REDVET - Revista electrónica de Veterinaria - ISSN 1695-7504
Vol 25, No. 2 (2024)
http://www.veterinaria.org
Article Received: Revised: Accepted:

Effect of Helicobacter pylori infection on TNF-α level in patients with diabetes and thyroid disorder

Methaq Hadi Lafta[1], Dr. Nowroz Dalirezh[2]

[1'2]Department of Microbiology, Faculty of Veterinay Medicine, Urmia University, Urmia, Iran E-mail:
[1]Mithaqiraqi@gmail.com, [2]n.delirezh@urmia.ac.ir

Abstract

The study was conducted on 88 influencers, 46 of whom were male, 42 samples from Haddith that were still present and still visible, diabetes, those infected with H. pylori, and uninfected persons, and their ages were between (35-70) years from (1/1/2023 - 1/1/2024) From Al-Diwaniyah General Hospital in Al-Diwaniyah Governorate, where numbers were collected from visitors and healthy people and were separated by the Central Croatian device, then the biochemical test was measured, which showed (TNF-α, FBS, Lipids profal).

The results of the current research showed a significant increase in the levels of (TNF-α, FBS.) in the blood serum of patients compared to the control group, with no significant differences in the levels of (T.G, Cholesterol, HDL,LDL) in both groups, and at its level, the probability of $P \leq 0.05$.

Key words / TNF-α, FBS, T.G, Cholesterol, HDL,LDL.

Introduction

Helicobacter pylori (H. pylori) infection has been increasingly recognized as a potential contributor to autoimmune thyroid diseases (AITD). Multiple studies have demonstrated a positive correlation between H. pylori infection and AITD, with particular emphasis on the role of cytotoxin-associated gene A (CagA) positive strains [(1,2)]. The presence of CagA-expressing H. pylori has been linked to more severe progression of AITD, suggesting a strain-specific impact on thyroid autoimmunity. This association is thought to be mediated through molecular mimicry, where bacterial antigens cross-react with thyroid tissues, and through the modulation of the host immune response. The resulting chronic inflammation and altered cytokine profiles may contribute to the initiation or exacerbation of thyroid autoimmunity, highlighting the complex interplay between infectious agents and endocrine disorders.

The prevalence of Helicobacter pylori (H. pylori) infection among individuals with diabetes has been a subject of significant research interest. A comprehensive meta-analysis has revealed a pooled prevalence of 54% in patients with diabetes [(3)]. This finding suggests that more than half of diabetic individuals may harbor H. pylori, highlighting the potential importance of this bacterial infection in the context of metabolic disorders. The prevalence rate in diabetic populations is notably higher than in the general population, raising questions about the bidirectional relationship between H. pylori infection and diabetes. Factors such as altered gastric motility, changes in glucose metabolism, and impaired immune responses in diabetic patients may contribute to this increased prevalence. Understanding the epidemiology of H. pylori infection in diabetic populations is crucial for developing targeted screening and management strategies.

The relationship between H. pylori infection and autoimmune disorders extends to type 1 diabetes mellitus (T1DM), where a significant association with thyroid autoimmunity has been observed. Research has revealed elevated levels of H. pylori IgG antibodies in T1DM patients, along with increased thyroid-stimulating hormone (TSH), anti-thyroglobulin, and anti-thyroid peroxidase antibodies [(4)] . This constellation of findings suggests a potential synergistic effect between H. pylori infection and the autoimmune processes underlying both T1DM and thyroid dysfunction. Moreover, a study focusing on pediatric populations with AITD found a high prevalence of H. pylori infection, which was associated with lower triiodothyronine (T3) levels [(3)] . These observations underscore the potential impact of H. pylori on thyroid hormone balance, particularly in younger individuals with developing immune systems.

In contrast to diabetic populations, individuals with thyroid disorders exhibit an even higher prevalence of H. pylori infection. Studies have reported strikingly high rates, with 93.3% prevalence in cases of Hashimoto's thyroiditis (HT) and 92.7% in Graves' disease (GD) [(1)]. These figures underscore a potentially significant relationship between H. pylori colonization and autoimmune thyroid conditions. The near-universal presence of H. pylori in these thyroid disorders suggests that the bacterium may play a role in the pathogenesis or progression of autoimmune thyroid diseases. The mechanisms underlying this high prevalence may involve shared genetic susceptibilities, environmental factors, or direct effects of H. pylori on thyroid function. These findings emphasize the need for healthcare providers to consider H. pylori infection when managing patients with autoimmune thyroid disorders.

The presence of H. pylori infection has been consistently associated with autoimmune thyroid diseases, particularly Hashimoto's thyroiditis and Graves' disease [(5)]. This significant positive relationship suggests that H. pylori may contribute to the development or exacerbation of thyroid autoimmunity. Several mechanisms have been proposed to explain this association, including molecular mimicry between H. pylori antigens and thyroid tissues, bystander

activation of autoreactive T cells, and modulation of the host immune response. The chronic inflammatory state induced by H. pylori infection may also play a role in breaking thyroid self-tolerance. Furthermore, the potential role of specific H. pylori virulence factors, such as CagA, in triggering or perpetuating thyroid autoimmunity warrants further investigation. Understanding these associations could lead to novel approaches in the prevention and treatment of autoimmune thyroid diseases.

Helicobacter pylori infection in individuals with diabetes mellitus has been associated with distinct alterations in cytokine profiles. Research has demonstrated significant changes in pro-inflammatory and anti-inflammatory cytokines, particularly interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and interleukin-10 (IL-10) [(1)]. These cytokine alterations are of particular concern in the diabetic population due to their potential impact on renal function. The heightened inflammatory state induced by H. pylori infection, as evidenced by elevated IL-6 and TNF-α levels, may contribute to the progression of diabetic nephropathy. Conversely, changes in anti-inflammatory cytokines like IL-10 may compromise the body's ability to regulate inflammatory responses. The complex interplay between H. pylori infection, diabetes, and cytokine dysregulation underscores the need for comprehensive management strategies that address both glycemic control and potential infectious complications.

The complex interplay between H. pylori infection, cytokine dysregulation, and the pathogenesis of diabetic and thyroid disorders highlights the need for a multifaceted approach to patient care. The chronic inflammatory state induced by H. pylori, characterized by elevated pro-inflammatory cytokines, may exacerbate existing metabolic and autoimmune conditions. In diabetic patients, the increased inflammatory burden could accelerate the progression of microvascular complications, particularly diabetic nephropathy. For individuals with autoimmune thyroid diseases, the H. pylori-induced cytokine alterations may perpetuate or amplify the autoimmune response against thyroid tissue. Furthermore, the local cytokine changes in the gastric mucosa underscore the importance of vigilant monitoring of H. pylori-infected patients for the development of gastric pathologies. These findings collectively emphasize the need for comprehensive management strategies that address not only the primary diabetic or thyroid disorder but also consider the potential impact of H. pylori infection on disease progression and treatment outcomes. The word lipid has been used for a long time to describe groups of heterogeneous chemicals that do not dissolve in water but do dissolve in organic solvents. Lipids are ionic or polar derivatives of hydrocarbons, and they are dimeric compounds because they contain ionic or polar groups that are water-loving and non-polar groups that are not water-loving and are not attracted to water [(6).]

It is an important nutritional component because it is rich in energy and contains fat-soluble vitamins and essential fatty acids. It has many benefits as it is considered a source of energy stored in adipose tissue [(7).] An increasing number of studies have analyzed the relationship between fats and various malignant tumors: breast cancer. , prostate cancer, ovarian cancer, hepatocellular carcinoma, lung cancer, pancreatic cancer, and bladder cancer [(8).] Through the high level (TNF-α, FBS), the current research aims to Effect of Helicobacter pylori infection on TNF-α level in patients with diabetes and thyroid disorder.

Collection of specimens

The study was conducted on 88 influencers, 46 of whom were male, 42 samples from Haddith that were still present and still visible, diabetes, those infected with H. pylori, and uninfected persons, and their ages were between (35-70) years from (1/1/2023 - 1/1/2024) From Al-Diwaniyah General Hospital in Al-Diwaniyah Governorate, where numbers were collected from visitors and healthy people and were separated by the Central Croatian device, then the biochemical test was measured, which showed (TNF-α, FBS, Lipids profal).

• **Estimating levels FBS in blood serum:**

The level of FBS in blood serum was measured by the Spanish company BioSystems, using an assay kit prepared using the enzymatic method followed by Young (2001) [(9)].

• **Estimating of serum cholesterol concentration**

The concentration of cholesterol in the blood serum was measured using a kit (kit) [(10).]

• **Estimating of Serum triglycerides Level**

Triglycerides are estimated after enzymatic hydrolysis by the enzyme lipase to release glycerol (alcohol) and free fatty acids. Glycerol is converted to glycerol-3-phosphate by the enzyme glycerol kinase (GK). Glycerol-3-phosphate is converted to dihydroxyacetone in the presence of the enzyme glycerol-3-phosphate oxidase (GPO). The quinonimine colored product is obtained in the presence of the enzyme Peroxidase (POD), which is measured spectrophotometrically at the wavelength of 500 nanometers [(11).]

• **Estimating of Serum HDL-C concentration**

LDL-C, VLDL and chylomicrons chylimmicrons (CM) were precipitated by addeding phosphotungstic acid (PTA) and magnesium chloride salt. ready-made cholesterol [(12).]

Statistical Analysis

The process of collecting data for the samples used for the study and analyzing them statistically was done using the SPSS system by extracting the arithmetic mean and standard deviation. The test was also used to analyze the differences between the group of patients and healthy people. Significant differences were chosen for these groups under a probability level of $P \leq 0.05$.

REDVET - Revista electrónica de Veterinaria - ISSN 1695-7504
Vol 25, No. 2 (2024)
http://www.veterinaria.org
Article Received: Revised: Accepted:

and Desiccation

Result

• Measuring the levels of biochemical variables for the samples under study:

Table No. (1) shows the mean ± standard deviation of the biochemical variables for the samples under study

The results showed a significant increase in both levels (TNF-α, FBS). In the blood serum of patients infected with H. pylori and diabetes compared with the control group, there was a significant decrease in the level of (T.G, Cholesterol, HDL,LDL) in both groups, as in the following figures.

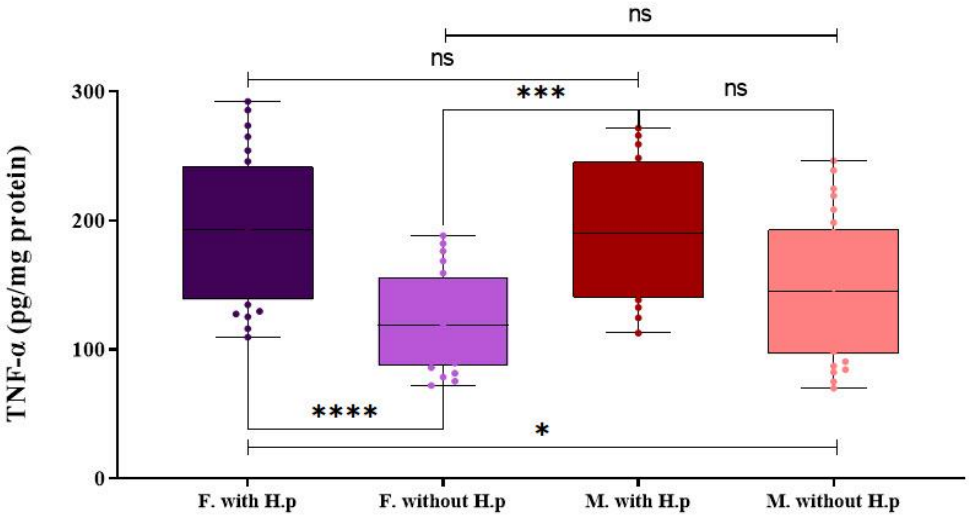

Figure (1) TNF-α in the blood sera of the samples under study

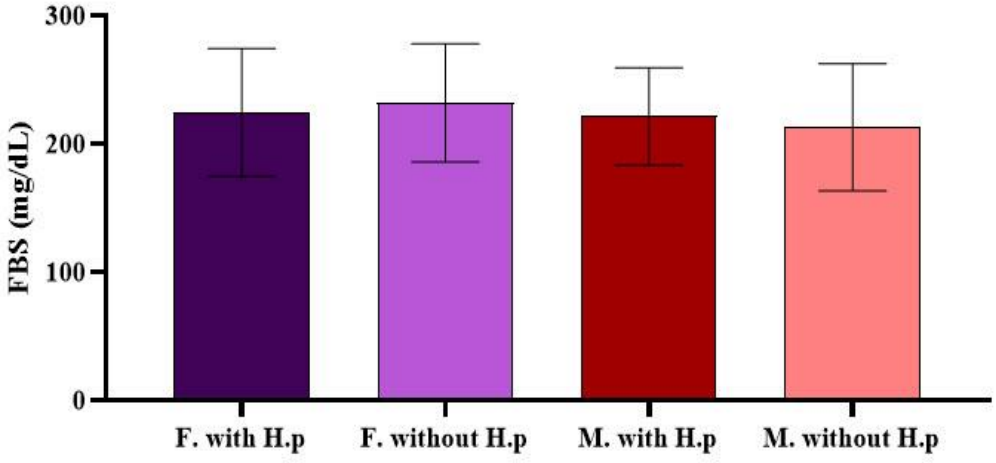

Figure (2) : FBS in the blood sera of the samples under study

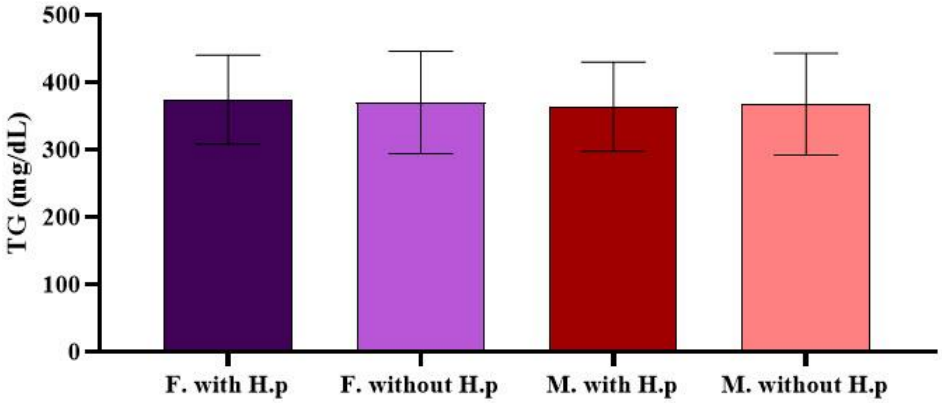

Figure (3) : T.G in the blood sera of the samples under study

REDVET - Revista electrónica de Veterinaria - ISSN 1695-7504
Vol 25, No. 2 (2024)
http://www.veterinaria.org
Article Received: Revised: Accepted:

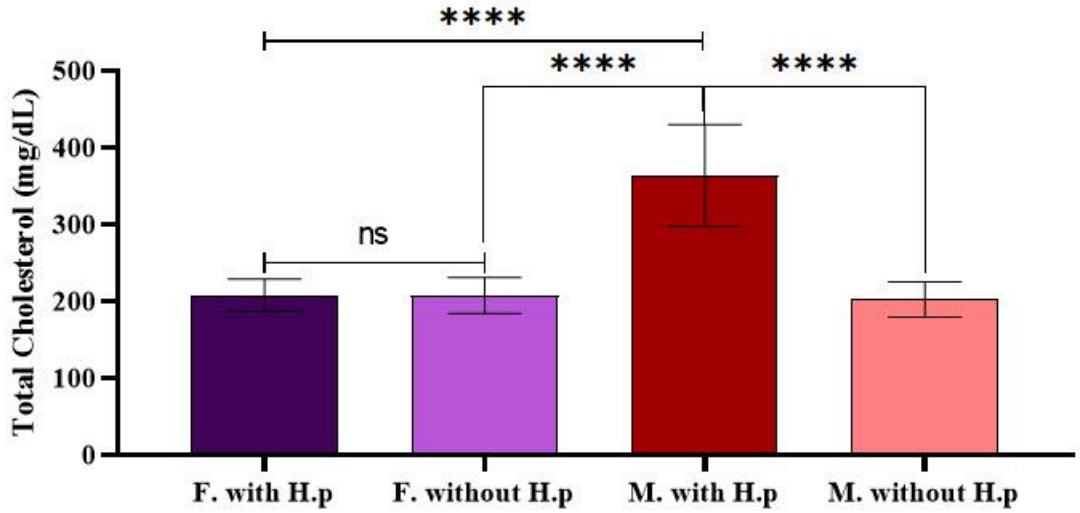

Figure (4) : Cholesterol in the blood sera of the samples under study

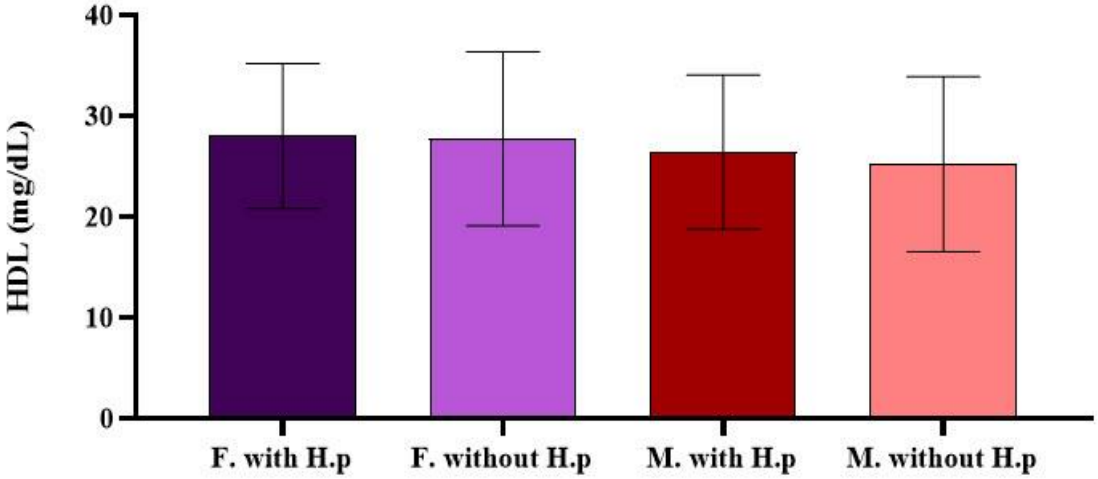

Figure (5) : HDL in the blood sera of the samples under study

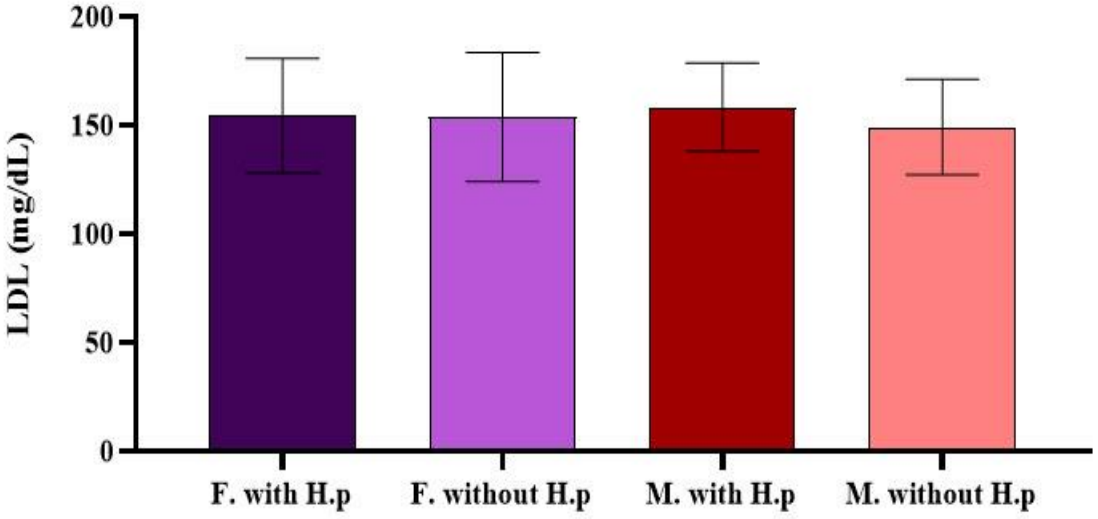

Figure (6) : LDL in the blood sera of the samples under study

REDVET - Revista electrónica de Veterinaria - ISSN 1695-7504
Vol 25, No. 2 (2024)
http://www.veterinaria.org
Article Received: Revised: Accepted:

Desiccation

The present investigation reveals a substantial augmentation in the circulating levels of the pro-inflammatory cytokines tumor necrosis factor-alpha (TNF-α) among individuals harboring Helicobacter pylori infection in comparison to uninfected controls. This elevated pro-inflammatory milieu was consistently observed across both male and female participants, underscoring a robust association between H. pylori infection and a systemic inflammatory response. These findings contribute to the growing body of evidence implicating H. pylori as a potential instigator of chronic inflammation.

The marked elevation of (TNF-α) observed in H. pylori-positive individuals is consistent with the established paradigm that chronic H. pylori infection triggers a persistent inflammatory response within the gastric mucosa. These pro-inflammatory cytokines, as pivotal mediators of inflammation, have been extensively implicated in the pathogenesis of a spectrum of gastrointestinal disorders, including peptic ulcer disease and gastric adenocarcinoma, both of which are well-documented sequelae of chronic H. pylori infection. Our findings thus corroborate the notion that H. pylori-induced inflammation extends beyond the gastric mucosa to elicit a systemic inflammatory response. The observed positive association between H. pylori infection and elevated levels of IL-1β and TNF-α is corroborated by a substantial body of literature. Several studies have consistently reported increased circulating levels of these pro-inflammatory cytokines in individuals harboring H. pylori [13,14,15]. These findings collectively support the notion of a systemic inflammatory response triggered by H. pylori infection. It is noteworthy, however, that a subset of studies, exemplified by some stadies, have failed to detect a significant association between H. pylori status and cytokine levels [16,17].

Analyzing metabolic parameters and thyroid function tests in the context of H. pylori infection has yielded intriguing insights. Within the scope of our study, an intriguing trend was observed where fasting blood sugar (FBS) levels were elevated in participants with H. pylori infection compared to those without. However, it is critical to note that these differences did not reach statistical significance. This finding suggests that while there may be a tendency for higher FBS in the presence of H. pylori, the effect is not pronounced enough to conclude a definitive impact of the infection on glycemic control.

The lack of significant differences in FBS levels aligns with the complex and sometimes contradictory findings in existing literature regarding the role of H. pylori in glucose metabolism. Some studies have proposed that H. pylori infection may contribute to insulin resistance and, consequently, elevated blood sugar levels. However, the mechanisms underlying this association are not fully understood, and the relationship appears to be influenced by multiple factors, including the host's immune response, genetic predispositions, and environmental influences.

Comparing our findings to those of other studies reveals a heterogeneous landscape. Research such as Eslami et al., 2017 has indicated a stronger correlation between H. pylori infection and increased FBS levels, suggesting a potential contributory role of the infection in the development of insulin resistance or type 2 diabetes [18]. On the other hand, several stadies have found no significant association, which is more in line with our results [19,20,21]. The variation in these findings may be attributable to differences in study design, population demographics, the criteria for defining H. pylori infection, and the methods used to assess FBS.

Our study's investigation into lipid profile parameters with H. pylori infection status and gender revealed several key points. Triglyceride levels did not differ significantly between males and females, nor did they vary with H. pylori infection status. Total cholesterol levels were also consistent across all groups, suggesting no impact from either H. pylori infection or gender. Similarly, HDL cholesterol levels showed no clear variation due to infection status or between genders. However, a trend toward higher LDL cholesterol levels was observed in individuals with H. pylori infection when compared to non-infected individuals, irrespective of gender. This trend necessitates further statistical evaluation to determine its significance.

The absence of significant differences in triglycerides, total cholesterol, and HDL cholesterol levels aligns with some scientific studies that have found limited or no association between H. pylori infection and these lipid profile parameters. The observed trend towards higher LDL cholesterol levels in infected individuals may suggest a possible link between H. pylori infection and lipid metabolism. This is consistent with the hypothesis that chronic infections like H. pylori could contribute to a pro-inflammatory state, potentially influencing lipid metabolism and the distribution of cholesterol fractions.

If further analysis confirms the trend in LDL cholesterol levels, it could imply that H. pylori infection might play a role in the pathophysiological mechanisms of chronic inflammation and its subsequent impact on cardiovascular health. Chronic inflammation is known to affect lipid metabolism, and an increase in LDL cholesterol is considered a risk factor for the development of atherosclerosis. The potential influence of H. pylori on LDL cholesterol could, therefore, be of significance in understanding the broader implications of chronic infections on lipid profiles and cardiovascular risk.

The findings of this study appear to be in line with research such as that by several stadies, who reported no significant changes in triglycerides and total cholesterol levels with H. pylori infection [22,23,24]. However, our observations of a trend in LDL cholesterol differ from some studies, which found no association between LDL levels and H. pylori status [25,26] . On the contrary, several studies have identified a potential link between H. pylori infection and elevated LDL cholesterol, supporting the hypothesis that H. pylori may contribute to dyslipidemia and its related conditions [27,28].

These discrepancies underscore the need for further research to clarify the relationship between H. pylori infection and lipid metabolism, considering factors such as the duration of infection, bacterial strain virulence, and host factors like genetics and lifestyle.

References

1-Abdollahi, H., Shams, S., Zahedi, M. J., Moghadam, S. D., Hayatbakhsh, M. M., & Jafarzadeh, A. (2011). IL-10, TNF-α and IFN-γ levels in serum and stomach mucosa of Helicobacter pylori-infected patients. Iranian Journal of Allergy, Asthma and Immunology, 267-271.

2- Abdu, A., Cheneke, W., Adem, M., Belete, R., & Getachew, A. (2020). Dyslipidemia and associated factors among patients suspected to have Helicobacter pylori infection at Jimma University Medical Center, Jimma, Ethiopia. International journal of general medicine, 311-321.

3- Dore, M. P., Bilotta, M., Malaty, H. M., Pacifico, A., Maioli, M., Graham, D. Y., & Realdi, G. (2000). Diabetes mellitus and Helicobacter pylori infection. Nutrition, 16(6), 407-410.

4- Eslami, O., Shahraki, M., Shahraki, T., & Ansari, H. (2017). Association of Helicobacter pylori infection with metabolic parameters and dietary habits among medical undergraduate students in southeastern of Iran. Journal of Research in Medical Sciences, 22(1), 12.

5- Ghazvini, K., Yamaoka, Y., Karbalaei, M., & Keikha, M. (2022). Extragastric infection of Helicobacter pylori and alopecia areata: a systematic review and meta-analysis. Reviews and Research in Medical Microbiology, 33(1), e114-e118.

6- Al-Tamery .y.,and Mahmood A.A, (2006) : The Influence of Iraqi Mothers Socioeconomic status on their Milk – lipid Content . .E.J Clin Nutr , 60 : pp.1400 – 1405 .

7- Sun, J., Rijpkema, S. J., Luan, J., Zhang, S., & Wilson, D. A. (2021). Generating biomembrane-like local curvature in polymersomes via dynamic polymer insertion. Nature communications, 12(1), 1-10.

8-Tamery .y. and Mohammd A.A. (2008) : *Lipid Compon Ents and Fatty acid Composition of Iraqi subjects who Smoke and Cosume dairy products* . Nurt , Metab , Cardiovase Dis ., 14:94-96.

9- Young, D. S., & Friedman, R. B. (2001). Effects of disease on clinical laboratory tests (Vol. 1). Amer Assn for Clinical Chemistry.2001.

10- Tietz,N. W. (1999). Textbook of clinical chemistry. 3rded. C.A.Burtis, E.R.Ashwood,W.B.Saunders. pp: 819-861,1245-1250.

11- Burtis,C. A. and Ashwood,E. R. (1999). Teitz Text Book of Clinical Chemistry, 3rded.,W.B.Saunders Company,London,UK., pp: 840-843.

12- MedCalc Statistical Software version 16.4.3 (MedCalc Software bvba, Ostend, Belgium; https://www.medcalc.org; 2016)" IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM.

13- Hamajima, N., Shibata, A., Katsuda, N., Matsuo, K., Ito, H., Saito, T., . . . Tominaga, S. (2003). Subjects with TNF-A-857TT and-1031TT genotypes showed the highest Helicobacter pylori seropositive rate compared with those with other genotypes. Gastric Cancer, 6, 230-236.

14- Outlioua, A., Badre, W., Desterke, C., Echarki, Z., El Hammani, N., Rabhi, M., . . . Khalil, A. (2020). Gastric IL-1β, IL-8, and IL-17A expression in Moroccan patients infected with Helicobacter pylori may be a predictive signature of severe pathological stages. *Cytokine, 126*, 154893.

15- Pasha, H. F., Tantawy, E. A., Radwan, M. I., Hagrass, H. A., Al-Monem, A., & AL-Karamany, A. S. (2020). Influence of Cytokine Gene Polymorphisms on the Risk of Gastric Disorders in H. pylori Infected Patients. *Afro-Egyptian Journal of Infectious and Endemic Diseases, 10*(4), 397-406.

16- Abdollahi, H., Shams, S., Zahedi, M. J., Moghadam, S. D., Hayatbakhsh, M. M., & Jafarzadeh, A. (2011). IL-10, TNF-α and IFN-γ levels in serum and stomach mucosa of Helicobacter pylori-infected patients. *Iranian Journal of Allergy, Asthma and Immunology*, 267-271.

17- Zhao, Y., Wang, J.-W., Tanaka, T., Hosono, A., Ando, R., Tokudome, S., . . . Achwan, E. W. A. (2013). Association between TNF-α and IL-1β genotypes vs Helicobacter pylori infection in Indonesia. *World journal of gastroenterology: WJG, 19*(46), 8758.

18- Eslami, O., Shahraki, M., Shahraki, T., & Ansari, H. (2017). Association of Helicobacter pylori infection with metabolic parameters and dietary habits among medical undergraduate students in southeastern of Iran. *Journal of Research in Medical Sciences, 22*(1), 12.

19- Dore, M. P., Bilotta, M., Malaty, H. M., Pacifico, A., Maioli, M., Graham, D. Y., & Realdi, G. (2000). Diabetes mellitus and Helicobacter pylori infection. *Nutrition, 16*(6), 407-410.

20- Jeon, C. Y., Haan, M. N., Cheng, C., Clayton, E. R., Mayeda, E. R., Miller, J. W., & Aiello, A. E. (2012). Helicobacter pylori infection is associated with an increased rate of diabetes. *Diabetes care, 35*(3), 520-525.

21- Mansori, K., Moradi, Y., Naderpour, S., Rashti, R., Moghaddam, A. B., Saed, L., & Mohammadi, H. (2020). Helicobacter pylori infection as a risk factor for diabetes: a meta-analysis of case-control studies. *BMC gastroenterology, 20*, 1-14.

22- Izhari, M. A., Al Mutawa, O. A., Mahzari, A., Alotaibi, E. A., Almashary, M. A., Alshahrani, J. A., . . . AlGarni, A. K. A. (2023). Helicobacter pylori (H. pylori) infection-associated dyslipidemia in the Asir region of Saudi Arabia. *Life, 13*(11), 2206.

23-Ozturk, S., Dursun, M. A., Yildirim, T., Sargin, F., Sargin, Z. G., & Ozan, Z. T. (2024). Traditional and nontraditional lipid parameters in Helicobacter pylori infection. *Biomarkers in Medicine*(0).

24-Sung, K. C., Rhee, E. J., Ryu, S. H., & Beck, S.-H. (2005). Prevalence of Helicobacter pylori infection and its association with cardiovascular risk factors in Korean adults. *International journal of cardiology, 102*(3), 411-417.

25- Kim, H.-L., Jeon, H. H., Park, I. Y., Choi, J. M., Kang, J. S., & Min, K.-W. (2011). Helicobacter pylori infection is associated with elevated low density lipoprotein cholesterol levels in elderly Koreans. *Journal of Korean medical science, 26*(5), 654.

26-Tali, L. D. N., Faujo, G. F. N., Konang, J. L. N., Dzoyem, J. P., & Kouitcheu, L. B. M. (2022). Relationship between active Helicobacter pylori infection and risk factors of cardiovascular diseases, a cross-sectional hospital-based study in a Sub-Saharan setting. *BMC Infectious Diseases, 22*(1), 731.

27-Abdu, A., Cheneke, W., Adem, M., Belete, R., & Getachew, A. (2020). Dyslipidemia and associated factors among patients suspected to have Helicobacter pylori infection at Jimma University Medical Center, Jimma, Ethiopia. *International journal of general medicine*, 311-321.

28- Riad, M. (2021). Association of Helicobacter pylori infection with coronary artery disease: is it an independent risk factor? *The Egyptian Heart Journal, 73*, 1-6.