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Lamina Cribrosa Anatomical Parameters Effects on Optic Disc Clinical Parameters and Visual Field in Primary Open-Angle Glaucoma Cases and Controls

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ABSTRACT

Background: Lamina cribrosa (LC) anatomical characteristics have strong association with visual field (VF) disorders in Primary Open-angle Glaucoma (POAG). To relate these results with clinical examination findings hence it reflects significant information to clinicians is the core emphasis of study. **Objective:** To relate anterior lamina cribrosa depth (ALCD), lamina cribrosa thickness (LCT), retinal nerve fiber layer thickness (RNFLT), mean deviation (MD), pattern standard deviation (PSD) with clinical findings in POAG cases and age-matched healthy controls. **Study Design:** Study design was case-control. **Settings:** Al-Ain Eye Institute, Karachi Pakistan. **Duration:** November 2018 to February 2019. **Methods:** Eye specialist selected 57 POAG cases with visual field (VF) disorders and 46 age-matched healthy controls without VF disorders as study samples, after sanction from Ethical Review Committee (ERC) of Bahria University Health Sciences (BUHSC). Slit-lamp bio-microscopy, tonometry, Humphrey Field Analyzer and spectral domain ocular coherence tomography with enhanced depth imaging (EDI-OCT) were used. Independent sample T-test, Fischer exact and Mann Whitney-U tests were used for statistical analysis. **Results:** Significant results obtained between cases with VF disorders and controls without VF disorders for LCT (218.07 ± 79.80 µm Vs 271.77 ± 64.45 µm), RNFLT (73.21 ± 13.63µm Vs 78.85 ± 13.63 µm), parapapillary atrophy (PPA) (3.63 ± 0.77 Vs 3.15 ± 0.76). Highly significant findings observed for intraocular pressure (IOP) (20.05 ± 2.47 Vs 15.59 ± 3.46) and vertical cup-to-disc ration (VCDR) (0.86 ± 0.24 Vs 0.54 ± 0.19). **Conclusion:** There is high association between optic nerve clinical parameters, RNFLT and LCT.

Keywords: *ALCD, LCT, RNFLT, EDI-OCT.*

INTRODUCTION

Glaucoma, leading cause of blindness[1] is a chronic ocular condition established to produce optic nerve head damage[2] by deterioration of retinal ganglion cells. POAG is the most prevalent type of glaucoma worldwide and in Pakistan as well.[3]

Early measures to halt the catastrophe of POAG are of utmost importance. LC is a flourishing research prospect of great interest globally, that promises to be the candidate parameter when primary prevention of the disease is sought for. LC anatomical parameters of ALCD and LCT have been proved to have strong ties with progression of POAG.[4] Imaging of LC in the early phases of disease can thus prove beneficial. POAG has been seen to produce alterations in optic nerve head findings, like in VCDR, disc area and rim area.[5]

These are easy findings which when notice if coupled with LC structural variables can prove valuable. Easy and highly precise non-invasive imaging of optic nerve head LC can be done using highly specific SD-OCT with enhanced depth imaging (EDI).[6] The deeper structures of the optic nerve head can easily be observed by this highly

sophisticated technology[7] and the pin point diagnosis can be approached using this technique.[8]

The scope of the present study revolves around ascertaining the optic nerve head clinical findings and LC anatomical parameters in POAG cases with VF defects and age-matched healthy controls without VF defects and exploring a link between them.

METHODS

This case-control study was conducted at Al-Ain Eye Institute, Karachi Pakistan. The duration of the study was 4 months from November 2018 to February 2019. Non probability purposive sampling employed sampling technique was used.

POAG cases enlisted had IOP of >22mmHg, with visualization of open-angle glaucoma tested by slit-lamp and stereoscopic ophthalmology. Controls selected had IOP of < 21 mmHg, with no optic disc defects were included in the study.

Other types of glaucoma, autoimmune illnesses, diabetic and hypertensive retinopathies, neurological conditions and head traumas were excluded from the study.

The study included 103 subjects with 57 cases of POAG and 46 age-matched healthy controls. Ethical approval taken by ERC of BUHS (ERC 60/2018). For cases with POAG, set measurement of IOP was > 22 mmHg (Goldmann Applanation tonometry, At-900, Haag Striet, Switzerland). Open angle of the anterior chamber was viewed using Slit-lamp biomicroscope (Topcon SL-D 7, Topcon Corporation, Tokyo, Japan and stereroscopic ophthalmoscopy Welch Allyn, USA). Optic disc, rim and cup area, VCDR and cup-to-disc ratio observed by Slit-lamp biomicroscope and stereroscopic ophthalmoscopy.

ALCD, LCT and RNFLT measured by EDI-OCT (REVO nx/SOCT Copernicus REVO OPTOPOL Technology, Wavelength 830nm, Axial resolution 2µm, scan speed 1,10,000 scans/sec, scan time 1.37seconds, OPTOPOL Technology Sp. Z o.o, ul. Zabia 42, 42-400 Zawiercie, Poland) with standard guidelines.[9] ALCD demarcated as a track in the middle of the ends of Bruch's membrane and anterior border of LC. LCT gauged by measuring the width sandwiched between the anterior and posterior borders of LC.

Visual field calculation done as external normal limits on glaucoma hemifeild test, with three unusual points with P <5% probability of being normal, 1 with P<1% by pattern deviation, pattern standard deviation of <5% on automated Humphry 50-2 VF analysis ((Medmont M 700 Automated Perimeter, fast threshold, Vermont, Australia) for visual field analysis).[10,11,12]

Participants recruited after informed consent. Sample size designed using method of comparing two means. Cases were tailored using the baseline study by Kim et al, 2016.[10,13] For Statistical analysis of the study, SPSS 23 version was utilized Margin of error for sample size calculation was 5% with confidence interval for mean 95%. Fischer exact test for parapapillary atrophy, Mann-Whitney-U test for cup area, cup-to-disc ratio, VCDR, IOP and RNFLT and independent sample T-tests for disc and rim area comparison were used. P-value of < 0.05 was taken as significant.

RESULTS

The present study included study participants (n=103), 57 out of which were POAG cases, identified with VF defects [10], and the 46 age-matched healthy controls without VF defects. Participants included of both genders of all the ages except pediatric age group (1-10 years of age).

Table 1 exhibits statistically significant results for RNFLT [cases 73.21 ± 13.63µm Vs 78.85 ± 13.63 µm, P-value 0.018] and parapapillary atrophy [cases 3.63 ± 0.77 Vs 3.15 ± 0.76, P-value of 0.002]. Highly significance can be observed in the findings for VCDR and IOP, where P-value of 0.000 is obtained when comparison was made between cases with VF defects and controls without VF defects.

Table 1: Calculation of Optic Disc Clinical Parameters using EDI-OCT between POAG Cases with Visual Field Defects and Healthy Controls without Visual Field Defects (N=103)

Parameters	Case with VFD (n=57)	Control without VFD (n=46)	P-value
Disc Area (mm²)	2.46 ± 0.93	2.45 ± 0.68	0.975 †
Rim Area (mm²)	1.00 ± 0.53	1.10 ± 0.50	0.326 †
Cup Area (mm²)	1.40 ± 1.09	1.34 ± 0.73	0.737 §
Cup-to-Disc Ratio	0.59 ± 0.27	0.55 ± 0.32	0.518 §
Vertical Cup to Disc Ratio	0.86 ± 0.24	0.54 ± 0.19	0.000* §
Retina Nerve Fiber Layer Thickness (µm)	73.21 ± 13.63	78.85 ± 13.63	0.018* §
Intraocular Pressure (mmHg)	20.05 ± 2.47	15.59 ± 3.46	0.000* §
Parapapillary Atrophy	3.63 ± 0.77	3.15 ± 0.76	0.002* ɤ

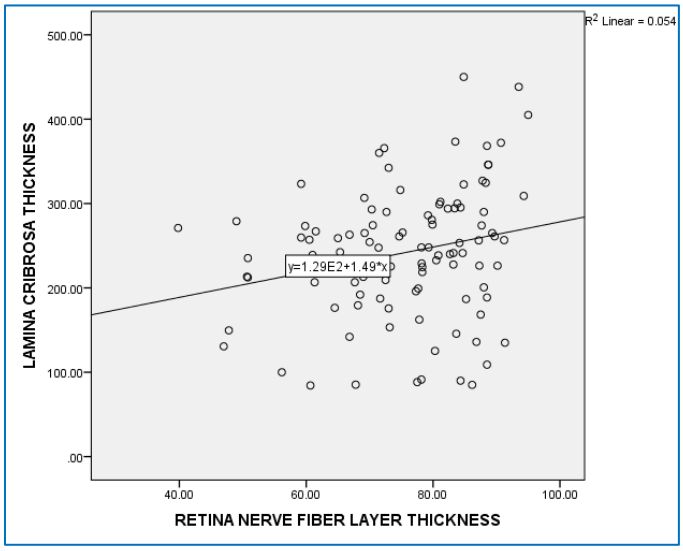
P-value of ≤0.05 is significant and shown with asterisk, †-Independent sample T-test, §- Mann Whitney-U test, ɤ- Fisher exact test, Units used: mm²-millimeter square, µm- micrometer, mmHg- millimeter of mercury*

"ALCD and RNFLT" have inverse relations with each other which had been explored by previous. Figure 1 clearly demonstrates that lesser the RNFLT, the greater will be the depth for ALCD in study subjects.

Figure 1: Scatter plot showing the inverse relation of anterior lamina cribrosa depth (ALCD) and retinal nerve fiber layer thickness (RNFLT)

Greater thickness of retina can be seen in figure 2 is associated with a greater thickness of LC in the study participants.

Figure 2: Scatter plot showing the relation of anterior lamina cribrosa thickness (LCT) and retinal nerve fiber layer thickness (RNFLT)



DISCUSSION

The current study is based upon documenting the structural damage consequences of POAG and to associate them with the clinical findings that is attained during the course of the ailment. LC anatomical parameters have been thoroughly investigated globally, but here in Pakistan this domain had never been researched. This study of LC can be regarded as the primary study done in this field.

The researcher's world over had shown significant findings for LCT when compared with RNFLT. These two seem to have a directly proportional relationship, increase in one automatically suggests a rise in the thickness of other[14] as can also be judged in our work. This proportionality had also been linked with the functional aspect of visual field. The greater thickness of LC had demonstrated better fields of vision.[15]

Parapapillary atrophy is the area of optic nerve head lacking the retinal pigment epithelium. The clinical finding of parapapillary atrophy had produced significant results in our study. Similar findings had also been find previously and parapapillary atrophy had thus been regarded as a clinical risk factor for the progression of POAG.[16] Parapapillary atrophy is strongly reported in other researches and these variables had also been linked with optical errors; like myopia.[17]

The main causative factor around which the pathogenesis of glaucoma revolves is increased intraocular pressure (IOP). Elevations in IOP had been documented to exert pressure effects on the ocular structures, and thus researchers had found significant results when IOP was compared with LC variables. Interventional studies in which trabulectomy had been employed showed significant results when IOP and LC parameters had been compared.[18] Our study had also shown strong association between greater IOP in cases and controls.

The discovery of RNFLT defects holds significance as the structural damage to the optic nerve head precedes the development of visual errors.[19] Universally it has been established that the progression of POAG is interrelated with advanced loss of retinal ganglion cells. Analogous results can also be comprehended from current study and it can be paralleled with other research works.[20]

As had been discovered by previous studies, VCDR alterations occur invariably in POAG. Transformed VCDR should warn the ophthalmologist about the developing biomechanical and structural changes occurring in the optic nerve head. Various studies had shown highly significant results for VCDR[21] like our study. VCDR can also be regarded as a clinical risk factor for progression of POAG.[22]

CONCLUSION

The study concludes that alterations of optic nerve head clinical parameters can heavily be linked with LC stuctural derangments, and both can be associated with the increase in the severity of POAG.

LIMITATIONS

EDI-OCT is an expensive instrument and few are available at some places. Researches conducted on this

topic have to opt for EDI-OCT, hence this present research till date is the only one done ever in Pakistan. Moreover, due to this fact this study had to be carried out at a single center.

SUGGESTIONS / RECOMMENDATIONS

More studies over the histological, biomechanical and molecular level of LC should be done.

CONFLICT OF INTEREST / DISCLOSURE

There is no conflict of interest.

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