ORIGINAL ARTICLE

Impact of *Helicobacter pylori* eradication therapy on quality of life and symptoms in osteoarthritis symptoms in infected patients: A nonblinded clinical trial

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Background: Osteoarthritis (OA) is a disease whose treatment is essential due to various complications, such as pain, inflammation, and disturbance in patients' quality of life (QOL). This study aimed to determine the effect of *Helicobacter pylori* eradication therapy on QOL and arthritis symptoms in patients with OA who are infected with *H. pylori.* **Materials and Methods:** In this clinical trial, 62 OA patients were categorized into two groups based on diagnostic tests: *H. pylori* positive and negative. The negative group received only standard OA treatment, while the positive group underwent eradication therapy in addition to standard treatment. Patients were assessed and compared before, 4 weeks, and 8 weeks after treatment using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), Visual Analog Scale (VAS), and European Quality of Life Questionnaire. Data were analyzed using the SPSS software. **Results:** Comparison of the two groups revealed a significant reduction in physical function, joint stiffness, pain, total WOMAC, and VAS scores in the *H. pylori* positive group over the study period ($P < 0.05$), whereas no significant changes were observed in the negative group ($P > 0.05$). QOL scores improved significantly in the eradicated group ($P < 0.05$). Significant improvements were seen between the eradicated and noneradicated subgroups in physical function, pain, total WOMAC, and VAS scores, with more significant improvements in the eradicated group ($P < 0.05$). After the intervention, self-care and QOL scores differed significantly between the groups, with the eradicated group showing better outcomes ($P < 0.05$). **Conclusion:** In OA patients with *H. pylori* infection, eradication therapy improves specific symptoms, pain, and QOL.

Key words: *Helicobacter pylori*, inflammation, osteoarthritis, pain, quality of life

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INTRODUCTION

Osteoarthritis (OA) is one of the most common forms of arthritis worldwide, especially among the geriatrics.[1] It is characterized by progressive cartilage matrix degradation, joint pain, loss of function, stiffness, chronic inflammation of the synovial lining, and loss of mobility.[2,3] All of these symptoms crucially impair quality of life (QOL), particularly in terms of physical activity and social functioning and lead to significant disability in daily living.[2,4] In addition, because of high morbidity, OA imposes heavy medical costs on affected individuals and the healthcare system of societies.[5] Despite extensive research into the pathogenesis of OA, its exact causes remain multifactorial. Recent studies have confirmed the involvement of immune cells (dendritic cells and macrophages) and pro-inflammatory cytokines such as interleukin-6 (IL-6), IL-1 β, nuclear factor kappa B (NF-κB) activation, tumor necrosis factor-alpha (TNF-α), and C-reactive protein can lead to inflammatory synovium/synovitis and have

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a critical role in the development and progression of OA.[6-8] Pathogens such as bacteria and viruses can trigger immunological responses and aggregate inflammation in OA patients.[9,10] Furthermore, molecular mimicry and immune system activation may lead to autoimmunity or heightened inflammatory responses in joint tissues. The translocation of bacterial antigens or products into the bloodstream can further stimulate the synovial membrane, resulting in synovitis and cartilage degradation, both of which are the characteristic features of OA.[11,12] In this regard, *Helicobacter pylori* is a high-prevalence spiral, flagellated, and Gram-negative microaerophilic bacillus.[13] *H. pylori* infection causes various gastric pathologies, such as gastritis and peptic ulcers, and chronic affection may cause gastric cancer. *H. pylori* infection has also been associated with several extragastric complications, anemia (lack of iron and B12), immune thrombocytopenic purpura, insulin resistance, cardiovascular diseases, and certain neurological disorders.[14,15] Recent studies have shown that eradicating *H. pylori* effectively reduces inflammatory factors and the course of some inflammatory and autoimmune diseases.[11,16]

Given the high prevalence of both *H. pylori* infection and OA and the scarcity of clinical studies examining their relationship, this study was conducted to investigate the impact of *H. pylori* eradication therapy on QOL and disease symptoms in OA patients infected with *H. pylori*.

MATERIALS AND METHODS

Study design, setting, and population

This study is a nonblinded nonrandomized clinical trial conducted among OA patients referred to the Imam Ali Clinic, Hajir Hospital, and Kashani Hospital in Shahrekord (South-east of Iran) from 2023 to 2024. Sixty-two patients were categorized into two groups (31 in each group) based on *H. pylori* status: positive and negative [Figure 1].

Inclusion and exclusion criteria

Age above 50 years, diagnosis of OA confirmed by radiographic findings, clinical examination, and a specialist physician's diagnosis, confirmation of *H. pylori* infection based on endoscopy, fecal antigen test, or serum antibody testing (for the experimental group), and consent to participate in the study were considered as inclusion criteria. Exclusion criteria included recent antibiotic use, the presence of immunodeficiency disorders, musculoskeletal abnormalities, previous fractures around the joint, surgical procedures on lower limb joints, active cancer, or other rheumatological diseases.

Sample size and sampling method

Based on the study by Honcharuk *et al*. in 2021, with a significance level of 5% (Z = 1.96) and a statistical power of 80% (*Z* = 0.84), a minimum standardized effect size of 0.8 was

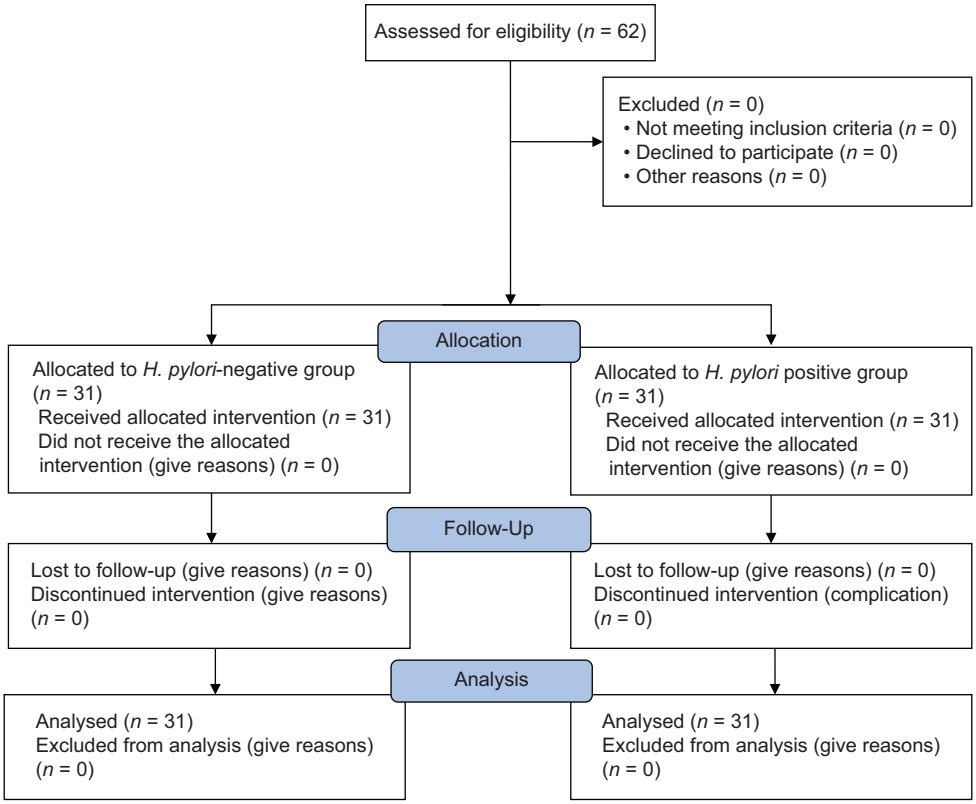

Figure 1: CONSORT flow diagram of the study population

required for the various dimensions of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and pain as the primary variables of interest. Thus, the sample size was determined to be 26 participants per group according to formula 1, considering a dropout rate of 20%, resulting in 30 participants per group.[17]

$$n = \binom{1+\varphi}{\varphi}\frac{(Z_1 - \alpha/2 + Z_{1-\beta})^2}{\Delta^2} + \frac{z_1^2 - \alpha/2}{2(1+\varphi)}$$

The sampling method in this study was nonrandom and based on convenience sampling.

Data collection methods and instruments

Data were collected using a demographic and clinical checklist (age, gender, marital status, level of education, smoking status, duration of illness, and medications) and the following validated questionnaires:

WOMAC: A 24-item questionnaire assessing pain (5 items), joint stiffness (2 items), and physical function (16 items) in OA patients. Each item is scored from 0 to 4, with a total score ranging from 0 to 96. The WOMAC questionnaire's validity and reliability ranged from 0.8 to 0.96.[18]

The Visual Analog Scale (VAS): A 10-cm line used to assess pain, with scores ranging from 0 (no pain) to 10 (worst pain). The reliability of the VAS has been reported as 0.97 based on the correlation coefficient (ICC) in osteoarthritic knee pain.[19]

European Quality of Life Questionnaire (EQ-5D): This includes a descriptive section with five single-item dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) scored on three levels (no problems, some problems, and severe problems) and a VAS ranging from 0 (worst imaginable health state) to 100 (best imaginable health state). The Persian version of the EQ-5D demonstrated good validity and reliability, with a coefficient of 0.8.[20]

Intervention and assigning groups

Once the study objectives were explained, the participants signed written informed consent. Participants were assigned to intervention and control groups based on their *H. pylori* infection status, as determined by endoscopy, fecal antigen testing, or serum antibody testing.

The control group (*H. pylori* negative) received standard OA treatment only. The intervention group (*H. pylori* positive) received standard OA treatment along with an *H. pylori* eradication regimen comprising levofloxacin (500 mg twice daily), amoxicillin (1 g twice daily), tinidazole (500 mg twice daily), and pantoprazole (40 mg twice daily) for 5 days (39). Medications were sourced from Obidi Pharmaceutical Company (levofloxacin and pantoprazole), Farabi Pharmaceutical Company (amoxicillin), and Tehran Darou Pharmaceutical Company (Tinidazole).

Four weeks after treatment initiation, *H. pylori* eradication was assessed using a fecal antigen test. Given the approximate 10% failure rate for *H. pylori* eradication with this regimen (39), the intervention's outcomes were statistically analyzed, categorizing patients into three subgroups based on the fecal antigen test results: *H. pylori*-negative, successfully eradicated *H. pylori* positive, and unsuccessful eradication *H. pylori* positive.

Outcomes assessed included the WOMAC score, VAS score, and EQ-5D score, which were evaluated before and 4 weeks posttreatment. To investigate the durability of the eradication effect on arthritis symptoms and pain in the intervention group, patients with confirmed eradication through fecal antigen testing were re-evaluated for pain intensity, WOMAC score, and QOL 8 weeks posttreatment. Any potential drug-related side effects from the *H. pylori* eradication regimen were monitored throughout the study.

Randomization

Patients were divided into intervention and control groups without randomization based on the presence of *H. pylori* infection, as determined by endoscopy, fecal antigen test, or serum antibody test results.

Blinding

This study was nonblinded, meaning the patients and researchers knew the intervention type. While the interventions were not blinded, outcome assessment was conducted by evaluators blinded to participants' group assignment to reduce detection bias.

Ethical considerations

This clinical trial was conducted after receiving the required approvals from the Research Deputy and the Biomedical Ethics Committee of Shahrekord University of Medical Sciences, with ID: IR.SKUMS.MED.REC.1402.076. The study protocol was also registered and approved under ID: IRCT20231216060428N1 on the Iranian Registry of Clinical Trials.

Statistical analysis

Results were analyzed using the SPSS software version 20 (IBM Corp. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY, USA: IBM Corp; 2011). A significance level of $P < 0.05$ was considered statistically significant. The continuous variables were reported as mean and standard deviation, whereas categorical variables were reported as frequencies and percentages.

Baseline continuous and categorical demographic and clinical variables were compared between groups using the independent *t*-tests and Chi-square or Fisher exact tests, respectively. To evaluate the changes in primary continuous variables within each group and between groups, repeated-measures analysis of variance (ANOVA) was employed. Mauchly's test of sphericity was conducted, and if the assumption was violated, multivariate ANOVA was used for the conclusions. In the repeated-measures ANOVA conducted to compare the primary response variables between the two groups, baseline values were adjusted as covariates whenever significant differences were observed between the groups at baseline.

The means of each primary variable at preintervention, 4 weeks postintervention, and 8 weeks postintervention were compared using independent samples *t*-test. The changes in ordinal qualitative variables were analyzed using the Friedman test, with pairwise comparisons at each time point conducted between groups using the Mann–Whitney *U*-test.

RESULTS

According to the results in Table 1, there was no significant difference between the two groups regarding baseline quantitative and qualitative variables ($P > 0.05$).

According to Table 2, the mean physical function score before the intervention showed no significant difference between the *H. pylori*-positive and negative groups. However, at 4 and 8 weeks postintervention, the physical function score was significantly lower in the positive group than in the negative group ($P < 0.05$*)

Repeated-measures ANOVA revealed a significant improvement in mean physical function scores over time within the *H. pylori*-positive group ($P < 0.001$*). In contrast, no significant change was observed in the *H. pylori*-negative group ($P = 0.294$). However, when comparing the two groups overall, the difference in physical function scores was not statistically significant ($P = 0.103$). However, after adjusting for the mean preintervention physical function score (as a confounding factor), there was a significant difference between the two groups ($P < 0.001$*).

The mean joint stiffness score showed no significant difference between the two groups. Repeated-measures ANOVA indicated a significant change in the mean joint stiffness score over the study period in the *H. pylori*-positive group ($P < 0.001$*). However, no significant change was observed in the negative group ($P = 0.094$). Overall, the two groups had no significant difference ($P = 0.476$). However, after adjusting for the preintervention joint stiffness score (as a confounding factor), there was a significant difference between the two groups ($P = 0.003$*).

The mean WOMAC score did not differ significantly between the two groups before the intervention. However, at 4 and 8 weeks postintervention, the score was significantly lower in the *H. pylori*-positive group than in the negative group ($P < 0.05$ and $P < 0.001$, respectively*).

Table 1: Comparison of quantitative and qualitative variables in *Helicobacter pylori* -positive and negative groups

Variable	*H. pylori* positive group (*n*=31), *n* (%)	*H. pylori* negative group (*n*=31), *n* (%)	*P*
Age (years), mean±SD	66.29±8.48	66.00±6.72	0.882*
Duration of illness (years), mean±SD	10.61±5.51	9.77±4.39	0.510*
BMI (kg/m^2), mean±SD	26.51±2.69	27.50±2.40	0.140*
Gender			
Male	14 (45.2)	17 (54.8)	1**
Female	14 (45.2)	17 (54.8)	
Education			
Illiterate	12 (38.7)	11 (35.5)	0.502**
Below diploma	6 (19.4)	8 (25.8)	
Diploma	8 (25.8)	4 (12.9)	
Bachelor	5 (16.1)	8 (25.8)	
NSAID use			
No	7 (22.6)	12 (38.7)	0.168**
Yes	24 (77.4)	19 (61.3)	
Smoking status			
No	23 (74.2)	28 (90.3)	0.096**
Yes	8 (25.8)	3 (9.7)	
Marital status			
Single	27 (87.1)	30 (96.8)	0.354**
Married	4 (12.9)	1 (3.2)	

*Independent *t*-test; **Chi-square or Fisher's exact test. BMI=Body mass index; NSAIDs=Nonsteroidal anti-inflammatory drugs; *H. pylori=Helicobacter pylori*; SD=Standard deviation

Table 2: Comparison of disease status in *Helicobacter pylori* -positive and negative groups at different time points

Variable	Time	*H. pylori* positive group (*n*=31), mean±SD	*H. pylori* negative group (*n*=31), mean±SD	*P* (*t*-test)
Physical function	Before intervention	34.03±10.23	30.19±10.89	0.158
	4 weeks postintervention	22.54±8.93	30.77±10.10	0.001*
	8 weeks postintervention	22.80±9.09	30.16±10.33	0.002*
P	Trend over time	<0.001	0.294	
Joint stiffness	Before intervention	3.93±1.31	3.51±1.72	0.287
	4 weeks postintervention	2.48±1.15	3.00±1.03	0.068
	8 weeks postintervention	2.51±1.17	3.03±1.04	0.074
P	Trend over time	<0.001	0.094	
Pain	Before intervention	10.25±2.78	8.19±3.43	0.012*
	4 weeks postintervention	6.00±2.04	8.00±2.75	0.002*
	8 weeks postintervention	6.12±2.17	7.96±2.76	0.005*
P	Trend over time	<0.001	0.500	
WOMAC score	Before intervention	48.35±13.64	41.09±15.21	0.084
	4 weeks postintervention	31.03±11.20	41.80±12.82	<0.001
	8 weeks postintervention	31.45±11.50	41.61±13.01	0.002*
P	Trend over time	<0.001	0.373	
VAS score	Before intervention	5.54±1.47	4.51±1.52	0.009*
	4 weeks postintervention	3.29±1.18	4.45±1.17	<0.001
	8 weeks postintervention	3.29±1.18	4.45±1.17	<0.001
P	Trend over time	<0.001	0.758	

*P<0.05 indicates significant differences. WOMAC=Western Ontario and McMaster Universities Osteoarthritis Index; VAS=Visual Analog Scale; *H. pylori=Helicobacter pylori*; SD=Standard deviation

Repeated-measures ANOVA showed that the mean WOMAC score significantly changed over time in the *H. pylori*-positive group ($P < 0.001$) but not in the negative group ($P = 0.373$). Overall, no significant difference was found between the two groups ($P = 0.133$). However, after controlling for the preintervention WOMAC score (as a confounding factor), there was a significant difference between the two groups ($P = 0.003$*).

The mean pain score (VAS) before the intervention was significantly higher in the *H. pylori*-positive group than in the negative group ($P < 0.05$*). However, at 4 and 8 weeks postintervention, the pain score was significantly lower in the positive group than in the negative group ($P < 0.001$*). Repeated-measures ANOVA showed that the mean VAS pain score significantly changed over time in the *H. pylori*-positive group ($P < 0.001$*). However, no significant change was observed in the negative group ($P = 0.758$). There was no significant difference between the two groups ($P = 0.162$). However, after adjusting for the preintervention pain score as a confounding variable, a statistically significant difference emerged between the two groups ($P < 0.001$*).

According to the results in Table 3, the mean scores for mobility, self-care, usual activities, pain/discomfort, and final component of the QOL significantly improved over time in the *H. pylori*-positive group ($P < 0.001$*), while no significant changes were observed in the *H. pylori*-negative group.

Based on Table 3, at 4 and 8 weeks postintervention, usual daily activities, and pain/discomfort, these scores were significantly lower in the *H. pylori*-positive group compared to the negative group ($P < 0.05$*).

Repeated-measures ANOVA showed that the mean score for this component significantly changed in the positive group during the study period ($P < 0.001$*). However, no significant change was observed in the negative group ($P = 0.071$). There was also no significant difference between the two groups ($P = 0.227$). However, after adjusting for the preintervention score (confounding factor), the score for this component was significantly higher in the positive group compared to the negative group ($P < 0.001$*).

Table 4 indicated that, there was a significant difference between the eradicated and noneradicated *H. pylori*-positive groups in terms of age and adverse effects variables ($P < 0.05$*). Moreover, according to the results presented in Table 4, there was no significant difference in baseline quantitative and qualitative variables between the noneradicated *H. pylori*-positive group and the *H. pylori*-negative group, except for age and duration of infection, which were higher in the noneradicated group ($P > 0.05$).

The mean physical performance score at baseline, 4 weeks, and 8 weeks after the intervention was significantly lower in the *H. pylori*-eradicated group compared to the noneradicated group ($P < 0.05$*). Repeated-measures ANOVA indicated that the mean physical performance score changed significantly during the study period in both

Table 3: Comparison of the mean scores of the quality of life questionnaire components between *Helicobacter pylori*-positive and *Helicobacter pylori*-negative groups at different time points

Variable	Time	*H. pylori*-positive group (*n*=31), mean±SD	*H. pylori*-negative group (*n*=31), mean±SD	*P* (Chi-square test)
Mobility	Before intervention	2.19±0.40	2.06±0.57	0.305
	4 weeks after intervention	1.77±0.42	2.00±0.44	0.047*
	8 weeks after intervention	1.77±0.42	2.00±0.44	0.047*
P (Friedman test)		<0.001	0.67	
Self-care	Before intervention	2.25±0.72	1.93±0.72	0.086
	4 weeks after intervention	1.38±0.49	1.74±0.51	0.009*
	8 weeks after intervention	1.38±0.49	1.74±0.51	0.009*
P (Friedman test)		<0.001	0.223	
Usual activities	Before intervention	2.29±0.58	1.93±0.72	0.040*
	4 weeks after intervention	1.45±0.50	1.83±0.63	0.012*
	8 weeks after intervention	1.41±0.50	1.83±0.63	0.007*
P (Friedman test)		<0.001	0.589	
Pain/discomfort	Before intervention	2.41±0.50	2.16±0.58	0.067
	4 weeks after intervention	1.67±0.54	2.09±0.30	<0.001*
	8 weeks after intervention	1.67±0.54	2.09±0.30	<0.001*
P (Friedman test)		<0.001	0.670	
Anxiety/depression	Before intervention	1.83±0.58	1.58±0.56	0.082
	4 weeks after intervention	1.38±0.49	1.48±0.56	0.474
	8 weeks after intervention	1.38±0.49	1.48±0.56	0.474
P (Friedman test)		<0.001	0.276	
The final component of the QOL	Before intervention	41.22±21.58	50.19±18.15	0.082
	4 weeks after intervention	67.09±16.23	54.80±17.74	0.006*
	8 weeks after intervention	67.09±16.23	54.80±17.74	0.006*
P (Friedman test)		<0.001*	0.071	

*P<0.05 indicates statistical significance. QOL=Quality of life, *H. pylori=Helicobacter pylori*; SD=Standard deviation

groups ($P < 0.001$*), and there was a significant difference between the two groups ($P = 0.007$*).

There was no significant difference in mean joint stiffness scores between the eradicated and noneradicated groups at the time points studied. However, repeated-measures ANOVA showed that the mean joint stiffness score changed significantly over time in both groups ($P < 0.001$), but there was no significant difference between the groups ($P = 0.195$).

At baseline, there was no significant difference in the mean pain score between the *H. pylori*-eradicated and noneradicated groups. However, at 4 and 8 weeks postintervention, the pain score was significantly lower in the eradicated group compared to the noneradicated group ($P < 0.05$*). Repeated measures ANOVA revealed a significant change in the mean pain score over time in both groups ($P < 0.001$*), and there was a significant difference between the two groups ($P = 0.014$*).

There was no significant difference in the total WOMAC score between the *H. pylori*-eradicated and noneradicated groups at baseline. However, at 4 and 8 weeks postintervention, the total WOMAC score was significantly lower in the eradicated group ($P < 0.05$*). Repeated measures ANOVA showed that the total WOMAC score changed significantly during the study period ($P < 0.001$), with a significant difference between the two groups ($P = 0.010$*).

At baseline, the mean VAS score was not significantly different between the eradicated and noneradicated groups. However, at 4 and 8 weeks postintervention, the VAS score was significantly lower in the eradicated group ($P < 0.05$*). Repeated-measures ANOVA indicated a significant improvement in VAS scores over time in both groups ($P < 0.001$*), with a significant difference between the groups ($P = 0.001$*).

Repeated-measures ANOVA indicated that the physical functioning score significantly decreased over the study period ($P < 0.001$*), but there was no significant difference between the two groups ($P = 0.198$). After controlling for preintervention time as a confounding factor, the physical functioning score still significantly decreased over the study period ($P < 0.001$*), with a significant difference between the groups ($P = 0.016$*).

Repeated-measures ANOVA showed a significant improvement in joint stiffness over the study period ($P < 0.001$*), with no significant difference between the groups ($P = 0.415$).

Table 4: Comparison of quantitative and qualitative basic variables of participants between noneradicated positive *Helicobacter pylori* subgroups groups and eradicated and negative *Helicobacter pylori* subgroups groups at study time points groups

Variable	Subgroups		*P*	Subgroups		*P*
	Noneradicated *H. pylori* group (*n*=4), *n* (%)	Eradicated *H. pylori* group (*n*=27), *n* (%)		*H. pylori* positive noneradicated group, *n* (%)	*H. pylori* negative group, *n* (%)	
Age (years), mean±SD	74.50±9.81	65.07±7.75	0.036*	4.50±9.81	66.00±7.72	0.030*
Duration of illness (years), mean±SD	26.75±3.02	26.48±2.71	0.858*	15.50±7.72	9.77±4.39	0.031*
BMI (kg/m^2), mean±SD	15.50±7.72	9.88±4.89	0.056*	26.75±3.02	27.50±2.40	0.572*
Gender						
Male	2 (50)	12 (44.4)	0.835**	14 (45.2)	0.857**	0.857**
Female	2 (50)	15 (55.6)		17 (54.8)	17 (54.8)	
Education						
Illiterate	3 (75)	9 (33.3)	0.277**	11 (35.5)	0.412**	0.412**
Below diploma	0	6 (22.2)		8 (25.8)	8 (25.8)	
Diploma	0	8 (29.6)		4 (12.9)	4 (12.9)	
Bachelor	1 (25)	4 (14.8)		8 (25.8)	8 (25.8)	
NSAID use						
No	1 (25)	6 (22.2)	0.901**	12 (38.7)	0.599**	0.599**
Yes	3 (75)	21 (77.8)		19 (61.3)	19 (61.3)	
Smoking status						
No	4 (100)	19 (70.4)	0.206**	28 (90.3)	0.521**	0.521**
Yes	0	8 (29.6)		3 (9.7)	3 (9.7)	
Marital status						
Single	3 (75)	24 (88.9)	0.439**	30 (96.8)	0.082**	0.082**
Married	1 (25)	3 (11.1)		1 (3.2)	1 (3.2)	
Adverse effects						
None	2 (50)	25 (92.6)	0.018**	2 (50)	-	-
Nausea	1 (25)	0		1 (25)	1 (25)	
Bloating	1 (25)	1 (3.7)		1 (25)	1 (25)	
Constipation	0	1 (3.7)				

*Resulted from independent samples *t*-test; **Resulted from Chi-square or Fisher exact tests. BMI: Body mass index; NSAIDs: Nonsteroidal anti-inflammatory drugs, SD: Standard deviation

Repeated-measures ANOVA indicated a significant decrease in the WOMAC score over the study period ($P < 0.001$*), with no significant difference between the groups ($P = 0.214$). After controlling for preintervention time, there was a significant decrease in the WOMAC score ($P < 0.001$*) and a significant difference between the groups ($P = 0.047$*).

Repeated-measures ANOVA indicated a significant improvement in pain scores over the study period ($P < 0.001$*), with no significant difference between the groups ($P = 0.378$).

Repeated-measures ANOVA showed a significant improvement in VAS scores in both groups over the study period ($P < 0.001$*), with no significant difference between the groups ($P = 0.061$).

Table 5 summarizes the mean and standard deviation of various health metrics measured before and after intervention for the noneradicated and eradicated groups of *H. pylori*-positive patients. Moreover, Table 5 summarizes the mean and standard deviation of various health-related outcomes for the noneradicated and negative *H. pylori* groups at different study times.

The self-care score did not differ significantly between the two groups before the intervention. However, after the intervention, a significant difference was observed at 4 and 8 weeks, with the noneradicated group exhibiting worse self-care status ($P = 0.008$*). There was a significant difference in mobility status between the two groups before the intervention ($P = 0.003$*).

There was no significant difference in the mean score of the last component of the QOL questionnaire between the two groups before the intervention ($P = 0.065$). However, significant differences were observed after 4 (0.020*) and 8 (0.028*) weeks, with the noneradicated group showing worse QOL status ($P < 0.05$*). Repeated-measures ANOVA indicated that the mean score of the last component of the QOL questionnaire significantly changed during the study period ($P < 0.001$), and there was a significant difference between the two groups ($P = 0.048$*).

Table 5: Comparison of disease status in non-eradicated positive *Helicobacter pylori* subgroups groups and eradicated and negative *Helicobacter pylori* subgroups groups at study time points

Variable	Time	Subgroups		*P*	Subgroups		*P*
		Noneradicated *H. pylori* group, mean±SD	Eradicated *H. pylori* group, mean±SD		Noneradicated *H. pylori* positive group, mean±SD	*H. pylori* negative group, mean±SD	
Physical performance	Before intervention	43.50±10.10	32.62±9.87	0.045*	43.50±10.10	30.19±19.89	0.025*
	4 weeks after intervention	34.50±10.10	20.77±7.70	0.003*	34.50±10.10	30.77±18.18	0.489
	8 weeks after intervention	34.50±10.10	21.98±7.07	0.004*	34.50±10.10	30.61±10.33	0.476
Joint stiffness	Before intervention	4.50±1.00	3.85±1.35	0.366	4.50±1.00	3.51±1.72	0.277
	4 weeks after intervention	3.25±0.95	2.14±1.37	0.157	3.25±0.95	3.00±1.03	0.650
	8 weeks after intervention	3.25±0.95	2.14±1.37	0.187	3.25±0.95	3.04±1.03	0.696
Pain	Before intervention	11.00±2.16	10.14±2.87	0.576	11.00±2.16	8.19±3.43	0.124
	4 weeks after intervention	8.50±1.73	5.62±1.84	0.007*	8.50±1.73	8.00±2.75	0.728
	8 weeks after intervention	8.50±1.73	5.62±1.84	0.017*	8.50±1.73	7.96±2.76	0.711
WOMAC score	Before intervention	59.00±11.13	46.77±13.43	0.095	59.00±11.13	41.90±15.21	0.038*
	4 weeks after intervention	46.25±10.50	28.77±9.55	0.002*	46.25±10.50	41.80±12.82	0.513
	8 weeks after intervention	46.25±10.50	29.05±10.25	0.004*	46.25±10.50	41.61±13.01	0.500
VAS score	Before intervention	6.75±2.06	5.37±1.33	0.082	6.75±2.06	4.51±1.52	0.012*
	4 weeks after intervention	5.25±1.50	3.00±0.83	0.054	5.25±1.50	4.45±1.17	0.224
	8 weeks after intervention	5.25±1.50	3.00±0.83	0.054	5.25±1.50	4.45±1.17	0.224

*Indicated statistically significant at P<0.05. WOMAC=Western Ontario and McMaster Universities Osteoarthritis Index; VAS=Visual Analog Scale; *H. pylori=Helicobacter pylori*; SD=Standard deviation

The last component of QOL in *H. pylori* eradicated and noneradicated groups were compared and found to have no significant differences before ($P = 0.272$) and significant differences after intervention ($P = 0.017$*).

The results of the Chi-square indicate significant differences in mobility status ($P = 0.032$*) and self-care ($P = 0.040$*) components before the intervention, while other variables showed no significant differences after 4 and 8 weeks.

Comparison of the last component of QOL in noneradicated and negative *H. pylori* groups revealed significant differences between groups at baseline ($P = 0.043$*). However, this relationship was not significant at 4 and 8 weeks of treatment ($P = 0.572$).

DISCUSSION

This study aimed to determine the effect of *H. pylori* eradication therapy on QOL and arthritis symptoms in patients with OA who are infected with *H. pylori*. The results of this study indicate a significant relationship between the eradication of *H. pylori* and enhancements in OA symptoms and overall QOL in these patients.

Patients diagnosed with *H. pylori* and receiving eradication treatment experienced significant improvements in physical function, joint stiffness, and pain, as demonstrated by decreases in WOMAC scores for physical function, joint stiffness, overall WOMAC scores, and VAS pain scores. These improvements were statistically significant, whereas no significant changes were observed in the *H. pylori*-negative group. These results confirm the bacteria's role in intensifying pain and disease symptoms.

A literature review found no study examining the relationship between *H. pylori* infection and OA symptoms. However, in line with our results, Düzenli *et al*. conducted a study in 2021 to assess the association between *H. pylori* infection, knee pain, and femoral cartilage thickness in adults. The thickness of the femoral articular cartilage was measured in patients with *H. pylori* infection and *H. pylori*-negative individuals. The study found that the thickness of the medial condyle of the right and left femur was thinner in patients with *H. pylori* infection compared to those without it, suggesting that *H. pylori* infection may affect femoral cartilage thickness and potentially increase the risk of cartilage degeneration, a critical factor in the development of OA. Another finding indicated a higher prevalence of knee pain in the *H. pylori*-positive group compared to the negative group.[21]

H. pylori infection activates inflammatory and immune processes that can lead to chronic infection, neoplasia progression, higher risk for autoimmune disease and extragastric manifestations.[22,23] *H. pylori* infection may induce systemic inflammation by increasing inflammatory cytokines such as NF-κB activation, TNF-α expression, IL-1, IL-6, IL-8, IL-17, IL-23, IL-1 β, and IL-1α, and these factors can significantly disrupt the bone and cartilage health.[24-26] It also aggregates the inflammatory environment by increasing monocyte chemoattractant protein-1, transforming growth factor-β, and causes neutrophil and macrophage activation and accumulation.[25] Systemic inflammation during *H. pylori*

infection occurs due to two main mechanisms. First, *H. pylori* triggers the release of pro-inflammatory mediators derived from epithelial cells, such as chemokines. Second, bacterial virulence factors can induce both specific and nonspecific immune responses, releasing various cytokine pathways.[27] The findings of this study support the growing evidence that systemic inflammation plays a significant role in the advancement of OA and that *H. pylori* infection may contribute to the incensement of inflammatory cytokines. By targeting and eradicating *H. pylori*, patients experience relief from gastrointestinal symptoms and a general reduction in inflammation, leading to improved management of OA symptoms. These discoveries are especially pertinent for OA patients who require long-term nonsteroidal anti-inflammatory drugs (NSAIDs) intake, as NSAIDs are known to worsen gastrointestinal disorders such as gastroduodenopathies in individuals with *H. pylori* infection.[17,28] Honcharuk *et al*. conducted a study on patients with OA who also had gastroduodenopathy associated with *H. pylori* infection and NSAID use in support of our findings. They observed higher levels of TNF-α in these patients compared to healthy individuals. Additionally, *H. pylori* eradication therapy was significantly associated with a reduction in TNF-α levels.[17] In a study by Mendez *et al*., it was also observed that antibiotic prophylaxis (ampicillin/neomycin) reduced or improved the outcomes of trauma-induced OA by reducing the inflammatory state in mice.[29]

Although our goal was to eradicate *H. pylori* to reduce OA symptoms, a study showed no association between *H. pylori* infection and the level of gastritis in OA patients who use sodium diclofenac.[30] On the other hand, an experimental study also reported that administration of *H. pylori* γ-glutamyl-transpeptidase (a bacterial virulence factor) in rats can effectively alleviate joint pain and CXCL1/IL-6 in levels of blood.[31] Despite these discrepancies with the results of our study, which may be due to differences in study objectives and design, it seems necessary to conduct more studies in this regard.

Although the impact of *H. pylori* eradication on the clinical course of OA has not yet been thoroughly studied, the efficacy of bacterial eradication in improving symptoms and outcomes of other inflammatory and autoimmune diseases has been reported in several studies. In the Zentilin *et al*. study, *H. pylori* eradication was associated with reduced disease activity, fewer swollen and painful joints, less morning stiffness, and decreased pain in patients with rheumatoid arthritis.[32] These findings regarding improving joint stiffness and pain in patients undergoing eradication therapy are similar to our results.

El-Hewala *et al*. also demonstrated that *H. pylori* eradication reduced the number of tender and swollen joints, disease activity, and pain severity in patients with rheumatoid arthritis,[33] which aligns with the findings of the present study.

The data from the QOL assessment shows a mixed result of improvement and decline based on specific factors and time points. For the self-care component, a significant decline was observed in the noneradicated *H. pylori* group after the intervention, indicating a worsening condition compared to the eradicated group. However, for other aspects, such as daily activities, pain/discomfort, and anxiety/depression, there were no significant differences between the groups at any time point. Notably, in the last component of the QOL questionnaire, significant improvements were recorded in the eradicated group at 4 and 8 weeks postintervention. In contrast, the noneradicated group showed a decline. Overall, the eradicated group exhibited better outcomes in self-care and other QOL aspects. Although no study has investigated the QOL of OA after treatment, a study measuring the QOL of people with this disorder using EQ-5D reported a 0.72 (0.508–0.796) score on this questionnaire, and pain was one of the most important factors affecting it negatively. Overall, OA can impair the patient's health-related QOL.[34] Another study also reported that the SF-36 emotional domain had the highest mean score of 60 ± 38.43, indicating a relatively low impact on patients' QOL.

In contrast, the lowest mean score in the role physical domain was 35.33, with a standard deviation of 32.67, suggesting a significant impact on patients' ability to carry out physical tasks. Based on the WOMAC index, patients reported experiencing the most pain when climbing stairs, stiffness in the morning, and difficulty with heavy domestic work.[35] In our study, physical factors showed more changes than psychological factors. However, it seems that the determinants of pain in OA can be affected by independent risk factors such as gender, pain sites, and mental health.[36] In another study, in addition to improving the overall WHO's generic QOL-BREF and WOMAC score, surgery also positively affected the social relationship subscale.[37] QOL is a subjective perception that varies from person to person.[38] Therefore, the different results and the difference in the importance of some domains can be caused by this issue.

The study's sample size was relatively small, and it did not investigate the long-term effects of *H. pylori* eradication on OA symptoms. Furthermore, focusing on the specific mechanisms by which *H. pylori* infection exacerbates OA and how its eradication mitigates these effects would further clarify the relationship between the two disorders.

It is important to note that these subgroup analyses were conducted *post hoc*, and as such, the results should be

interpreted with caution. We recommend that future studies with larger sample sizes and robust subgroup designs further investigate these findings to validate and expand upon our results.

CONCLUSIONS

In OA patients with *H. pylori* infection, eradication therapy improves specific symptoms and QOL. On the other hand, the significant enhancements in physical function, pain, WOMAC total score, and the last component of QOL among the *H. pylori*-positive, eradicated group underscore the potential therapeutic significance of *H. pylori* eradication in treating OA. Although the mechanisms of eradication of arthritis have not been fully established, the decrease in gastrointestinal symptoms and overall inflammation may contribute to improved management of OA symptoms and enhanced physical function.

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Conflicts of interest

There are no conflicts of interest.

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