

# Eradication Treatment of *Helicobacter pylori* Infection: Evaluation of Therapeutic Strategies in N'Djamena

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## Abstract

**Background:** *Helicobacter pylori* (Hp) infection is the most widespread bacterial infection in the world. The infection is generally acquired in childhood, but can persist into adulthood. Eradication therapy has undergone several modifications. The aim of this study was to evaluate the different therapeutic strategies used in the eradication of *Helicobacter pylori* infection in the Centre Hospitalier Universitaire La Reference Nationale of N'Djaména. **Patients and Methods:** This was a prospective, descriptive analytical study spread over one year, from September 2021 to September 2022. Patients at least 15 years of age presenting with dyspeptic symptoms, seen consecutively in a hepato-gastroenterology consultation and with a positive stool test for *H. pylori* infection, were included in the study. Equally, 1/3 of patients were treated with dual or triple therapy. The remaining third received quadritherapy. **Results:** A total of 268 patients were included in the study (mean age  $38.40 \pm 14.66$  with extremes of 16 and 80 years). Males predominated in 58% of cases. Overall therapeutic efficacy was 88.9%. According to different therapeutic strategies, efficacy was 90.75% for dual therapy with PPI (Rabeprazole) and Amoxicillin. On the other hand, efficacy was 87% and 88.88% for PPI-based triple therapy and dual antibiotic therapy, and for PPI-based quadruple therapy and triple antibiotic therapy. **Conclusion:** *H. pylori* infection is a common disease in Chad. Dual therapy with rabeprazole combined with a high dose of amoxicillin over a period of at least two weeks showed similar if not better efficacy than triple or quadruple therapy.

## Keywords

*Helicobacter pylori*, Therapeutic Strategies, Eradication, Dyspepsia, Chad

## 1. Introduction

*Helicobacter pylori* is a spiral-shaped, flagellated, motile Gram-negative bacterium. It was first isolated and cultured from gastric biopsies in 1982 by two Australian researchers, J. Robin Warren and Barry J. Marshall. This discovery was awarded the Nobel Prize for Physiology and Medicine in 2005 [1].

Transmission of *Helicobacter pylori* infection is human-to-human, and usually occurs during infancy via the oral or fecal-oral route [2]. As the human stomach is the only reservoir for *Helicobacter pylori*, the bacterium is able to survive and multiply in the stomach thanks to a highly active enzyme that converts urea into ammonia and carbon dioxide, thereby increasing the PH and neutralizing gastric acidity. This bacterium was recognized as a type 1 carcinogen by the WHO in 1994, and plays a major role in the onset of numerous digestive pathologies such as peptic ulcer disease, MALT-type lymphoma, dyspepsia, gastro-oesophageal reflux disease, gastric cancer and other extradigestive pathologies [2].

*Helicobacter pylori* infection is the most widespread bacterial infection, affecting almost 50% of the world's population. Prevalence varies according to geographical origin, age and socio-economic status [3]. Its management has undergone several modifications, ranging from dual to triple and quadruple therapy.

In Chad, prevalences of 83.7% and 60.2% were reported in dyspeptic patients undergoing upper digestive endoscopy at the Internal Medicine and Gastroenterology department of the National Reference University Hospital Center (CHU-RN) [4] [5]. Despite the high prevalence, we do not have data relating to the evaluation of therapeutic strategies in the eradication of *Helicobacter pylori* infection. Hence the need to conduct this study in order to promote better management of this condition.

## 2. Patients and Methods

This was a prospective, descriptive and analytical study spread over a one-year period from September 2021 to September 2022. The setting was the Department of Internal Medicine and Gastroenterology at "Référence Nationale" Teaching Hospital. The study population consisted of patients aged at least 15 years, of all sexes, seen in consultations during the study period. Consenting patients presenting with digestive symptoms and a positive diagnosis of *H. pylori* infection based on stool testing for Hp antigen were included. Patients under 15 years of age were not included in this study. Consent was verbal. Socio-demographic, clinical and paraclinical variables were used. The draw was random during the consultation if a first case is put on dual therapy, the second will be put on triple therapy and the third on quadruple therapy.

Therapeutically, the distribution was equitable, with 1/3 of the study population on a dual-therapy protocol consisting of: Proton Pump Inhibitor (Rabeprazole-type PPI) and amoxicillin 3 g/d. We also put 1/3 on a triple-therapy proto-

col (PPI (Rabeprazole) + Amoxicillin + Metronidazole or PPI (Rabeprazole) + Amoxicillin + Clarithromycin). Finally, we started the remaining 1/3 of the study population on quadritherapy consisting of: PPI + Amoxicillin + Metronidazole + Clarithromycin. Half of this population was subjected to sequential quadritherapy and the other half to concomitant quadritherapy.

The daily dose of amoxicillin was 3 g for 14 days. Metronidazole was 1 g/d, as was clarithromycin. The dose and duration of PPI varied according to endoscopic lesions in patients who underwent upper GI endoscopy.

One month after the end of treatment, all treated patients underwent a follow-up examination for Hp infection in the stool. Any patient with a negative control result one month after the end of treatment was considered cured. However, in patients with positive control results, the protocol used was deemed ineffective and another protocol was proposed with the patient's consent. Thus, the efficacy of the protocol used was judged by the negatization of the control result.

The chi-square test<sup>2</sup> was used to analyze the data.

### 3. Results

Of a total of two hundred and sixty-eight (268) patients seen consecutively for dyspeptic symptoms, 162 had a positive result, *i.e.* a prevalence of 60.44%. This series was predominantly female (58%).

The mean age was  $38.40 \pm 14.66$ , with extremes of 16 and 80 years. The 20 - 29 and 30 - 39 age groups were the most represented (55.6%). Reasons for consultation were dominated by epigastralgia and dyspepsia, which accounted for over 70% of cases. Endoscopic lesions were dominated by gastropathy (27.7%) and peptic esophagitis (13.5%). Upper GI endoscopy was normal in 8% of cases (**Table 1**).

**Table 1.** Sociodemographic characteristics.

<b>Ages (Year):</b>	Numbers (n)	Percentage (%)
<20 years old	7	4.3
20 to 29 years old	45	27.8
30 to 39 years old	45	27.8
40 to 49 years old	28	17.3
50 to 59 years old	20	12.3
60 to 69 years old	11	6.8
70 and more	6	3.7
<b>Social economic level</b>		
Weak	117	72.22
Middle	33	20.38
High	12	7.4
Total	162	100

### 3.1. Evolution after Treatment

#### Dual therapy

Among the 54 patients treated with a dual-therapy protocol of Amoxicillin 3 g for 14 days combined with a Rabeprazol 20 mg double-dose PPI of variable duration, 49 patients (90.75%) had a negative result one month after the end of treatment.

For triple therapy, which consists of:

- Amoxicillin + Clarithromycin + PPI;
- Amoxicillin + Metronidazole + PPI;
- Amoxicillin + Clarithromycin + PPI.

Forty-seven of the 54 patients had a negative control result one month after the end of treatment, giving a cure rate of 87%.

For patients on a quadritherapy regimen (concomitant and sequential), therapeutic success was 88.88%.

In this study, 88.9% of all treatment protocols were cured.

### 3.2. Analytical Study

There was a statistically significant relationship between Hp eradication and the different treatment regimens: dual, triple and quadruple therapy, with  $p = 0.00$  (see **Table 2**).

## 4. Discussion

This work, carried out in a country with limited resources, was not done without difficulties; we certainly had the consent of the patients before their inclusion, but the additional examinations and prescribed medications were the responsibility of the patients. As patients were not insured, this was a handicap for follow-up. The high number of people lost to follow-up would be linked to this situation. The number of our enchantments should be significant if care was provided to patients.

In this study, the prevalence of *Helicobacter pylori* infection was 60.40%. This prevalence is similar to that of Nadlaou *et al.* in 2021 [5]. This result is also close to the Ivorian study by Doffou *et al.* who reported a prevalence of 57.8% [6]. It is, however, lower than that of Moussa *et al.* who obtained a prevalence of 83.7% in a study carried out at the Teaching Hospital “la Référence Nationale” in N'Djamena [4]. It is also lower than certain African data which report 66.12% and 69.5% respectively in Egypt and Nigeria [7] [8]. This drop is probably due to improved living conditions and, above all, to the overuse of antibiotics and self-medication with PPIs in our African context. The prevalence of infection varies, and is partly linked to socio-economic conditions. The prevalence of *H. pylori* in Europe (Germany) published in 2018 was said to be 20% - 40% [9].

Mean age was  $38.40 \pm 14.66$  years, with extremes of 16 and 80 years. The 20 - 39 age group is predominant (55.6%). This result is similar to those of Doffou *et al.*, who found a frequency of 57.7% in the 21 to 40 age brackets [6]. *H. pylori*

**Table 2.** Efficacy of Hp eradication according to treatment regimens.

Treatments	Control		Total	Khi <sup>2</sup>	p
	Negative	Positive			
Dual therapy	49	5	54	5.52	0.000
Tritherapy	47	7	54	11.82	0.000
Quadritherapy	48	6	54	2.38	0.000
<b>Total</b>	<b>144</b>	<b>18</b>	<b>162</b>		

infection certainly occurs in relatively young subjects, given that transmission takes place during childhood. However, Moussa *et al.*'s assertion that age has no influence on *H. pylori* infection status seems plausible and remains valid today [4].

In this study, women predominated. Women accounted for 58% versus 42% of men (sex ratio: 0.7). This female predominance has also been reported by several authors, notably Joutei *et al.* in Morocco, who obtained 53% in women and 47% in men [10]. Other authors have reported a male predominance, notably Firmin *et al.* in Cameroon and Amel *et al.* in Morocco [7] [11]. It has been shown in the literature that gender has no influence on the status of *H. pylori* patients [4]. The only factors favoring the appearance of *H. pylori* are immaturity of the gastric mucosa, low socio-economic status, hygiene, gastrointestinal enteritis and promiscuity. The female predominance found in the Moroccan series and ours could be related to the global demographic situation which is in favor of women.

Numerous studies have confirmed the association of *H. pylori* infection with socio-economic and living conditions: poor hygiene, promiscuity and communal living are all risk factors favoring *H. pylori* infection. In this series, *H. pylori* infection was found in 72.22% of cases in subjects with a low socioeconomic level, confirming the data in the literature. These unstudied parameters will be the subject of future work.

#### Clinical and paraclinical aspects

Clinically, the main reasons for consultation are dominated by epigastralgia (58.6%), followed by dyspepsia (14.2%). Other complaints (nausea, vomiting and fever) accounted for 13.5%. Hematemesis and pyrosis are equally important, accounting for 6.8% each. This result is comparable to those of Nadloua *et al.* who reported 54.2% for epigastralgia [5]. In the same context, Ontsira reported 64.3% for epigastralgia [12]. The result is also similar to those of Doffou *et al.* who found epigastralgia to be the main reason in 82.7% of cases [6].

Endoscopically, the main lesions were gastropathy (27.7%). Gastric ulcers were found in 11.7% of cases, duodenal ulcers in 9.2% and esophagitis in around 13.5%. This result is close to that of the Cameroon study by Ankouane *et al.*, who found a predominance of gastropathy (49.7%), followed by peptic esophagitis and peptic ulcer disease (29.8%) [7]. It is also close to that of Onstira, who found gastropathy (22.4%) and peptic ulcer disease (17.4%), although over 36%

had normal endoscopy [12].

### **Progression according to different therapeutic strategies**

The aim of this study was to evaluate some treatment strategies for the eradication of *H. pylori* infection. A total of 54 patients were treated equally with dual therapy, 54 with triple therapy and 54 with quadruple therapy. The overall success rate in this study was 88.90%. This result is higher than those of Ndjitoyap *et al.* in a study carried out in Yaoundé, Cameroon, in 2019, which found an overall success rate of 73.9% [13]. However, it is close to the Korean study by Bang *et al.* which found an efficacy of over 80% [14].

Dual therapy was first introduced in the 1990s as a first-line treatment for the eradication of *H. pylori* infection. After the discovery of the bacterium by Marshall in 1982, the treatment used was a combination of amoxicillin and a proton pump inhibitor [6]. Over time, since PPI-amoxicillin combination therapy at the standard dose did not produce satisfactory therapeutic results, it was used as a rescue treatment. As a result, dual therapy was abandoned in favor of triple and then quadruple therapy. Recent studies have revisited this combination therapy, which combines amoxicillin and rabeprazole for 14 days. The novelty lies in the improved efficacy, probably due to the optimization of treatment by the 14-day duration, the increase in PPI doses and the distribution of amoxicillin doses, more in line with its pharmacokinetics [15] [16].

In this series, treatment with dual therapy in our 54 patients showed a cure rate of 90.7% after control of *H. pylori* infection in the stool. This result is comparable to those of Yang *et al.* who, in a study carried out in China in 2015, showed a 95.3% efficacy rate for dual therapy with rabeprazole 20 mg combined with amoxicillin 3 g/day, for a total treatment duration of 14 days, in both naïve patients and those who had already received previous treatment [16]. However, these results are superior to those of Sapmaz *et al.* in a study carried out in Turkey in 2017, which showed 87.8% efficacy [17]. The advantage of this discontinued dual therapy is tolerance and cost. Thus, dual therapy with rabeprazole combined with high-dose amoxicillin could overcome the intolerance of quadritherapy (today's reference treatment) if the experimental studies currently underway are validated [15] [18].

After noting the resistance of dual therapy in the 1990s, triple therapy was introduced. This consists of using a PPI and two antibiotics against *H. pylori* infection for 7 to 14 days. The antibiotics used are generally amoxicillin, clarithromycin, metronidazole and/or levofloxacin. In this study, the eradication rate for this therapeutic line was 87%.

This result is superior to those of Tai *et al.* who, in a Chinese study, showed that triple therapy (amoxicillin-levofloxacin PPI) used in patients failing standard triple therapy was more effective when prescribed for a total duration of 14 days compared with 10 days, and showed a prevalence of 84.8% versus 67.1% [19]. This result is also superior to those of Lahbabi *et al.* who, in a study using AM and AC-based protocols (amoxicillin and metronidazole, amoxicillin and clarithromycin) found eradication rates of 53.1% and 64.6% respectively [20].

The effectiveness of HP infection eradication was probably linked to treatment compliance and tolerance in our context. The high level of resistance to metronidazole and clarithromycin in our country would also play a significant role [5] [7].

As for quadritherapy, both forms (sequential and concomitant) were used in this study. In general, the sequential regimen consisted of simple dual therapy comprising standard-dose proton pump inhibitors twice daily plus amoxicillin 1 g twice daily for the first 5 days, followed by triple therapy comprising a standard-dose PPI twice daily plus clarithromycin 500 mg and metronidazole 500 mg twice daily. For the remaining 5 days. Concurrent quadritherapy consists of the combination of 3 antibiotics (amoxicillin, clarithromycin and metronidazole) with a PPI. In this series, the efficacy of quadritherapy was 88.88%. This result is superior to those of Agdal *et al.* in Rabat, Morocco, in 2017, who found an eradication rate of 84.21%. In the same Moroccan study, bismuth quadritherapy was the least prescribed but the only one with an eradication percentage of 100% [21]. On the other hand, it is lower than those of Sardarianh *et al.* in a study carried out in Iran in 2013, who found efficacy at 90% of patients subjected to quadritherapy [22]. They are, however, close to those of Apostolopoulos *et al.* in a study in Greece, who found 87% efficacy for a 10-day non-bismuth quadritherapy [23]. However, Saudi Arabia reported very poor eradication rates of 63.4% for sequential therapy [24].

## 5. Conclusion

Although on the decline, HP infection remains frequent in Chad. For reasons of resistance, treatment has undergone several modifications. This study shows that the abandoned dual therapy is still effective and gives practically the same, if not better, results than triple and quadruple therapy, if the duration of treatment is extended with an increase in the dose of amoxicillin. Treatment by BI, TRI and Quad therapy are effective with a positive statistical relationship.

## Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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