



Evaluation of Peripapillary RNFL (Retinal Nerve Fiber Layer) in Sickle cell disease at a Tertiary Care Centre

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Abstract

Aims: To evaluate peripapillary retinal nerve fiber layer thickness (RNFL) in patients with sickle cell disease by Optical Coherence Tomography (OCT) and to correlate any changes with macular thinning on OCT.

Method: The clinical, prospective study was carried out with 50 Sickle cell disease (SCD) patients & 50 control patients. For the study Glaucoma & other ocular diseases were excluded. Complete ophthalmic evaluation & OCT was performed. The patients were divided in 2 groups, focal macular thinning & no macular thinning made and Peripapillary RNFL thickness was measured.

Result: It was found that Sickle Cell patients with macular thinning had thinner mean peripapillary RNFL thickness in nasal sector compared with control eyes & in superotemporal sector compared with Sickle Cell patient eyes without macular thinning. In severe macular thinning, mean peripapillary RNFL thickness was significantly thinner than controls.

Conclusion: Sickle Cell patients without glaucoma & with focal macular thinning have thinner peripapillary RNFL than controls & those without macular thinning. Degree of RNFL thinning correlates with severity of temporal macular thinning. These patients may require different peripapillary RNFL thickness thresholds for future glaucoma evaluations.

Introduction

Anemia is a widespread public health problem, and iron deficiency is the commonest cause of anemia^[1]. Patients with sickle cell haemoglobinopathies inherit an abnormal globin protein chain that results in occlusions in various vascular systems. Vascular occlusions occur from sickling of the erythrocytes, increased viscosity, and venostasis, especially in the setting of hypoxia, acidosis, and inflammation.^[2] In the retina, common findings include salmon-patch hemorrhages, iridescent spots, and black sunbursts. Non-proliferative sickle retinopathy

with arteriolar occlusions and arteriovenous anastomoses can progress to proliferative sickle retinopathy with sea-fan neovascularization, vitreous hemorrhage, and retinal detachment.^[3]

Normal myelination requires iron and oligodendrocytes normally contain high concentrations of iron-containing enzymes^[4] Although sickle retinopathy occurs primarily in the retinal periphery, structural macular changes have been well documented by clinical examination^[5] fluoresceinangiography, histopathological analysis, and more recently, spectral-domain optical coherence tomography (SD OCT)^[6,7] It is

well known that retinal ischemia plays a significant role in development and progression of many ocular disorders as diabetic retinopathy, glaucoma, vascular occlusion, retinopathy of prematurity and sickle cell anemia.^[8] These changes include enlargement of the foveal avascular zone with perifoveal capillary dropout, nerve fiber layer infarcts, and vascular abnormalities including microaneurysm-like dots and hairpin-shaped venular loops.^[9] Optical Coherence Tomography (OCT) is a noninvasive technique that performs high resolution in vivo imaging of retinal, choroidal and optic nerve head structures. Peripheral changes secondary to proliferative sickle retinopathy were associated with thinning of macular inner retinal layers and thickening of central fovea. Ancillary OCT has demonstrated a recent finding associated with macular (paramacula) thinning. A study using Spectral-Domain Optical Coherence Tomography (SD-OCT) showed correlating macular thinning in about 50% of eyes with SCD^[10]. This may be a direct result of chronic ischemia affecting the retinal ganglion cells and retinal nerve fibers as they course temporally toward the optic nerve. In one study, results showed that sickle cell retinopathy eyes with macular thinning had thinner mean peripapillary RNFL in the nasal and superotemporal sectors than controls^[11].

Aims

- To evaluate peripapillary retinal nerve fiber layer thickness (RNFL) in patients with sickle cell disease by OCT.
- To correlate any changes with macular thinning on OCT.

Material and Methods

This was a clinical, prospective, diagnostic study conducted in Tertiary Eye care Centre. Study was performed over a period of 6 months. The protocol for present study as followed as per reported method.

Patient enrollment

Patients were diagnosed using electrophoresis confirmed Sickle cell hemoglobinopathy present at Sickle cell OPD in Government Medical College and Hospital were included for further study.

Exclusion criteria

The patients excluded were those with Glaucoma, Diabetes mellitus, Uncontrolled hypertension, maculopathies, previous Laser therapy and dense Cataract. Medical history, treatment history and type of SCD were recorded. Best Corrected Visual Acuity by Snellens chart, Applanation tonometry, slit lamp biomicroscopy, dilated fundus examination was done. All patients and controls underwent Spectral domain optical coherence tomography (SD OCT) of the Optic nerve head and macula. Patients with Sickle cell haemoglobinopathy (total-94) were divided in two groups: Group A-focal macular thinning (50), and Group B- no macular thinning (44). SCD with macular thinning was subdivided into

- Mild (mean value within 1 standard deviation of mean of control group),
- Moderate (between 1 to 2 Standard deviation less than mean of controls),
- Severe (more than 2 standard deviations less)

OCT for optic nerve head were taken in 6 regional fields

1. Nasal,
 2. Inferonasal,
 3. Superonasal,
 4. Temporal,
 5. Superotemporal,
 6. Inferotemporal
- along with global values.

Results

It was found that 94 eyes of 50 patients of SCD were included (n=94). The number of eyes of patients with SCD with macular thinning were 50 and those eyes without macular thinning were 44. 42 eyes of similar age of 25 control patients were selected for study. SCD with macular thinning of

50 eyes of 25 patients were divided into mild (n=7), moderate (n=9), severe (n=34). Patients with macular thinning had significantly thinner RNFL thickness in nasal sector compared with control (p=0.01). In Superotemporal sector RNFL thickness was significantly lower in macular thinning group compared with no thinning group. (p=0.01) In severe macular thinning group mean peripapillary RNFL thickness was significantly thinner than that of controls in 6 of 7 sectors.

Table 1: Data of macular thinning in optic nerve head

Sector	Controls (n=42)	No Macular thinning (n=44)	Macular thinning (n=50)
1) Nasal	80.5	73.2	72.7
2) Inferonasal	128.3	123.2	126
3) Inferotemporal	151.6	150.7	142.1
4) Temporal	71.9	75.3	70.4
5) Superotemporal	133.7	135.9	125.5
6) Superonasal	117.5	115.3	114.4
7) Global	104.6	102.8	99.4

Discussion

It was observed that in age matched groups thinning of peripapillary retinal nerve fiber layer in sickle cell hemoglobinopathy patients is statistically significant and p value is >0.05. This was much more evident in severe thinning group. Peripapillary RNFL thinning occurs in diabetic patients^[12] glaucoma, BRAO, CRAO^[13] also. Since, glaucoma and sickle cell disease are both prevalent in Central India, it would be worth to know that RNFL thinning in SCD can be due to systemic illness itself. At present, there is no data to show the prevalence of glaucoma in sickle cell patients. There is effect of vessel diameter on peripapillary RNFL thickness measurement. Based on a previous report by Hood and associates, the retinal vessels contribute approximately 13% of the peripapillary RNFL thicknesses^[14]. Zheng and associates also showed that retinal vessel caliber has a direct relationship with peripapillary RNFL thickness in a Malay population^[15] Sickle-cell disease patients are known to have more dilated vessels^[15,16] This may contribute to thicker peripapillary RNFL

measurements in sickle-cell disease patients. Besides increases in vessel diameter, sickle-cell disease patients also are known to have more vessel tortuosity.^[17,18] We suspect that tortuosity of vessels within the peripapillary RNFL can cause expansion of the peripapillary RNFL, especially if the vessels loop on themselves within the RNFL layer.

Histopathological studies of sickle-cell disease patients with vaso-occlusive diseases have shown atrophy and thinning of the inner retinal layers, including the ganglion cell and inner nuclear layer.^[6,7,19] Macular SD OCT images from our sickle-cell disease patients as well as a recent report also confirmed loss of the inner retinal layers in the temporal macula. Because the macular RNFL and ganglion cell layer contribute to the peripapillary RNFL, perhaps it is not surprising to see peripapillary RNFL thinning in sickle-cell disease patients with macular thinning.

In present study Sickle Cell patients with macular thinning had thinner mean peripapillary RNFL thickness in nasal sector compared with control eyes & in superotemporal sector compared with Sickle Cell patient eyes without macular thinning. In severe macular thinning, mean peripapillary RNFL thickness was significantly thinner than controls. Peripapillary RNFL thinning on SD OCT can be associated with macular thinning in Sickle cell disease patients due to their systemic disease in absence of glaucoma. The degree of peripapillary RNFL thinning correlated with the severity of macular thinning.

References

1. Fairbanks VF. Iron-deficiency anemia. In: Mazza JJ, editor. Manual of Clinical Hematology. Philadelphia, USA: Lippincott Williams & Wilkins; 2002. pp. 17–38.
2. Emerson, GG.; Harlan, JB.; Fekrat, S., *et al.* Hemoglobinopathies. In: Ryan, SJ., editor. Retina. 4th ed.. Elsevier; Philadelphia, PA: 2006. p. 1429-1445.
3. Goldberg MF. Classification and pathogenesis of proliferative sickle

- retinopathy. *Am J Ophthalmol.* 1971; 71(3):649–65. [PubMed: 5546311]
4. Connor JR, Menzies SL. Relationship of iron to oligodendrocytes and myelination. *Glia* 1996; 17:83-93.
 5. Goldbaum MH. Retinal depression sign indicating a small retinal infarct. *Am J Ophthalmol* 1978;86(1):45–55.
 6. Acacio I, Goldberg MF. Peripapillary and macular vessel occlusions in sickle cell anemia. *Am J Ophthalmol.* 1973; 75(5):861–866. [PubMed: 4706419]
 7. Romayanada N, Goldberg MF, Green WR. Histopathology of sickle cell retinopathy. *Trans Am Acad Ophthalmol Otolaryngol.* 1973; 77(5):OP642–76. [PubMed: 4784908]
 8. Chow CC, Shan RJ, Lim JI, *et al.* Peripapillary retinal nerve fiber layer thickness in sickle-cell hemoglobinopathies using spectral-domain optical coherence tomography. *Am J Ophthalmol* 2013; 155: 456- 464.e2?
 9. Asdourian GK, Nagpal KC, Busse B, *et al.* Macular and perimacular vascular remodelling sickling haemoglobinopathies. *Br J Ophthalmol.* 1976; 60(6):431–453. [PubMed: 952816] .
 10. Hoang QV, Chau FY, Shahidi M, Lim JI. Central macular splaying and outer retinal thinning in asymptomatic sickle cell patients by spectral-domain optical coherence tomography. *Am J Ophthalmol* 2011;151(6):990–994.
 11. Lonneville YH, Ozdek SC, Onol M, *et al.* The effect of blood glucose regulation on retinal nerve fiber layer thickness in diabetic patients. *Ophthalmologica* 2003;217 (5): 347–350.
 12. Lim MC, Tanimoto SA, Furlani BA, *et al.* Effect of diabetic retinopathy and panretinal photocoagulation on retinal nerve fiber layer and optic nerve appearance. *Arch Ophthalmol* 2009;127 (7): 857–862.
 13. Leung CK, Tham CC, Mohammed S, *et al.* In vivo measurements of macular and nerve fibre layer thickness in retinal arterial occlusion. *Eye (Lond)* 2007;21 (12):1464–1468.
 14. Hood DC, Salant JA, Arthur SN, *et al.* The location of the inferior and superior temporal blood vessels and interindividual variability of the retinal nerve fiber layer thickness. *J Glaucoma* 2010;19(3):158–166.
 15. Zheng Y, Cheung N, Aung T, *et al.* Relationship of retinal vascular caliber with retinal nerve fiber layer thickness: the Singapore Malay Eye Study. *Invest Ophthalmol Vis Sci* 2009; 50(9):4091–4096.
 16. Retinopathy in ophthalmologically asymptomatic patients with abnormal hemoglobins. *Ann Ophthalmol* 1979; 11(3):365–369.
 17. Welch RB, Goldberg MF. Sickle-cell hemoglobin and its relation to fundus abnormality. *Arch Ophthalmol* 1966;75(3): 353–362.
 18. Majekodunmi SA, Akinyanju OO. Ocular findings in homozygous sickle cell disease in Nigeria. *Can J Ophthalmol* 1978; 13(3):160–162.
 19. Knapp JW. Isolated macular infarction in sickle cell (SS) disease. *Am J Ophthalmol.* 1972; 73(6): 857–859. [PubMed: 5032692]