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Interocular Variation in Retinal Nerve Fibre Layer Thickness of the Natives of High Altitude Versus Low Altitude

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Purpose*: To study Interocular variation in RNFL thickness of the natives of high altitude versus low altitude in the hilly terrain of Himachal Pradesh.*
Method*s: A hospital based prospective observational study was conducted from July2017 to June2018 in the ophthalmology department at Indira Gandhi Medical College Shimla. Total of 200 healthy subjects underwent retinal nerve fibre layer thickness analysis by Spectral domain OCT. Of the 200 subjects, 100 subjects residing at a height, greater than 2000m above the sea level were included in the study group (cases), 100 subjects residing at a height of less than 2000m above the sea level were included in the control group.*
Results*: The study population consisted of 200 healthy subjects from 30 to 69 years of age. There were 49 males and 51 females were in the both the groups. In our study the average RNFL thickness for high altitude (cases) in right eye was 97.56± 6.81 and in the left eye was 97.76± 7.30. In our study the average RNFL thickness for low altitude (controls) in right eye was 102.69 ±7.02 and in the left eye was 102.49± 7.20. Average RNFL thickness in right eye and the left eye for high altitude (cases) and low altitude (controls) was statistically insignificant with p value is more than 0.05*
Conclusion*: This study concluded that average RNFL thickness in right eye and the left eye for high altitude (cases) and low altitude (controls) was statistically insignificant. For both the eyes RNFL thickness of high altitude residents was significantly lower than those of low altitude.*

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I. Introduction

Glaucoma is an optic neuropathy associated with accelerated apoptosis of retinal ganglion cells (RGCs) that manifests as increased cupping of the optic disc and thinning of the retinal nerve fiber layer (RNFL). The diagnosis of glaucoma is currently based on the appearance of the optic disc, RNFL, and standard achromatic perimetry. The optic disc is quite variable in appearance in the normal population; hence, a progressive change in the appearance of the disc architecture compared with a baseline condition is a more robust criterion for diagnosing glaucoma damage.[1] Optical coherence tomography (OCT) is an imaging device, which produces high resolution, cross-sectional images of retinal nerve fiber layer (RNFL) and optic nerve head (ONH).[2]

It is known that the quantity of UV light increases with increasing altitude at a rate of 4% for each 300 m ascent), low latitude, and in highly reflective environments. For example, the reflection of ultraviolet increases two times from the surface of water and eight times from snow when compared to the reflection from a field of grass. The combination of altitude and snow at 2000 m results in a doubling of the quantity of UV light compared to sea level; damage to almost all eye tissues (eye lids, cornea, conjunctiva and lens) could occur. Disturbance in visual function can result from the hypoxia of altitude and the effects of cold. High altitude and hypoxia also affect the retina.[3]

This study was being conducted to assess any difference in right and left eye RNFL thickness in natives of high altitude as compared to that of low altitude.

II. Material And Methods

A hospital based prospective observational study was conducted from July2017 to June2018 in the ophthalmology department at Indira Gandhi Medical College Shimla. The study population consisted of 200 healthy subjects from 30 to 69 years of age. Of the 200 subjects, 100 subjects residing at a height, greater than 2000m above the sea level were included in the study group (cases), 100 subjects residing at a height of less than 2000m above the sea level were included in the control group. The study was conducted in accordance with Declaration of Helsinki and the guidelines for good ethical clinical practice. The study was approved by our institute ethics committee. Informed consent was obtained from all subjects. A complete ocular examination including visual acuity, refractive error, anterior and posterior segment examination, intraocular pressure (IOP) with Goldman applanation tonometry, Gonioscopy with Goldman single mirror was done to rule out any anterior and posterior segment pathology. Patients excluded were those with history of ocular trauma, intraocular surgery/ laser, diabetes mellitus, family history of glaucoma, some ocular/neurological disease affecting ONH or causing RNFL thinning. OCT was done on 3D OCT-1 maestro. Pupils were dilated by using one to two drops of 5% phenylephrine and 0.8% tropicamide. The desired scanning protocol i.e. 3D Disc was selected by double clicking on it.

Statistical Analysis: Data collected during study period is transferred to MS excel sheet for further process and analysis. Means and standard deviations were calculated for continuous variables. Comparison of means was done on two groups using statistical software SPSS version 20. Parametric tests of significance i.e. ANOVA was used to determine statistical significance and p value.

III. Result

The study population consisted of 200 healthy subjects from 30 to 69 years of age. The mean age of cases (high altitude residents) and controls (low altitude residents) were 46.87±9.32 years and 46.65 ±9.68 years respectively. There were 49 males and 51 females in the both the groups.

RNFL Thickness in right and Left eye of High Altitude (Cases)

RNFL Thickness in different quadrants, for high altitude residents – Average inferior RNFL thickness in right eye was 126.56±10.57 and in left eye was 125.02±11.25, average superior RNFL thickness in right eye was 114.47±10.01 and in left eye was 117.93±10.72, average nasal RNFL thickness in right eye was 81.86±10.37 and in left eye was 83.12±9.89, average temporal RNFL thickness in right eye was 67.49±7.38 and in the left eye was 65.02±7.71, average RNFL thickness of all quadrants in right eye was 97.56± 6.81 and in the left eye was 97.76± 7.30. The p value for inferior and temporal quadrants in the right and left eye was less than 0.05 which is statistically significant, but p value for average RNFL thickness and superior and nasal quadrants was more than 0.05 which is statistically insignificant. This has been depicted in table 1

Table 1: RNFL Thickness in right and Left eye of High Altitude (Cases)

RNFL Thickness	Right eye (n=100)	Left eye (n=100)	p value
Inferior	126.56± 10.57	125.02± 11.25	0.019
Superior	114.47± 10.01	117.93± 10.72	0.32
Nasal	81.86± 10.37	83.12±9.89	0.38
Temporal	67.49± 7.38	65.02± 7.71	0.022
Average	97.56± 6.81	97.76± 7.30	0.84

RNFL Thickness in right and Left eye of Low Altitude (Controls)

RNFL Thickness parameters, for low altitude residents – Average inferior RNFL thickness in right eye was 129.77±11.45 and in left eye was 129.61±10.80, average superior RNFL thickness in right eye was 120.54±10.52 and in left eye was 123.48±10.67, average nasal RNFL thickness in right eye was 88.02±9.48 and in left eye was 88.02±9.56, average temporal RNFL thickness in right eye was 72.08±6.85 and in the left eye was 69.04±7.09, average RNFL thickness of all quadrants in right eye was 102.69 ±7.02 and in the left eye was 102.49± 7.20. The p value for average RNFL and inferior, superior and nasal quadrants in the right and left eye was more than 0.05 which is statistically insignificant, except for temporal quadrant in which p value is less than 0.05. This has been depicted in table 2

Table 2: RNFL Thickness in right and Left eye of Low Altitude (Controls)

RNFL Thickness	Right eye (n=100)	Left eye (n=100)	p value
Inferior	129.77± 11.45	129.61± 10.80	0.09
Superior	120.54± 10.52	123.48± 10.67	0.92
Nasal	88.02± 9.48	88.02± 9.56	1.00
Temporal	72.08± 6.85	69.04± 7.09	0.002
Average	102.69± 7.02	102.49 ± 7.20	0.84

RNFL Thickness in right eye of high altitude (Cases) and low altitude (Controls)

RNFL Thickness parameters, for right eye – Average inferior RNFL thickness in right eye was 126.56±10.57 in cases 129.77±11.45 in controls, average superior RNFL thickness in right eye was 114.47±10.01 in cases and 120.94±10.52 in controls, average nasal RNFL thickness in right eye was 81.86±10.37 in cases and 88.02±9.48 in controls , average temporal RNFL thickness in right eye was 67.49±7.38 in cases and 72.08±6.85 in controls, average RNFL thickness of all quadrants in right eye was 97.56± 6.81in cases and 102.69±7.02 in controls. The p value for RNFL Thickness of right eye in high altitude and low altitude was less than 0.05 which is statistically significant. This has been depicted in table 3

Table 3
RNFL Thickness in right eye of high altitude (Cases) and low altitude (Controls)

RNFL Thickness	High Altitude (Rt eye, n=100)	Low Altitude (Rt eye, n=100)	p value
Inferior	126.56±10.57	129.77±11.45	0.041
Superior	114.47±10.01	120.94±10.52	0.00
Nasal	81.86±10.37	88.02±9.48	0.00
Temporal	67.49±7.38	72.08±6.85	0.00
Average	97.56±6.81	102.69±7.02	0.00

RNFL Thickness parameters, for left eye – Average inferior RNFL thickness in left eye was 125.02±11.25 in cases 129.61±10.84 in controls, average superior RNFL thickness in left eye was 117.93±10.72 in cases and 123.48±10.67 in controls, average nasal RNFL thickness in left eye was 83.12±9.89 in cases and 88.02±9.56 in controls , average temporal RNFL thickness in left eye was 65.02±7.71 in cases and 69.04±7.09 in controls, average RNFL thickness of all quadrants in left eye was 97.76± 7.30 in cases and 102.49±7.20 in controls. The p value for RNFL Thickness of left eye in high altitude and low altitude was less than 0.05 which is statistically significant. This has been depicted in table 4

Table 4
RNFL Thickness in Left eye of cases and controls

RNFL Thickness	High Altitude(Lt eye, n=100)	Low Altitude(Lt eye, n=100)	p value
Inferior	125.02±11.25	129.61±10.84	0.004
Superior	117.93±10.72	123.48±10.67	0.00
Nasal	83.12±9.89	88.02±9.56	0.00
Temporal	65.02±7.71	69.04±7.09	0.00
Average	97.76±7.30	102.49±7.20	0.00

IV. Discussion

Glaucoma is a multifactorial, chronic optic nerve neuropathy that is characterized by progressive loss of retinal ganglion cells (RGC), which leads to structural damage to the optic nerve head (ONH), retinal nerve fiber layer (RNFL), and consequent visual field defects. Optical coherence technology (OCT) is playing an increasing role in glaucoma diagnosis, monitoring of disease progress, and quantification of structural damage. Peripapillary RNFL analysis is the most commonly used scanning protocol for glaucoma diagnosis, as it samples RGCs from the entire retina.[4]

In our study the average RNFL thickness for high altitude (cases) in right eye was 97.56± 6.81 and in the left eye was 97.76± 7.30. The p value for inferior and temporal quadrants in the right and left eye was less than 0.05 which is statistically significant, but p value for average RNFL thickness and superior and nasal quadrants was more than 0.05 which is statistically insignificant.

In our study the average RNFL thickness for low altitude (controls) in right eye was 102.69 ±7.02 and in the left eye was 102.49± 7.20. The p value for average RNFL and inferior, superior and nasal quadrants in the right and left eye was more than 0.05 which is statistically insignificant ,except for temporal quadrant in which p value is less than 0.05.In a study conducted by Budenz et al (2008) [5] on symmetry between the right and left eyes of the normal retinal nerve fiber layer found that there was a small, but statistically significant, difference between mean RNFL thickness measurements of the 2 eyes. The right eye measured 1.3 μm thicker than the left on the standard scan (SD 4.7, 95% CI 0.4-2.2, P = .004) and 1.2 μm thicker on the fast scan (SD 5.2, 95% C.I.

0.1-2.2, P = .026). The quadrant and clock-hour differences were sometimes larger in the right eye and sometimes the left eye. While in our study there was no statistically difference between mean RNFLT in the right and left eye but there was some difference in quadrant wise RNFLT. The difference in right and left eye may be due to error related to measuring RNFL thickness with the Stratus OCT in their study.

On the other hand, Huynh and associates (2007) [6], in their large study of symmetry of optical coherence tomography retinal measurements in young children , did not find any difference in mean RNFL thickness between right and left eyes of the same individuals. Similar results were found in our study

Average RNFL thickness in right eye was 97.56± 6.81in high altitude (cases) and 102.69±7.02 in low altitude **(**controls). The p value for RNFL Thickness of right eye between high altitude and low altitude was less than 0.05 which is statistically significant. Average RNFL thickness in left eye was 97.76± 7.30 in high altitude (cases) and 102.49±7.20 in low altitude **(**controls). The p value for RNFL Thickness of left eye between high altitude and low altitude was less than 0.05 which is statistically significant.

In a study conducted by Tarek Alasil et al (2013) [7]on analysis of normal retinal nerve fibre layer thickness by age, sex, and race showed that comparisons between ethnic groups revealed that Caucasians had mean RNFL values (96±9mm) slightly thinner than those of Hispanics (103±11mm; P=0.02) or Asians (101±8.5mm; P=0.009.Study done by Budenz et al (2007)[8] on Caucasian eyes showed that they had mean RNFL values of 100.1±11.6µm which was significantly less than Asians (105.8±9.2).

Difference in embryogenesis and variable expression of genes affecting retinal neurogenesis may be responsible for lower RNFLT in high altitude residents.

A difference may or may not exist can only be ascertained in a large sample, so a larger group of High and low altitude residents will be required to further potentiate the present study.

V. Conclusion

For both the eyes RNFL thickness of high altitude residents was significantly lower than those of low altitude. The average RNFL thickness in right eye and the left eye for high altitude (cases) and low altitude (controls) was statistically insignificant.

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