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# THE EFFECT OF CHRONIC ALCOHOL USE ON RETINAL NERVE FIBER LAYER THICKNESS

# **Ophthalmology**

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# ABSTRACT

Aim: To evaluate the effect of chronic alcohol intake on peripapillary retinal nerve fiber layer

(RNFL) thickness and to find any association between severity of alcohol addiction with the RNFL thickness.

Methods: This was a case control study of 70 cases of alcohol addiction for more than five years and 70 age-matched normal healthy persons as controls. The cases were interviewed with structured questionnaires of Alcohol Use Disorders Identification Test (AUDIT) to detect the severity of alcohol use. The peripapillary RNFL thickness was measured by 3D optical coherence tomography (OCT).

**Observation:** A total of 137 eyes of 70 cases of alcohol users and 139 eyes of 70 controls were included in the study. The average RNFL thickness of 95.12 $\pm$ 5.02 µm in chronic alcoholic users was found to be statistically significantly thinner compared to 99.37 $\pm$ 3.08 µm of the control group (p< 0.0001). The measurements of the RNFL thickness 78.45 $\pm$ 8.7 µm in temporal quadrant of chronic alcoholic users was statistically significantly (p<0.0001) thin from 83.55 $\pm$ 11.17 µm of control group. The measurements of the RNFL thickness in superior, inferior and nasal quadrant were not statistically significant between chronic alcoholic users and control groups (p=0.0779, p=0.1196 and p=0.0618 respectively). Thinning of RNFL in all the quadrants were more in cases with increase severity of alcohol use than others, though it was not statistically significant.

**Conclusion:** In this study, average and temporal quadrant RNFL thickness was thinner in chronic alcoholics than the controls. We therefore conclude that measurement of RNFL by OCT in chronic alcoholic cases could be a useful technique for early detection of retinal nerve fiber loss.

# **KEYWORDS**

Peripapillary RNFL, Optical Coherence Tomography, alcohol

## INTRODUCTION

Alcohol abuse in India is a substantive problem for the individual as well as for the society. The prevalence of alcohol intake in India ranges from 65.8% to 67.4%.<sup>1</sup> It varies in urban and rural areas with estimated 7.3 per 1000 in urban areas to 5.8 per 1000 in rural areas.<sup>2</sup> Alcohol intakes are more common among the poorer section of the society. Alcohol exerts its deleterious effect metabolically via oxidative or nonoxidative pathways by free radical production and lipid peroxidation, resulting in increase oxidative stress.<sup>3,4</sup> This oxidative stress is responsible for many ocular neurodegenerative disorders. The retina is the neurosensorial tissue and is extremely rich in membranes with polyunsaturated lipids.<sup>5</sup> It is highly sensitive to oxygen free radicals and lipid peroxidation.<sup>6</sup>

Toxic optic neuropathy is a condition that usually occurs in alcohol drinkers characterized by progressive painless visual impairment and central or centroceacal scotoma due to optic nerve damage. The exact pathogenesis of toxic optic neuropathy is not established though malnutrition due to alcohol intake appears to be the most important causative factor.<sup>5</sup> The mechanism of the primary damage to mitochondria that disrupts the process of oxidative phosphorylation causing axonal loss which preferentially affects the parvocellular neurons in papillomacular bundle of the retina, thus causes thinning of the retinal nerve fiber layer (RNFL).<sup>7,8</sup> Toxic optic neuropathy is usually an under diagnosed condition and patients usually present at late stage of the diseases when visual recovery is impossible.

OCT is a reliable reproducible noninvasive transpupillary diagnostic imaging that utilizes infrared wavelengths and enables quantitative in vivo high resolution measurement of peripapillary RNFL. The decreased thickness of RNFL has been reported in the literature for various neurological disorders.<sup>9-11</sup> The early diagnosis of thinning of RNFL by OCT in chronic alcoholics can prevent blindness due to toxic optic neuropathy.

Therefore, this study was aimed to measure and compare the thickness of peripapillary RNFL by OCT in chronic alcoholic cases and in healthy individuals which will improve our understanding of pathophysiology of toxic optic neuropathy.

### MATERIALAND METHODS

This was a case control study of 70 alcohol users for more than five years and 70 age-matched normal healthy persons as controls, conducted from January 2017 to December 2017 in a tertiary care teaching hospital. The cases were recruited from deaddiction clinic and age matched individuals without any history of alcohol addiction attending the ophthalmology outpatient department were taken as

controls. We included consecutive cases that were referred to us. This research protocol was approved by the Institutional ethics committee. All the investigations were done according to Helsinki declaration. The full informed consent was taken from all participants.

The cases were assessed with structured questionnaires of Alcohol Use Disorders Identification Test (AUDIT) to detect the severity of alcohol use. The participants in the study group with history of raised intracranial pressure, previous ocular surgeries, use of medicines ethambutol and isoniazide, systemic diseases like multiple sclerosis, Parkinson disease, Alzheimer disease and renal failure were excluded from the study.

Physical and neurological examinations were done in all the participants. Complete ophthalmological examination including visual acuity was measured with internally illuminated Snellen's chart and near vision was recorded at 33 cm with Jagger's chart under good illumination. Colour vision was tested with Ishihara's peudoisochromatic plates. Pupillary reaction was noted. Slit lamp biomicroscopy and fundus examination were done to rule out any anterior or posterior segment ocular pathology. Fundus photograph was taken to look for temporal pallor of the optic disc. Intraocular pressure was measured with Goldman tonometer.

The thickness of peripapillary RNFL was measured by 360° circular scanning around the optic nerve with 3D OCT after dilatation of the pupils with 0.5% tropicamide solution in patients with chronic migraine and in healthy individuals to compare between the two groups. The RNFL thickness parameters calculated by the OCT software (version 8.42.003.01) were average thickness and thickness in the superior, inferior, temporal and nasal quadrants. There were three colour coded modalities to represent RNFL thickness, a wave chart or graph, a radial diagram and a table.

Statistical analysis was done with software SPSS version 20.0 to analyze the data of the study. Differences were considered statistically significant at p < 0.05.

#### Observations

A total of 137 eyes of 70 cases alcohol users and 139 eyes of 70 controls were included in the study. All cases and controls in our study were male. The age of the cases the controls ranged from 18 to 45 years. The mean age of the cases was  $35.4\pm 8.9$  years and in controls was  $36.2\pm 4.9$  years (Table-1). In our study of 70 chronic alcoholics cases, on analysis of response for AUDIT questionnaires, we got 11 persons with AUDIT score greater than 20 and rest 59 cases had AUDIT score of less or equal to 20.

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The best corrected visual acuity (BCVA) with Snellen's chart was 6/6 in 132 eyes, 6/9 to 6/18 in 3 eyes and less than or equal to 6/24 in 2 eyes out of 137 eyes of alcohol users where as out of 139 eyes in the control group, BCVA was 6/6 in 138 eyes and 6/9 to 6/18 in 1 eye. Out of 137 eyes of the cases, 2 eyes had optic disc pallor which was more marked temporally with red green colour deficiency. All the participants in control group had normal fundus and normal colour vision.

The mean intra ocular pressure (IOP) in chronic alcoholic users was  $14.6\pm4.1 \text{ mm}$  of Hg and  $14.9\pm3.4 \text{ mm}$  of Hg in the control group. The IOP in chronic alcoholic users group and in controls was not statistically insignificant (p =0.6382). The mean axial length (AL) of eyeball was  $24.2\pm0.7 \text{ mm}$  in chronic alcoholic users and  $24.3\pm0.5 \text{ mm}$  in control group. The difference of axial length was not statistically significant between two groups (p=0.3325).

Table-1	Baseline	demographic	characteristic	with	intraocular
pressure	e and axial	llength			

Variables		chronic alcoholic users	Controls	P value
Age (years), mean±SD		35.4± 8.9	36.2± 4.9	0.5111
Visual acuity	6/6	132(96.3%)	138(99.3%)	
	6/9 -6/18	03(2.2%)	01(0.7%)	
	≤6/24	02(1.5%)	00	
IOP (mm of Hg), mean±SD		14.6±4.1	14.9±3.4	0.6382
Axial length( mm) mean±SD		24.2±0.7	24.3±0.5	0.3325

On optic nerve head (ONH) evaluation, the mean cup to disc ratio (CDR) in chronic alcoholic users group was  $0.34\pm0.03$  and in control group  $0.33\pm0.09$ . The difference was not statistically significant between two groups (p=0.2180) (Table-2).

The RNFL thickness was measured in all the quadrants of all the eyes in cases and controls. The average RNFL thickness was  $95.12\pm5.02$  µm in chronic alcoholic users group and  $99.37\pm3.08$  µm in control group. In our study, the average RNFL thickness in chronic alcoholic users was found to be statistically significantly thinner compared to the control group (p<0.0001).

The mean superior quadrant RNFL thickness was 115.13 $\pm$ 11.02 µm in chronic alcoholic users group and 117.78 $\pm$ 13.69 µm in control group. The measurements of the RNFL thickness in superior quadrant was not statistically significantly different between chronic alcoholic users and control groups (p =0.0779). The mean RNFL thickness in inferior quadrant was 124.19 $\pm$ 10.21 µm in chronic alcoholic users and 127.23 $\pm$ 11.45 µm in control group. The measurements of the RNFL thickness in inferior quadrant was not statistically significant between chronic alcoholic users and control group. The measurements of the RNFL thickness in inferior quadrant was not statistically significant between chronic alcoholic users and control groups (p =0.1196).

The measurements of the RNFL thickness in temporal quadrant was  $78.45\pm8.7 \ \mu\text{m}$  and  $83.55\pm11.17 \ \mu\text{m}$  in chronic alcoholic users and control groups respectively, were statistically significant thinner (p<0.0001). The mean RNFL thickness in nasal quadrant was  $70.13\pm10.81 \ \mu\text{m}$  in chronic alcoholic users and  $72.561\pm11.15 \ \mu\text{m}$  in control group. The measurements of the RNFL thickness in nasal quadrant were not statistically significant between chronic alcoholic users and control groups (p=0.0618).

Table-2 Comparison of retinal nerve fiber layer (RNFL) thickness in chronic alcoholic users and control group

	Variable	chronic	Control	P value
		alcoholic	group	
		users mean	mean	
Optic nerve	Average cup to	$0.34 \pm 0.03$	0.33±0.09	0.2180
head(ONH)	disc ratio(CDR)			
Retinal Nerve Fiber Layer (RNFL) in microns	Average	95.12±5.02	99.37±3.08	< 0.0001
	Superior	$115.13 \pm 11.02$	117.78±13.69	0.0779
	Inferior	$124.19{\pm}\ 10.21$	$127.23{\pm}11.45$	0.1196
	Nasal	70.13±10.81	72.61±11.15	0.0618
	Temporal	78.45±8.7	83.55±11.17	< 0.0001

The RNFL thickness on comparing with the severity of alcohol use, we found that thickness in all the quadrants were diminished in cases with

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AUDIT score greater than 20 compared to the cases with AUDIT score less or equal to 20. However, the comparison of RNFL thinning with AUDIT score was not statistically significant (Table-3).

Table-3 Comparison of retinal nerve fiber layer (RNFL) thickness
in chronic alcoholic users in relation with AUDIT score

Variable	Quadrant	AUDIT score $> 20$	AUDIT score $\leq$	P value
		mean±SD	20 mean±SD	
Retinal	Superior	$109.23 \pm 12.3$	$112.17 \pm 9.02$	0.3166
Nerve Fiber	Inferior	$123.59 \pm 7.6$	$124.89{\pm}9.9$	0.6721
Layer	Nasal	69.41±2.9	70.94±9.6	0.6016
(RNFL) in microns	Temporal	77.25±4.7	78.82±9.1	0.5735

#### DISCUSSION

A total of 1387 eyes of 70 cases alcohol users and 139 eyes of 70 controls were included in the study. All cases and controls in our study were male. The mean age of the cases was  $35.4\pm 8.9$  years and in controls was  $36.2\pm 4.9$  years.

The best corrected visual acuity (BCVA) with Snellen's chart was 6/6 in 132 eyes, out of 138 eyes of alcohol users where as in the control group; BCVA was 6/6 in 138 eyes out of 139 eyes. Hence, majority of the cases did not have diminution of vision. Out of 138 eyes of the cases, 2 eyes had optic disc pallor which was more marked temporally with red green colour deficiency. All the participants in control group had normal fundus and colour vision. In this study most of the participants had normal fundus.

The mean intra ocular pressure (IOP) in chronic alcoholic users was  $14.6\pm4.1 \text{ mm}$  of Hg and  $14.9\pm3.4 \text{ mm}$  of Hg in the control group. The IOP in chronic alcoholic users group and in controls was not statistically insignificant (p=0.6382). The mean axial length (AL) was  $24.2\pm0.7 \text{ mm}$  in chronic alcoholic users and  $24.3\pm0.5 \text{ mm}$  in control group. The difference of axial length was not statistically significant between two groups (p=0.3325). On optic nerve head (ONH) evaluation the mean cup to disc ratio (CDR) in chronic alcoholic users group was  $0.34\pm0.03 \text{ and } 0.33\pm0.09 \text{ in control group}$ . The difference was not statistically significant between two groups (p=0.2180).

The RNFL thickness was measured in all the quadrants of all the eyes in cases and controls. The average RNFL thickness was 95.12±5.02  $\mu$ m in chronic alcoholic users group and99.37±3.08  $\mu$ m in control group. In our study, the average RNFL thickness in chronic alcoholic users was found to be statistically significantly thinner compared to the control group (p<0.0001). Moura et al <sup>12</sup> also reported thinning of RNFL in their study. The measurement of the RNFL thickness in temporal quadrant was 78.45±8.7 $\mu$ m and 83.55±11.17  $\mu$ m in chronic alcoholic users and control groups respectively. The measurements of the RNFL thickness in temporal quadrant was statistically significant between two groups (p<0.0001).

The mean superior quadrant RNFL thickness was 115.13 $\pm$ 11.02 µm in chronic alcoholic users group and µm117.78 $\pm$ 13.69 in control group. The mean RNFL thickness in inferior quadrant was 124.19 $\pm$ 10.21µm in chronic alcoholic users and 127.23 $\pm$ 11.45 µm in control group. The mean RNFL thickness in nasal quadrant was 70.13 $\pm$ 10.81 µm in chronic alcoholic users and 72.61 $\pm$ 11.15 µm in control group. The measurements of the RNFL thickness in superior, inferior and nasal quadrant were not statistically significant between chronic alcoholic users and control groups (p =0.0779,p=0.1196 and p=0.0618 respectively).

In this study, more thinning of RNFL was observed in cases with increase in severity of alcohol intake with AUDIT score greater than 20 compared to the cases with AUDIT score less than or equal to 20. However the thinning of RNFL thickness was not statistically significant with AUDIT score. Ahuja et al<sup>13</sup> also reported more thinning of RNFL with severity of alcohol intake in their study

We therefore conclude that measurement of RNFL by OCT in chronic alcoholic cases could be a useful technique for early detection of retinal nerve fiber loss.

### REFERENCES

- Ghosh S, Samanta A, Mukherjee S. Patterns of alcohol consumption among male adults at a slum in Kolkata, India. J Health Popul Nutr 2012;30:73–81.
- Girish N, Kavita R, Gururaj G. Alcohol use and implications for public health: patterns of use in four communities. Indian J Community Med 2010;35:238–44.

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- Bondy SC, Guo SX. Regional selectivity in ethanol induced pro-oxidant events within brain.Biochemical Pharmacology. 1995;6: 69-72.
- Brain.Biocennical rnarmacology. 1993;6: 69-72.
  Ramachandran V, Watts LT, Maffi SK, Chen J, Schenker S, Henderson G. Ethanol-Induced Oxidative Stress Preceds Mitrochondrially Mediated Apoptotic Death of Cultured Fetal Cortical Neurons. J Neuroscience Research, 2003;74: 577-588.
   Kagan VE, Shvedova AA, Novikov KN, and Kozlov YP. Light-induced free radical
- Kagan VE, Shvedova AA, Novikov KN, and Kozlov YP. Light-induced free radical oxidation of membrane lipids in photoreceptors of frog retina. Biochimica et Biophysica Acta, 1973;330:76-79.
- Bazan NG. The metabolism of omega-3 polyunsaturated fatty acids in the eye: the possible role of docosahexaenoic acid and docosanoids in retinal physiology and ocular pathology. Progress in Clinical Biology and Research, 1989;312: 95-112.
  Lessel S. Toxic and deficiency optic neuropathies. In: Miller N, Newman NJ, eds. Walsh
- Lessel S. Toxic and deficiency optic neuropathies. In: Miller N, Newman NJ, eds. Walsh and Hoyts clinical neuro-ophthalmology. 5th edn. Vol 1. Baltimore: Williams and Wilkins. 1998;663–79.
- Sharma P, Sharma R. Toxic optic neuropathy. Indian J Ophthalmol 2011;59:137–41.
  Huang D, Swanson EA, Lin CP, Schuman JS, Stinson WG, Chang W. Optical coherence
- Huang D, Swanson EA, Lin CP, Schuman JS, Stinson WG, Chang W. Optical coherence tomography. Science 1991;254:1178-81.
   Schuman JS, Pedut-Kloizman T, Hertzmark E, Hee MR, Wilkins JR, Coker JG.
- Schuma JS, Fedur-Kiotzman I, Hertzmark E, Hee MR, Wilkins JK, Coker JJ. Reproducibility of nerve fiber layer thickness measurements using optical coherence tomography. Ophthalmology 1996;103:1889-98.
   Blumenthal EZ, Williams JM, Weinreb RN, Girkin CA, Berry CC, Zangwill LM.
- Blumenthal EZ, Williams JM, Weinreb RN, Girkin CA, Berry CC, Zangwill LM. Reproducibility of nerve fiber layer thickness measurements by use of optical coherence tomography. Ophthalmology 2000;107:2278-82.
- Moura FC, Monteiro ML. Evaluation of retinal nerve fiber layer thickness measurements using optical coherence tomography in patients with tobacco-alcoholinduced toxic optic neuropathy. Indian J Opthalamlo 2101(58:143–6.
- induced toxic optic neuropathy. Indian J Ophthalmol 2010;58:143–6.
  Ahuja S, Kumar PS, Kumar VP, Kattimani S, Akkilagunta S. Effect of chronic alcohol and tobacco use on retinal nerve fibre layer thickness: a case-control study.BMJ Open Ophth 2016;1:e000003.doi10.1136/bmjopth-2016-000003