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# Helicobacter Pylori gastritis and risk of ischaemic stroke

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## Abstract

**Objective:** To identify the association between H. Pylori gastritis and stroke.

**Method:** Patients with biopsy proven H.Pylori gastritis and non H.Pylori gastritis were enrolled. Patients were followed for a period of two years.

**Results:** A total of 326 patients were included in the study. 162 patients were with H.Pylori gastritis. There was no significance difference in age, sex and duration of symptoms in the two groups. Three patients in H.Pylori group had stroke or TIA as compared to one in non H.Pylori group. Patients with H Pylori gastritis were more likely to die or have cardiac and or neurological event as compared to Non H pylori gastritis (OR 1.23, 95% CI 0.89-1.67). This relationship was not significant after adjusting for cardiovascular risk factors (AOR 0.85, 95% CI 0.45- 1.31).

**Conclusion:** H. Pylori gastritis is not independently associated with increased risk for stroke. Larger, randomized studies are needed to confirm our findings (JPMA 58:368;2008).

## Introduction

An association between chronic infections and atherosclerosis has been a topic of great interest for researcher for the last decade.<sup>1</sup> The association between Helicobacter Pylori infection and atherosclerosis and coronary artery disease has long been debated.<sup>2</sup>

An association between Helicobacter Pylori infection and stroke has been recently suggested.<sup>3-5</sup> Recent studies suggested that H Pylori infection is more likely to be related to large vessel or small vessel stroke as compared to cardioembolic stroke. Masoud et al from Iran reported an association between H Pylori infection and non cardioembolic ischemic stroke.<sup>6</sup> Investigators from Korea identified that H Pylori seropositivity was significantly more common in Large artery stroke patients as compared to control group (87% vs 60%,  $P < 0.001$ ).<sup>7</sup> H Pylori seropositivity was associated with all stroke subtypes (OR 1.63, 95%CI: 1.02-2.60), lacunar or small artery strokes (OR 2.21, 95%CI: 1.12-4.38) and large vessel stroke (OR 2.58, 95%CI: 1.44-4.63) in another study.<sup>8</sup> Heuschmann showed that chronic H Pylori infection was associated with higher

risk of small artery stroke (OR 3.31, CI 1.15-9.56). It was not a significant factor for all stroke subtypes.<sup>9</sup> Pietroiusti et al reported high likelihood of large vessel stroke as compared to cardioembolic stroke (OR 3.04, CI 1.43-6.49) and as compared to control subjects (OR 4.3, CI 2.12-8.64).<sup>10</sup>

More recent data suggested that a specific strain of H Pylori (CAG-A positive strain) was more strongly associated with risk of stroke as compared to other strains.<sup>11-13</sup> All these studies have looked for antibodies against H Pylori among stroke patients and compared them with control population. Our study is the first study to follow patients with proven H Pylori gastritis over a period of time to identify risk of stroke in comparison to a control population.

## Patients and Methods

Patients with biopsy proven H Pylori gastritis and non- H pylori gastritis (control group) were enrolled in the study at The Aga Khan University, Karachi during 1999-2000. All patients were evaluated for cardiac or stroke risk factors including Hypertension, Diabetes and Smoking. Patients were followed for a mean of two years by telephone or office visits. Stroke or TIA was defined as primary end

point. Angina or Myocardial infarction was defined as secondary endpoint. These patients were divided in two groups based on visualization of Helicobacter Pylori on H&E and or Giemsa stain. Patients with no H Pylori on gastric biopsy were labeled as non- H Pylori gastritis.

All patients with H Pylori gastritis were treated with standard treatment and patients with non H Pylori gastritis were treated with proton pump inhibitors, H2 receptor antagonists and Antacid preparations. Patients with Hypertension and Diabetes were treated with standard anti Hypertensive and ant Diabetic medications. Diagnosis of stroke or TIA was confirmed by a neurologist based on neurological history and exam and MRI findings and diagnosis of Angina or Myocardial infarction was established by a cardiologist based on EKG findings and cardiac enzymes.

We performed chi square tests for significance between two groups (H Pylori gastritis and non H Pylori gastritis). Association between death or neurological event (stroke or TIA) or cardiac event (Angina or MI) and H Pylori gastritis was analyzed by Logistic regression analysis. Adjusted analysis was done after adjusting for stroke or cardiac risk factors (Hypertension, Diabetes and Smoking).

## Results

Four hundred thirty four patients with sub acute to chronic gastritis were enrolled (H Pylori group= 210, Non

**Table. Comparison of baseline characteristics and follow up data.**

	H Pylori (n=162)	Non H pylori (n= 164)	P value
<b>Baseline:</b>			
Age:	18-69	20-68	
Range	46 (SD??)	46 (SD??)	0.15
Mean (SD)	90 (56%)	82 (50%)	
Male	72 (44%)	82 (50%)	
Females			
Duration of symptoms (Mean)	5 weeks	7 weeks	NS
Hypertension	33 (20%)	17 (10%)	0.05
Diabetes	15 (9%)	9 (5%)	0.09
Cigarette smoking	26 (16%)	17 (10%)	0.088
Previous stroke	1	0	NS
<b>Follow up:</b>			
Duration:			
Range	20-38	24-37 months	
Mean	28 months	29 months	NS
<b>Death or cardiac or neurological event, any</b>			
	12 (7%)	4 (2%)	0.05
Stroke	2	1	NS
Transient ischaemic attack	1	0	NS
Myocardial infarction	0	1	NS
Angina	6	1	NS
Death	3	1	NS
No cardiac/ neurological events	149 (92%)	159 (97%)	0.059

H Pylori group= 224), of these 108 (25%) were lost for follow up and 326 patients were included in the study (H Pylori group= 162 patients, Non H Pylori group= 164).

Risk factors profile of two groups was not significantly different except Hypertension was more prevalent in H Pylori group (Table). Three patients in H Pylori group had stroke during two years follow up (stroke=2, TIA=1) as compared to one in non H Pylori group. All four patients had positive risk factors for stroke. Three patients died in H Pylori group as compared to one in non H Pylori group. The cause of death was cardiac= 2 patients, gastrointestinal bleeding=1 patient and unknown=1 patient. Patients with H Pylori gastritis were more likely to die or have cardiac and or neurological event as compared to Non H pylori gastritis (OR 1.23, 95% CI 0.89-1.67). This relationship was not significant after adjusting for cardiovascular risk factors (AOR 0.85, 95% CI 0.45- 1.31).

## Discussion

Our study failed to show an independent association between H pylori gastritis and stroke. Combined risk of cardiac or neurological event and death was increased among patients with H Pylori gastritis but this was not significant after adjusting for cardiovascular risk factors.

There are many limitations to our study. About 25% patients were lost to follow up. Major reason for loss to follow up was non availability of telephone. Incidence of stroke among patients or controls was extremely low and non significant. Atherosclerosis and associated coronary or cerebrovascular disease is probably associated with prolonged, untreated H Pylori infection. Most of the published studies have looked at the IgG antibodies against H Pylori as evidence of infection. These antibodies remain positive even after eradication of the organism from gastric mucosa and complete relief of symptoms. Previous studies have not mentioned if those patients with positive IgG against H Pylori had symptoms of H Pylori gastritis or their status of treatment or eradication. It is likely that only patients with chronic, untreated H Pylori infections develop atherosclerotic complications like stroke. It is possible that this treatment may have decreased their risk of stroke up to the level of control population in our study.

Another limitation of our study is the period of follow up. There is no data to suggest time lag between H Pylori infection and development of atherosclerosis. It is possible that two years time is not enough for development of stroke and these patients may need a longer follow up.

A much larger sample size would be required to detect a statistically significant difference when comparing this group to patients with non H Pylori gastritis. An ideal

cohort to follow according to this study design would be the patients with H.Pylori in appropriate age group and followed for 10 - 15 years may give us the answer.

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