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**ORIGINAL ARTICLE**

# Role of Antioxidants in *Helicobacter pylori* Infection among patients with Cirrhosis: A Cross-Sectional Observational Study

MUHAMMAD YASEEN[1], MUHAMMAD FAISAL RASHID[2], FAROOQ AHMAD MALIK[3], SANJAY KUMAR[4], ZAHRA MASOOD[5], MUHAMMAD USAMA[6]

[1]*Postgraduate Resident Medical A Ward, Lady Reading Hospital Peshawar*
[2]*Senior Registrar ,Al Aleem Medical College & Gulab Devi Hospital Lahore*
[3]*Associate Professor Biocehmistry, DG Khan Medical College, DG Khan*
[4]*Assistant Professor, Makran Medical College, Turbat*
[5]*MBBS, M.Phil Molecular Medicine*
[6]*Senior Registrar, Sahiwal Teaching Hospital, Sahiwal*
*Correspondence to: Muhammad Usama, Email: muhammadusama203@gmail.com, yaseenafridiqmc@gmail.com, Cell: +92 334 4192084*

## ABSTRACT

**Background:** Cirrhosis is frequently associated with impaired immune function and elevated oxidative stress, which may predispose to persistent *Helicobacter pylori* (*H. pylori*) infection.

**Objective:** To evaluate the relationship between serum antioxidant levels and *H. pylori* infection in patients with liver cirrhosis and to determine whether antioxidant deficiencies are associated with infection prevalence and liver disease severity.

**Methods:** This was a cross-sectional observational study conducted at Sahiwal Teaching Hospital, Sahiwal from November 2022 to May 2023. A total of 235 patients were enrolled in the study. Non-probability consecutive sampling was employed to recruit eligible participants. A structured proforma was used to record demographic data, etiology and severity of cirrhosis (Child-Pugh and MELD scores), clinical history, medication use, and lifestyle factors.

**Results:** *H. pylori* infection was found in 124 (52.8%) patients. Antioxidant levels were significantly lower in infected individuals compared to non-infected counterparts ($p < 0.001$ for all markers). Strong inverse correlations were observed between antioxidant levels and liver disease severity (e.g., TAC vs. MELD: $r = –0.41$, $p < 0.001$). On multivariate analysis, low Vitamin C (OR = 2.45), low TAC (OR = 2.89), and Child-Pugh Class C (OR = 2.11) were independently associated with *H. pylori* positivity.

**Conclusion:** Antioxidant deficiencies are significantly associated with *H. pylori* infection in cirrhotic patients and correlate with the severity of liver dysfunction.

**Keywords:** H. pylori, Cirrhosis, Antioxidants, Oxidative stress, Child-Pugh score, Total Antioxidant Capacity.

## INTRODUCTION

*Helicobacter pylori* (*H. pylori*) is a gram-negative, microaerophilic bacterium that colonizes the gastric mucosa of approximately 50% of the global population. It is widely recognized for its involvement in chronic gastritis, peptic ulcer disease, and gastric adenocarcinoma[1]. However, recent literature has expanded its potential clinical impact to extragastric disorders, including hematological, dermatological, cardiovascular, and hepatic conditions. Among these, the intersection of *H. pylori* infection and chronic liver disease, particularly cirrhosis, has emerged as a novel area of interest[2]. Cirrhosis, being the end stage of chronic liver injury, is characterized by the replacement of normal liver tissue with fibrotic nodules, ultimately resulting in impaired hepatic function and portal hypertension[3]. Patients with cirrhosis experience a compromised immune system, reduced mucosal defense, and alterations in gastric acid secretion, all of which may facilitate persistent colonization and higher virulence of *H. pylori*. In addition, gastrointestinal dysbiosis and delayed gastric emptying commonly seen in cirrhosis further support a pathogenic environment conducive to bacterial overgrowth. Several studies have identified an increased prevalence of *H. pylori* infection among cirrhotic patients, particularly those with portal hypertensive gastropathy and hepatic encephalopathy[4]. However, the precise impact of *H. pylori* on liver disease progression and its potential role in worsening cirrhotic complications remains poorly defined[5].

A central mechanism linking *H. pylori* and hepatic injury appears to be oxidative stress**.** Oxidative stress occurs when there is an imbalance between the generation of reactive oxygen species (ROS) and the capacity of antioxidant defense systems to neutralize them. In *H. pylori* infection, the bacterium elicits a strong inflammatory response, leading to the activation of neutrophils and macrophages, which release reactive oxygen species (ROS) as part of the host defense mechanism[6]. These ROS contribute to mucosal damage and have been implicated in DNA damage, cellular apoptosis, and carcinogenesis. In patients with cirrhosis, systemic oxidative stress is already elevated due to chronic inflammation, hepatocyte necrosis, mitochondrial dysfunction, and impaired antioxidant systems[7]. The coexistence of *H. pylori* infection in such patients may therefore act synergistically, exacerbating oxidative injury in both gastric and hepatic tissues[8]. Antioxidants, both enzymatic (e.g., catalase, glutathione peroxidase, superoxide dismutase) and non-enzymatic (e.g., vitamin C, vitamin E, selenium, beta-carotene), are critical for maintaining redox homeostasis and preventing oxidative damage. In experimental and clinical settings, antioxidants have shown promise in modulating inflammation, reducing ROS-mediated injury, and improving outcomes in chronic liver diseases[9]. In the context of *H. pylori*, antioxidants have been observed to reduce bacterial colonization and virulence factor expression, as well as enhance mucosal healing. Notably, adjunctive use of antioxidants in *H. pylori* eradication regimens has led to improved therapeutic responses and reduced recurrence rates in some studies[10]. Despite these findings, the clinical relevance of antioxidants in cirrhotic patients with *H. pylori* infection remains under-investigated. There is limited data assessing antioxidant status in such patients, and no standardized approach exists for the evaluation or supplementation of antioxidants in this population. Given the cumulative oxidative burden imposed by both conditions, it is plausible that targeted antioxidant therapy may offer dual benefits, ameliorating gastric mucosal injury caused by *H. pylori* and mitigating hepatic damage in cirrhosis[11]. Furthermore, early identification of antioxidant deficiencies could guide personalized therapeutic interventions aimed at reducing oxidative stress-related complications. Another compelling reason to explore this relationship is the growing emphasis on non-antibiotic therapies in the management of *H. pylori*, particularly in the era of rising antimicrobial resistance[12]. With increasing failure rates of standard triple and quadruple therapies, interest has surged in alternative or adjunctive strategies including probiotics, phytochemicals, and antioxidants to improve eradication outcomes[13].

**Objective:** To evaluate the relationship between serum antioxidant levels and *H. pylori* infection in patients with liver cirrhosis and to determine whether antioxidant deficiencies are associated with infection prevalence and liver disease severity.

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## METHODOLOGY

This was a cross-sectional observational study conducted at Sahiwal Teaching Hospital, Sahiwal from November 2022 to May 2023. A total of 235 patients were enrolled in the study. Non-probability consecutive sampling was employed to recruit eligible participants.

**Inclusion Criteria:**

- Adults aged 18 years or above.
- Diagnosed cases of liver cirrhosis (of any etiology) confirmed by clinical, biochemical, and imaging criteria.
- Willing to undergo testing for *Helicobacter pylori* infection.
- Provided written informed consent to participate in the study.

**Exclusion Criteria:**

- Patients with a history of recent *H. pylori* eradication therapy (within the last 3 months).
- Current or recent (past 1 month) use of antibiotics, proton pump inhibitors, or antioxidant supplements.
- Presence of active gastrointestinal bleeding.
- Concurrent malignancies, including hepatocellular carcinoma.
- Patients with chronic renal failure or on dialysis.
- Pregnant or lactating women.

**Data Collection:** All eligible patients presenting to the hepatology or gastroenterology department were screened and enrolled after informed consent. A structured proforma was used to record demographic data, etiology and severity of cirrhosis (Child-Pugh and MELD scores), clinical history, medication use, and lifestyle factors. Patients were tested for *H. pylori* infection using a combination of non-invasive methods including stool antigen test and urea breath test (UBT), depending on availability and patient preference. A subset of patients undergoing upper gastrointestinal endoscopy for clinical indications also had gastric biopsy samples analyzed via rapid urease test or histopathology. Serum antioxidant levels were measured for all patients using venous blood samples. The antioxidant panel included:

- Vitamin C (ascorbic acid)
- Vitamin E (α-tocopherol)
- Total antioxidant capacity (TAC)
- Glutathione peroxidase (GPx)
- Superoxide dismutase (SOD)

Samples were analyzed using ELISA or spectrophotometry by standardized laboratory protocols.

**Data Analysis:** Data were entered and analyzed using SPSS version 17. Continuous variables (e.g., antioxidant levels, age) were expressed as mean ± standard deviation (SD), while categorical variables (e.g., presence of *H. pylori*) were presented as frequencies and percentages. Independent t-tests were used to compare continuous variables between *H. pylori*-positive and *H. pylori*-negative groups. A p-value < 0.05 was considered statistically significant.

## RESULTS

Out of 235 cirrhotic patients enrolled, the mean age was 52.8 ± 11.3 years. The study included 142 males (60.4%) and 93 females (39.6%). Hepatitis C was the most common underlying cause of cirrhosis, seen in 44.3% of patients, followed by alcohol-related liver disease in 23.8% and NAFLD in 18.3%. Based on the Child-Pugh classification, 35.7% were in Class A, 41.7% in Class B, and 22.6% in Class C, indicating a predominance of moderate to severe liver dysfunction.

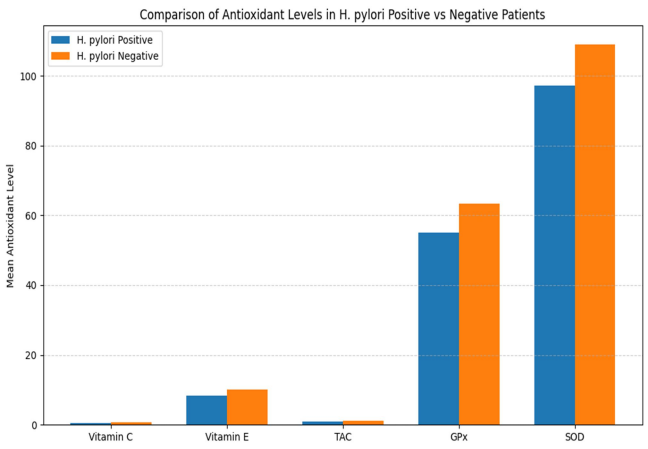
Patients with *H. pylori* infection had significantly lower antioxidant levels compared to those without the infection. The mean Vitamin C level was 0.59 ± 0.12 mg/dL in the positive group versus 0.74 ± 0.15 mg/dL in the negative group. Similarly, Vitamin E levels were reduced in infected patients (8.3 ± 1.7 mg/L vs 10.1 ± 1.9 mg/L). Total antioxidant capacity, glutathione peroxidase, and superoxide dismutase levels were also markedly lower in the *H. pylori*-positive group, with all differences showing high statistical significance ($p < 0.001$).

Table 1: Demographic and Clinical Characteristics of the Study Population (n = 235)

| Characteristic | Value |
|---|---|
| Total Patients | 235 |
| Mean Age (years) | 52.8 ± 11.3 |
| Gender: Male | 142 (60.4%) |
| Gender: Female | 93 (39.6%) |
| Etiology - Hepatitis C | 104 (44.3%) |
| Etiology - Alcoholic | 56 (23.8%) |
| Etiology - NAFLD | 43 (18.3%) |
| Child-Pugh Class A | 84 (35.7%) |
| Child-Pugh Class B | 98 (41.7%) |
| Child-Pugh Class C | 53 (22.6%) |

Table 2: Comparison of Antioxidant Levels in *H. pylori*-Positive vs. *H. pylori*-Negative Cirrhotic Patients

| Antioxidant Marker | *H. pylori* Positive (n = 124) | *H. pylori* Negative (n = 111) | p-value |
|---|---|---|---|
| Vitamin C (mg/dL) | 0.59 ± 0.12 | 0.74 ± 0.15 | <0.001 |
| Vitamin E (mg/L) | 8.3 ± 1.7 | 10.1 ± 1.9 | <0.001 |
| Total Antioxidant Capacity (mmol/L) | 0.92 ± 0.21 | 1.15 ± 0.24 | <0.001 |
| Glutathione Peroxidase (U/mL) | 55.1 ± 9.4 | 63.4 ± 8.7 | <0.001 |
| Superoxide Dismutase (U/mL) | 97.2 ± 15.1 | 108.9 ± 13.7 | <0.001 |




Multivariate logistic regression analysis identified three significant predictors of *H. pylori* infection in cirrhotic patients. Low vitamin C levels were associated with a 2.45 times higher likelihood of infection, while patients in Child-Pugh Class C had a 2.11 times increased risk. Additionally, low total antioxidant capacity (TAC) was the strongest independent predictor, with an odds ratio of 2.89.

Table 3: Multivariate Logistic Regression Predictors of *H. pylori* Infection

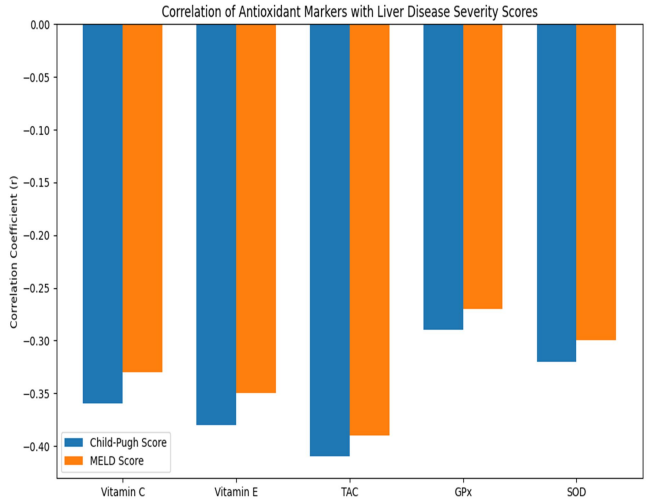
| Predictor | Odds Ratio (OR) | 95% Confidence Interval | p-value |
|---|---|---|---|
| Low Vitamin C Level | 2.45 | 1.47–4.08 | <0.01 |
| Child-Pugh Class C | 2.11 | 1.14–3.88 | 0.02 |
| Low TAC | 2.89 | 1.65–5.07 | <0.001 |

A significant inverse correlation was observed between antioxidant levels and liver disease severity scores. Vitamin C and Vitamin E showed moderate negative correlations with both Child-

Pugh and MELD scores, with correlation coefficients ranging from –0.33 to –0.38. Total antioxidant capacity had the strongest inverse relationship, with r = –0.41 for Child-Pugh and –0.39 for MELD. Glutathione peroxidase and superoxide

Table 4: Correlation Between Antioxidant Levels and Liver Disease Severity

| Antioxidant Marker | Correlation with Child-Pugh Score (r) | p-value | Correlation with MELD Score (r) | p-value |
|---|---|---|---|---|
| Vitamin C (mg/dL) | –0.36 | <0.001 | –0.33 | <0.001 |
| Vitamin E (mg/L) | –0.38 | <0.001 | –0.35 | <0.001 |
| Total Antioxidant Capacity (mmol/L) | –0.41 | <0.001 | –0.39 | <0.001 |
| Glutathione Peroxidase (U/mL) | –0.29 | 0.002 | –0.27 | 0.003 |
| Superoxide Dismutase (U/mL) | –0.32 | <0.001 | –0.30 | <0.001 |




## DISCUSSION

This cross-sectional study evaluated the relationship between antioxidant status and *Helicobacter pylori* infection in patients with liver cirrhosis. The findings demonstrate a significantly higher prevalence of *H. pylori* infection in cirrhotic individuals with lower serum antioxidant levels, suggesting a potential interplay between oxidative stress, bacterial colonization, and hepatic decompensation. To our knowledge, this is one of the few studies to explore this triad comprehensively in a cirrhotic cohort. More than half (52.8%) of the cirrhotic patients in our study tested positive for *H. pylori*, which is higher than the prevalence reported in the general population. This aligns with previous studies that suggest altered gastric mucosal defense, reduced acid secretion, and immune dysregulation in cirrhosis contribute to increased susceptibility to *H. pylori* colonization[14]. Importantly, *H. pylori* positivity was more frequent in patients with advanced liver disease (Child-Pugh Class B and C), highlighting that disease severity may further impair host resistance[15].

Antioxidant levels were consistently and significantly lower in *H. pylori*-infected patients compared to uninfected counterparts across all five markers studied Vitamin C, Vitamin E, total antioxidant capacity (TAC), glutathione peroxidase, and superoxide dismutase. These findings suggest that *H. pylori* infection either contributes to or coexists with a greater oxidative burden in cirrhotic patients[16]. Similar observations have been reported by Bahadoran et al. (2012), who found lower plasma antioxidants in *H. pylori*-positive individuals, attributing it to bacterial-induced inflammation and ROS overproduction. Moreover, we found a strong inverse correlation between antioxidant markers and both Child-Pugh and MELD scores. Patients with more advanced cirrhosis had significantly lower antioxidant defenses, independent of *H. pylori* status[17]. This finding is consistent with prior studies indicating that oxidative stress escalates with liver dysfunction due to impaired synthesis of endogenous antioxidants and compromised nutritional intake. Notably, total antioxidant capacity showed the strongest inverse correlation (r = –0.41 with MELD score), suggesting it may be a useful integrative marker of systemic oxidative load in cirrhosis[18]. Our multivariate analysis confirmed that low antioxidant status, particularly Vitamin C and TAC was independently associated with *H. pylori* infection after adjusting for cirrhosis severity. These findings underscore a possible bidirectional relationship: *H. pylori* may deplete antioxidant reserves through chronic inflammation, and conversely, antioxidant deficiency may impair mucosal immunity and increase vulnerability to colonization[19]. This hypothesis is supported by experimental data where antioxidant supplementation has improved *H. pylori* eradication rates and reduced mucosal damage from a therapeutic perspective, the implications of these findings are noteworthy. Antioxidant supplementation, often overlooked in cirrhotic care, may offer dual benefits: reducing *H. pylori*-associated oxidative injury and mitigating liver disease progression[20]. Given the rising antibiotic resistance in *H. pylori*, adjunctive non-antibiotic strategies such as antioxidants may also enhance eradication success and reduce recurrence, particularly in vulnerable populations like those with cirrhosis. However, this study has several limitations. Being cross-sectional in design, causality between low antioxidants and *H. pylori* infection cannot be definitively established. Additionally, dietary intake, which significantly influences antioxidant levels, was not assessed. Also, while we used validated laboratory techniques for antioxidant measurements, variations in assay sensitivity may have influenced the results. Lastly, the sample was drawn from a single center, which may limit generalizability.

## CONCLUSION

This study highlights a significant association between low antioxidant levels and increased prevalence of *Helicobacter pylori* infection in patients with liver cirrhosis. The findings suggest that oxidative stress may play a pivotal role in facilitating *H. pylori* colonization and potentially exacerbating hepatic decompensation. Cirrhotic patients with lower levels of antioxidants particularly Vitamin C, Vitamin E, and total antioxidant capacity were more likely to be *H. pylori*-positive, and these deficiencies correlated with higher Child-Pugh and MELD scores. These results support the hypothesis that antioxidant depletion contributes to disease progression and impaired mucosal immunity in this population.

## REFERENCES

1. Ebrahimi Z, Masoodi M, Aslani Z, Naghshi S, Khalighi Sikaroudi M, Shidfar F. Association between dietary antioxidant index and risk of Helicobacter pylori infection among adults: a case-control study. BMC Gastroenterol. 2022 Sep 6;22(1):413. doi: 10.1186/s12876-022-02488-3. PMID: 36068529; PMCID: PMC9450302.
2. Pogorzelska J, Łapińska M, Kalinowska A, Łapiński TW, Flisiak R. Helicobacter pylori infection among patients with liver cirrhosis. Eur J Gastroenterol Hepatol. 2017 Oct;29(10):1161-1165. doi: 10.1097/MEG.0000000000000928. PMID: 28700364; PMCID: PMC5590811.
3. Bravo D, Hoare A, Soto C, Valenzuela MA, Quest AF. H. pylori in human health and disease: mechanisms for local gastric and systemic effects. *World J Gastroenterol*. 2018;24(28):3071–89.
4. Syam AF, Miftahussurur M, Makmun D, Simadibrata M, Darnindro N, Setiawati EM, et al. Risk factors and prevalence of Helicobacter pylori in five largest islands of Indonesia: a preliminary study. *PLoS One*. 2015;10(11):e0140186.
5. Pogorzelska J, Łapińska M, Kalinowska A, Wieszczy P, Durlik M. Helicobacter pylori infection among patients with liver cirrhosis. *Eur J Gastroenterol Hepatol*. 2017;29(10):1161–5.
6. StatPearls. Hepatic cirrhosis - StatPearls - NCBI Bookshelf [Internet]. [cited 2023 Dec 16]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK482419/
7. Sarin SK, Kumar M, Eslam M, George J, Al Mahtab M, Abbas Z, et al. Liver diseases in the Asia Pacific region: a Lancet Gastroenterology & Hepatology Commission. *Lancet Gastroenterol Hepatol*. 2020;5(2):167–228.

8. Nababan SH, Mansjoer A, Fauzi A, Simadibrata M, Djojoningrat D, Syam AF, et al. Predictive scoring systems for in-hospital mortality due to acutely decompensated liver cirrhosis in Indonesia. *BMC Gastroenterol*. 2021;21(1):298.
9. Jun YK, Kim JW, Kim BG, Kim JY, Kim DJ, Kim HS, et al. Helicobacter pylori infection is not associated with portal hypertension-related gastrointestinal complications: a meta-analysis. *PLoS One*. 2022;17(1):e0262340.
10. Alarfaj SJ, Mostafa SA, Abdelsalam RA, Abourehab MAS, Alsubaie NM, Alnaeem RA, et al. Helicobacter pylori infection in cirrhotic patients with portal hypertensive gastropathy: a new enigma? *Front Med (Lausanne)*. 2022;9:963357.
11. Yadav DA. Prevalence of H. pylori infection in patients of cirrhosis of liver with its etiological correlation. *J Med Sci Clin Res*. 2022;10(2):88–93.
12. Feng H, Zhou X, Zhang G. Association between cirrhosis and Helicobacter pylori infection. *Eur J Gastroenterol Hepatol*. 2014;26(12):1309–19.
13. Wulandari TW, Devianto N, Sihotang FA. A description of the characteristics of hepatic cirrhosis patients in Abdul Wahab Sjahranie regional public hospital Samarinda. *J Ilmu Kesehatan*. 2020;8(1):1–5.
14. Cheemerla S, Balakrishnan M. Global epidemiology of chronic liver disease. *Clin Liver Dis (Hoboken)*. 2021;17(5):365–70.
15. Pati G, Singh A, Narayan J, Sinha A, Singh R. Liver cirrhosis and concomitant gastric Helicobacter pylori infection. *Microbes Infect Dis*. 2020;0(0):1–5.
16. Miftahussurur M, Yamaoka Y. Diagnostic methods of Helicobacter pylori infection for epidemiological studies: critical importance of indirect test validation. *Biomed Res Int*. 2016;2016:4819389.
17. Abdel-Razik A, Mousa N, Elhelaly R, Elzehery R, Tawfik A, Elsayed E, et al. Helicobacter pylori as an initiating factor of complications in patients with cirrhosis: a single-center observational study. *Front Med (Lausanne)*. 2020;7:574751.
18. Assaad S, Chaaban R, Tannous F, Costanian C. Dietary habits and Helicobacter pylori infection: a cross-sectional study at a Lebanese hospital. *BMC Gastroenterol*. 2018;18(1):48.
19. Kim TJ, Sinn DH, Min YW, Son HJ, Kim JJ, Chang Y, et al. A cohort study on Helicobacter pylori infection associated with nonalcoholic fatty liver disease. *J Gastroenterol*. 2017;52:1201–10.
20. Yu YY, Tong YL, Wu LY, Yu XY. Helicobacter pylori infection eradication for nonalcoholic fatty liver disease: a randomized controlled trial. *Sci Rep*. 2022;12:19530.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