Frequency of Helicobacter Pylori in Patients with Primary Open Angle Glaucoma

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Purpose: To find out the frequency of Helicobacter pylori (H. pylori) antibody in the serum of people with established POAG.

Study Design: Cross Sectional Study.

Place & Duration of Study: LRBT Free Eye Hospital, Lahore from 1st July 2012 to 1st January 2013.

Material and Methods: All patients attending the glaucoma unit of the outpatient department with primary open angle glaucoma willing to be included in the study were enrolled using consecutive sampling. After collecting demographic information of the patients 3 ml of venous blood was withdrawn. Later on processing was done using the chemiluminescent enzyme immunoassay of the Immulite 2000 systems analyzers H. pylori IgG detection kit. Quantitative variable such as age was presented as mean and standard deviation while qualitative variables such as gender and H. pylori status (positive or negative) were expressed as frequencies and percentages.

Results: There were 100 patients included in the study with mean age of 50.45 ± 6.16 years. There were 49 (49%) male and 51 (51%) female patients. The mean antibody level of patients was 3.80 ± 2.57 with a range of 9.39. The minimum and maximum antibody level were 0.07 and 9.46 respectively. There were 75 (75%) patients having primary open angle glaucoma who were diagnosed positive with H. pylori.

Conclusion: The study shows high frequency of H. pylori antibody in patients with Open Angle Glaucoma.

Key Words: Optic Neuropathy, Open angle Glaucoma, Helicobacter Pylori.

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Glaucoma is the terminology used to describe a disease which is characterized by optic neuropathy together with loss of visual field as damage progresses, and in which intraocular pressure is seen as the main modifying risk factor[1]. POAG is the most commonly encountered type of glaucoma and one of the most frequent causes of irreversible visual loss in adults. It is usually asymptomatic and diagnosed when the condition has progressed sufficiently to cause the patient to present with irreversible decreased vision. It can also be diagnosed in patients during routine screening process. The pathology of POAG has been attributed to 2 main reasons which include augmented hindrance at the level of the trabeculum, causing raised IOP leading to direct damage of retinal nerve fibers as they exit the lamina cribrosa and the other is ischemia of the optic disc due to compromised microvasculature which may be due to loss of capillaries, altered blood flow, interference between delivery of nutrients or removal of metabolic products. More recently, some studies are suggesting the possibility of immune-mediated mechanisms in the pathogenesis of POAG.[1]

H.pylori is a non-sporing, curvilinear gram-negative flagellated rod that colonizes the gastric mucosa. It has strong associations with diseases such as peptic ulcer, chronic gastritis, carcinoma of the stomach and gastric Mucosa Associated Lymphoid Tissue (MALT) lymphoma. Extragastric manifestations were seen in patients with hepatic and pancreatic diseases.[23] Its prevalence and distribution worldwide is variable but it has been detected in gastric mucosa of the population of the developing countries. Nowadays many tests are available for the detection of H.pylori, some are invasive (gastric endoscopy and mucosal biopsy) and other non-invasive (urease breath test, serum antibody detection, fecal bacterial detection).[2] H.pylori causes apoptosis of the gastric mucosa by the increased expression of the Fas-cell death receptor and sensitivity to Fas-mediated apoptosis. H.pylori antibodies circulating found in the blood cross the blood-aqueous barrier to enter the aqueous humor and cross-react with antigens on ciliary body epithelium. Apoptosis of the trabecular meshwork cells can be triggered through Fas/FasL pathway.[3-5]

A clinical study carried out at Aravind Eye Hospital, Madurai, India showed that there was a marked elevation in serum antibody titer against H.pylori in POAG (70%).[3]

In Peking University, Beijing, China, a study was done to establish a causality between Helicobacter pylori and POAG and found the frequency of Helicobacter pylori to be 54.2% positive.[6] Another study carried out at AHEPA Hospital, Greece revealed a frequency of 88% helicobacter pylori in patients of POAG.[7]

The rationale of this study is that, since no data is available in Pakistan regarding the frequency of helicobacter pylori in POAG, and multiple international research articles have been observed to show variability in their respective data, this study will set a baseline data in our population and also bring focus to a serious health issue and appropriate intervention that neeeds to be carried out.

It is has been established that about 60 million people globally are being treated for glaucoma and amongst which 8.4 million are blind in both eyes[8,9]. Many factors, including presence of H.pylori, which is associated with the occurrence of Alzheimer's disease, gastritis, gastric ulcers, and gastric carcinomas, have been implicated as the pathophysiology.[10-12] Recently, researchers have globally directed attention to this issue; however, the variable results have left the subject without a definitive conclusion. Further questions that will require answers are whether there is an association between H.pylori infection and POAG, and if ever these two diseases have a causal relationship or if they coincidentally have common triggering factors.[9]

H.pylori was detected by[13] C-urea breath test in a study and was found to be higher in patients with glaucoma (54.2%) than in control group (20.8%) [p = 0.017]. There was no statistical significance regarding the overall visual field loss and CD ratio of patients whether they were H.pylori-positive or H.pylori-negative.[13]

In Thessaloniki, a study observed that IOP was the sole risk factor involved with POAG and pseudoexfoliative glaucoma, but the strong presence of H. pylori infection in glaucoma patients of this area is also coincidentally high, hence demonstrating a common factor with probable association with POAG and pseudoexfoliative glaucoma in Greece.[14]

The test was positive if Anti-H.Pylori antibody was 1.1U/ml and above. The aim of this study is to obtain the frequency of H.pylori antibody in serum of patients of established POAG.

MATERIAL AND METHODS

A cross sectional study was carried out at LRBT Free Eye and Cancer Hospital, Lahore, for a duration of 6 months, from 01-07-2012 to 01-01-2013. With 95% confidence level, 9% margin of error and 70.0% expected percentage of positive results for Helicobacter pylori antibody in serum, 100 patients of POAG were selected from the glaucoma unit. Non probability purposive sampling was used.

Criteria for patient selection were age 40 to 60 years, both genders and patients with established POAG. Patients with history of ocular trauma or any systemic diseases or any systemic medications were not included. Patients with history of any ocular pathology other than Primary Open Angle Glaucoma e.g. corneal ulcer, uveitis, retinal detachment, vitreous hemorrhage were also excluded from this study.

Through consecutive sampling, a total of 100 patients fulfilling the inclusion criteria were taken from the Glaucoma Unit of LRBT Free Eye and Cancer Hospital Lahore. Informed consent was taken from all patients. Demographic information of patients (name, age, gender) was taken and then 3 mL of venous blood

from each subject was drawn, and processed through the chemiluminescent enzyme immunoassay of the Immulite 2000 Systems Analyzers H.pylori IgG detection kit from Siemens Healthcare Diagnostics Inc., United Kingdom. To avoid bias, all tests were carried out at Shaukat Khanum Memorial Cancer Hospital & Research Centre (SKMCH & RC) only. Reports were regarded as positive or negative and recorded on the proforma.

All the data collected was entered into SPSS version 22 and it was analyzed through its statistical package. The Quantitative variables such as age was presented as mean and standard deviations while qualitative variables such as gender and H.pylori status (positive or negative) were expressed as frequencies and percentages.

RESULTS

The mean age of patients was 50.45 ± 6.16 years with age range of 20 years. The minimum and maximum ages were 40 and 60 years respectively (**Table 1).**

There were 49 (49%) male and 51 (51%) female patients. The male to female ratio was almost same (**Table 2).**

Table 1: Descriptive Statistics of Age (Years).

	Age (Years)
Mean	50.45
Std. Deviation	6.16
Range	20.00
Minimum	40.00
Maximum	60.00

Table 2: Frequency Distribution of Gender.

	Frequency	Percent
Male	49	49
Female	51	51
Total	100	100.0

The mean antibody level of patients was 3.80 ± 2.57 with range of 9.39. The minimum and maximum antibody level was 0.07 and 9.46 respectively (**Table 3).**

According to operational definition Helicobacter pylori antibody was present in 75 (75%) patients. (**Table 4).**

Table 3: Descriptive Statistics of Antibody Level.

	Antibody Level
Mean	3.80
Std. Deviation	2.57
Range	9.39
Minimum	0.07
Maximum	9.46

Table 4: Frequency distribution of Helicobacter pylori antibody.

	Frequency	Percent
Yes	75	75.0
No	25	25.0
Total	100	100.0

DISCUSSION

Pathogenesis of glaucoma due to H.pylori infection is hypothesized to be through the following mechanisms. 1) Promoting platelet and platelet-leucocyte aggregation. 2) Releasing pro-inflammatory and vasoactive substances, such as cytokines, eicosanoids and acute phase proteins involved in a multitude of disorders mentioned in Weinreb and Khaw's report. 3) Stimulating monocytes to induce a tissue factor-like pro-coagulant activity, 4) Development of cross mimicry between endothelial and H.pylori antigens. 5) Producing oxidative stress and circulating lipid peroxides and 6) Promoting apoptotic cascade. These variables may also initiate or worsen the progression of glaucomatous neuropathy and other neurodegenerative disorders (GBS, Parkinsonism)[15]. Glaucoma is differentiated from other forms of acquired optic nerve pathologies by the typical optic disc cupping. In glaucoma, the rim of the optic nerve gradually thins over time, thereby enlarging the optic nerve cup. This is called optic disc cupping. It results from the loss of axons of the retinal ganglion cells, combined with glial tissue and vascular architecture. The remaining rim maintains a pinkish color. With the exception of arteritic ischemic optic neuropathy, an immune-mediated inflammatory entity in which cupping maybe observed, other optic nerve diseases lose their pink color and there is no cupping[16].

The key factor in the pathogenesis of POAG is believed to be IOP primarily. Other lesser understood risk factors have been included in its pathophysiology, such as; ischemia of the optic disc, vascular dysfunction or dysregulation (peripapillary and

systemic). These factors are believed to cause direct damage to the optic nerve tissue or augment its risk of getting more damaged. Recent studies suggest that alteration in endothelium-dependent vascular regulation, decreased blood supply to the ocular tissues, and cytokines can induce glaucoma related optic nerve damage[10,17].

Chen H et al found out that in their experimental model with mice, that IOP related T cell infiltration occurs in the retinal layers after transient raise in IOP which persists even after the IOP has been brought down to normal levels[22].

The prevalence of POAG varies geographically, racially and is affected by various demographic factors. It was estimated in one study that 1.6 million people of 40 years of age and above in the United States have POAG. The age adjusted prevalence rates of POAG were 4 times higher in African-Americans in comparison to Caucasians in this survey. Also, rates among African-Americans were as low as 1.23% in the 40-49 years group to as high as 11.26% in the 80 years or older, and Caucasians varied from 0.92% to 2.16%, respectively[18].

Until now, there has not been extensive investigation to determine the prevalence of H.pylori in glaucoma patients. Until recent, Kountouras and associates reported a higher figures of H.pylori in Greek patients with POAG as compared to a control group, a suggestion was made for a possible link between glaucoma and POAG in their population[14]. Studies from India and China have shown the frequency of H.pylori in patients of POAG to be 70% and 54.2% respectively[6,19].

A survey estimated 0.5% of the population of developed countries and a variable of 3-10% in developing countries are more likely to become infected with H.pylori[21].

Considering the fact that in our developing country, where the health facilities, diagnostic measures and treatment strategies are lacking already, early detection of such infections and their eradication can help greatly in the management of Primary Open Angle Glaucoma (POAG). In Pakistan, no study has been conducted to see the frequency of H.pylori in POAG population. Multiple international studies have shown variability in their results. Hence, we aimed to conduct this study with our primary objective to determine the frequency of H.pylori antibody in serum of patients with established POAG.

The mean age of patients was 50.45 ± 6.16 years

with age range of 20 years. The minimum and maximum ages were 40 and 60 years respectively. There were 49 (49%) male and 51 (51%) female patients. The male to female ratio was almost same. Ida Dielemans and coworkers showed in their study that the overall prevalence of POAG was 1.10%. The prevalence increased from 0.2% in the 55-59 years group, to 3.3% in the 85-89 years group. Men were found be 3 times more prone than women (odds ratio, 3.6) [19,20].

Another study conducted in Iran showed that mean age of patients of POAG was 61.11 ± 11.1 with a female to male ratio to be 7:13. Furthermore, they showed that the average concentration of anti-H. pylori IgG antibodies of patients with POAG was 0.44 ± 0.64 U/ml.[5] In our study, the mean antibody level of patients was 3.80 ± 2.57 with range of 9.39. The minimum and maximum antibody level was 0.07 and 9.46 respectively.

The Helicobacter pylori antibody was present in 75 (75%) patients. Another study showed that patients with glaucoma had a more strong presence of H.pylori infection than controls, 36 (88%) of 41 glaucoma cases, including 6 patients who tested negative in the gastric mucosa urease test, and in 14 (47%) of the 30 control subjects. The mean serum Ig G anti–H.pylori level was also more in POAG population (35.6 ± 31.1 U/mL) than in the control group (17.03 ± 18.1 U/mL; P = .002)[7]. Another study showed that 43 of their 51 POAG cases (84.3%) and 17 of their 35 control subjects (48.6%) were tested positive for H. pylori[21].

Zeng et al suggested through their meta-analysis that there is strong association between H. pylori and Open Angle Glaucoma[24].

Few studies found no correlation between H.pylori and POAG. This is based on the fact that eradication of H.pylori did not help increase or decrease the prevalence of POAG in those patients. A study by Noche et al saw that there was no statistical significance in their case-control study regarding the prevalence of H.pylori in the POAG group and the normal group, 74% and 87% respectively[25,26].

The results of current study were compatible with other international studies and showed a higher than normal frequency of H.pylori in a population of POAG. The results urge for making it essential to detect the presence of this bacteria and pursue its eradication among such patients. This could potentially help in better clinical management of the disease.

The limitation of our study was the small sample size and single center used for data collection. Further studies are required to obtain more generalizable results.

CONCLUSION

The results of our study show that the frequency of Helicobacter pylori antibody is H.pyloci antibody is as high as a 75% in patients with primary open angle glaucoma. We must focus on this serious health issue and should start appropriate intervention to prevent Helicobacter pylori antibody at an early stage of this disease.

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