

Bilateral Retinal Artery Occlusion; A Retrospective Analysis of Clinical Presentation and Management

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Abstract

Purpose; Retinal artery occlusion (RAO) is an ophthalmologic emergency and involvement of both eyes is rare. The aim of this study was to determine the pattern of presentation of bilateral RAO in south India and the associated systemic disorders.

Methods; A retrospective review of the medical records of patients with bilateral RAO seen at a tertiary eye hospital in south India over a period of eight years was carried out. The patients' demographic and clinical data were extracted from the case files, and analysed using Epi Info statistical software.

Results; Six hundred and seventy-four eyes of 662 patients were seen with RAO during the period of the study with 12 (1.8%) patients having bilateral involvement. The mean age of the patients was 58.3 years and males comprised 66.7%. There were 22 (91.7%) eyes with CRAO, and two (8.4%) with branch RAO. Three (25%) patients had simultaneous RAO. The median interval for involvement of the fellow eye was 90 days. Hypertension and diabetes were the most common associated systemic disorders.

Conclusion; Bilateral RAO is very rare and usually nonsimultaneous. Patients need to be aware of the possibility of involvement of the fellow eye after a unilateral RAO, and the importance of seeking medical care promptly if this occurs.

Introduction

Retinal artery occlusion (RAO) is one of the leading causes of profound and permanent visual impairment [1]. It is an important emergent ocular problem due to the acute severe loss of vision, and the increased risk of further vascular events such as stroke, and acute coronary syndrome [2,3]. Retinal arterial occlusions are divided into central and branch groups depending on the precise site of occlusion [4]. Each group comprises of multiple distinct entities differing in aetiology, pathogenesis, clinical features, and management [5]. Central retinal artery occlusion (CRAO) consists of four categories; non-arteritic (NA) CRAO, transient NA-CRAO, NA-CRAO with cilioretinal artery sparing, and arteritic CRAO with giant cell arteritis [6]. Branch retinal artery occlusion (BRAO) consists of BRAO and cilioretinal artery occlusion (CLRAO) with the latter comprising of NA-CLRAO alone, arteritic CLRAO associated with giant cell arteritis, and CLRAO associated with central retinal vein occlusion[7].

Retinal artery occlusions are rare events with CRAO occurring more frequently than BRAO [4]. Recent estimates put the incidence of RAO at 0.85 per 100,000 per year [8]. Mean age at presentation is early in the seventh decade of life, and men have a slightly higher incidence than women [8]. Retinal artery occlusion most often affects one eye with bilateral involvement occurring in 1-2% of cases [9]. Previous reports on bilateral RAO in India have primarily been case reports [10-14]. An earlier hospital-based retrospective study on RAO also in India reported bilateral involvement in 3 patients which constituted 10% of the study population [15]. This study was, however, carried out in young adults less than 40 years of age. The purpose of this study, therefore, was to determine the pattern of presentation and management of bilateral RAO in south India and the associated systemic risk factors.

Methods

A retrospective record analysis of patients with bilateral RAO presenting at a tertiary eye hospital in Tamil Nadu, south India between January 2012 and December 2019 was carried out. Follow-up cases of bilateral RAO seen during this period but diagnosed before January 2012 were excluded from the study. The cases were identified from the electronic medical records. The casefiles were then retrieved and the demographic characteristics of the patients, as well as the clinical findings extracted. Information retrieved on clinical findings included; duration of visual loss, history of cigarette smoking and alcohol consumption, associated ophthalmic and systemic diseases, best corrected visual acuity (BCVA) at presentation and at the last follow-up visit, and diagnosis. All the patients underwent a comprehensive ophthalmic history and examination. Results of optical coherence tomography scans and fundus fluorescein angiograms were reviewed were available. Investigations were done according to associated history and clinical findings. These included carotid Doppler, echocardiography, computer tomography (CT)/magnetic resonance imaging (MRI) scan of the brain, haemogram with erythrocyte sedimentation rate (ESR), C reactive protein, lipid profile, renal function tests, vasculitis screening profile, homocysteine levels, and coagulation profile. Treatment given in each case was also recorded.

The study adhered to the tenets of the declaration of Helsinki, and was approved by the Institutional Review Board of the hospital. Data analysis was done using Epi Info statistical software version 7.2.3.0 developed by the Centre for Disease Control, Georgia, USA. Frequencies and percentages were computed for qualitative variables while mean and standard deviation was computed for quantitative variables.

Results

Six hundred and seventy-four eyes of 662 patients were seen with RAO during the period under review. There were 12 (1.8%) patients with bilateral involvement comprising eight (66.7%) males, and four (33.3%) females (Table 1). The mean age of the patients was 58.3 years (range; 31-73years, SD; 12.7), and the age range 60-69 years had the highest proportion of patients (Figure 1).

There were 22 (91.7%) eyes with CRAO, and one (4.2%) eye each with CLRAO alone (Figure 2) and BRAO. One eye with CRAO had cilioretinal artery sparing. The majority of eyes (20 eyes) had acute events with patients presenting within 8hours to 30 days of onset of visual loss (mean 6.9 days, SD 4.9). The remaining four eyes of four patients were old CRAOs which had occurred at two, six, 24 and 36 months respectively before presentation. Only two patients (two eyes, 8.3%) were seen within 24 hours of loss of vision and three (25%) patients complained of noticing visual loss in both eyes at the same time. In the remaining nine (75%) patients the interval between the first CRAO and involvement of the second eye was from three days to 1095 days (median 90 days, SD 410.4). The majority of arterial occlusions were non-arteritic with only two eyes (8.3%) of one patients with arteritic CRAO.

Associated orbital/ocular disorders were present in both eyes of three patients (Table 1) while systemic disorders were present in 10 (83.3%) patients (Figure 3). The most common disease was hypertension

(58.3%), and eight (66.7%) patients had at least two systemic disorders. There was a 57 year old man with subacute pancreatitis who had a history of heavy alcohol consumption and no other systemic disorder. Two (16.7%) patients with diabetes and hypertension had a history of stroke. In the first patient this occurred two years after the first episode of arterial occlusion, and five days before involvement of the fellow eye. In the second patient stroke occurred three years before the first episode of RAO. Three (60%) out of five patients with documented brain MRI or CT scan reports had areas of infarction in the brain. Cardiac abnormalities were present in four (50%) of eight patients that had echocardiography, and these included calcified posterior mitral leaflet and left ventricular hypertrophy, dilated left atrium with sclerosed aortic valve, calcified mitral valve, and left ventricular hypertrophy with aortic regurgitation. Carotid Doppler reports was available for eight patients and revealed calcifications in the right carotid bulb in two (25%) of these patients.

Twenty (83.3%) eyes were blind (BCVA < 20/400) at presentation and at the last clinic visit. The BCVA in eyes with CRAO is illustrated in figure 4. The two eyes with BRAO had a BCVA of 20/40 and above at presentation as well as at the last clinic visit (Table 1).

Treatment was given in six (30%) of the 20 eyes with acute CRAO, and included ocular massage with anterior chamber paracentesis in two eyes, ocular massage alone in three eyes, and ocular massage followed by pars plana vitrectomy in one eye. These patients presented within 10 days of loss of vision in the affected eyes. Improvement in BCVA was, however, documented in only two (33.3%) of these eyes (same patient) following ocular massage from hand movement and light perception in the right eye and left eye respectively to 20/600. The patient presented within 24 hours of the first RAO, and 48 hours of involvement of the second, in the left eye which occurred a year later. One patient had arteritic CRAO. He was a 70-year old man with presumed giant cell arteritis and was treated with intravenous methylprednisolone one gram daily for 3 days after developing CRAO in the right eye. He, however, still developed CRAO in the left eye 5 days later. His ESR and C reactive protein were both elevated. He was referred for temporal artery biopsy but defaulted. His final BCVA was no light perception in both eyes.

There were three (12.5%) eyes with iris neovascularization and one (4.2%) eye with neovascular glaucoma. Neovascularization developed within 10 days, 29 days and two years respectively of loss of vision in the involved eyes. Two eyes had panretinal laser photocoagulation with regression of new vessels in both cases.

Discussion

Bilateral RAO is extremely rare and constitutes less than 2% of cases of RAO [9]. In this current study bilateral RAO accounted for 1.8% of cases of RAO seen in our centre. Similarly, Schmidt *et al.* reported a prevalence less than 2% (0.5%) in a retrospective study of patients with non-inflammatory RAO in Germany [16]. Hayreh *et al.* on the contrary reported a much higher incidence of 13.7% in a prospective study on RAO in Iowa, USA over a period of 27 years [5]. The majority of patients in this study were males, which is consistent with findings from earlier studies on RAO [5,15-17]. The mean age in our cohort of

patients (58.3 years), however, contrasts with higher mean ages of 66 years and 74 years reported in patients with RAO in Germany [16] and America [17] respectively. These findings, though suggestive of RAO occurring at an earlier age in Indian patients, needs to be interpreted with caution considering the small number of cases in this study. A review of all cases of RAO seen in our centre will determine if this is the case. Most cases of RAO in this study were nonsimultaneous, and the median interval for involvement of the fellow eye was 90 days. Even though bilateral RAO is extremely rare, patients need to be aware of not only the risk of subsequent cerebral stroke and ischemic heart disease, but also of the fellow eye suffering a similar event.

Systemic cardiovascular diseases have a well-known association with RAO [5]. Arterial hypertension, diabetes mellitus, hyperlipidaemia, carotid artery disease, coronary artery disease, transient ischaemic attack, cerebrovascular accident, and tobacco smoking have been described as significantly more common among these patients than in the general population [5,18]. Most of the patients in this current study had more than one risk factor with hypertension being the most common. This is consistent with the findings by Schmidt *et al* [16]. Twenty percent of patients in this study had a history of stroke while an additional 60% of brain MRI/CT scans revealed areas of infarction in the brain. In a case-control study on the correlation of the history of stroke and RAO by Xiao *et al*, 40% of patients with RAO had a stroke prior to developing the arterial occlusion while another 22% had areas of infarction in the brain on cranial MRI/CT scan [19]. Abnormal findings were noted on echocardiography and carotid Doppler in 50% and 25% respectively of patients that had these procedures in this study. In contrast, Xiao *et al* found more patients with abnormalities on carotid ultrasound, 89% as against 32% with abnormalities on echocardiography [19]. Acute pancreatitis which was seen in one patient in this study has been associated with bilateral RAO [20]. It is postulated that arterial occlusion occurs as a result of complement activation with subsequent leukoembolization [20]. Aggressive management of modifiable risk factors is essential in preventing a repeat arterial occlusion in the fellow eye following a unilateral RAO as well as other life threatening vascular events.

Visual outcome was poor in the majority of eyes in this study which is in agreement with previous studies. Several factors play a crucial role in determining the visual outcome of CRAO, and these include duration of retinal ischaemia, type of CRAO, cause of CRAO, site of occlusion in the central retinal artery, residual retinal circulation, and presence and area of supply by a patent cilioretinal artery [21]. The duration of RAO is, however, almost always the principal determining factor in the production of irreversible retinal damage, that is, the longer the ischemia, the more marked the retinal damage, and the worse the visual outcome [21]. The majority of patients in this study presented after 24 hours of loss of vision with a mean duration 6.9 days in eyes with acute RAO. This is higher than 3.4 days reported by Xiao *et al* [19]. Retinal artery occlusion is an ocular emergency, and any intervention is best done within four to 6.5 hours which is the retinal ischaemia tolerance time, before irreversible damage occurs [22,23]. A recent review by Tobalem *et al.*, however, suggests that this critical time limit for inner retinal non-perfusion has been greatly overestimated, and that irreversible retinal ganglion cell death occurs after 12-15 minutes of complete CRAO in humans [24]. Patients with unilateral RAO, therefore, should be made to

understand the importance of prompt presentation to the hospital if loss of vision occurs in the fellow eye.

Ocular neovascularization (ONV) is an important complication of CRAO and is a less-frequent complication of BRAO. Patients with ocular ischaemic syndrome, and type 2 diabetes are particularly at risk of developing this complication following occlusion of the central retinal artery [21,25]. About 13% of eyes had ONV in this current study which compares favourably with 14.5% reported by Mason *et al* [25]. However, neovascular glaucoma was reported in only one (4%) of these eyes in this current series in contrast to 83% reported by Mason *et al* [25].

Our study had a few limitations including its retrospective nature, and incomplete data in some case files. The sample size was small but this is not unconnected with the rarity of the condition. It was also difficult to determine if the simultaneous cases were truly simultaneous as these patients were seen within seven days to a month of development of visual loss.

In conclusion, bilateral RAO is very rare and usually nonsimultaneous with a median interval of 90 days for involvement of the fellow eye. The majority of patients presented outside of the window period for any meaningful intervention even when the fellow eye developed the same symptoms. Patients with previous unilateral RAO, therefore, need to be educated not only about the potentially fatal complications that could be associated with the condition, but also the possibility of the fellow eye suffering a similar event, and the importance of prompt presentation to the hospital if this occurs. This along with management of associated risk factors may go a long way in preventing catastrophic visual loss in probably the only seeing eye.

Declarations

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Code availability; Not applicable

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Consent to participate; Not applicable

Consent for publication; Not applicable

References

1. Chang YS, Ho CH, Chu CC, Wang JJ, Tseng SH, Jan R (2018) Risk of retinal artery occlusion in patients with diabetes mellitus: a retrospective large-scale cohort study. *PLoS One* 13(8): e0201627. doi.org/10.1371/journal.pone.0201627.
2. Chang YS, Jan RL, Weng SF, et al (2012) Retinal artery occlusion and the 3-year risk of stroke in Taiwan: a nationwide population-based study. *Am J Ophthalmol* 154(4):645-652.
3. Chang YS, Chu CC, Weng SF, Chang C, Wang JJ, Jan RL (2015) The risk of acute coronary syndrome after retinal artery occlusion: a population-based cohort study. *Br J Ophthalmol* 99(2):227-231.
4. Caglar C, Caglar Z, Gul A (2013) The central retinal artery occlusion in the right eye followed by a branch retinal artery occlusion in the left eye four days later. *Indian J Ophthalmol* 61(11):667-669.
5. Hayreh SS, Podhajsky PA, Zimmerman MB (2009) Retinal artery occlusion: associated systemic and ophthalmic abnormalities. *Ophthalmology* 116(10):1928-1936.
6. Hayreh SS, Zimmerman MB (2005) Central retinal artery occlusion: visual outcome. *Am J Ophthalmol* 140(3):376–391.
7. Hayreh SS, Podhajsky PA, Zimmerman MB (2009) Branch retinal artery occlusion: natural history of visual outcome. *Ophthalmology* 116(6):1188-1194.
8. Feldman B, Juang PSC. Retinal artery occlusion (RAO). Available at <https://emedicine.medscape.com/article/799119>. Accessed 8th August, 2020.
9. Joanna S, Joanna S, Maria B, Paweł R, Bartosz S (2018) Through the eyes to the heart - bilateral non-simultaneous retinal artery occlusion in 33-year-old female probably associated with a paradoxical embolism. *Biomed J Sci &Tech Res* 6(3);5298-5303.
10. Bansal R, Jain S, Gupta V, Sharma A, Bal A, Jain S (2018) Bilateral central retinal artery occlusion as presenting manifestation of human immunodeficiency virus infection. *Indian J Ophthalmol* 66(3):466-468.
11. Sinha S, Rau AT, Kumar RV, Jayadev C, Vinekar A (2018) Bilateral combined central retinal artery and vein occlusion in a 3-year-old child with nephrotic syndrome. *Indian J Ophthalmol* 66(10):1498-1501.
12. Shilpa Y D, Kalpana B N, Devaru S (2018) Bilateral central retinal artery occlusion in a case of eclampsia. *Egypt Retina J* 5(2):50-52.
13. Ghose S, Subhabrata P (2011) Bilateral central retinal arterial obstruction following head trauma: a very rare case report. *Indian J Ophthalmol* 59(1):66-68.
14. Pauranik A, Parwani S, Jain S (1987) Simultaneous bilateral central retinal arterial occlusion in a patient with Sneddon syndrome: case history. *Angiology* 38(2 Pt 1):158-163.
15. Ratra D, Dhupper M (2012) Retinal arterial occlusions in the young: systemic associations in Indian population. *Indian J Ophthalmol* 60(2):95-100.
16. Schmidt D, Hetzel A, Geibel-Zehender A, Schulte-Mönting J (2007) Systemic diseases in non-inflammatory branch and central retinal artery occlusion: An overview of 416 patients. *Eur J Med Res* 12(12):595-603.

17. Leavitt JA, Larson TA, Hodge DO, Gullerud RE (2011) The incidence of central retinal artery occlusion in Olmsted County, Minnesota. *Am J Ophthalmol* 152(5):820-823.
18. Klein R, Klein BE, Moss SE, Meuer SM (2003) Retinal emboli and cardiovascular disease: the Beaver Dam Eye Study. *Arch Ophthalmol* 121(10):1446-1451.
19. Xiao YY, Wei WB, Wang YX, et al (2020) Correlation of the history of stroke and the retinal artery occlusion: a nested case-control study. *Int J Ophthalmol* 13(3):431-437.
20. Timoney PJ, Pate JC, Pearson PA, Crandall J (2009) Bilateral central retinal artery occlusion in a patient with acute pancreatitis. *Retin Cases Brief Rep* 3(3):308-309.
21. Hayreh SS. Central retinal artery occlusion (2018) *Indian J Ophthalmol* 66(12):1684-1694.
22. Hayreh SS, Zimmerman MB, Kimura A, Sanon A (2004) Central retinal artery occlusion. Retinal survival time. *Exp Eye Res* 78(3):723-736.
23. Chen CS, Lee AW, Campbell B, *et al* (2011) Efficacy of intravenous tissue-type plasminogen activator in central retinal artery occlusion: Report from a randomized, controlled trial. *Stroke* 42(8):2229-2234.
24. Tobalem S, Schutz JS, Chronopoulos A (2018) Central retinal artery occlusion – rethinking retinal survival time. *BMC Ophthalmol* 18:101. doi.org/10.1186/s12886-018-0768-4.
25. Mason JO 3rd, Patel S, Feist R, *et al* (2015) Ocular neovascularization in eyes with a central retinal artery occlusion or a branch retinal artery occlusion. *Clin Ophthalmol* 9:995-1000.

Tables

Table 1; Demographic profile and systemic abnormalities in patients with bilateral RAO

S/n	Age (years)	Sex	BCVA at last visit		Type of RAO		Ocular Associations	Systemic Associations
			Right eye	Left eye	Right eye	Left eye		
1.	66	F	PL	NPL	CRAO	CRAO	Bilateral optic disc drusen	Diabetes, hypertension
2.	31	M	1/60	PL	CRAO	CRAO	Bilateral rhino-orbital mucormycosis	Diabetes, chronic kidney disease, chronic smoker
3.	49	F	6/60	6/36	CRAO	CRAO		Hypertension, chronic renal failure
4.	70	M	NPL	NPL	CRAO	CRAO		Ischaemic heart disease
5.	64	M	HM	NPL	CRAO	CRAO		Diabetes, hypertension, stroke
6.	63	M	1/60	6/12	CRAO	BRAO	POAG	Diabetes, hypertension, stroke
7.	57	M	2/60	2/60	CRAO	CRAO		Subacute pancreatitis, alcoholic
8.	42	F	6/9	HM	CLRAO	CRAO		Hypertension, ischaemic heart disease, seizure disorder
9.	70	M	HM	HM	CRAO	CRAO		Hypertension, ischaemic heart disease, chronic smoker
10.	52	F	HM	HM	CRAO	CRAO		Hypertension, diabetes
11.	63	M	PL	HM	CRAO	CRAO		
12.	73	M	NPL	PL	CRAO	CRAO		

HM; hand movement, PL; perception of light, NPL; no perception of light, PAOG; primary open-angle glaucoma

Figures

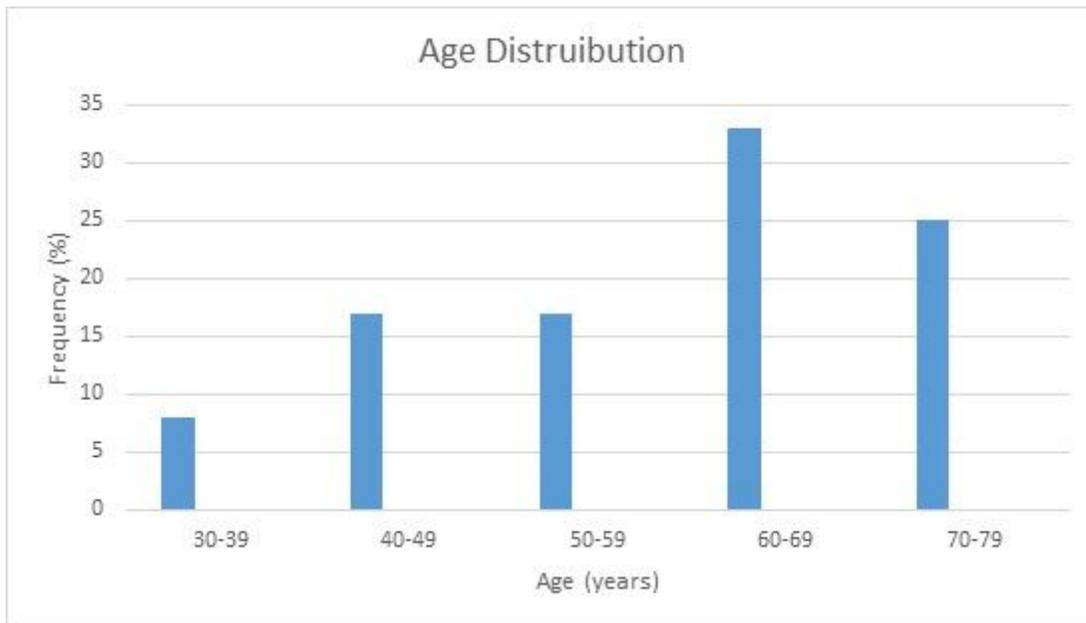


Figure 1

Age distribution of patients

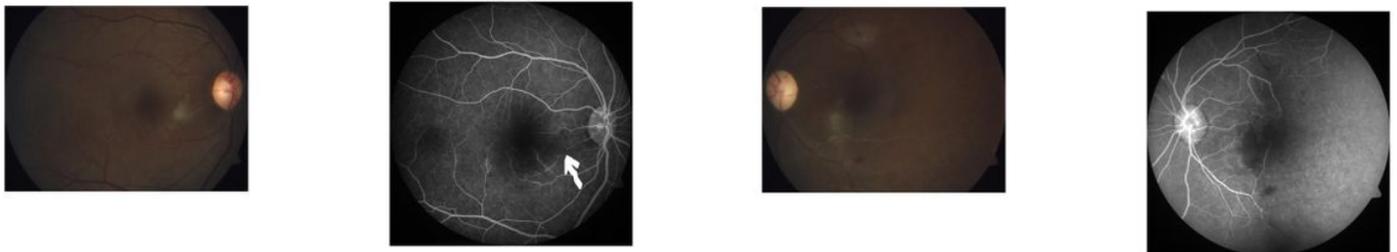
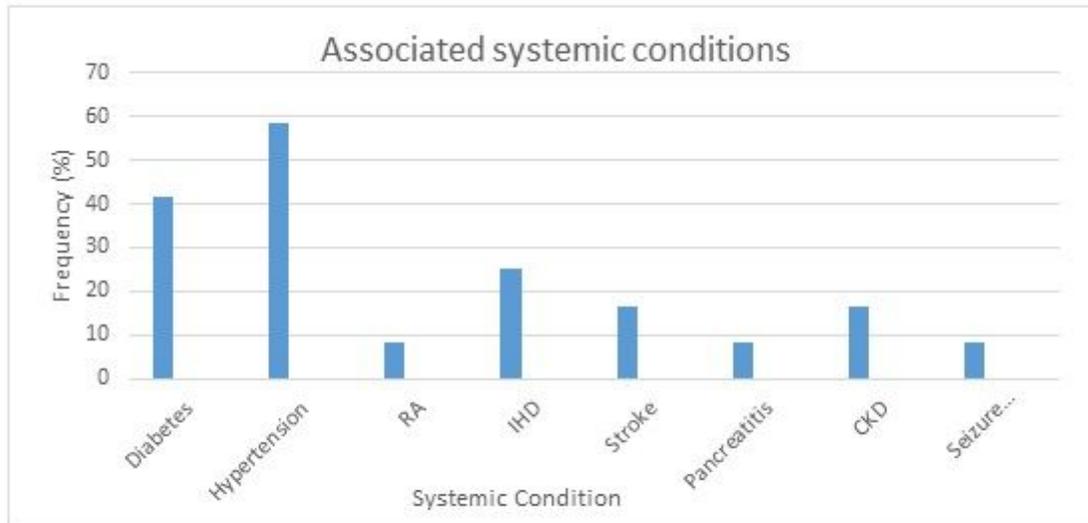


Figure 2

a; Fundus photograph showing right cilioretinal artery occlusion b; Fundus fluorescein angiography (FFA) showing occluded cilioretinal artery c; Fundus photograph showing central retinal artery occlusion (CRAO) in left eye of same patient d; FFA of left eye showing CRAO



CKD; chronic kidney disease, IHD; ischaemic heart disease, RA; rheumatoid arthritis

Figure 3

Associated systemic conditions

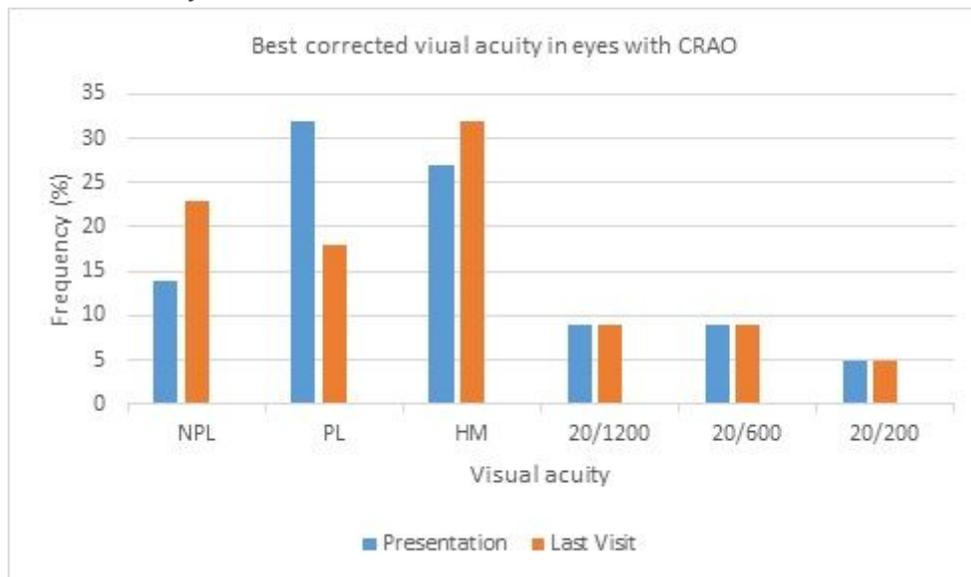


Figure 4

Best corrected visual acuity in eyes with CRAO

Supplementary Files

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- [BILATERALRAO.xlsx](#)