. Global epidemiology of nonalcoholic fatty liver disease—Meta-analytic assessment of prevalence, incidence, and outcomes. Hepatology,pp. 64, 73-84, 2016.

10. Pellicano, R., Ribaldone, D. G., Fagoonee, S., Astegiano, M., Saracco, G. M. & Mégraud, F. A 2016 panorama of Helicobacter pylori infection: key messages for clinicians. Panminerva medica. Vol. 58,pp. 304-317, 2016.

11. Polyzos, S. A., Kountouras, J., Papatheodorou, A., Patsiaoura, K., Katsiki, E., Zafeiriadou, E., et al. Helicobacter pylori infection in patients with nonalcoholic fatty liver disease. Metabolism-Clinical and Experimental. Vol. 62,pp. 121-126, 2013.

12. Khalil, A. E.-H. E., Lashin, H. E., Metwally, M. M. & Rady, M. A Study of Helicobacter Pylori Infection in Patients with Non-Alcoholic Fatty Liver Disease. The Egyptian Journal of Hospital Medicine. Vol. 77,pp. 4855-4860, 2019.

13. Kang, S. J., Kim, H. J., Kim, D. & Ahmed, A. Association between cagA negative Helicobacter pylori status and nonalcoholic fatty liver disease among adults in the United States. PLOS ONE. Vol. 13,pp. e0202325, 2018.

14. Ozhan, H., Aydin, M., Yazici, M., Yazgan, O., Basar, C., Gungor, A., et al. Mean platelet volume in patients with non-alcoholic fatty liver disease. Platelets. Vol. 21,pp.29-32, 2010.

15. Almobarak, A. O., Barakat, S., Khalifa, M. H., Elhoweris, M. H., Elhassan, T. M. & Ahmed, M. H. Non alcoholic fatty liver disease (NAFLD) in a Sudanese population: What is the prevalence and risk factors? Arab Journal of Gastroenterology. Vol. 15,pp.12-15, 2014.

16. Okushin, K., Takahashi, Y., Yamamichi, N., Shimamoto, T., Enooku, K., Fujinaga, H., et al. Helicobacter pylori infection is not associated with fatty liver disease including non-alcoholic fatty liver disease: a large-scale cross-sectional study in Japan. BMC gastroenterology. Vol. 15, 25, 2015.

17. 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. Vol. 12, 168-172, 2019.

18. Marchesini, G., Brizi, M., Bianchi, G., Tomassetti, S., Bugianesi, E., Lenzi, M., et al. Nonalcoholic fatty liver disease: a feature of the metabolic syndrome. Diabetes. Vol. 50, 1844-1850, 2001.

19. Pacifico, L., Bonci, E., Andreoli, G. M., Di Martino, M., Gallozzi, A., De Luca, E., et al. The Impact of Nonalcoholic Fatty Liver Disease on Renal Function in Children with Overweight/Obesity. Int J Mol Sci. Vol. 17, 2016.

20. Corey, K. E. & Chalasani, N. Management of dyslipidemia as a cardiovascular risk factor in individuals with nonalcoholic fatty liver disease. Clinical Gastroenterology and Hepatology. Vol. 12,pp.1077-1084, 2014.

21. Cai, O., Huang, Z., Li, M., Zhang, C., Xi, F. & Tan, S. Association between Helicobacter pylori Infection and Nonalcoholic Fatty Liver Disease: A Single-Center Clinical Study, 2018.

22. Kim, T. J., Sinn, D. H., Min, Y. W., Son, H. J., Kim, J. J., Chang, Y., et al. A cohort study on Helicobacter pylori infection associated with nonalcoholic fatty liver disease. Journal of gastroenterology. Vol. 52,pp.1201-1210, 2017.

23. Sumida, Y., Kanemasa, K., Imai, S., Mori, K., Tanaka, S., Shimokobe, H., et al. Helicobacter pylori infection might have a potential role in hepatocyte ballooning in nonalcoholic fatty liver disease. Journal of gastroenterology. Vol. 50, pp. 996-1004, 2015.

24. Polyzos, S., Kountouras, J., Papatheodorou, A., Patsiaoura, K., Katsiki, E., Zafeiriadou, E., et al. Helicobacter pylori infection in patients with nonalcoholic fatty liver disease. Metabolism: clinical and experimental. Vol. 62, 2012.

25. Fukuda, Y., Hashimoto, Y., Hamaguchi, M., Fukuda, T., Nakamura, N., Ohbora, A., et al.

Triglycerides to high-density lipoprotein cholesterol ratio is an independent predictor of incident fatty liver; a population-based cohort study. Liver International. Vol. 36,pp.713-720, 2016.

26. Abangah, G., Yousefi, A., Asadollahi, R., Veisani, Y., Rahimifar, P. & Alizadeh, S. Correlation of body mass index and serum parameters with ultrasonographic grade of fatty change in non-alcoholic fatty liver disease. Iranian Red Crescent Medical Journal. Vol. 16, 2014.

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