Is Raised *Helicobacter pylori* Antibody Titre Enough to Decide Retreatment?

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**Abstract**

**Background:** *Helicobacter pylori* infection causes a rise in its antibodies which take almost a year to come to baseline following successful eradication treatment. Checking these values in between a year may give falsely high values and many patients may thus be over treated.

**Aims:** To serially determine *Helicobacter pylori* antibody titres in patients after giving them triple therapy for *H. pylori* eradication and see how these values drop over time.

**Study type, Settings and duration:** Longitudinal study conducted in Department of Gastroenterology and Hepatology, Pakistan Medical Research Council, Research Centre, Jinnah Post Graduate Medical Centre, Karachi, from May 2006 to April 2010.

**Subjects and Methods:** Over the period of four years, 186 patients who were found positive for campylobacter like organism test during endoscopy were further tested for anti *H. pylori* IgG titre before being treated for *H.pylori*. Patients were given triple therapy comprising of Omeprazole (20mg twice daily), Amoxicillin (1gm twice daily) and Clarithromycin (500mg twice daily) for a week and were followed at 1, 3, 6 and 12 months to check symptomatic relief and they were tested again for *H.Pylori* antibody titres. Data was collected on pre-designed proforma which included patient’s demography, symptoms and diagnosis.

**Results:** Out of 186 patients who had a positive campylobacter like organism test, 173 patients consented to participate in the study. Serology for *H.Pylori* was positive in 119(68%) cases. A decline in mean antibody titres was observed as 11%, 21.5%, 54.7% and 59.2% at 1, 3, 6 and 12 months respectively.

**Conclusions:** Sensitivity of serology for diagnosing *H. pylori* infection is good but using these as a tool for monitoring response to treatment is doubtful. A slow drop in *H. pylori* antibodies was seen over 12 months and therefore, physicians are cautioned not to retreat the already treated cases till about one year post treatment.

**Policy message:** *H. pylori* antibodies should be checked on regular basis to diagnose new cases but it should not be used in previously treated patients to retreat.

**Key words:** *Helicobacter pylori*, antibody titres, triple therapy.

**Introduction**

*Helicobacter pylori* is a spiral shaped, gram negative fastidious organism. Since the discovery of *H. pylori* as an infective agent the organism has been described as etiological agent in the development of gastritis, gastro-duodenal ulcers and gastric malignancies.

A number of tests are available for diagnosis of *H. pylori* infection which include invasive (Campylobacter like organism, Histopathology and culture) and non invasive tests (*H. pylori* stool antigen test, IgG serology). Invasive and non invasive tests have their own advantages and limitations. Invasive tests are usually considered more appropriate for assessing pretreatment status of patient as endoscopy also reveals treatment indications e.g. presence of ulcers or gastritis.

Non invasive tests particularly serology are usually preferred for diagnostic purpose as they are cost effective and convenient. Enzyme linked Immunosorbent Assay (ELISA) for detection of serum IgG against *H. pylori* are reported to be 93% sensitive and 90% specific for diagnosing *H. pylori* infection in comparison to the urea breath test. But after treatment, serum IgG antibodies may not be useful as an effective diagnostic tool for *H. pylori* infection as antibody titres remain elevated for a longer periods of time after treatment. Hence serology results (both quantitative and qualitative) will yield a false positive reaction resulting in repeated treatment of patients even after eradication.
This study was carried out to determine *H. pylori* antibody titres of patients who had received *H. pylori* treatment to find out the time taken for *H. pylori* antibody titres to drop after treatment and hence to decide that whether raised *H. pylori* titre is an indication for retreatment?

**Subjects and Methods**

This was a longitudinal study carried out from March 2006 to May 2010. The study was conducted in PMRC Research Centre specialized for Gastroenterology & Hepatology, Jinnah Postgraduate Medical Center (JPMC), Karachi.

All patients presenting with dyspeptic symptoms and referred for upper GI endoscopy to establish their diagnosis were checked for campylobacter like organism test using antral biopsy during endoscopy. Those who yielded a positive campylobacter like organism test were included in the study after taking informed consent. Patients who had a history of using proton pump inhibitor or antibiotics in the last two weeks and previously treated cases of *H. pylori* were excluded from the study. A questionnaire was filled for each patient to collect necessary data about patient demographics, symptoms and diagnosis. Five ml blood was collected for baseline *H. pylori* IgG titres before initiation of therapy and patients were prescribed triple therapy comprising of Clarithromycin (500mg twice daily), Amoxicillin (1gm thrice daily) and Omeprazole (20mg twice daily) for one week. Patients were issued follow-up cards for revisits, where apart from clinical evaluation they were also subjected to a repeat blood test for *H. pylori* IgG titres at 1, 3, 6 and 12 months post therapy. Sera were separated and stored at -20°C until test was performed. Antibody titres were determined by ELISA method. HpG screen ELISA kit made by Genesis company England was used and cut off points were described as per manufacturer’s guidelines.

Study was approved by local advisory committee and informed consent was obtained before including the patients in the study.

The data feeding and analysis is done on computer package “Microsoft Excel”. The results are given in the text as mean (X) ± standard deviation (S.D) for continuous variables like age, antibody titres and percentage for categorical variables like gender and proportion of patients with positive or negative antibody titres.

**Results**

During the 4 years of study period, a total of 186 patients showed a positive campylobacter like organism test performed on antral biopsy collected during endoscopy. Eleven patients did not consent to participate in the study thus leaving 175 patients. Of 175 cases, 114(65%) patients were males and 61(35%) females. Age range of patients was 13-70 years with a mean age of 39.6 ±12.2 years.

Out of 175 patients, 119(68%) had positive *H. pylori* IgG antibody titres. Mean antibody titre of these patients before therapy was 42.4 U/ml. Mean antibody titres dropped by 11% after one month of triple therapy. At 3-months post treatment mean drop in IgG titres was 21.5%. Antibody titres further dropped to 54.7% and 59.2% at 6 and 12-months respectively.

When analyzed on the basis of positive antibody titres, number and percentages of positive patients at 1, 3, 6 and 12 months are shown in Table-1.

**Table 1: Number and percentage of patients with positive *H. pylori* antibody titres during followup period.**

<table>
<thead>
<tr>
<th>Follow-up period</th>
<th>Total # of patients followed</th>
<th>No. (%) of patients with positive antibody titre i.e. &gt;?</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 month</td>
<td>175</td>
<td>119(68)</td>
</tr>
<tr>
<td>1 month</td>
<td>74</td>
<td>44(59.4)</td>
</tr>
<tr>
<td>3 months</td>
<td>54</td>
<td>24(44.4)</td>
</tr>
<tr>
<td>6 months</td>
<td>37</td>
<td>5(13.6)</td>
</tr>
<tr>
<td>12 months</td>
<td>27</td>
<td>6(22.2)</td>
</tr>
</tbody>
</table>

**Discussion**

In the present study, out of 175 patients who were positive on campylobacter like organism test, serology for *H. pylori* was positive in only 119(68%) patients indicating a lower sensitivity of serology for diagnostic purposes. Non invasive tests for *H. pylori* are considered an important tool in primary health care for both initial diagnosis of infection and confirmation of eradication. Despite being cost effective and convenient, there are serious doubts regarding their accuracy in terms of sensitivity and specificity.

Although the sensitivity of serology described in literature is higher than that observed in this study but it varies considerably within the different kits and population. Only campylobacter like organism test is not enough to establish sensitivity and specificity as histopathology (which is considered gold standard for diagnosis of *H. pylori* infection) and culture results should also be correlated.

In the present study, after one month of treatment 11% fall in antibody titres was observed which is in concordance with other studies. Laheij et al reported that a drop in antibody titres at 1-month post therapy in patients who failed to eradicate the infection hence showing that drop in antibody titres cannot be taken as part of successful eradication. At 3, 6 and 12 months post treatment a sequential drop in antibody titres was observed which is similar to other studies.
show that a significant drop in antibody titres is seen after 6-months of treatment where a fall of more than 50% is seen.10

Similarly, when analyzed on the basis of normalization of antibody titres post treatment only 40% patients showed normal titres after 1-month of treatment. At 6-months of treatment antibody titres normalized in 86% patients which dropped to 78% at 1-year. Normalization of antibody titres in up to 81% patients is reported by others11 and was also seen in our study but decrease from 86% to 78% at 12-months probably indicates some re-infection which is described as a common phenomenon in H. pylori patients14.

This study and other studies support the idea that although serology is a non invasive and easy method for monitoring the treatment response but H. pylori antibody titres drop very slowly and may take several months to yield negative results. Hence physicians should be careful in choosing serology alone for diagnostic purposes and retreatment in those with previous history of anti H. pylori treatment.

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References