

Association between *Helicobacter pylori* infection and primary open-angle glaucoma

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Article Info

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Received: 12 November 2018
Accepted: 3 February 2019
Available Online: 14 March 2019

ISSN: 2224-7750 (Online)
2074-2908 (Print)

DOI: 10.3329/bsmmuj.v12i1.40484

Cite this article:

Sultana S, Khan N, Islam MS. Association between *Helicobacter pylori* infection and primary open-angle glaucoma. Bangabandhu Sheikh Mujib Med Univ J. 2019; 12: 25-28.

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A Journal of Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh

Abstract

The pathological processes of primary open-angle glaucoma is unknown. Several studies show the relation between *Helicobacter pylori* infection and primary open-angle glaucoma. The purpose of this study was to assess the association between *H. pylori* infection and primary open-angle glaucoma. Forty patients of diagnosed primary open-angle glaucoma were selected as case and 40 participants without primary open-angle glaucoma were selected as control as per inclusion and exclusion criteria. Complete clinical evaluation including history, physical examination, relevant ocular examinations and laboratory investigations were performed. Serologic evidence of *H. pylori* infection was found in 75% of patients with primary open-angle glaucoma and 30% of patients without primary open-angle glaucoma which achieved statistically significant difference ($p=0.000$, $OR=7.00$ and $CI\ 95\% =2.61-18.74$). ^{13}C urea breath test was positive in 70% in case group and 37.5% in control group which also achieved statistically significant difference ($p=0.003$, $OR=3.89$ and $CI\ 95\% =1.53-9.87$). The findings revealed significant association between *H. pylori* infection and primary open-angle glaucoma.

Introduction

Primary open-angle glaucoma is the most common cause of irreversible blindness worldwide.¹ It is usually bilateral which is adult onset characterized by an intraocular pressure more than 21 mmHg at some stage, glaucomatous optic nerve damage, an open anterior chamber angle, characteristic visual field loss as damage progresses, absence of signs of secondary glaucoma or a non-glaucomatous cause for the optic neuropathy. The pathologic processes of glaucoma still remains hidden in many points. Agedness, hereditary and raised intraocular pressure may be responsible factors. Changes in endothelin-dependent vascular regulation, cytokine-dependent platelet aggregation which impaired ocular blood flow, influencing apoptotic process and apoptotic loss of optic disk neurons and other autoimmune mechanisms which may induce and/or exacerbate glaucomatous optic neuropathy.²⁻⁴

Helicobacter pylori is a Gram negative bacterium which causes many upper gastrointestinal diseases. It mainly resides in the stomach, but it also produces a systemic host immunologic response and the release of various vasoactive and pro-inflammatory substances. Thus, *H. pylori* may be partly responsible for the occurrence of diseases in extradigestive areas such as ischemic heart disease, cardiovascular

disease, Raynaud's phenomenon and migraine. Another likely association is the glaucoma which thought to linked with *H. pylori* through some mechanisms include: Stimulating aggregation of platelet and platelet-leucocyte, stimulating release of pro-inflammatory and vasoactive substances, inducing cross mimicry between endothelial and *H. pylori* antigens and promoting apoptotic process.⁵ Recently various debate about their association.⁶ Some studies in Greece, china, Iran, and Australia have reported relatively higher association between *H. pylori* infection and open-angle glaucoma.⁷⁻¹¹ However, other studies in Canada and Iran have not reported statistically significant differences between them.¹²⁻¹⁴ Other studies found that eradication of *H. pylori* may be beneficial in the management of chronic open-angle glaucoma.¹⁵ Thinking about these dispute, this study was done to compare the association of *H. pylori* infection in patients having primary open-angle glaucoma and control group of participants.

Materials and Methods

This study was carried out from March, 2015 to August, 2017. Forty patients with primary open-angle glaucoma were selected as case and 40 patients as control group as per inclusion and exclusion criteria. The selection criteria of cases



were age between 40-80 years, intraocular pressure ≥ 21 mmHg, open anterior chamber angle in gonioscopy, optic nerve head changes as glaucomatous, visual field changes such as generalized depression, paracentral scotoma, nasal step. The patient with history of angle closure glaucoma or other kinds of glaucoma, diabetes mellitus, severe systemic disease and neoplasm, other serious eye diseases (corneal opacity, uveitis, central serous chorioretinopathy), previous gastric surgery or treatment of *H. pylori* eradication were excluded from the study. Inclusion criteria of the controls were age between 40-80 years, intraocular pressure < 21 mmHg, normal perimetry, without any glaucomatous optic nerve changes and normotension. The patient with history of angle closure glaucoma or other kinds of glaucoma, diabetes mellitus, severe systemic disease and neoplasm, serious eye disease (corneal opacity, uveitis, central serous chorioretinopathy), previous gastric surgery or treatment of *H. pylori* eradication were excluded from the control. The purpose and procedures were briefly explained to all participants. Following inclusion and exclusion criteria, samples were collected by purposive sampling.

The complete clinical evaluation including history, physical examination, relevant ocular examinations, fundus examination, some special ocular examinations like - intraocular pressure, visual field analysis, gonioscopy were done.

Serologic assays

Table I

Demographic characteristics, gender, antibody titre and ^{13}C -urea breath test positivity

	Primary open-angle glaucoma (n ₁ = 40)	Control (n ₂ = 40)	p value	Odds	95% CI
Mean age (range)	51.4 \pm 10.1 (40 - 75)	51.2 \pm 9.9 (40 - 70)	0.929		
Gender (male/female)	24/16	24/16	1		
Antibody titer positivity	30	12	0.000	7.00	2.61 to 18.74
^{13}C urea breath test positivity	28	15	0.003	3.89	1.53 to 9.87

Table II

Intraocular pressure of study subjects

	Right eye (mm of Hg)	Left eye (mm of Hg)
Patient with primary open angle glaucoma	21.8 \pm 1.6	21.8 \pm 1.3
Patient without primary open angle glaucoma	11.2 \pm 2.5	11.2 \pm 2.5
p value	<0.01	<0.01

For the determination of serum levels of anti-pylori IgG antibody, blood samples were collected and evaluated by ELISA method (DRG *H. pylori* IgG kit-EIA-3057) (positive if anti H-pylori IgG level > 20 U/mL).

Urea breath test

After an abstinence of proton pump inhibitor for 14 days and fasting for 2 hours, all patients were subsequently subjected to a ^{13}C -urea breath test, performed accordance with the manufacturer's recommendations (HCBT-01, Headway ^{13}C -Urea Breath Analyzer, China). Patient went through for procedure: a) Blow up the first collection bag; b) take one ^{13}C -urea capsule (75 mg urea); c) wait for 30 min; d) blow up the second collection bag and e) test two bags of breath samples with the analyzer. The results were obtained on-site and expressed as positive or negative.

Statistical analysis

All data were analyzed by using statistical package for social sciences (SPSS). Associations between two variables were measured by Chi-square test. A probability 'p' value of 0.05 or less was considered as significant. Strength of association was determined by estimating odds ratio (OR) and their 95% confidence intervals (CI).

Results

The mean age of the patients of both groups were similar. Positive serology of *H. pylori* infection was found in 75% of patients with primary open-angle glaucoma and 30% of patients without primary open-angle glaucoma, which was statistically significant ($p=0.000$, OR=7.00 and CI 95% =2.61-18.74). ^{13}C -urea breath test was positive in 70% in case group and 37.5 % in control group, which was significant ($p=0.003$, OR=3.89 and CI 95% =1.53-9.87).

The mean intraocular pressure in right eye and left eye of the patients primary open-angle glaucoma were 21.8 \pm 1.6 and 21.8 \pm 1.30 mm of Hg respectively whereas in control group, the values were 11.2 \pm 2.5 and 11.2 \pm 2.5 mm of Hg respectively for right eye and left eye (Table II). The p value was found significant (< 0.01).

Discussion

Comparing serology and urea breath test results reveals significantly higher prevalence of *H. pylori* infection in patients with primary open-angle glaucoma.

In the last few years, many studies had conducted for the relationship between *H. pylori* infection and

the pathological processes of few ocular disorders, such as central serous chorioretinopathy,^{16,17} glaucoma,¹⁸⁻²² blepharitis, and uveitis. The present study found a significant association between *H. pylori* infection and glaucoma.

In the previous studies, only serological method (ELISA) was used to detect *H. pylori* infection because it's a simple test and good for population studies. But it conveys high false positive rates.^{23,24} Besides, urea breath test shows higher sensitivity (91.4%) and higher specificity (93.8%) respectively and accuracy (90-93%) which was nearer with the values for histological examination in the elderly.²⁵ Therefore, we preferred the ¹³C-urea breath test and serological method both. Endoscopic biopsy is an invasive method and noninvasive tests are more accessible for screening.¹

Greece done the larger period study of this association, used histologic analysis, rapid urease slide test (CLO test) for biopsy, saliva samples and serologic tests, found more frequency of *H. pylori* in glaucoma patients than anemic control group ($p < 0.001$).⁸ Other study announced that eradication of *H. pylori* effectively upgrade glaucoma parameters ($p < 0.001$ for intraocular pressure; $p \leq 0.01$ for visual field), giving the idea about their causal relationship.¹⁵ Another article explained the inductive theory of apoptosis with *H. pylori* infection.⁵ Another study gave the idea about their possible genetic relationship, proposed this infection as an environmental risk factor for primary open-angle glaucoma.⁶ Another study in china performing ¹³C-urea breath method reported significantly higher prevalence of *H. pylori* in patients with primary open-angle glaucoma (54.2%) than in control group (20.8%) ($p = 0.017$ OR=4.49 CI 95%= 1.26-16.01).⁷

Another study in Iran found significant difference in seroprevalence of *H. pylori* infection in patients with primary open-angle glaucoma and control group, 89.1 and 59.5% respectively ($p = 0.008$).²²

Tsolaki et al. (2015) explain the supposed association between various forms of dementia, including Alzheimer's disease, primary open-angle glaucoma and *H. pylori* infection in all possible combinations.²⁶

Zeng et al. (2015) in their meta-interpretive literature found no significant difference regarding the rates of *H. pylori* infection and ¹⁴C-urea breath test positivity were observed between the study and control groups ($p = 0.473$).²⁷

Some studies reported diverging results. For instance, in one study seropositivity of *H. pylori* and serum level of cytotoxin associated gene-A product was evaluated in both groups, reported that either *H. pylori* infection or seropositivity for virulent cytotoxin associated gene-A bearing *H. pylori* strains do not have significant association with any type of glaucoma ($p = 0.88$ for *H. pylori* and

$p = 0.67$ for Cag-A).¹² Other disagreeing studies about the relation between *H. pylori* infection and primary open-angle glaucoma carried out in Canada and Iran.^{13, 11} Regarding this conflicting results, we used both methods serological test and urea breath test for more accuracy.

In Bangladesh, the prevalence of *H. pylori* infection is high. More than 90% apparently healthy adults have antibody to *H. pylori* in the blood.²⁸

Possible explanation of this association is the auto-immune reaction, stimulating platelet and platelet leucocyte aggregation, releasing vasoactive and pro inflammatory factors, sharing common genetic factors which causes apoptosis, impaired ocular circulation, ultimately induces or aggravate glaucomatous damages.¹

Conclusion

There is significant association between *H. pylori* infection and primary open-angle glaucoma.

Ethical Issue

The research protocol was approved by the ethical review committee of BSMMU before starting this study. Informed consent was taken from all participants.

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