Helicobacter Pylori Positive Dyspepsia in Relation to Ocular Manifestations and Primary Open Angle Glaucoma

Delhi J Ophthalmol 2014; 24 (4): 237-240
DOI: http://dx.doi.org/10.7869/djo.50

*Aim:* To find out the correlation between H. Pylori infection and various ocular manifestations including Primary open angle (POAG) glaucoma, uveitis, blepharitis, CSR and dry eye syndromes.

**Materials and Methods:** Patients of dyspepsia visiting gastroenterology department (Gastrogroup-100 patients) were subjected to detailed ocular examination and patients visiting eye OPD (POAG- 50 patients) were subjected for endoscopic and histopathological examination for the confirmation of H. Pylori (HP) infection. In gastrogroup, we have included 50 H. pylori positive and 50 H. pylori negative patients.

**Results:** In Gastrogroup (HP+ve) – glaucoma in 3 (6%), blepharitis in 7 (14%) and dry eye in 5(10%) patients were detected. In Gastrogroup (HP-ve) - glaucoma in 1 (2%), blepharitis in 2 (4%) and dry eye in 2 (4%) patients were found. No patient was detected positive for CSR and uveitis in both the groups. Out of 50 patients, 44 subjects were HP+ve and 6 were HP-ve.88% of patients were found positive for H. Pylori infection in POAG group.

**Conclusions:** The prevalence of dry eye, POAG was found higher in H. pylori positive patients as compared to H. pylori negative patients. This correlation of H. pylori positivity and H. pylori negativity was not statistically significant in present study (p=0.12 for POAG, p=0.24 for Dry eye). In POAG group, prevalence of H. pylori infection seems to be high (88%), but general population of north India found to have same infectivity rate. The prevalence of blepharitis was found higher in H. pylori positive individuals in present study (p=0.03). It is suggested that any patient with recurrent gastritis should be subjected for detailed ocular examination.

**Keywords:** H.pylori • dyspepsia • primary open angle glaucoma

Glaucma is the second leading cause of blindness in the world after cataract and the leading cause of irreversible blindness. Many aspects of its pathogenesis remain unknown. Helicobacter pylori infection is also one of the world’s most common infection. In recent years, a possible association between H. pylori infection and eye diseases including glaucoma, Sjogren's syndrome, blepharitis, central serous chorioretinopathy and uveitis has been proposed. The relationship between these different eye diseases and H. Pylori infection is not clear.** The present study is an attempt to study any correlation of H. pylori positive gastritis in relation to ocular diseases especially in relation to diagnosed cases of POAG.

**Material & Methods**

One hundred and fifty subjects were recruited in this study from July 2010 to June 2011. Informed consent was obtained from all participants before ophthalmic examination as well as before endoscopic procedure approved by ethical committee of IGMC, Shimla. Subjects were divided in to two groups as: Gastrogroup – one hundred subjects from Gastroenterology department. In Gastro group, we have included fifty H. pylori positive and fifty H. pylori negative subjects confirmed by histopathological examination. Second group was POAG group - fifty subjects from Ophthalmology department.

**Inclusion Criteria**

Age > 40 Years, Patients have...
established POAG presenting in Ophthalmology department. Patients having acid-peptic ulcer disease who presented in Gastroenterology department were included in the study.

**Exclusion Criteria**

Patient with history of H. pylori eradication therapy (one week triple therapy a full dose proton pump inhibitor, with either amoxicillin 1g and clarithromycin 500mg or metronidazole, 400mg and clarithromycin 250mg, all given twice daily), history of any systemic disease require chronic medication, patient having any systemic disease as a cause for ocular manifestations other than H. pylori infection, subjects who had undergone previous gastric surgery, patients on anticoagulant therapy, history of any cardiopulmonary disease were excluded from the study.

Gastro group was subjected to detailed ocular examination including slit lamp bimicroscopy, fundus examination, Goldman applanation tonometry, gonioscopy, automated perimetry (Octopus 900) for detection of following ocular diseases: glaucoma, uveitis, blepharitis, central serous chorioretinopathy and dry eye syndrome. POAG was defined as IOP higher than 22 mmHg without medication and measured at least on two consecutive occasions separated by an interval of at least 2 hours, plus glaucomatous visual field or optic disc changes.

POAG group subjected to endoscopic examination. Before procedure an informed consent was taken from all the patients, approved by ethical committee of IGMC, Shimla. During endoscopy three biopsy specimens were obtained from both the antrum and the gastric corpus. Specimens were subjected to rapid urease test followed by Haematoxylin & eosin and Gimsa staining. Data was analyzed using Commercial SPSS 17 trial version. Chi square, Mann Whitney and Student t tests were used depending on various variables. The p value was calculated and value less than 0.05 implied statistically significant at 5% confidence limit.

**Results**

There was no statistically significant difference in age and sex between the groups (Table-1). Using Chi-square test visual acuity revealed no statistically significant differences among the groups. Mean intraocular pressure in Right eye of G (HP + ve) group was 17.4±1.4 mm of Hg while in G (HP - ve) group was 16.9±2.1 mm of Hg. Student t test showed no statistical significant difference. Mean IOP left eye of cases were 17.8±1.6 mm of Hg while in control were 16.9±2.0 mm of Hg. Student t test revealed significant statistical difference between two groups (Table-2). Mean value of vertical cup disc ratio was higher in G (HP + ve) group as compared to G (HP - ve) group which was found statistically significant by Mann Whitney test (Table-2).

In H. pylori positive group, three patients have POAG, while in control group only one patient has POAG (Table-3, Figure 1). Seven patients (14%) have blepharitis in G (HP + ve) group and two (4%) in G (HP - ve) group. Five patients (10%) have dry eye in G (HP + ve) and two (4%) patients in G (HP - ve) group. No patient came positive for CSR and uveitis in our study. Second part of study includes established cases of Primary open angle glaucoma (POAG) group. These patients were subjected to endoscopy followed by Rapid urease test and histopathological examination. In POAG group 44 (88%) patients are positive and 0(12%) are found negative for H. pylori infection. General population of North India have same infectivity rate (88%) according to World Gastroenterology Organisation Global Guidelines 2010.8

**Discussion**

The present study is an attempt to study any correlation of H. pylori positive gastritis in relation to ocular diseases especially in relation to POAG and patients suffering from POAG have been subjected to Gastro endoscopy, rapid urease test and histopathological examination. There was no difference between G (HP + ve) and G (HP - ve) group with...
could reflect the severity of glaucomatous damage in these aqueous humour of POAG patients, suggesting that this with the concentration of H.pylori-specific IgG in the
In our study we have found that there is discrepancy between optic nerve head cupping and IOP in right eye. The reason may be the intraocular pressure. Although we have used Goldman applanation tonometry for recording IOP but discrepancy may be due to interobserver error or instrumental error. The Optic cup disc ratio (OCD) is more reliable criteria as compared to IOP. The chances of error in OCD calculation is less as compared to IOP as calculation in OCD is computer based. We calculated OCD ratio using KOWA-VX fundus camera The edge of optic disc was then detected by use of a Canny edge detection filter. The profile was then obtained around the center of the optic disc. Subsequently, the edges of the cup area were determined by classification of the profiles based on zero-crossing method. Lastly, the cup-to-disc ratio was calculated

In our study, POAG was found in three patients in G (HP + ve) group. In control group, open angle glaucoma was present in only one patient. There was no statistically significant difference found between two groups in relation to POAG by chi-square test at p value = 0.12 (Figure 1). In a study by Ozturk et al the POAG was found in one patient. In the histological H. pylori (-) group, no patient had POAG. Statistically, there was no difference found with respect to presence of POAG between H. pylori infected and non-infected patients. When observed, the results of our study were precisely similar to the compared study. In our study, it has been found that 44 patients are H. pylori positive whereas rest six are H. pylori negative in POAG group as confirmed by biopsy (a Gold standard method).This shows that infectivity of H. pylori is much higher among POAG group up to 88%. A similar study by Kountouras et al reported 87.5% H. pylori positivity in POAG group as confirmed by biopsy. These results are precisely same. The general population of North India also found to have the same infectivity rate (88%) according to World Gastroenterology Organisation Global Guidelines 2010. So, further studies based on large sample size is required to confirm this possible relationship.

Kountouras et al first reported an association between glaucoma and H.pylori infection. Even Ozturk et al have demonstrated a link between glaucoma and H.pylori serology. Kountouras et al investigated 41 glaucomatous patients (78% with primary open-angle glaucoma, 12% with pseudoexfoliative glaucoma - PXFG) and 30 age-matched anaemic controls. All 71 subjects underwent diagnostic gastroscopy and gastric mucosa biopsies to determine H.pylori infection by means of histopathologic analysis and urease test. The prevalence of H.pylori infection and serum levels of IgG anti-H.pylori were significantly higher among glaucoma patients than controls. This result has been confirmed by a Chinese report but other studies did not detect any association between glaucoma and H.pylori infection. Kountouras et al examined H.pylori infection directly by searching for H.pylori in endoscopic specimens, while the other studies examined H.pylori infection indirectly by detecting the antibodies produced against the bacterium. Kurtz et al also evaluated seropositivity to the cytotoxin-associated gene A (CagA) antigen, an important virulence marker of some strains of Helicobacter pylori. They found no association between seropositivity for virulent CagA-bearing H.pylori strains and the occurrence of glaucoma among the patients in their study. It should be noted that the detection of anti-H.pylori antibodies serum does not only reflect current infection but may also be a hallmark of eradicated infections. Furthermore, serum antibodies are not sensitive markers of H.pylori infection, as this bacterium does not penetrate into the blood stream but localizes between the gastric mucosa and the mucus layer, mainly inducing the production of mucosal IgA rather than serum IgG. Consequently, evaluations of H.pylori infection status by serum ELISA and the histological examination of gastric mucosa may not always be congruent. In addition, the ELISA technique of detecting H.pylori infection has been
reported to have suboptimal sensitivity and specificity. On the basis of different studies we have discussed, some show positive correlation regarding infectivity of H. pylori towards glaucoma while others show no relation. The difference in the studies may be due to racial differentiation, using different control group, site specificity of sample, method of detection of H. pylori, sample size etc. In G (HP + ve) group 7 patients found to have blepharitis while in control only two patients had blepharitis. Chi-square test revealed statistically significant difference between two groups (Table-3). A retrospective study by Sacca SC et al showed H. pylori infection prevalence of approximately 76.3% in blepharitis group, compared with those of 42.3% of the control group.

Main difference between the two lies in the nature of study. Our study has a prospective nature whereas the other is of retrospective nature. In our study we observed that five patients had dry eyes in G (HP + ve) group and two in G (HP - ve) group. However, incidence of dry eye was higher in G (HP + ve) group but Chi-square test had not revealed any statistically significant difference between two groups (Table3). Blomberg et al has found correlation between H. pylori infection and dry eye. Fifty three patients were examined retrospectively, Thirty three patients were found H.pylori negative and twenty were H.pylori positive. Most of the patients (35.8%) belong to sicca–stage I. In the statistic evaluation, the H.pylori positive patients have enhanced susceptibility to quantitative moisturizing disorders (e.g. reduced Schirmer’s test). Qualitative parameters (break up time and lid parallel conjunctival folds) showed no relation to H.pylori infection but were significantly age related (p < 0.01). Difference in studies may be due to prospective nature of our study as compared to retrospective nature of other study. No patient was found positive for CSR and Uveitis in both the groups. Cottecelli et al observed that prevalence of H. pylori infection was 78.2% in CSR patients and 43.5% in control subjects (p<0.03 by two-tailed Fisher exact test). The difference in our study may be due to the fact that these diseases are more common in younger age group whereas our study included patients more than 40 yrs of age. The present study explores correlation between H.pylori positive gastritis and ocular diseases, especially the all diagnosed cases of POAG as per the criteria subjected to gastro endoscopy by gastroenterologist, rapid urease test and histopathological examination. The prevalence of some ocular diseases i.e. Dry eye, POAG was found higher in H. pylori positive patients as compared to H. pylori negative patients. This correlation of H. Pylori positivity and H. pylori negativity was not statistically significant in present study. The prevalence of blepharitis was found higher in H. pylori positive individual in present study. Thus, the present study probably seems to confirm a relationship between blepharitis and H. pylori positivity. It is suggested, any patient with recurrent gastritis should be subjected for detailed ocular examination. There was no statistical significant correlation of POAG between H. pylori positive and H. pylori negative patients. In POAG group, prevalence of H. pylori infection seems to be high (88%), but general population of north India found to have same infectivity rate(88%) according to World Gastroenterology Organisation Global Guidelines 2010. POAG and H. pylori positivity cannot strictly correlated, but correlation may exist. In final conclusion, multicentric studies involving large number of patients in H. pylori positive group subjected to detailed ocular examinations and large number of POAG patients subjected to gastro endoscopy may be helpful in attributing role of H. Pylori infection of some significance in relation to ocular changes and open angle glaucoma in future.

Financial & competing interest disclosure
The authors do not have any competing interests in any product/ procedure mentioned in this study. The authors do not have any financial interests in any product / procedure mentioned in this study.