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H. PYLORI INDUCED CHRONIC GASTRITIS: A PATHWAY TO GASTRIC MUCOSA ASSOCIATED LYMPHOID TISSUE LYMPHOMA; REVIEW OF CURRENT DIAGNOSTIC AND TREATMENT MODALITIES

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Abstract – MALT-type marginal zone lymphomas are B-cell neoplasms that include extra-nodal tissues and exhibit a slow clinical course. The stomach is the predominant area, and most people are afflicted with *Helicobacter pylori*. Recently, there has been an increase in the bacterium's resistance to several antibiotics, necessitating a change of treatment protocols. In regions where clarithromycin resistance surpasses 15%, it is necessary to discontinue the traditional triple therapy, and new therapies called quadruple regimens, including or excluding bismuth, are now suggested. Consequently, persons diagnosed with stomach MALT lymphoma linked with *H. pylori* must adhere to these revised eradication treatment protocols.

Keywords: Chronic gastritis, MALT lymphoma, *H. pylori* infection, *H. pylori* eradication, Gastric MALT lymphoma.

INTRODUCTION

Among chronic gastric infections, Infection caused by *Helicobacter pylori* (*H. pylori*) is not uncommon globally. Infection rates vary by nation; overall, 55% of the global population has *H. pylori* infection[1]. Furthermore, the infection caused by *H. pylori* is the main etiologic factor for low-grade MALT lymphoma in the gastric region[1]. International recommendations emphatically advocate for the elimination of pathogens in all individuals having stomach MALT lymphoma, particularly in the 1st stages of low-grade mucosa-associated lymphoid tissue lymphoma. Elimination of *H. pylori* might attain a cure rate of 60%-80%[2-5]. Primary gastrointestinal lymphoma

constitutes 30% to 40% of all extranodal lymphomas. The prevalence of primary gastric lymphoma has risen in recent decades[6]. The culprit found in around 75% of gastric cancers and 5.5% of all worldwide malignancies is *H. pylori* infection. Infection rates differ by country: China exhibits rates between 55% and 80%, Hong Kong at 15%, and Taiwan at 40%[7]. Hispanics, African Americans, and the elderly exhibit a higher prevalence of *H. pylori* infections in the United States, with Hispanics 60%, 54% of Blacks, and 20% of Whites. Similar infection rates were found in both sexes. The estimated prevalence in the US is 20% for those under thirty and 50% for those over sixty years[8].

Gastric mucosa-associated lymphoid tissue lymphoma is a neoplasm of clonal B-cells originating from post-germinal center B-cells inside the lymphoid follicles' marginal zone. Over 30 years ago, people with chronic gastritis discovered *H. pylori* in their stomach mucosa[9]. Infection caused by *Helicobacter pylori* is regarded as a primary reason for chronic gastritis and a significant reason for stomach MALT lymphoma. After the recognition of the correlation between *H. pylori* gastritis and stomach MALT lymphoma, comprehensive foundational research and clinical trials have been undertaken globally, resulting in the establishment of treatment protocols for *H. pylori*-related gastritis and stomach MALT lymphoma[7,10,11]. Gastric MALT lymphoma is a sporadic condition. The projected prevalence of stomach lymphoma in Europe was around 0.3-0.8 per 100,000 persons[10]. Recent research indicated that the prevalence of stomach MALT lymphoma was around 0.38 per 100,000 individuals in the USA. The rate of incidence increased with advancing age[12]. This study reviewed the English-language literature about *H. pylori* gastritis and stomach MALT lymphoma, assessing recent advancements in their diagnosis and treatment. The existing difficulties in diagnosing and managing the illness are also discussed.

HELICOBACTER PYLORI

Overview

Helicobacter pylori, a spiral-shaped bacterium that stains pink on gram staining (gram -IVe), is among the most common etiological agents of gastric infections worldwide, affecting 20%-50% of individuals in the USA and Europe and up to 70% in underdeveloped nations[13,14]. The illness is often latent and asymptomatic, with a well-documented association with dyspepsia, peptic ulcer, chronic gastritis, gastric MALT lymphoma, and gastric cancer. WHO has classified *H. pylori* as a Group I carcinogen. The elimination of *H. pylori* alleviates gastritis and precludes additional complications. Currently, all individuals diagnosed with an infection of *H. pylori* should get elimination therapy[15]. In most recent decades, this bacterium has shown heightened resistance to the predominant medications used in the treatment. It is also strongly linked with gastric MALT lymphoma[14]. Consequently, it is essential to reevaluate its current treatment protocols.

Diagnostic Methods

Helicobacter pylori infection can be diagnosed either by invasive test or non-invasive (Table 1). Noninvasive testing is more convenient, more endured, and cheap. The carbon-13 (13C)-labeled urea breath test, following the addition of citric acid, is the most specific and sensitive noninvasive procedure., making it the ideal technique for detecting *H. pylori* infection[16]. A monoclonal ELISA stool test may detect its antigen and be a valid, non-invasive alternative[11,14]. Serological investigations for *H. pylori* are not universally suggested for diagnosis due to their significant variability and inadequate ability to differentiate between current infection and past exposure. They may be beneficial for individuals with MALT lymphoma or other disorders that markedly diminish infection risks, like severe intestine metaplasia or atrophy, individuals having recently completed antibiotic therapy, or individuals who are unable to stop prior treatment with PPIs[3]. The definitive noninvasive diagnostic method for *H. pylori* infections is an endoscopic stomach biopsy accompanied by a Giemsa stain analysis, which has a sensitivity of 95% and a specificity of 98%. Moreover, the rapid urease test is a feasible and satisfactory substitute for histological evaluation[17].

TABLE 1. *HELICOBACTER PYLORI* DIAGNOSTIC TESTS.

Investigation	First diagnosis	Diagnosis following treatment	Sensitivity/ specificity	Advantages	Limitations
Noninvasive 13C-labeled urea breath test	+++	+++	>95%/>95%	Reliable, easy, easily accessible, and rapid	The analysis requires a specific instrument
Antigen detection using a monoclonal ELISA stool test	+++	+++	>95%/>95%	Reliable, easy, and speedy.	Patient rejection
IgG serology	+	–	75%-85%/ 79%-90%	Easily accessible and capable of discovering virulence factors	Persistent +ive findings after eradication of the bacteria and poor sensitivity
Rapid invasive urease test	+++	+	80%-95%/ 97%-99%	Reliable and fast.	A high bacterial l oad is required
Histology	++	++	60%-95%/ >98%	Excellent sensitivity and secondary diagnostic information. An immunohistochemical study boosts sensitivity.	Significant interobserver variability. This takes a long time. Immunohistochemical studies are more costly and slower

Treatment

Recent revisions to the worldwide and national consensus guidelines for the treatment and management of *H. pylori* infections specify that a therapy is deemed successful when it has an eradication rate of no less than 90%, replacing the previously acceptable threshold of 80%[3,14,18]. These underscore the bacteria's increasing antibiotic resistance and the need to access homegrown bacterial resistance data to choose a suitable medication in an individual context. The consensus recommendations suggest replacing the existing triple therapy (OCA: omeprazole, clarithromycin, and amoxicillin) with a quadruple regimen, including or excluding bismuth, to enhance the success of treatment. *H. pylori* infection management can be enhanced by observing these three fundamental guidelines: examine the patients' previous antibiotic exposure, provide substantial doses of PPIs, and refrain from continuing an unsuccessful treatment regimen[14,19].

First-Line Treatment

The United States has a notable clarithromycin resistance rate of 13%[20]. Present global and local guidelines for eliminating *H. pylori* recommend discontinuing old triple therapy with OCA in regions with increased resistance to clarithromycin, such as the USA and Southern Europe, and instead utilizing simultaneous quadruple therapies with or without bismuth. The international consensus advises a fourteen-day course of treatment using a concurrent quadruple regimen excluding bismuth (OCAM: PPIs, clarithromycin, amoxicillin, and metronidazole), which is linked to eradication rates of 86%-92%[16,21]. A 10-day treatment of concurrent quadruple therapy of bismuth (OBMT: PPIs, bismuth, metronidazole, and tetracycline) is advised as well. For regions with metronidazole-resistant bacteria, increasing the treatment period to fourteen days can enhance effectiveness. Since 2016, bismuth subcitrate potassium, tetracycline, and metronidazole in a fixed-dose and a single capsule combination have streamlined the therapy, accompanied by a proton pump inhibitor for 10 days. Eradication rates of 85% are reported with the quadruple bismuth regimens, and they are typically tolerated well[14,21].

Second-Line Treatment

2nd line treatment is dependent on the results of the first. Therefore, if initial clarithromycin therapy is ineffective, the consensus of Spain recommends a therapy course that includes levofloxacin, ideally in a quadruple format (OLAB: PPIs, levofloxacin, amoxicillin, and bismuth); alternatively, quadruple bismuth therapy (OBMT) is also a viable option (Table 2). In the event of a failed initial first-line quadruple therapy using bismuth, a treatment plan comprising either quadruple or triple therapy with levofloxacin (OLA ± bismuth) is advised. These pharmacological combinations have an eradication rate of around 90%[3,16,21].

Third- and Fourth-Line Treatment

The necessity to eliminate the illness, as well as the patients' assessment of compliance with the therapy, must be prioritized. After the unsuccessful administration of the first-line and second-line treatments, international guidelines advocate for a quadruple therapy that incorporates bismuth. Additionally, a treatment regimen featuring levofloxacin is advised after the ineffectiveness of first-line clarithromycin treatment and subsequent quadruple therapy using bismuth. Patients with MALT lymphomas require a fourth-line of elimination therapy. Under these conditions, a therapeutic regimen with rifabutin is advised, such as proton pump inhibitors, amoxicillin, and rifabutin[14,19,21].

Historical Evidence Correlating *H. pylori* Infection with Gastric MALT Lymphomas

The first study linking *H. pylori* to gastric MALT lymphoma was performed in 1991[22]. *H. pylori* infection increased the risk of stomach MALT lymphoma since most patients had it. Typical stomach lymphoid tissue is unorganized. *H. pylori*-infected people establish lymphoid follicles and produce morphologically similar lymphoid tissue. In addition, case-control studies have linked *H. pylori* infection to primary gastric lymphoma[23]. Studies that found the lymphoma B-cell clone in biopsy specimens of chronic gastritis that preceded lymphoma and *in vitro* studies that showed *H. pylori* strain-specific T cells could stimulate lymphoma growth in crude lymphoma cultures

TABLE 2. *HELICOBACTER PYLORI* TREATMENT REGIMENS[14].

Treatment regimen	Agents	Duration
Quadruple concurrent therapy excluding bismuth (OCAM)	Omeprazole 20 mg every 12 hours, Clarithromycin 500 mg every 12 hours, Amoxicillin 1 g every 12 hours, Metronidazole 500 mg every 12 hours.	14 days
Quadruple regimen with bismuth (OBMT)	Omeprazole 20 mg every 12 hours; Bismuth subcitrate 240 mg every 12 hours or 120 mg every 6 hours. Metronidazole 500 mg every 8 hours; Doxycycline 100 mg every 12 hours.	10 to 14 days
A single capsule contain 140 mg of bismuth subcitrate potassium, 125 mg of tetracycline, and 125 mg of metronidazole, with a dosage of 3 capsules used four times day + omeprazole.	Omeprazole 20 mg every 12 hours Bismuth subcitrate potassium 420 mg every 6 hours Metronidazole 375 mg every 6 hours; Tetracycline 375 mg every 6 hours	10 to 14 days
Triple therapy using levofloxacin (OLA), with or without bismuth	Omeprazole 20 mg every 12 hours Levofloxacin 500 mg per 24 hours Amoxicillin 1 g every 12 hours ± Bismuth subcitrate 240 mg every 12 hours	14 days
Triple therapy using rifabutin, with or without bismuth	Omeprazole 20 mg every 12 hours, Rifabutin 150 mg every 12 hours, Amoxicillin 1 g every 12 hours ± Bismuth subcitrate 240 mg every 12 hours	14 days

provided direct evidence for *H. pylori*'s role in gastric MALT lymphoma's pathogenesis[24]. Finally, Wotherspoon et al[25] in 1993 showed that antibiotics alone eliminated *H. pylori* and regressed stomach MALT lymphoma by 75%. Most of these individuals with antibiotic-eradicated lymphomas have achieved long-term clinical remission[26].

These pioneering experiments showed that antibiotics alone could remove a malignant tumor. Additionally, sero-epidemiologic case-control studies strongly suggested that *H. pylori* infection raised stomach cancer risk. In 1994, the International Agency for Research on Cancer designated *H. pylori* as a Group I carcinogen[27].

GASTRIC MALT LYMPHOMAS

MALT lymphomas have a very slow clinical course and arise in the stomach, salivary glands, lungs, thyroid, and other organs. They are a kind of extranodal B-cell lymphoma that occurs from a structure similar to Peyer's patches. According to the WHO categorization, they are classified as extranodal marginal zone lymphomas with the subtype of MALT[28,29]. Despite a recent rise in prevalence, MALT Lymphomas have incidence rates of 1.53 and 1.61 per 100,000 individuals in the USA for men and females, respectively[30].

Pathogenesis

After the establishment of the association between peptic ulcer, gastritis, and *H. pylori* infections[9] at the beginning of the 1990s, Peter Isaacson first reported a significant prevalence of gastritis (in individuals with MALT lymphoma) because of *Helicobacter pylori* infection, along with the presence of lymphoid follicles resembling those found in MALT of the infected individuals, but without lymphoma[22]. This study indicated the enhancement of the Malt lymphoma in the stomach due to the presence of *H. pylori*, given that the stomach typically lacks organized lymphoid tissue. Subsequently, the same research group revealed the complete remission of MALT lymphoma with the elimination of *H. pylori*, in five out of six instances[25]. Many clinical studies show that after the elimination therapy of *H. pylori*, there is complete histological remission of MALT Lymphoma[31]. The pathogenesis of mucosa-associated lymphoid tissue lymphoma has been thoroughly examined in various scholarly articles; in summary, MALT lymphoma shows a multistage progression, with the first development of chronic gastritis triggered by *H. pylori* that stimulates the infiltration of the lymphocytes in gastric mucosa[27]. B cells transform into the neoplasm having genetic defects under the impact of *H. pylori*-specific T cells and autoantigens, which is exaggerated by the free radicals[32,33]. The development of genetic aberrations may correlate with reduced reliance on antigenic stimulation and histological changes[31].

MALT Lymphoma Pathogenesis Pathways

Gastric MALT lymphoma seems to develop *via* two primary molecular pathways originating from the stomach's oncogenic inflammatory environment. The other case was associated with a methylator-prone phenotype (CIMP), the other fully dependent on the t(11;18) translocation. In both cases, H. pylori infection leads to chronic gastritis, marked by a strong inflammatory response, increased epithelial cell turnover, and oxidative damage from reactive oxygen species. In susceptible individuals, this environment can promote the development of malignancies. Clonal evolution into MALT lymphoma is more likely when the tumor exhibits a converging methylator phenotype, which may result from sustained proliferation in the presence of microorganisms. The accumulation of these genetic abnormalities – primarily gains rather than losses – through frequent, mutually exclusive events observed with increased frequency in specific gastric DLBCLs suggests a predisposition to histologic transformation. Alternatively, the lesion may evolve into a MALT lymphoma, which can eventually grow independently of *H. pylori*, often characterized by the t(11;18) translocation, a non-methylator phenotype, and additional genetic alterations. These instances rarely evolve to DLBCL but do represent more

advanced disease and show clinically aggressive behavior. However, a similar carcinogenic mechanism is observed in *H. pylori*-negative counterparts of these MALT lymphomas (Figure 1), supporting the proposed pathogenesis of H. pylori-induced MALT lymphoma[27].

Histopathological Diagnostics and Genetic Modifications

The 79% prevalence of *H. pylori* infections in subjects with stomach MALT lymphoma is widespread, yet from research, this varies[34]. Gastric MALT lymphoma usually includes a thick, homogenous infiltration of small cytoid cells with a small round nucleus and a little or moderate amount of pale cytoplasm. A few show a marked plasmocytic differentiation associated with small lymphocytes. Lymphocytes often infiltrate glandular epithelial tissue to form lymphoepithelial lesions that are suggestive, but not diagnostic, of MALT lymphoma because the latter may also be caused by other lymphoma types. B cell lineage markers, such as CD79a and CD20 are expressed by lymphocytes; abnormal CD43 expression can distinguish MALT lymphoma from other non-neoplastic disorders, including chronic gastritis. This may allow differentiation of certain lymphomas affecting the stomach that would otherwise lack other markers, such as CD10 or CD5, including follicular lymphoma and mantle cell lymphoma[35]. Following the documentation of a continuum of histological alterations of the stomach mucosa, including active chronic gastritis and MALT lymphoma (Table 3), the authors detected a TSD localization of MALT lymphomas along the esophageal fatty streaks. If the histology findings are inconclusive, then a rearrangement in the immunoglobulin heavy chain variable region (Ig VH) and other molecular approaches might be useful[36]. IgVH monoclonality has thus been suggested to be of value in the diagnosis of MALT lymphoma[37]. Lymphoid infiltration in all strong lymphomas should only be performed when it is diagnosed, and MALT lymphoma should not be diagnosed in the absence of decisive

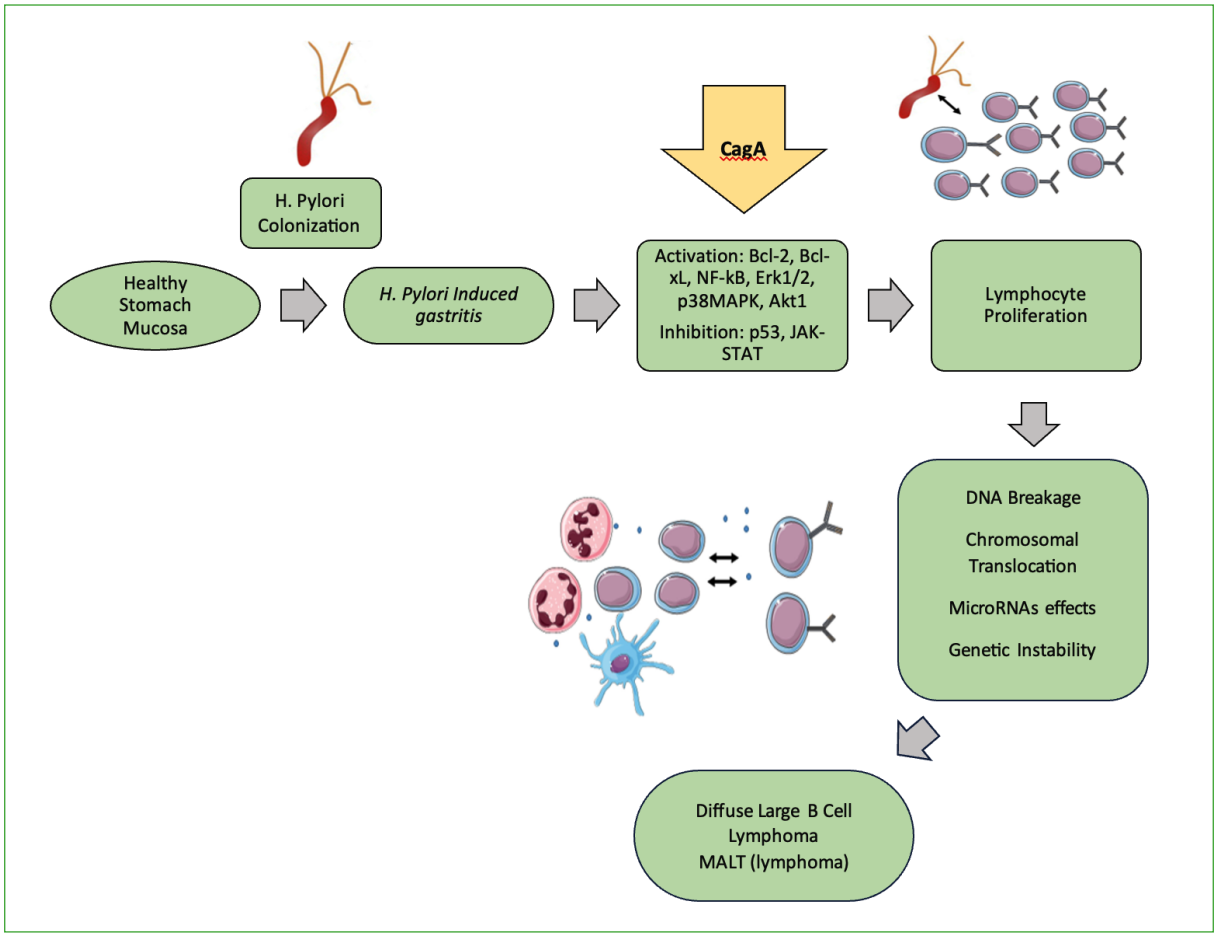

Figure 1. *H. pylori* induces MALT lymphoma.

TABLE 3. HISTOLOGICAL CRITERIA FOR DIAGNOSING STOMACH MALT LYMPHOMA[14].

Grade	Description	Histological findings
0	Normal	Plasma cells dispersed inside the lamina propria. Lack of lymphoid follicles
1	Active chronic gastritis	Lymphocytes minor aggregates inside the amina propria. Lack of lymphoid follicles or lymphoepithelial lesions
2	Active chronic gastritis with prominent lymphoid follicles	Distinguished lymphoid follicles encircled by a mantle zone and plasma cells
3	Suspicious and possibly reactive lymphoid infiltrate	Centrocyte-like cells encircling Lymphoid follicles that widely infiltrate the lamina propria and, intermittently, the epithelium.
4	Suspicious lymphoid infiltrate suggestive of lymphoma	Centrocyte-like cells encircling the Lymphoid follicles that diffusely penetrating the l amina propria and epithelium in small clusters.
5	MALT lymphoma	Presence of a diffuse dense infiltration of centrocyte-like cells into the lamina propria, together with significant lymphoepithelial lesions

histological evidence. Gastric MALT lymphoma is typically slow-growing but has the potential to progress in approximately 4-8% of cases to more aggressive forms, such as diffuse large B-cell lymphoma (DLBCL)[38,39]. Therefore, we consider that the former 'high-grade MALT lymphoma' has become dated and that this term is now replaced by DLBCL with or without regions of MALT lymphoma in accordance with the latest WHO classification. The major numerical change identified in stomach MALT lymphoma is 3 trisomy (30%), and the most frequent translocation is t(11;18)(q21;q21), seen in 20% of patients. In MALT lymphomas, where afflicted patients usually do not respond to *H. pylori* eradication therapy and do not develop DLBCL, the translocation has been detected[40].

Extension Studies and Staging Systems

Like other lymphomas, gastric MALT lymphoma is staged. Waldeyer's tonsillar ring is assessed, as well as CBC, LFTs, RFTs, serum LDH, 2-microglobulin, and blood coagulation profile. Assessment of the co-morbidities that can affect the treatment, for example, the infection caused by HBV, HCV, and HIV must be made. All cases are recommended to undergo a CT of the chest, abdomen, and pelvis[41]. Patients without regional lymphadenopathy do not require a bone marrow biopsy since the role of bone marrow in stomach MALT lymphoma is considered. Musshoff and Ann Arbor revised the traditional staging method for gastric MALT lymphomas[42]. Most cases are in the early local stages, i.e., stage I1E – lymphoma localized to the stomach mucosa or lamina propria – or stage I2E, involving the superficial lamina propria, according to the standardized use of endoscopic ultrasonography[43]. The diagnostic research toward a more accurate assessment of disease infiltration to the gastric wall has resulted in staging systems that included Lugano and Paris staging (Table 4)[44].

Treatment

Precise diagnosis and staging are critical before starting treatment[46,47]. As infiltration is restricted to mucosa and submucosa of MALT lymphoma (stage I1E)[41], it often provides full remission after eradication of *H. pylori*. Therefore, surgical and chemotherapeutic intervention is deferred until after *H. pylori* eradication (Table 4). More than 90% of primary MALT lymphomas are low-grade and usually limited to the mucosal or submucosal layers, and eradicating *H. pylori* becomes less effective with deeper infiltration. Evaluations of gastric wall involvement by EUS are therefore

TABLE 4. STAGING SYSTEMS FOR GASTRIC LYMPHOMA[45].

Ann Arbor by Musshoff	Paris system	Tumor size
I1E	T1m N0 M0	Mucosa
I1E	T1sm N0 M0	Submucosa
I2E	T2 N0 M0	Muscularis propia, subserosa
I2E	T3 N0 M0	Serosa
II1E	T1-3 N1 M0	Lymph nodes of Peri gastric area
II2E	T1-3 N2 M0	Distant regional lymph nodes
I2E	T4 N0-2 M0	Adjacent invasion of surrounding organs with without involvement of abdominal lymph nodes
IIIE IV	T1-4 N3 M0 T1-4 N3 M1	Extra abdominal lymph nodes Diffuse or disseminated invasion of remote or extragastrointestinal organs
	B1	Involvement of bone marrow

important, and MALT lymphoma often has modest progression with a favorable prognosis when the disease is localized before the advanced stage[46,48-50]. However, the progress high-grade lymphoma progresses with the duration of the disease with increased incidence. Therefore, early identification and intervention are essential.

Eradication of *H. pylori*

Multiple research studies have shown that MALT lymphoma of the stomach may achieve complete regression, endoscopically and histologically, and on molecular criteria after *H. pylori* eradication[1,48]. Additional research assessing the efficacy of eradicating *H. pylori* in stage IE1 demonstrated complete remission rates ranging from 60% to 92%[51,52]. Typically, *H. pylori*-positive patients get triple or quadruple therapy for a duration of 1-2 weeks, followed by retesting 4-8 weeks thereafter[48]. Bismuth-based quadruple therapy (that excludes antibiotics that have already been administered) is indicated if the first medication proves unsuccessful[53]. Gastric MALT lymphoma *H. pylori* prevalence rates documented range from 0% to 38%[54]. Factors contributing to false negative *H. pylori* include eradication of *H. pylori*, recovery of *H. pylori* infection, and recovery from non-*H. pylori* infections such as *Helicobacter felis* or *Helicobacter heilmannii*, and autoimmunity may cause false negative *H. pylori* in early gastric MALT lymphoma. That's why carrying out various evaluations for *H. pylori* infection and a detailed medical history is essential.

Management of High-Grade MALT Lymphoma

H. pylori changes are independent of *H. pylori* antigen proliferation, and there is a correlation between increasing stage or histologic grade and decreasing rates of *H. pylori* infection[55]. 80% of patients with stage IIE lymphoma are documented to have undergone total gastrectomy and have same-side lymph node invasion of the diaphragm[56]. It has a very great effect on the quality of life[57]. On the other hand, with extensive field radiation of 30-40 Gy over four weeks to the stomach and perigastric nodes, there was a full remission rate of 90%-100%, with an estimated 5-year disease-free survival of 80%. In contrast, 30-40 Gy of field radiation given over 4 weeks to stomach and perigastric nodes has yielded a full remission rate of 90 to 100% and long-term disease-free survival of about 80%[58]. Patients with severe sickness, who are *H. pylori* negative, or who have had *H. pylori* for a long time after eradication respond best to radiotherapy[59]. Treatment alternatives include chemotherapy, immunotherapy, or a combinatorial combination of these therapies. It was shown that a chimeric monoclonal antibody (Rituximab) targeting the B cell-specific antigen CD20 is valid in patients with follicular lymphomas[60]. In addition, it has been

further used therapeutically with this antibody in a wide variety of non-Hodgkin lymphomas with improved results as monotherapy or in combination with chemotherapy[61-64]. MALT lymphoma of the stomach, which is resistant to treatment, and *H. pylori*-negative responds to rituximab[65,66]. If such high-grade MALT lymphoma is shown to be positive for *H. pylori* infection, *H. pylori* eradication treatment should be considered because the presence of *H. pylori* may favor recurrence, but eradication in these patients is still disputed[1].

Prevention

Although *H. pylori*, as a tumor-inducing pathogen, is implicated in both carcinoma and lymphoma, it does not lead to malignant disease in most of the patients. Hence, vaccination programs need to take into account *H. pylori's* co-evolution with humans, and various host-pathogen interactions may be beneficial. *H. pylori* has been found to protect against the acidic environment of the antrum (Cardia). Eradicating bacterium could have consequences that cannot be envisioned. As *H. pylori* correlates with cancer progression, the interest in immunization is expected to grow. A wide variety of innovative techniques have been evaluated in human and animal subjects. Sutton et al[67] showed that *H. felis*-infected BALB/c mice for 22 months had devastating lymphoepithelial lesions similar to what is seen in human MALT lymphomas. Eradication of the bacterial infection led to a noteworthy reduction in the incidence of MALT lymphoma in mice, and mice immunized prophylactically and later exposed to *H. felis* have not shown lymphocytic infiltration and follicle development in infection response, as compared with control. As such, researchers concluded that preventive vaccination for *H. felis* could prevent stomach MALT lymphoma.

CONCLUSIONS

There is a strong association between *H. pylori* infection and the development of gastric malt lymphoma, and there is a need for new treatment guidelines on how to treat gastric MALT lymphoma along with new antibiotics for the elimination of *H. pylori* which are essential in its management.

AI Disclosure

The authors made use of Grammarly to correct the grammar issue of the manuscript, and Mendeley reference manager was used to properly reference the manuscript and assist with the drafting of this article. Both tools were obtained from the official websites and used without modification.

Conflict of Interest

The authors declare that they have no conflict of interest.

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