Review article: Helicobacter pylori infection and gastric outlet obstruction — prevalence of the infection and role of antimicrobial treatment

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SUMMARY
The prevalence of *Helicobacter pylori* infection in peptic ulcer disease complicated by gastric outlet obstruction seems to be, overall, lower than that reported in non-complicated ulcer disease, with a mean value of 69%. However, *H. pylori* infection rates in various studies range from 33% to 91%, suggesting that differences in variables, such as the number and type of diagnostic methods used or the frequency of non-steroidal anti-inflammatory drug intake, may be responsible for the low prevalence reported in some studies.

The resolution of gastric outlet obstruction after the eradication of *H. pylori* has been demonstrated by several studies. It seems that the beneficial effect of *H. pylori* eradication on gastric outlet obstruction is observed early, just a few weeks after the administration of antimicrobial treatment. Furthermore, this favourable effect seems to remain during long-term follow-up. Nevertheless, gastric outlet obstruction does not always resolve after *H. pylori* eradication treatment and an explanation for the failures is not completely clear, non-steroidal anti-inflammatory drug intake perhaps playing a major role in these cases. Treatment should start pharmacologically with the eradication of *H. pylori* even when stenosis is considered to be fibrotic, or when there is some gastric stasis.

In summary, *H. pylori* eradication therapy should be considered as the first step in the treatment of duodenal or pyloric *H. pylori*-positive stenosis, whereas dilation or surgery should be reserved for patients who do not respond to such medical therapy.

INTRODUCTION
Chronic peptic ulcers in either the stomach or duodenum may cause scarring and may impair gastric emptying, a condition known as ‘gastric outlet obstruction’. In adults, peptic ulcer disease is the major cause of benign gastric outlet obstruction. Most cases are associated with duodenal or pyloric channel ulceration, with gastric ulceration accounting for only 5% of cases. Although the role of *Helicobacter pylori* infection in non-complicated peptic ulcer disease has been definitively established, the exact relationship between the organism and complicated ulcer disease has not been studied in any detail. The true prevalence of *H. pylori* infection in ulcer disease complicated by gastric outlet obstruction remains a matter of debate, and the effect of *H. pylori* eradication on this complication has not been fully established. In this respect, although surgery or balloon dilation has been classically considered to be necessary to relieve the symptoms of gastric outlet obstruction in most patients, more recently resolution of this complication has been reported in patients with peptic ulcers infected by *H. pylori* after eradication of the organism. Our aim was to review the studies assessing the prevalence of *H. pylori* infection in...
patients with gastric outlet obstruction, and to evaluate
the effect of eradication of the infection on the
resolution of this important complication.

Bibliographical searches were performed in the Pub-
Med (Internet) database, including studies available
until October 2001, looking for the following words (all
fields): (Helicobacter pylori OR H. pylori) and (obstruction
OR stenosis OR gastric outlet obstruction). References
from reviews on gastric outlet obstruction in peptic
ulcer disease, and from the articles selected for the
study, were also examined in search of articles meeting
the inclusion criteria. Articles published in any lan-
guage were included. The prevalence of H. pylori
infection in patients with gastric outlet obstruction in
each study was recorded, and the diagnostic methods
used to detect the organism were also identified. The
weighted mean (taking into account the number of
patients in each study) of prevalence and the 95%
confidence interval were calculated. The effect of
eradication of the infection on the resolution of gastric
outlet obstruction was assessed in all studies.

PREVALENCE OF H. PYLORI INFECTION
IN GASTRIC OUTLET OBSTRUCTION

The prevalence of H. pylori infection in non-complicated
peptic ulcer disease has been reported to be very high,
especially if patients taking non-steroidal anti-inflam-
atory drugs (NSAIDs) are excluded.\(^2,^3\) However, the
prevalence of the organism in complicated ulcer disease,
and specifically in those patients with gastric outlet
obstruction, has not been assessed in detail, although it
appears to be lower than that in uncomplicated ulcer
disease.\(^4\) Some authors have reported quite a low
prevalence of H. pylori infection in gastric outlet
obstruction, with values ranging from 33% to 69%.\(^5^-^9\)
These results suggest, as has been proposed in the case
of perforation,\(^10\) that ulcer disease complicated by
obstruction has a different pathogenesis from chronic
peptic ulcer disease, and that the first should not be
regarded simply as a complication of the second. In the
study with the lowest prevalence of H. pylori,\(^5\) the
presence of the infection was examined in patients
undergoing resection for gastric outlet obstruction. The
organism was detected in only 33% of cases using
Steiner stain from either pre-operative endoscopic
biopsy or, in most patients, final surgical specimens.
This low prevalence could be explained, at least in part,
by the use of only one diagnostic method to detect
H. pylori, and by the inclusion of patients taking
NSAIDs. However, in other studies with low infection
rates,\(^7,^8\) the presence of the organism was investigated
by means of two diagnostic methods (rapid urease test
and histology), and NSAID use was absent or not
remarkable, suggesting that the low prevalence of
H. pylori may be a true situation and not a false
negative result. Nevertheless, it has been postulated that
the true prevalence of the infection would be higher as
H. pylori may not survive as well in the milieu of an
obstructed stomach.\(^7\)

On the other hand, some authors have concluded that
gastric outlet obstruction is associated with a high
H. pylori infection rate.\(^11,^12\) Taskin et al. studied 10
consecutive patients presenting with clinically and
diagnostically significant gastric outlet obstruction.\(^11\)
During each endoscopy, seven gastric biopsy specimens
were obtained (from the antrum, corpus and fundus)
and analysed for H. pylori colonization by both rapid
urease test and histological methods. The antral
mucosal biopsy specimens were positive for H. pylori
in nine patients, that is, in 90% of patients. The use of
more than one diagnostic method and the high number
of biopsies taken could explain the high prevalence of
the infection reported in this study. In summary, from
the seven studies shown in Table 1, including 187
patients with gastric outlet obstruction, an overall
H. pylori infection rate (weighted mean) of 69% is
calculated (95% confidence interval, 62–76%), a value
that is, effectively, relatively low.

Although prevalence studies are interesting, case–
control studies comparing patients with gastric outlet
obstruction with those with non-complicated ulcer
disease provide more information. In this respect, Kate

<table>
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<th>Reference</th>
<th>No. of patients</th>
<th>Diagnosis of H. pylori</th>
<th>H. pylori infection (%)</th>
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<tbody>
<tr>
<td>Gibson et al.(^5)</td>
<td>24</td>
<td>Steiner stain</td>
<td>33</td>
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<tr>
<td>Perng et al.(^6)</td>
<td>19</td>
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<td>Lam et al.(^7)</td>
<td>19</td>
<td>RUT, H</td>
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<tr>
<td>Awan et al.(^8)</td>
<td>13</td>
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<td>Boylan &amp; Gradzka(^9)</td>
<td>13</td>
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<td>69</td>
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<td>Taskin et al.(^11)</td>
<td>10</td>
<td>RUT, H</td>
<td>90</td>
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<tr>
<td>Kate et al.(^12)</td>
<td>66</td>
<td>RUT, H, S</td>
<td>91</td>
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H. histology; RUT, rapid urease test; S, serology.
Overall H. pylori infection rate (weighted mean) = 69% (95% confi-
dence interval, 62–76%).

et al. included 103 patients in their study: 37 had duodenal ulcer (Group I), 35 duodenal ulcer disease with gastric outlet obstruction with the presence of an active ulcer in the duodenum (Group II), and 31 duodenal ulcer disease with gastric outlet obstruction but no active ulcer (Group III). The presence of *H. pylori* infection was determined by urease test, serology and/or histology. The prevalence of *H. pylori* infection in the three groups was not significantly different (95%, 91% and 90%, respectively). The conclusion of this study was that the prevalence of *H. pylori* infection was high in patients with duodenal ulcer and was unaltered by the presence of gastric outlet obstruction.

**ROLE OF ANTIMICROBIAL TREATMENT IN GASTRIC OUTLET OBSTRUCTION**

The standard treatment for benign, non-resolving gastric outlet obstruction is either endoscopic balloon dilation or surgery. More recently, the resolution of gastric outlet obstruction after the eradication of *H. pylori* has been described in several studies, summarized below. de Boer & Driessen reported the first case of the resolution of gastric outlet obstruction after the eradication of *H. pylori*. In the same year, Annibale et al. reported the case of a patient with duodenal bulb stenosis and active ulcer in whom 4 months of omeprazole (40 mg/day) had not modified the endoscopic picture. The diagnosis of *H. pylori* infection and its treatment led to the cure of both duodenal ulcer and bulbar stenosis. This case illustrates that *H. pylori* eradication is able to cure refractory duodenal ulcer and stenosis which have not responded to previous treatment with potent antisecretors, such as proton pump inhibitors. In 1996, Tursi et al. prescribed *H. pylori* eradication therapy to two patients with duodenal and pyloric stenosis, and reported the resolution of both the symptoms and the endoscopic lesions. One year later, Lam et al. treated nine patients with *H. pylori*-positive benign gastric outlet obstruction with triple therapy (bismuth, tetracycline and metronidazole) for 1 week without acid suppression. Six patients also underwent incremental endoscopic balloon dilation. All of the six patients treated by endoscopic balloon dilation and *H. pylori* eradication remained symptom free for a median follow-up of 16.5 months. In contrast, outcomes for *H. pylori*-negative patients, whether treated with dilation or long-term acid suppression, were much less favourable.

In 1998, Malik et al. studied six patients with duodenal ulcer-related gastric outlet obstruction positive for *H. pylori*, and treated them with eradication therapy. Repeated endoscopic follow-ups revealed a significant dilation and clinical improvement in all patients, and none required surgery. In the same year, Diaz Blasco & García Valriberas reported the case of one patient with pyloric stenosis and secondary gastric outlet obstruction in whom *H. pylori* was treated, with clinical improvement of the patient. Misra et al. reported a patient in whom endoscopic examination revealed findings suggestive of gastric outlet obstruction with nodularity of the antral mucosa leading to deformity of the pylorus. Endoscopic biopsies from the nodular antral mucosa showed the presence of *H. pylori*-induced lymphonodular hyperplasia without evidence of mucosa-associated lymphoid tissue lymphoma. Anti-*H. pylori* therapy resulted in the eradication of the infection and the signs and symptoms of gastric outlet obstruction. Finally, in 2001, Choudhary et al. reported the first case of *H. pylori*-related gastric outlet obstruction successfully treated with parenteral antibiotics in a patient who was unable to take oral medication.

The time-span from *H. pylori* eradication to gastric outlet obstruction resolution represents a relevant aspect of this type of treatment. Brandimarte et al. studied 22 patients with benign peptic stenosis and *H. pylori* infection who were treated with anti-*H. pylori* therapy, with endoscopic controls after the end of therapy, at 2 and 6 months, and then every 6 months. Peptic stenosis disappeared completely in 20 of the 22 cases (17/20 after 2 months and 3/20 after 6 months) after *H. pylori* eradication, and in all of these patients the symptoms disappeared within 2 months. These data are similar to those reported by Taskin et al., where the resolution of gastric outlet obstruction with eradication therapy was maximal at the end of the first month of treatment. Therefore, it seems that the beneficial effect of *H. pylori* eradication on gastric outlet obstruction is observed early, just a few weeks after the administration of antimicrobial treatment.

The long-term duration of the beneficial effects of *H. pylori* eradication, after the initial disappearance of the microorganism, is unknown. In one study, at a median follow-up of 12.4 months after *H. pylori* eradication therapy, the patients remained asymptomatic, without recurrence of stenosis, and required no medication. This observation suggests that the favourable
effect of *H. pylori* eradication — that is, the resolution of gastric outlet obstruction — remains for at least 1 year.

The question may be raised as to whether gastric outlet obstruction always resolves after *H. pylori* eradication treatment and, if not, what is the explanation for the negative response. Boylan & Gradzka reviewed a series of patients treated with balloon dilation and assessed the factors that affected the success rate. The eradication of *H. pylori* in nine patients was associated with the successful relief of obstruction without surgery. Only one case in this group of *H. pylori*-eradicated patients required surgery, and this patient was found to be a surreptitious NSAID user. Thus, NSAID intake should be excluded in cases with ulcer disease complicated by gastric outlet obstruction, and also in previously infected patients that do not respond or recur (especially after balloon dilation).

In another study, although the resolution of gastric outlet obstruction was generally observed, stenosis did not disappear in one patient despite *H. pylori* eradication and continuous proton pump inhibitor treatment. Furthermore, other authors have reported experience against an important role of antimicrobial treatment in gastric outlet obstruction. Thus, Gibson et al. prescribed eradication therapy alone (without endoscopic balloon dilation) to three *H. pylori*-positive patients with gastric outlet obstruction, this regimen being unsuccessful in avoiding operation. In this same study, it was suggested that patients negative for *H. pylori* responded poorly to pneumatic dilation, suggesting that they should be strongly considered for an early, definitive, acid-reducing surgical procedure.

Rinaldi et al. reported the case of a patient who had two active ulcers with duodenal stenosis. After *H. pylori* eradication, the ulcer healed, although central duodenal bulb stenosis, caused by fibrotic scarring, persisted. The authors concluded that fibrotic scarring may not regress after *H. pylori* eradication. However, as pointed out by de Boer, after close examination of the report by Rinaldi et al., it becomes evident that they actually report the successful medical treatment of duodenal stenosis. Their patient presented with pain and vomiting and was found to have active ulcers with stenosis of a deformed bulb. After diagnostic endoscopy, they prescribed *H. pylori* eradication treatment and thereafter the patient became completely symptom free. Similarly, De Francesco et al. presented the cases of two patients with endoscopically confirmed duodenal stenosis, caused by an active duodenal ulcer, and concomitant *H. pylori* infection. After the eradication of the organism, the radiographic study confirmed duodenal ulcer healing, but duodenal stenosis persisted unmodified. Nevertheless, both patients demonstrated relief from their symptoms. Thus, even though an anatomic stenosis identified only by endoscopy persisted, functional stenosis was no longer present (and, after 4 months, further endoscopic examination showed that the duodenal stenosis was still stable). These observations suggest that the main clinical issue is the patient’s symptoms and not the width of the pyloric opening itself.

It has been suggested that, in active duodenal ulcer, it is possible to identify two successive steps: duodenal ulcer activity, characterized by oedema and duodenospasm; and duodenal ulcer healing, characterized by collagen synthesis and fibrosis. Thus, gastric outlet obstruction may occur because of two underlying mechanisms. First, an acute ulcer can produce sufficient inflammation and oedema and/or muscular spasm to obstruct the lumen. Second, chronic scarring associated with fibrosis may cause narrowing and subsequent pyloric channel or duodenal obstruction. The supporters of *H. pylori* eradication as therapy for benign gastric outlet obstruction suggest that, because *H. pylori* infection causes severe inflammation with impressive oedema, the gastric outlet obstruction is provoked more by oedema than by fibrosis, and *H. pylori* eradication reduces oedema and permits resolution of the gastric outlet obstruction.

Nevertheless, Borody et al. believe that even tight stricturing and (presumably) associated fibrosis may be reversible. They postulated that the resolution of associated luminal oedema following *H. pylori* eradication allowed early improvement in gastric emptying and symptoms. One could, however, speculate that such an approach might only be useful in the subset of patients with benign gastric outlet obstruction and an acute, oedematous ulcer, as opposed to the situation in patients who present with a non-ulcerated, fibrotic stricture (after having been afflicted with recurrent ulcers over many years), in whom antimicrobial therapy alone would not be sufficient to resolve the problem. Nevertheless, although fibrosis may be an irreversible (or at best only partially reversible) phenomenon, *H. pylori* eradication is followed by duodenal ulcer healing and decreases in oedema and spasm, which may explain the symptomatic improvement even in (presumably) fibrotic stenosis. Furthermore, some studies have demonstrated...
that the ‘fibrotic’ pylorus may open up over time, thus suggesting that a few months of follow-up might not have allowed some authors to witness this. In this context, some authors have proposed that endoscopic balloon dilation could be used first to dilate the fibrous stricture, followed by anti-

\textit{H. pylori} therapy to prevent re-ulceration and re-stenosis. Finally, some observations suggest that, even when the stomach is not emptying adequately, oral antibiotics can eradicate \textit{H. pylori}, presumably by their topical action. That topical therapy can be used successfully is further supported by Kimura et al., who created pyloric obstruction with a balloon before administering an antimicrobial ‘cocktail’. In summary, it can be advised that treatment should start pharmacologically with the eradication of \textit{H. pylori} even when stenosis is considered to be fibrotic or when there is some gastric stasis. As suggested by de Boer & Driessen, because these patients have ulcer disease, they therefore need eradication therapy, and the aforementioned results suggest that it is best given right from the start.

It is unknown whether maintenance treatment with antisecretory drugs is necessary after \textit{H. pylori} eradication has been achieved and gastric outlet obstruction resolved. In a recent study, Taskin et al. administered \textit{H. pylori} eradication therapy to 10 patients presenting with gastric outlet obstruction. The infection was eradicated and complete ulcer healing was observed in all patients. Nevertheless, one patient had duodenal perforation and underwent surgical intervention following medical treatment, despite the eradication of \textit{H. pylori}. Furthermore, ulcer recurrence was noted in two of the other nine patients, and in one the recurrent ulcer was complicated by obstruction. Because \textit{H. pylori} could not be detected at the time of ulcer recurrence, it could not be attributed to \textit{H. pylori} re-infection or recrudescence. Thus, some authors have suggested that the long-term use of acid suppression despite \textit{H. pylori} eradication in ulcer disease complicated by gastric outlet obstruction may be justified. It is clear that further studies with a higher number of patients and longer follow-up are necessary to conclude whether the \textit{H. pylori} eradication regimen should be followed by antisecretory maintenance treatment in all cases.

CONCLUSIONS

The prevalence of \textit{H. pylori} infection in peptic ulcer disease complicated by gastric outlet obstruction seems to be, overall, lower than that reported in non-complicated ulcer disease, with a mean value of 69%. However, \textit{H. pylori} infection rates in various studies range from 33% to 91%, suggesting that differences in variables, such as the number and type of diagnostic methods used or the frequency of NSAID intake, may be responsible for the low prevalence reported in some studies. The resolution of gastric outlet obstruction after the eradication of \textit{H. pylori} has been demonstrated by several studies. It seems that the beneficial effect of \textit{H. pylori} eradication on gastric outlet obstruction is observed early, just a few weeks after the administration of antimicrobial treatment. Furthermore, this favourable effect seems to remain in long-term follow-up. Nevertheless, gastric outlet obstruction does not always resolve after \textit{H. pylori} eradication treatment, and the explanation for the failures is not completely clear, NSAID intake perhaps playing a major role in these cases. Treatment should start pharmacologically with the eradication of \textit{H. pylori} even when stenosis is considered to be fibrotic or when there is some gastric stasis. In summary, \textit{H. pylori} eradication therapy should be considered the first step in the treatment of duodenal or pyloric \textit{H. pylori}-positive stenosis, whereas dilation or surgery should be reserved for patients who do not respond to such medical therapy.

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REFERENCES


