IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 18, Issue 4 Ser. 2 (April. 2019), PP 18-22
www.iosrjournals.org

To Evaluate the Prevalence of Primary Open Angle Glaucoma/ Ocular Hypertension In Patients Infected With Helicobacter Pylori

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Abstract: ***Aim:*** *Helicobacter pylori (Gram negative bacilli), a commensal of gastrointestinal system is associated with many ocular manifestations. One of the associated links is proposed with glaucoma. Since the data on Indian population is lacking, we have devised this study to evaluate the prevelance of primary open angle glaucoma/ ocular hypertension in patients infected with Helicobacter pylori.*

Materials and Methods: *This observational study included helicobacter pylori seropositive patients on the basis of Rapid stool antigen test. Seropositive patients were then evaluated for glaucoma and prevalence of primary open angle glaucoma/ ocular hypertension was evaluated in such patients.*

Results: *Mean age of 100 patients was 55.93 (±9.91) years, of which 36% were females and 64% were males. Mean visual acuity, intraocular pressure, cup-disc ratio and mean deviation was 0.90±0.18 and 0.87±0.21, 16.74±2.28 and 16.53±2.42 mmHg, 0.37±0.05 and 0.37±0.07 and -1.75±0.48 and -1.65±0.39 for left and right eyes respectively. Total prevelance of glaucoma was 7% (5% had Ocular hypertension and 2% had Primary open angle glaucoma).*

Conclusion: *Since prevelance of glaucoma was higher in cases with H. Pylori infection and being the irreversible damage caused by glaucoma, seropositive helicobacter pylori patients were recommended ophthalmological examination for glaucoma evaluation.*

Keywords: *helicobacter pylori, prevelance, primary open angle glaucoma, ocular hypertension*

Date of Submission: 20-03-2019 Date of acceptance: 06-04-2019

I. Introduction

Glaucoma is not a single clinical entity but a group of ocular diseases with various causes that ultimately are associated with a progressive optic neuropathy leading to loss of visual function. About 8.4 million persons worldwide are bilaterally blind as a result of glaucoma.[1] Primary open angle glaucoma (POAG) is a chronic, progressive disease that often presents with characteristic optic nerve (ON) damage, retinal nerve fiber layer (NFL) defects, and subsequent visual field (VF) loss. The majority of persons with POAG have elevated intraocular pressure (IOP). Although 21 mm Hg is considered the upper limit of statistically normal IOP, at least one-sixth of patients with POAG have IOP levels below 21 mm Hg, which is considered statistically normal (in the 95th percentile range). Moreover, certain people have IOP levels >21 mm Hg (statistically abnormal) but don't have evidence of ON damage or loss of vision function. This condition is known as ocular hypertension (OHT).[2]

Helicobacter Pylori (H. pylori) is a gram-negative spiral bacteria found on the luminal surface of the gastric epithelium and was first isolated by Warren and Marshall in 1983.[3] Approximately two-thirds of the world's population is infected with H. Pylori. It is mainly found in the gastric mucous layer or adherent to the epithelial lining of the stomach. It is theorized that oxidative stress by H. Pylori plays an important role in inducing damage both in trabecular meshwork as well as optic nerve head. There are three major stimuli for retinal apoptotic death, i.e., hypoxia, neurotrophin withdrawal and glutamate mediated toxicity. The most import remains to be oxidative stress.[4]

Various authors have conducted studies to find the association between two. Not only H. Pylori antigens are found in aqueous of glaucoma patients but it has also been seen that eradication of H. Pylori has decreased the prevelance of glaucoma in such patients. Although many studies have produced frank association between two entities, still there are controversies related to it. .[5] Since the data on Indian population is lacking, therefore we have devised this study.

II. Materials And Methods

This observational study was conducted in the Department of Ophthalmology, Government Medical College Patiala in collaboration with Department of Medicine of same college. The aim of this clinical study was to evaluate the prevelance of primary open angle glaucoma/ ocular hypertension in patients infected with Helicobacter pylori. This study was conducted after permission from college's ethics committee and keeping in view the Declaration of Helsinki. From August 2016 to July 2018, 100 patients conforming to eligibility criteria were selected. Informed consent was taken from all patients prior to their inclusion in the study.

100 patients between 18- 80 years, willing for enrollment and diagnosed with H. pylori infection on the basis of sign and symptoms, confirmed by Rapid stool antigen test were included in the study. Patients already on triple therapy for H. pylori or anti-glaucoma medication, steroids or history of previous gastric surgery were excluded. Patients coming to medicine OPD with complaints of gastritis, burning abdominal pains, bloating and loss of appetite were diagnosed for presence of H. Pylori bacteria in their gut through Rapid stool antigen test.

Rapid stool antigen for H. Pylori is a qualitative immunochromatographic membrane-based assay using monoclonal antibodies and amplification technology for the direct detection of H. pylori antigens in human feces. The test has two capture lines, one coated with an H. pylori-specific amplified capture reagent (test line) and one with a control capture reagent (control line). Stool sample was applied in cassette along with few drops of reagent. One capture line suggested absence of H. Pylori antigens in stool, since it is a control line. Two lines suggested presence of H. Pylori antigens in stool.[68] Positive cases were then enrolled in the study. Demographic data such as age, sex, residence as well as complete clinical history was taken. Systemic examination was done, followed by detailed ophthalmic examination.

Snellen's Visual acuity (decimal interconversion) was measured and slit lamp as well as gonioscopic examination (Goldmann three mirror Gonio-prism) was done. Any patient with angle of Shaffer grade <III was excluded. Average of two Goldmann applanation tonometric reading was taken as IOP (one reading at 10 am and second at 1 pm). Automated static perimetry was done using Humphrey static perimeter. Settings were central 30-2 threshold test with background illumination of 31.5 apostilbs (asb), stimulus III white with SITA-standard strategy and 3mm pupil diameter. The single field analysis printouts were taken. Grey scale pattern, mean deviation, pattern standard deviation and glaucoma hemifield test was noted in selected patients. Modern Anderson's criteria were used to detect early-localized field defects due to glaucoma. Indirect Slit-lamp Bimicroscopy with 90D lens was used to do fundus examination. Cup to disc ratio, disc size, shape contour, neuroretinal rim, nerve fiber layer and peripapillary area was noted.

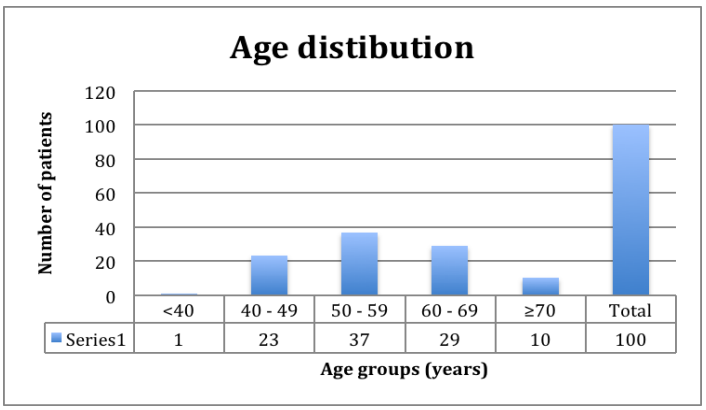
Disc changes persistent with glaucomatous damage included splinter hemorrhages, localized optic disc notch or thinning of the rim, non-maintenance of ISNT rule (inferior>superior>nasal>temporal rim thickness), an asymmetry of cup/disc ratios by > 0.2 between both eyes and/or retinal nerve fiber layer defect. Subjects were classified as having abnormal visual fields if they had atleast (a) 3 consecutive points depressed by 5 dB with one of the points being depressed by at least 10 dB, (b) 2 adjacent points depressed by 10 dB, or (c) a 10 dB difference across the nasal horizontal meridian in 2 adjacent points. Only reliable fields were included in the study, that is, false positive and false negative responses <30% and fixation losses <10%.

Statistical Analysis:

The mean age of study was 55.93±9.91years. 1 (1.00%) had age <40 years, 23 (23.00%) between 40-49 years, 37 (37.00%) between 50-59 years, 29 (29.00%) between 60-69 years and 10 (10.00%) with ≥70 years. Most of the patients belonged from 50-59 years- 37 patients (37.00%). The age distribution is as follows:

Graph 1:

Age Distribution



Of the 100 (100%) patients, 36 (36%) were females and 64 (64%) were males. The mean value, standard deviation and p-value of visual acuity, intraocular pressure, vertical cup-disc ratio (CDR) and central corneal thickness is as follows. P-value <0.05 was taken to be significant.

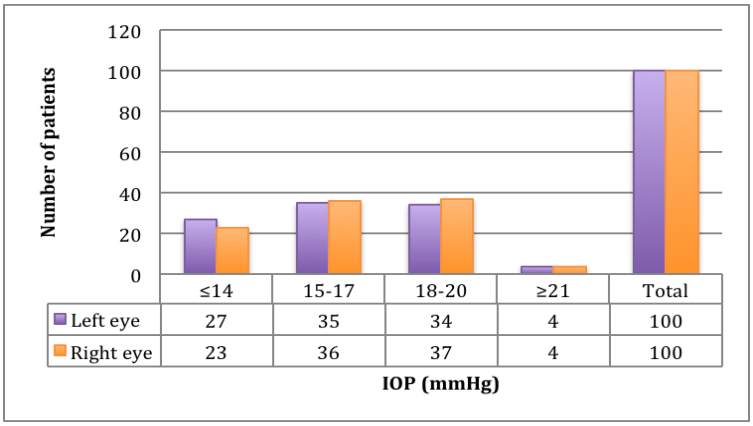
TABLE 1:

DATA	LEFT EYE (MEAN±SD) (n=50)	RIGHT EYE (MEAN±SD) (n=50)	p-value
1. Visual acuity	0.90±0.18	0.87±0.21	0.27 (NS)
2. Intraocular pressure (mmHg)	16.74±2.28	16.53±2.42	0.52 (NS)
3. Vertical Cup-disc ratio	0.37±0.05	0.37±0.07	0.83 (NS)
4. Mean deviation	-1.75±0.48	-1.65±0.39	0.11 (NS)

*NS means non-significant (p>0.05)

The distribution data of IOP is as follows:

GRAPH 2:
IOP DISTRIBUTION



Goldmann applanation tonometry was done and average of two readings were recorded. 27 (27.00%) patients had IOP between 12-14 mmHg, 35 (35.00%) had IOP between 15-17 mmHg, 34 (34.00%) had IOP between 18-20 mmHg and 4 (4.00%) had IOP ≥21 mmHg in left eyes. 23 (23.00%) patients had IOP between 12-14 mmHg, 36 (36.00%) had IOP between 15-17 mmHg, 37 (37.00%) had IOP between 18-20 mmHg and 4 (4.00%) had IOP ≥21 mmHg in right eyes. 200 eyes of 100 patients were evaluated gonioscopically. Grading was done based upon Shaffer's classification. In left eyes, 95 (95.00%) had Shaffer grade IV and 5 (5.00%) had Shaffer grade III. In right eyes, 96 (96.00%) had Shaffer grade IV and 4 (4.00%) had Shaffer grade III.

1 left eye had peripapillary atrophy as well as disobeyed ISNT rule. Rest of the fundus examinations was within normal limits. 1 right eye disobeyed ISNT rule. Rest of the fundus examinations was within normal limits. Fundus findings for left and right eyes is as follows:

TABLE 2-
FUNDUS FINDINGS

Fundus Examination		**Left Eye**	**Right Eye**
Peripapillary Atrophy	Present	1	0
	Absent	99	100
Maintenance of ISNT Rule	Present	1	1
	Absent	99	99
Splinter Hemorrhages	Present	0	0
	Absent	100	100
RNFL Defects	Present	0	0
	Absent	100	100

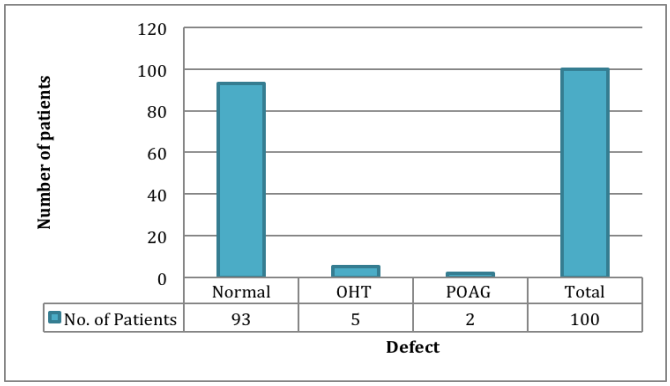
200 eyes underwent visual field analysis. The test employed was 30-2 SITA STANDARD with Humphrey Automated Perimeter. In left eyes, 95 (95.00%) had normal visual fields, 4 (4.00%) had generalized depression and 1 (1.00%) had glaucomatous defect. In right eyes, 92 (92.00%) had normal visual fields, 7 (7.00%) had generalized depression and 1 (1.00%) had glaucomatous defect. Glaucomatous defect was superior arcuate scotoma.

TABLE 3:
VISUAL FIELD DEFECTS

Visual Field Defects	Left eye		Right eye	
	No. of Patients	Percentage	No. of Patients	Percentage
Normal	95	95.00%	92	92.00%
Generalized Depression	4	4.00%	7	7.00%
Glaucomatous Defect	1	1.00%	1	1.00%
Total	100	100%	100	100%

Total prevelance of glaucoma found in study was 7% (5% of OHT and 2% of POAG).

GRAPH 3:
DISTRIBUTION OF GLAUCOMATOUS DEFECTS



III. Results:

The patients were between the age group of 38 to 77 years (inclusion criteria-18 to 80 years). The mean age of patients was 55.93 (±9.91) years. In this study of 100 patients, 36 (36%) were females and 64 (64%) were male. Female to male ratio was 1.89: 1. Mean±SD for visual acuity, IOP, vertical CDR and mean deviation was 0.90±0.18 and 0.87±0.21, 16.74±2.28 and 16.53±2.42 mmHg, 0.37±0.05 and 0.37±0.07 and -1.75±0.48 and -1.65±0.39 for left and right eyes respectively. None of the findings were significant.

200 eyes of 100 patients were evaluated gonioscopically. Grading was done based upon Shaffer's classification. In left eyes, 95 (95.00%) had Shaffer grade IV and 5 (5.00%) had Shaffer grade III. In right eyes, 96 (96.00%) had Shaffer grade IV and 4 (4.00%) had Shaffer grade III.

1 left eye had peripapillary atrophy as well as disobeyed ISNT rule. Rest of the fundus examinations was within normal limits. 1 right eye disobeyed ISNT rule. Rest of the fundus examinations was within normal limits. In left eyes, 95 (95.00%) had normal visual fields, 4 (4.00%) had generalized depression and 1 (1.00%) had glaucomatous defect. In right eyes, 92 (92.00%) had normal visual fields, 7 (7.00%) had generalized depression and 1 (1.00%) had glaucomatous defect. Glaucomatous defect was superior arcuate scotoma. Total prevelance of glaucoma found in study was 7% (5% of OHT and 2% of POAG).

IV. Discussion:

Over the last decades, various researchers have examined the existence of a possible link between H. pylori infection and glaucoma. Although some support this study but contradictory results from some other studies leave room for further research in this field. The establishment of such a casual relationship will probably have important practical applications in future as the eradication of H. Pylori may lead to halt of glaucoma. So keeping all this in mind, the present study was designed.

In present study, the patients were between the age group of 38 to 77 years (inclusion criteria-18 to 80 years). The mean age of patients was 55.93 (±9.91) years. Most of the patients belonged from 50-59 years- 37 patients (37.00%). The study conducted by Galloway et al[5] (2003) studied the serum positivity for H. Pylori in glaucoma patients. The mean age of study was 53.2 years. Razeghinejad et al[6] (2006) studied aqueous humor samples in glaucoma patients for presence of H. Pylori. The mean age of study was 61.1 years. In present study of 100 patients, 36 (36%) were females and 64 (64%) were male. Female to male ratio was 1.89: 1. Razeghinejad et al[6] (2006) studied aqueous humor samples in glaucoma patients for presence of H. Pylori.

Male: female ratio in study was 2:1. Vardhan et al[55] (2014) studied the prevelance of glaucoma in H. Pylori positive patients and was matched to control group and Male: female ratio in study was 1.72:1.

Mean visual acuity, intraocular pressure, cup-disc ratio and mean deviation was 0.90±0.18 and 0.87±0.21, 16.74±2.28 and 16.53±2.42 mmHg, 0.37±0.05 and 0.37±0.07 and -1.75±0.48 and -1.65±0.39 for left and right eyes respectively in our study. Vardhan et al[7] (2014) studied the prevelance of glaucoma in H. Pylori positive patients and was matched to control group. The decimal visual acuity was 0.87 in HP +ve group. The prevelance of glaucoma in H. Pylori positive patients and was matched to control group in same study. Mean IOP in H. Pylori + group was 17.4 and 17.8 mmHg of right and left eyes respectively. Mean CDR in H. Pylori + group was 0.44 and 0.42 in right and left eyes respectively. Study by Galloway et al[5] (2003) had Mean Deviation of -7.7, -7.9 and -6.9 in POAG, NTG and pseudoexfoliation group. MD was -0.97 in OHT group. Only the group with OHT matched mean deviation of present study because rest of the groups already had developed glaucoma. Study by Yaghoobi et al[8] (2013) had Mean Deviation of -1.63.

Yaghoobi et al[8] (2013) conducted a study to find any association between H. Pylori and ocular diseases. 35 patients participated in the study. This study showed that H. pylori infection is associated with two cases of cataract as well as two cases of glaucoma. Therefore prevelance was 5.7%. Vardhan et al[7] (2014) conducted a study in Gastrogroup (HP+ve). It had glaucoma in 3 (6%), blephritis in 7 (14%) and dry eye in 5(10%) patients. In Gastrogroup (HP-ve) - glaucoma in 1 (2%), blephritis in 2 (4%) and dry eye in 2 (4%) patients were found. All these findings were consistent with our study, which had prevelance of glaucoma as 7%.

However, there are certain limitations to the study. Visual field examination can be made more reliable, by doing second visual field in next visit. Tonography can be carried in patients to quantitate aqueous flow obstruction. The effect of treatment on outflow can also be studied. Previous literature suggests that eradication of H. Pylori by antibiotic therapy has caused reduction in outflow resistance.

V. Conclusion And Clinical Significance:

Since prevelance of glaucoma was high (7%) in cases with H. Pylori infection, it was recommended that such patients should have complete ophthalmological examination for glaucoma evaluation.

Acknowledgements:

We would like to thank the participants for the study as well as staff of Dept. of Ophthalmology, Government Medical College & Rajindra Hospital, Patiala.

Funding: None

Conflict of interest: None

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Dr. Harsimran Singh" To Evaluate the Prevelance of Primary Open Angle Glaucoma/ Ocular Hypertension In Patients Infected With Helicobacter Pylori" IOSR Journal of Dental and Medical Sciences (IOSR-JDMS), vol. 18, no. 4, 2019, 18-22.