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Original Research Article

Retinal changes in anemia - A comparative cross sectional study using SD-OCT

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ABSTRACT

Aim and Objective: To study the retinal changes in various grades of anemia and compare them with controls by analysing the peripapillary RNFL (retinal nerve fibre layer) thickness and CDR (cup-disc ratio) in OCT.

Introduction: Anemia is a common health problem, iron deficiency (IDA) being the most common type. It has deleterious visual effects through enhancement of ischemic effects.Changes in RNFL and CDR are seen in many ischemic retinal diseases.Optical coherence tomography (OCT) is a non invasive imaging modality that gives a cross-sectional topographic imaging of retina.Our study aims at analysing RNFL thickness and CDR by OCT in our subjects.

Materials and Methods: Our study was conducted including 44 each of anemic and non anemic people, after classifying the anemic group further based on WHO criteria. After detailed clinical examination, OCT was done and peri-papillary RNFL in 4 quadrants and vertical CDR were assessed and compared.

Results: Peripapillary RNFL thickness in anemia group was significantly thinner than controls, the change more pronounced in severe anemia than other groups. CDR was significantly high in severe anemia than others.

Conclusion: Retinal changes in anemia has a correlation with the severity of anemia. RNFL and CDR changes can predispose to serious visual defects in future. Hence, anemia screening and correction along with frequent clinical and OCT evaluation in such patients can be useful in early detection and prevention of anemic retinopathy.

1. Introduction

Hemoglobin (Hb) values below <13.0g/dL in males and <12.0g/dL in females are considered anemic, as per the WHO (World Health Organization).[1] However, ethnicity, sex and physiological health all affect the distribution of normal hemoglobin.[1] Anemia can be due to dietary Vitamin B12/ folate/ iron deficiency or chronic disease related anemia. Another one third may be "unexplained anemia" because it cannot be described by a pathological process or any underlying illness. A prolonged subclinical pro-inflammatory condition in the body may be the cause.[1] The most typical cause of anemia[2] is IDA (iron deficiency anemia), which is particularly prevalent in women of reproductive age. In addition to its crucial involvement in oxygen transport, iron also plays other functions in the CNS, such as myelination, the synthesis of neurotransmitters, and neuro- metabolism.[3]

Anemia may have a range of ocular symptoms. Every part of the eye and adnexa might be affected, although the most common symptoms are conjunctival pallor and retinal hemorrhages. Other ocular signs include optic disc edema, cotton wool patches, macular star, venous and

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arteriolar tortuosity. The severity of anemia is connected with its increasing occurrence. For the retina to retain its functional as well as structural integrity, it needs frequent oxygen supply.[2] Anemia decreases the substrate for retinal metabolism, which renders the tissue more vulnerable to hypoxic injury. The central retinal artery's superficial and deep capillary plexuses provide blood to the inner retinal layers, which makes them more vulnerable to hypoxic changes. It is well recognized that a decrease in the normal perfusion and oxygen saturation can harm the ganglion cells in the retina.[2]

RNFL (Retinal nerve fibre layer) thickness measurement offers crucial clinical data for determining retinal and optic nerve diseases.[2] Various ischemic retinal disorders have been related to lower RNFL thickness.[2] Additionally, some investigations on anemic mothers and children have shown thinning of the RNFL.[4] Although the precise etiology of fundus lesions is yet to be understood, hypoxia has been linked to them.[3] By using imaging, optical coherence tomography (OCT) has made it possible to do in-vivo quantitative analyses of peripapillary RNFL and other crucial characteristics.[4]

With anemia treated, anemic retinopathy is nearly always curable, hence the need for screening.[5] Here we intended to study the retinal changes and OCT values in patients with anemia and compare them with age and sex-matched control groups. Patients were screened for anemia and those found to be having anemia were classified into mild, moderate, and severe anemia based on WHO guidelines and were subjected to ophthalmologic examination. Fundusexamination using a fundus camera and direct/indirect ophthalmoscopy and Optical coherence tomography (OCT) was done and values recorded, mainly peripapillary RNFL thickness and cup disc ratio.

2. Materials and Methods

This comparative cross sectional study was conducted after the approval from the institutional ethics and research committees and informed consent was obtained from all participants before enrolment in the study. Study period was 18 months, from January 2021 to June 2022, in a multispeciality teaching hospital in Kerala. All patients in the age group 18-60 years satisfying our criteria, diagnosed with anemia from various clinical departments were selected, out of which first 44 (88 eyes) were included in the study. They were classified as mild, moderate and severe anemia based on WHO guidelines. A detailed history and ophthalmologic examination was done.

The non anemic control group was composed of 44 non anemic patients in the above said age group. They were also evaluated likewise.

Optical coherence tomography using CIRRUS HD OCT (spectral domain OCT, CarlZeiss) without pupillary dilatation and under the same intensity of dim room lighting was done and following parameters were evaluated:

1. Retinal nerve fibre layer (RNFL) thickness was measured with optic disc cube 200x200 scan protocol. Best scan with signal strength > 7 is used for analysis. Nasal, temporal, inferior, superior quadrant and average peripapillary RNFL measurements was noted.
2. Vertical optic cup- disc (C/D) ratio was measured in both the test and control group and values were compared.

3. Results

3.1. Age

In our study, mean age in anemia group was 39.97 ± 12.71 years and in control group was 42.4 ±12.12 years, which was not statistically significant.

3.2. Gender

In our study, the number of females and males were 35(79.55%) and 9(20.45%) in anemic group, 21(47.73%) and 23(52.27%) in control group. We noticed female predominance in anemic group.

3.3. Distribution of symptoms

Diminution of vision was most common symptom noticed -23(26.13%). The symptoms were more in severe anemia group (50%) compared to moderate, severe and control groups. Diminution of vision with floaters was seen only in severe anemia group (33.33%). We noticed that the pallor was found in moderate and severe anemia group only. All the patients in severe anemia group had pallor.

3.4. RNFL analysis

In right eye superior (p value 0.02) and inferior (p value 0.04) quadrant average RNFL thicknesses and left eye inferior quadrant (p value 0.004) RNFL thickness in anemia group were significantly thinner than the control group. The average, superior, temporal, inferior quadrant RNFL thickness of both eyes in the severe anemia group were thinner than the mild and moderate anemia groups (P = <0.05). Nasal quadrant RNFL thickness in left eye was slightly lower in mild anemia group (P- 0.37).

3.5. CDR and fundus changes

The CDR was comparable between anemic group and control group (p >0.05). Among the anemic groups CDR was significantly high in the severe anemic group compared to moderate and mild anemia groups and fundus changes were seen only in the severe anemia group in our study.

Table 1: RE RNFL among the anemic and control groups

RE RNFL	Anemia group		Control group		p- value
	Mean	SD	Mean	SD	
Average RNFL	92.84	7.55	95.63	7.35	0.07
Superior RNFL	118.95	13.12	125.79	12.65	0.02
Temporal RNFL	65.9	7.1	66.65	5.79	0.67
Nasal RNFL	66.31	8.23	63.9	9.26	0.1
Inferior RNFL	120.18	14.03	125.65	14.06	0.04

Table 2: LE RNFL among the anemic and control groups

LE RNFL	Anemia group		Control group		p- value
	Mean	SD	Mean	SD	
Average RNFL	93.65	7.45	97.79	6.8	0.01
Superior RNFL	122.81	10.7	126.72	12.4	0.11
Temporal RNFL	65.43	9.3	69.2	5.51	0.05
Nasal RNFL	65.84	8.7	66.56	8	0.58
Inferior RNFL	120.22	12.92	128.25	11.5	0.004

Table 3: RE RNFL among the anemic groups

RE RNFL	Mild Anemia group		Moderateanemia group		Severe anemia group		p- value
	Mean	SD	Mean	SD	Mean	SD	
Average RNFL	92.57	6.6	94.45	7.09	84.83	6.55	0.03
Superior RNFL	117.1	10.83	121.2	13.2	109.3	11.7	0.11
Temporal RNFL	67.85	5.69	66.9	6.77	58.5	6.8	0.03
Nasal RNFL	67.85	10.36	66.61	8.1	63	6.03	0.51
Inferior RNFL	118.1	12.86	122.7	14.22	109.1	9.41	0.05

Table 4: LE RNFL among the anemic groups

RE RNFL	Mild Anemia group		Moderateanemia group		Severe anemia group		p- value
	Mean	SD	Mean	SD	Mean	SD	
Average RNFL	93	5.41	95.12	7.26	86.83	7.52	0.04
Superior RNFL	123.2	8.57	124.3	10.83	114.5	10.19	0.18
Temporal RNFL	69.71	8.42	66.03	8.77	57.33	9.52	0.07
Nasal RNFL	62.42	10.37	66.87	8.82	64.5	6.5	0.37
Inferior RNFL	116.7	14.13	123	12.12	109.8	10.87	0.05

Table 5: CDR among the study groups

CDR	RE		LE	
	Mean	SD	Mean	SD
Anemia group	0.43	0.11	0.43	0.1
Control group	0.38	0.09	0.39	0.08
P-value	0.06		0.07	

Table 6: CDR among the anemic groups

CDR	RE		LE	
	Mean	SD	Mean	SD
Mild Anemia group	0.39	0.13	0.38	0.11
Moderate anemia group	0.42	0.11	0.42	0.09
Severe anemia group	0.54	0.06	0.55	0.08
p- value	0.03		0.01	

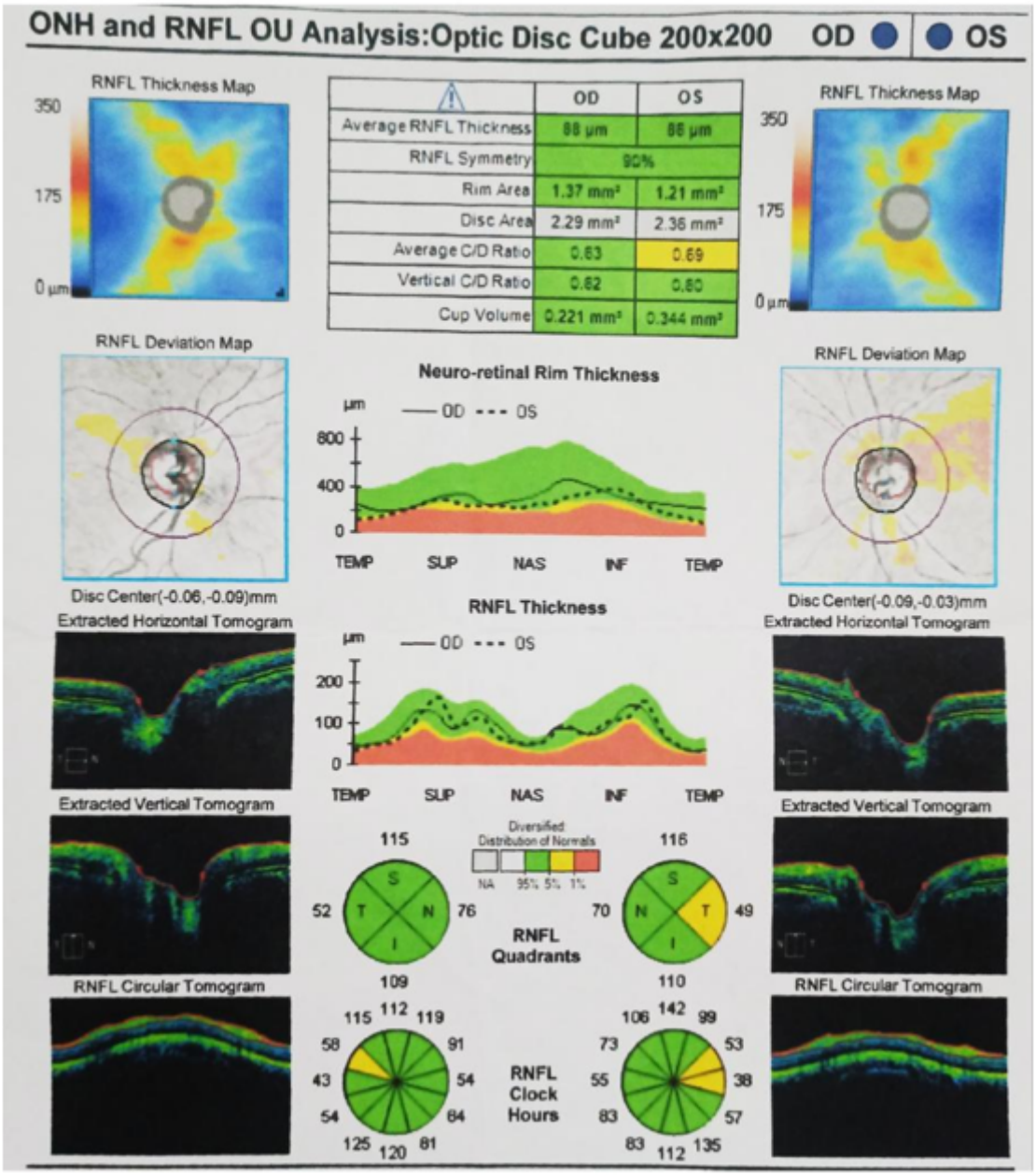


Figure 1: OCT-ONH of a study participant with moderate anemia group showing temporal thinning of RNFL in left eye and increased CDR in both eye

4. Discussion

4.1. Age, gender and distribution of symptoms

VE Raju et al conducted a study on Anemic people presenting with ocular manifestations. Their research shows that retinopathy is one of the most common signs of nutritional anemia. Hypoxia, venous stasis, angiospasm and increased capillary permeability all contribute to retinal injury. The severity of anemia increases the likelihood of developing retinopathy. The anemia severity depends on the extent of retinal hemorrhages. Early treatment of anemia and consequent cure of retinal hemorrhages are made possible by early detection of anemic retinopathy.[6–8]

4.2. RNFL distribution

Similarly in a study conducted by Ipek C and Seyda Ugurlu on peripapillary RNFL thickness in patients with iron deficiency anemia evaluated 102 anemic females with OCT and compared the results with 49 age and sex-matched non-

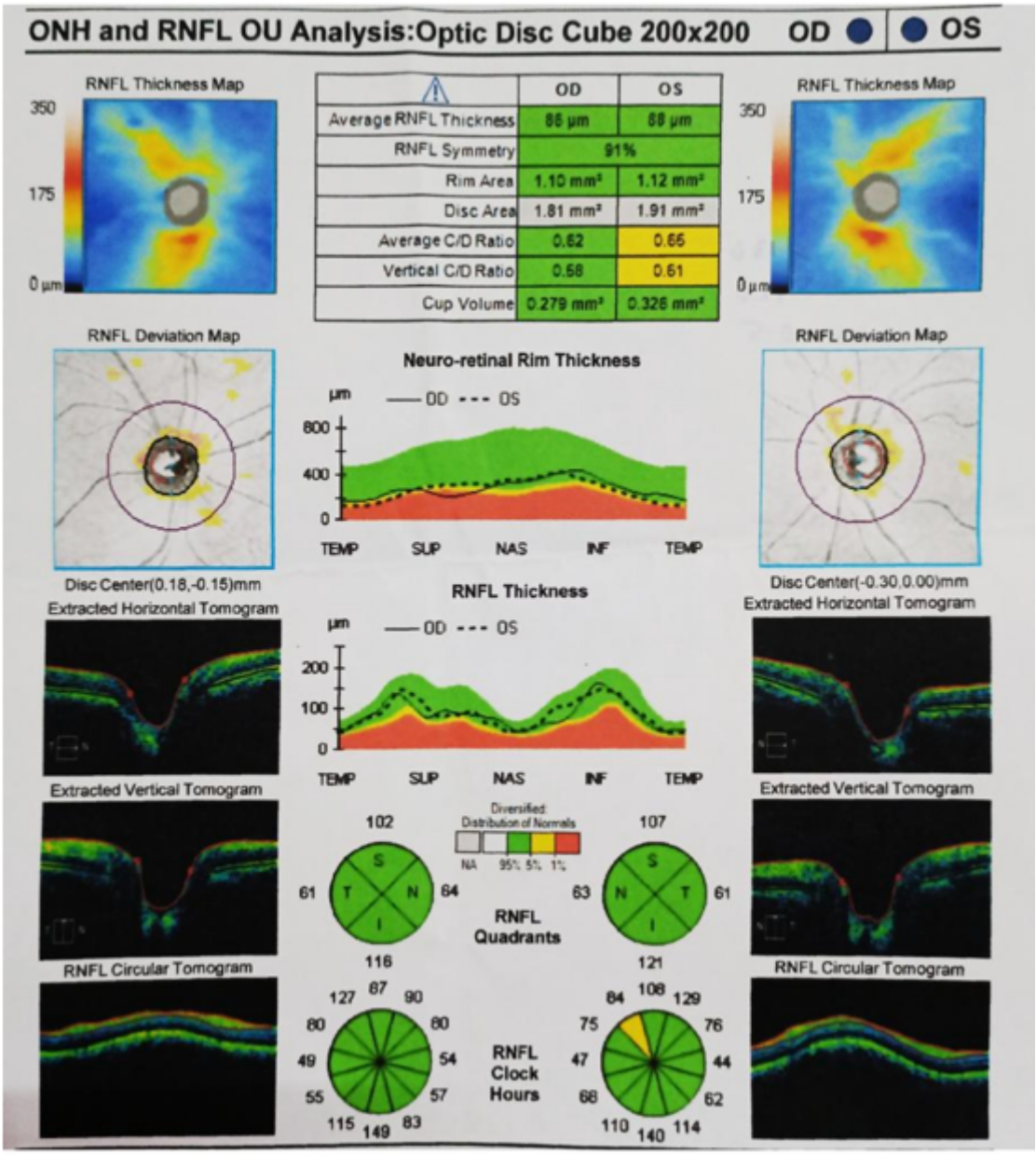


Figure 2: OCT-ONH of a study participant in mild anemic group showing increased CDR in left eye with normal RNFL thickness in both eyes

anemic individuals. According to the findings, individuals with anemia had thinner peripapillary RNFLs.[2]

Kemal et al. also found that average RNFL and RNFLs of the superior and inferior quadrants were significantly smaller in the anaemic group than in the control group.[3]

Mehmet Coskunl and Hurhayat's review of ocular results in women with iron and vitamin B12 deficiency anemia found that both patients with iron deficiency anemia alone and combined iron, vitamin B12 deficiency had reduced RNFL thickness compared to the normal control groups.[9]

In research by Nursen Oncel et al. found that peripapillary RNFL and ganglion cell inner plexiform layer in individuals with iron deficient anemia was thinner in the nasal inferior quadrant.[10]

Also in a study, children with IDA and thalassemia major in research by Aksoy A et al found considerable RNFL thinning in all 4 quadrants of patients with thalassemia major and thinning in the inferior quadrant of kids with iron deficient anemia.[11]

In research by Shreya Jateen et al. comparing the peripapillary RNFL thickness of iron deficiency anemia

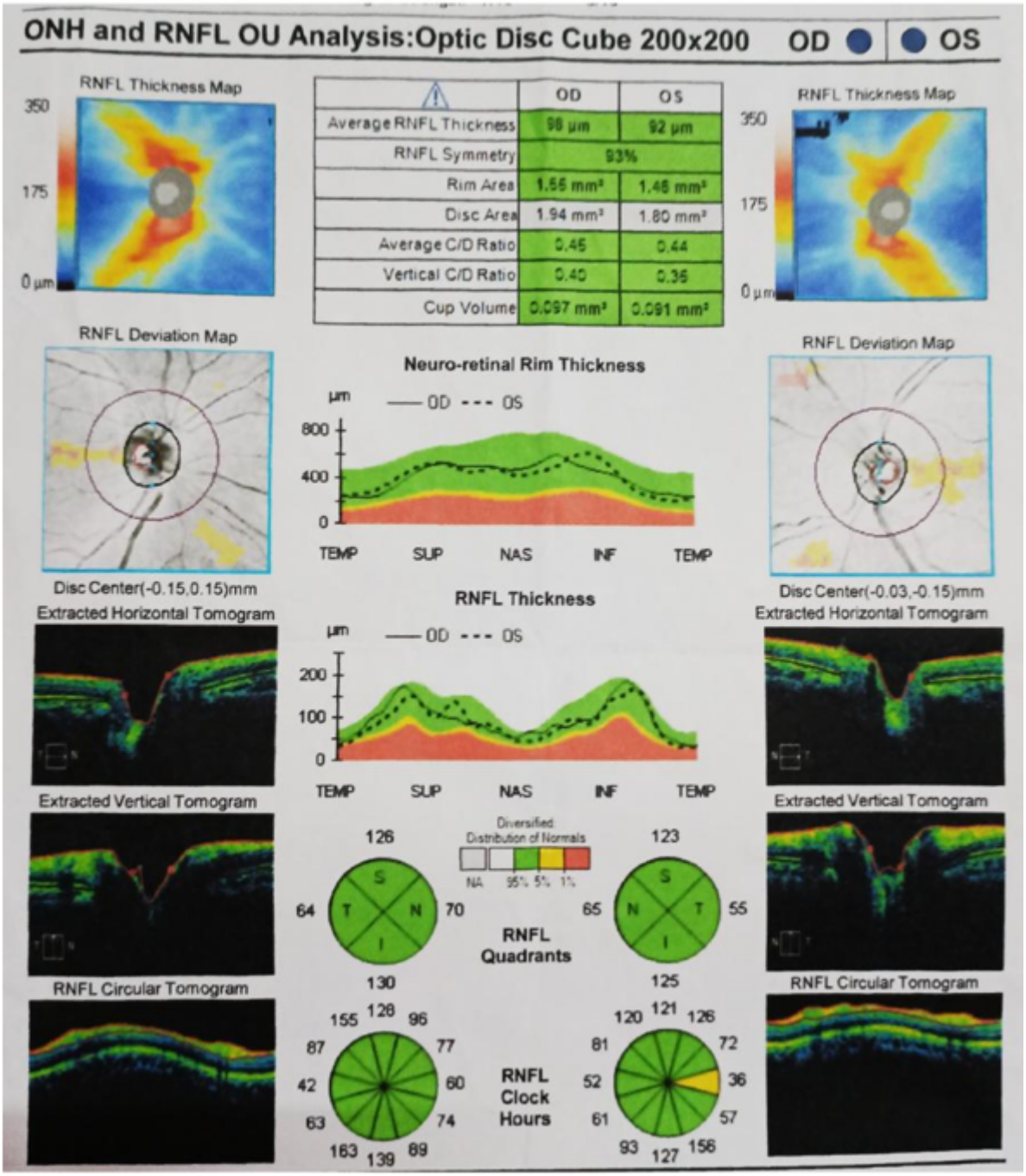
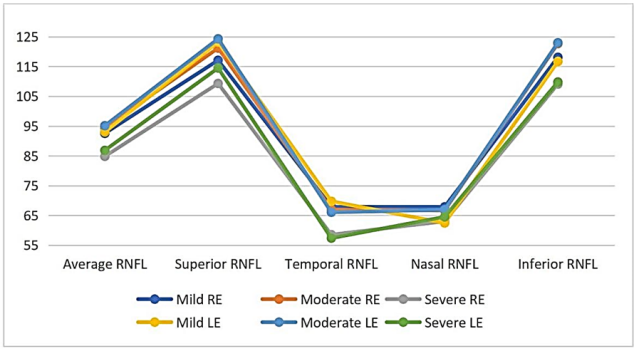
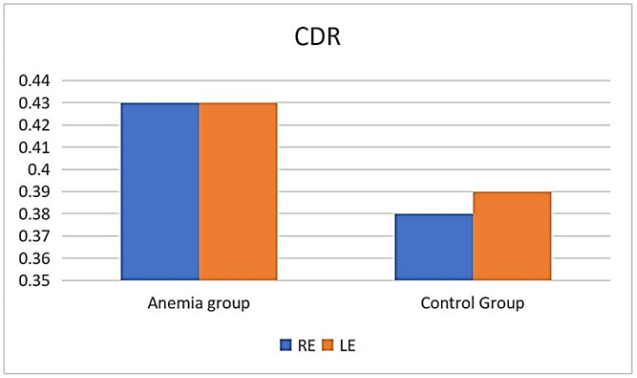


Figure 3: OCT-ONH of a study participant in non-anemic control group with normal CDR, RNFL values



Graph 1: RNFL variations in all 4 quadrants among anemic group



Graph 2: CDR among study groups

patients to normal controls, they discovered a statistically significant decrease in RNFL thickness in all 4 quadrants.[12]

According to research by Chow CC et al utilizing spectral domain OCT, individuals with non-glaucomatous sickle cell anemia who have focal macular thinning had considerably thinner peripapillary RNFL than those in the control group who don't have sickle cell hemoglobinopathies or macular thinning. The study included 151 eyes from 88 sickle cell patients and 55 eyes from 30 age- and race-matched controls.[13]

Our findings were consistent with all the similar studies performed before.

4.3. CDR changes

In a study by VE Raju et al suggested that a fundus examination should be performed on patients with moderate to severe anemia since this condition may be linked to anemic retinopathy.[6]

5. Conclusion

From our study we concluded that the retinal changes associated with anemia had a correlation with the severity of anemia. RFNL thickness significantly reduced and vertical CD ratio increased in severe anemia. Hence, anemia screening and correction along with frequent clinical and OCT evaluation in such patients can be useful in early detection and prevention of anemic retinopathy.

6. Limitations of the Study

The study was conducted in a small group of patients and was done at a single centre, both of which may limit the generalisability of the results. The exact duration of onset of anemia was also not taken into consideration as this was not practically possible to elicit in our scenario. Recent and long standing anemia would have had different outcomes, which could not be considered in our present study.

7. Source of Funding

None.

8. Conflicts of Interest

There are no conflicts of interest.

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