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Research Article

RETINAL NERVE FIBRE LAYER THICKNESS OF NATIVES OF HIGH ALTITUDE VERSUS LOW ALTITUDE (TOPCON 3D OCT-1MAESTRO BASED STUDY)

Dr. Seema[1], Dr. G. C. Rajput[2], Dr. Praveen Panwar[3] and Dr Devender Kumar[4]*

[1]M.B.B.S,M.S.Ophthalmology, Medical Officer,C.H.Sundernagar
[2]M.B.B.S,M.S.Ophthalmology, Professor, Department of Ophthalmology, Indira Gandhi Medical College Shimla
[3]M.B.B.S,M.S.Ophthalmology, Associate Professor, Department of Ophthalmology, Indira Gandhi Medical College, Shimla
[4]M.B.B.S, M.D. Community Medicine Assistant Professor Dr Radhakrishnan Government Medical College, Hamirpur

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A B S T R A C T

Purpose: To study Retinal nerve fibre layer thickness of natives of high altitude versus low altitudeat Indira Gandhi Medical College Shimla in the hilly terrain of Himachal Pradesh.
Methods: A hospitalbased 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. Average RNFL thickness in high altitude was 97.66 ± 7.04μm and 125.79 ± 10.91μm in inferior, 116.20 ± 10.49μm in superior, 82.49 ± 10.13μm in nasal and 66.26 ± 7.63μm in temporal quadrant. Average RNFL thickness in low altitude was 102.59 ± 7.10μm and 129.69 ± 11.12μm in inferior, 122.21 ± 10.64μm in superior, 88.02 ± 9.50μm in nasal and 70.56 ± 7.12μm in temporal quadrant.The high altitude group had thinner RNFL parameter than low altitude group, in data adjusted for age and gender (all $P < 0.05$). Normal RNFL thickness values follow the ISNT rule with decreasing RNFL thickness values starting from the thickest quadrant inferiorly to the thinnest quadrant temporally. Thinner RNFL measurements were associated with older age.
Conclusion: This study concluded that natives of high altitude have thinner RNFL values as compared to low altitude. Thinner RNFL measurements observed in older age group. There was no relationship between RNFL thickness and gender.

INTRODUCTION

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 fibre layer (RNFL), and consequent visual field defects. Early diagnosis and treatment of glaucoma has been shown to reduce the rate of disease progression, and improve patients' quality of life. The currently accepted gold standards for glaucoma diagnosis are optic disc assessment for structural changes, and achromatic white on-white perimetry to monitor changes in function. However, imaging technologies such as optic coherence technology (OCT) are playing an increasing role in glaucoma diagnosis, monitoring of disease progress, and quantification of structural damage.

Corresponding author:* **Dr Devender Kumar
M.B.B.S, M.D. Community Medicine Assistant Professor Dr Radhakrishnan Government Medical College, Hamirpur

[1]Life at high altitude differs from life at sea level in terms of numbers of factors. The unique environment of high altitude includes factors such as low air pressure, hypoxia, dry and cold weather, prolonged and increased exposure to sunlight, strong solar infrared light and UV radiation, and prolonged snow cover, which all have effects on the human body in general and the eyes in particular. The eye, like every other organ, is affected by the hypobaric hypoxia of high altitude[2,3]. This study was being conducted to assess RNFL thickness in natives of high altitude as compared to that of low altitude so, as to have baseline data of RNFL for higher altitude natives and to distinguish between disease-related RNFL changes and normal racial RNFL variations.

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. Subjects included were those of more than 30 years of age, with visual acuity of 20/20, refractive error less than ±3D, IOP less than 22mHg, a normal ONH with vertical CD ratio of less than or equal to 0.6 without asymmetry of more than 0.2.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. Peripapillary RNFL was measured along a circle having a nominal diameter of 3.46 mm centred on the optic disc.These include mean peripapillary RNFL thickness, 4 quadrant averages (temporal, superior, nasal and inferior), and 12 clock-hour averages. In this analysis, data from the mean RNFL thickness and quadrant averages are presented.

***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 <0.05 was considered statistically significant.

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. This is depicted in table 1& 2

Table 1 Demographic data for high altitude

Age in year	Total no of subjects	Gender male	Female
30-39	25	8	17
40-49	32	18	14
50-59	33	18	15
60-69	33	5	5
Total	100	49	51

Table 2 Demographic data for low altitude

Age in year	Total no of subjects	Gender male	Female
30-39	25	16	9
40-49	32	12	20
50-59	33	16	17
60-69	10	5	5
Total	100	49	51

RNFL Thickness of high altitude (H) and low altitude(L) gender wise

The average RNFL Thickness for high altitude residents (cases) in male was 96.77±6.28 and in the female was 98.52± 7.64. The average RNFL Thickness for low altitude residents (controls) in male was 102.38±7.13 and in the female was 102.79± 7.09. The RNFLT parameters were slightly thinner in males than females but difference was statistically insignificant with p value of less than 0.05. This has been depicted in table 3.

Table 3 RNFL Thickness of high altitude (H) and low altitude (L) gender wise

RNFL Thickness	Male (n = 49)	Female (n = 51)	p value
Inf- H	124.44± 10.01	127.09± 11.62	0.62
Inf-L	129.50± 11.46	129.87± 10.84	0.35
Sup-H	115.01± 10.19	117.34± 10.69	0.11
Sup-L	122.93± 10.07	121.52± 11.17	0.81
Nasal-H	81.99± 9.20	82.97± 10.97	0.086
Nasal-L	87.07± 9.78	88.93± 9.18	0.16
Temporal-H	65.86± 7.11	66.64± 8.12	0.47
Temporal-L	70.13± 6.95	70.97± 7.29	0.40
Average-H	96.77± 6.28	98.52± 7.64	0.078
Average-L	102.38± 7.13	102.79± 7.09	0.67

RNFL thickness for high altitude (H) and low altitude (L) stratified by age category

RNFL thickness was associated significantly with age. The RNFL thickness in all the quadrants decreased with age in both high and low altitude groups with p value of 0.00 for the age range 30-69 years included in this study.For every decade of higher age, the mean RNFL became thinner (p=0.00). This has been shown in table 4

Table 4 RNFL thickness for high altitude (H) and low altitude (L) stratified by age category

RNFL parameters	30-39 years	40-49 years	50-59 years	60-69 years	p value
Inf- H	133.82±8.08	127.78±7.69	121.94±10.38	112.05±9.01	0.00
Inf-L	140.48±7.20	131.22±8.38	123.94±8.84	116.80±7.56	0.00
Sup-H	123.88±7.33	118.27±8.95	112.42±9.48	102.85±5.83	0.00
Sup-L	131.00±7.81	124.19±8.76	117.30±8.74	110.10±7.51	0.00
Nasal-H	87.54±9.57	83.23±9.14	81.08±9.12	72.15±9.36	0.00
Nasal-L	95.36±5.94	89.27±7.63	84.26±9.22	78.10±8.37	0.00
Temporal-H	70.34±7.20	67.92±6.83	63.71±6.91	59.10±5.37	0.00
Temporal-L	75.44±5.22	72.08±5.88	67.97±6.04	62.05±7.17	0.00
Average-H	104.02±4.83	99.28±4.60	94.64±5.07	86.55±4.98	0.00
Average-L	110.58±2.80	104.25±3.40	98.21±4.77	91.75±4.86	0.00

Altitude wise RNFL thickness

Average RNFL thickness in high altitude was 97.66 ± 7.04µm and 125.79 ± 10.91µm in inferior, 116.20 ± 10.49µm in superior, 82.49 ± 10.13µm in nasal and 66.26 ± 7.63µm in temporal quadrant. Average RNFL thickness in low altitude was 102.59 ± 7.10µm and 129.69 ± 11.12µm in inferior, 122.21 ± 10.64µm in superior, 88.02 ± 9.50µm in nasal and 70.56 ± 7.12µm in temporal quadrant. The high altitude group had thinner RNFL parameter than low altitude group, in data adjusted for age and gender (all P <0.05). Normal RNFL thickness values follow the ISNT rule with decreasing RNFL thickness values starting from the thickest quadrant inferiorly to the thinnest quadrant temporally. This has been shown in table 5

Table 5 Altitude wise RNFL thickness

RNFL Thickness	High altitude residents (cases)	Low altitude residents (controls)	p value
Inferior	125.79±10.91	129.69±11.12	0.00
Superior	116.20±10.49	122.21±10.64	0.00
Nasal	82.49±10.13	88.02±9.50	0.00
Temporal	66.26±7.63	70.56±7.12	0.00
Average	97.66±7.04	102.59±7.10	0.00

DISCUSSION

Glaucoma is the second leading cause of blindness in the world accounting for upto 8% of total blindness. In India, glaucoma is the leading cause of irreversible blindness with atleast 12 million people affected and nearly 1.2 million people blind from the disease. More than 90 percent of cases of glaucoma remain undiagnosed in the community.[4] 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.[1]

In our study the mean age of the high altitude residents (cases) was 46.87 years and low altitude residents (controls) was 46.65 years. Similarly, in a study conducted by TarekAlasil *et al* (2013)[5] the mean age was 53.7±16.3 years. The discrepancy between the two studies is because in our study age range taken was 30-69 years where as in their study age range was 9-86 years.

The average RNFL Thickness for high altitude residents (cases) in male was 96.77±6.28 and in the female was 98.52± 7.64. The average RNFL Thickness for low altitude residents (controls) in male was 102.38±7.13 and in the female was 102.79± 7.09. The RNFLT parameters were slightly thinner in males than females but difference was statistically insignificant with p value of less than 0.05.

In a study conducted by Schuman *et al.*[6] on quantitative assessment of nerve fibre layer (NFL) thickness showed that RNFLT of men were usually thinner than that of women but not statistically significant. Similar results were found in our study. In a study conducted by Mansoori *et al* (2012)[7]in normal Indian eyes showed no significant gender-related difference in RNFLT.

The average RNFL for high altitude was 97.66 ± 7.04µm. The average RNFL for low altitude was 102.59 ± 7.10µm.The high altitude group had thinner RNFL parameter than low altitude group, in data adjusted for age and gender (all P <0.05).In a study conducted by Tarek Alasil *et al* (2013) [5]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). RNFL thickness in other Asian countries has also been seen to be on the higher side than Caucasians (Thai population= 109.3 ±10.5µm, Taiwanese= 108.7±9.4µm, Chinese=111.5 ±4.12) (Manassakorn *et al*, 2008[9]; Peng *et al*, 2008[10]. In a study conducted by TarannumMansoori *et al* (2012)[7] on quantification of retinal nerve fibre layer thickness in normal Indian population found significantly higher values of RNFLT in Indian eyes when compared to White eyes, and lower value when compared to RNFLT in normal Latino population.

So RNFL thickness has been seen to vary among ethnicities. Normal human ONH mean axonal population range from 700,000 to 1.2 million. Hence there is large variability of axonal numbers among normal eyes of approximately 200,000 fibres[11]. This variation in the number of nerve fibres may be responsible for thinner RNFL in natives of high altitude. The reflection of UV light increases 2 times from the surface of water and 8 times from snow when compared with 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 with sea level which can affect eye tissues.High altitude and hypoxia also affect the retina.[12]Retinal neurogenesis starts in the central optic cup region and then fans out concentrically in a wavelike pattern into the periphery. There is a basic topographic organization of the optic cup with dorsoventral and nasotemporal patterning, which involves certain genetic cues, including that of the Otx genes. Key regulatory genes involved in the early development of the eye and the fate of retinal cells include Pax6, Rxl, Six3/6, Lhx2, and certain basic helix-loop-helix transcription factors. 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.

CONCLUSION

For both the eyes RNFL thickness of high altitude residents was significantly lower than those of low altitude. Males in both the groups had slightly thinner RNFLT than female but it was not statistically significant.Thinner RNFL measurements observed in older age group. The conclusion drawn from the present study, may be authenticated by taking larger number of subjects in a multicentric study and hence confirming whether significant difference exists or not.

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