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HELICOBACTER PYLORI AND VASCULAR DISEASE

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ABSTRACT

Background: Helicobacter pylori infection is reported to have many varied extra gastrointestinal manifestation such as idiopathic thrombocytopenia, Iron deficiency anaemia, Ischemic heart disease (IHD), vascular disease, and neurological disorders (like stroke, Parkinson's disease and Alzheimer's disease)[1] Many studies conclude that the presence of chronic infection could be a risk factor for vascular disease leading to IHD.[2]

Objectives: The objective of this study was to find an association between H.pylori infection andlipidprofile and carotid intimal thickness which areestablished risk factors for vascular disease.

Methodology: A case control study of 356 patients who underwent Upper Glendoscopy and biopsy were included. Examination done on biopsied tissue divided the patients into H.pylori infected and non-infected groups. All patients underwent ultrasound Doppler of carotid arteries and lipid profile.

Results: Out of the 356 patients, 188 were found to have H.pylori infection (cases) and 168 did not (controls). The average carotid intima media thickness in H.pylori infected patients was 0.83mm, whereas in non-infected patients the average thickness was 0.72mm. Thus, there was a statistically significant correlation between carotid intimal media thickness and H.pylori infection (p=0.009). Dyslipidemia was seen in 172 patients. Dyslipidemia especially triglyceridemia correlated with increased CIMT but there was no significant correlation between deranged lipid profile and H.pylori infection.

Conclusion: This study found that Helicobacter pylori has a significant association with atherosclerosis and ischemic heart disease. The connection however is not by causing dyslipidemia and needs further studies to elucidate the pathogenesis.

KEYWORDS: Helicobacter pylori, Vasculardisease, CIMT

INTRODUCTION

The gastric spiral bacterium Helicobacter pylori infectsover 50% of the world population. [3] India has a larger share with 88% of the population infected with it.[4]

The 2005 Nobel Prize for Medicine went to Barry Marshall and Robin Warren for their demonstration of the causative link between gastric disease and H.pylori. Since then, the bacteria has been extensively investigated. In addition to its dominant causal role in peptic ulceration, it has been implicated in other gastric and even extra gastric diseases, includingchronic atrophic gastritis, gastric MALT lymphoma, gastric cancer, functional dyspepsia, idiopathic thrombocytopenic purpura (ITP), iron deficiencyanaemia, chronic urticaria,ischemic heart disease, and others[5]. Many studies have shown a strong link between ITP and H.Pylori infection.[6]There is fast accumulating data on the role of H.Pylori infection in iron deficiency anaemiaand ischemic heart disease.

The role of H.Pylori in causing ischemic heart disease remains controversial with some studies showing no correlation[7], while others showed a strong positive correlation. The mechanism by which H.Pylori causes vascular disease also remains a topic for speculation with many theories being put forward. One study showed an increase in levels of hsCRP, total cholesterol, LDL, oxidized LDL and apolipoprotein B in patients with H.Pylori infection. This was positively correlated with a severe coronary atherosclerosis in those patients.[8]

Another mechanism proposed based on a large study was that some strains of H.Pylori were able to bind to Von Willebrand factor and induce plateletaggregation in human[9]. This lead to a hypothesis that H.Pylori may elicit thrombosis leading to vascular disease.

A possible correlation between H.Pylori infection and ischemic heart disease has been explained due to cross mimicry between endothelial and bacterial antigens. It has been proposed that asymmetric dimethyl-arginine (inhibitor of nitric oxide synthase)levels are increased in H.Pylori infection leading to procoagulant state.[10]

Thus the link between IHD and H.Pylori remains largely unclear andour study was to establish the presence of this link and to elucidate the pathogenesis behind this link.

Abnormal lipid profile is a strong risk factor for atherosclerosis and Carotid intima media thickness (CIMT) measurement is awidely used surrogate marker for atherosclerosis.[11] In a recent meta-analysis, it was concluded that increments of 0.1mm in CIMT translated to a 10-15% increase in risk for having an myocardial infraction and 13-18% increased risk for stroke.[12] Therefore, we used these markers to correlate presence of vascular disease with H.Pylori infection and to test if the pathogenesis was due to derangement of lipid profile.

AIM & OBJECTIVES

The objectives of our study was two-fold:

- To evaluate if there was a link between vascular disease and H.Pylori infection in our patients.
- Is alink was established, to elucidate the mechanism by which H.Pylori could cause vascular disease.

MATERIALS AND METHODS

The study was done in Department of Medicine, from January 2013 to January 2014 after obtaining ethical clearance. It is a cross-sectional case-control study on 356 patients who underwent endoscopy for various reasons. Patients between the age of 18 years to 45 years without any of the traditional risk factors for vascular disease (hypertension, diabetes, hypothyroidism, BMI >23, nephrotic syndrome and history of smoking) were included in the study after written informed consent.

Gastric biopsy was taken from patients who underwent upper gastrointestinal endoscopy and was subjected to histopathological examination using special stains for presence of H.Pylori. Patients were assigned to case or control group based on presence of absence of H.Pylori infection respectively. Fasting lipid profile and measurement of Carotid Intima Media Thickness by ultrasound Doppler was done for all patients.

RESULTS

A total of 356 patients were included in the study with 208 males (58.4%) and 148 females (41.6%). Mean age of the patients studied was 33 years. 188 patients (52.8%) had H.Pylori infection and were grouped under Cases where as 168

patients (47.9%) were free of infection and grouped under Controls.

Table 1: Age Distribution of the Patients

Age group	18-24 Yrs	25-29 Yrs	30-34	35-39 Yrs	40-44 Yrs
H.Pylori positive	20	28	64	44	32
H.Pylori negative	16	48	28	40	36

Helicobacter pylori infection did not correlate significantly with the age of the patients (p=0.3) nor did it correlate with gender (p=0.27)

Table 2: Gender Distribution

	Males	Females
H.Pylori positive	104	84
H.Pylori negative	104	64

H. Pylori infection correlated positively and significantly with carotid intima media thickness (p=0.009). Patients infected with H.Pylori had higher carotid intimal thickness (above 0.8mm) whereas those in the non-infected group had lower CIMT. Mean CIMT in infected cases was 0.83 whereas in non-infected controls it was 0.72.

Table 3: CIMT Thikness with H. Pylori Positive and H. Pylori Negative

CIMT THIKNESS:	H. Pylori Positive	H. Pylori Negative
0.5-0.59	12	32
0.6-0.69	20	56
0.7-0.79	32	32
0.8-0.89	48	16
0.9-0.99	44	24
>1	32	8

Age can be confounding factor in the measurement of CIMT, but our study did not show a statistically significant correlation between age and CIMT. Highest CIMT was found in the age group of 30 to 34 years. Mean CIMT in males was 0.85 and in females it was found to be 0.66mm.CIMT correlated positively and significantly with dyslipidaemia especially hypertriglyceridemia (p=0.03). A total of 172 patients enrolled had dyslipidaemia with LDL and TAG elevated the most.

Table 4: CIMT THIKNESS: with Deranged TAG, Deranged LDL and Deranged HDL

CIMT THIKNESS:	Deranged TAG	Deranged LDL	Deranged HDL
0.5-0.59	8	4	4
0.6-0.69	12	16	8
0.7-0.79	12	16	4
0.8-0.89	32	32	4
0.9-0.99	20	36	12
>1	12	16	12

However H.Pylori infection did not correlate with dyslipidaemia with only 92 patients in the cases group having deranged lipid profile.

Table 5: H. Pylori Status

Pylori status	Dyslipidaemia	Normallipid Profile
H.Pylori Positive	92	96
H.Pylori Negative	80	88

DISCUSSIONS

The studies which indicate a link between H.Pylori and vascular disease have been sero-epidemiological and the issue remains controversial. One of the early studies, Mendall et al showed a higher prevalence of H. Pylori (IgG antibodies measured by ELISA) infection in patients with ischemic heart disease. [(13)] This was confirmed by many other studies. A study by Majka et al showed a significant reduction in plasma levels of total cholesterol, LDL, IL-8, and fibrinogen after eradication of H.Pylori.[14] In our study, 356 people without traditional risk factors for atherosclerosis were studied for the presence of Helicobacter pylori infection and it was found that 52.8%of the study population had the infection. This shows the high prevalence of a well treatable infection in the population. Further presence of Helicobacter pylori infection showed a statistically significant association with elevated carotid intima media thickness. Dyslipidemia also showed a strong correlation with elevated carotid intima media thickness. The dyslipidemia in the study population however did not show a statistically significant association with the presence of helicobacter pylori infection. This implies the existence of a missing link between the presence of helicobacter pylori infection and increased carotid intima media thickness, which calls for further studies.

CONCLUSIONS

Helicobacter pylori infection is very common with high prevalence rates in developing countries like India. It has an association with atherosclerosis which is gradually increasing even in lower socioeconomic strata of the society. However, the connecting link between Helicobacter pylori infection and atherosclerosis is not dyslipidemia and needs further studies to elucidate the pathogenesis. This infection should be recognized early since it is readily treatable. It can claim status of an infection cause for cerebrovascular accidents and cardiovascular disease.

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