

A 10-Year Study of Central Serous Chorioretinopathy: Recurrence Rate and Factors affecting Recurrence

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ABSTRACT

Purpose: To determine the recurrence rate of central serous chorioretinopathy and risk factors responsible for recurrence.

Methods: The study was designed as a hospital-based retrospective study. Medical records of all patients with CSCR, seen at the retina clinic from January 1999 to December 2008, were retrospectively analyzed. Univariate and multivariate analysis were done using statistical package for social sciences (SPSS).

Results: The recurrence rate of CSCR in 752 patients was 19.41%. The mean attack rate was 1.29. Using the Wilcoxon signed ranks test, it was found that in patients with and without recurrence, there was a significant improvement in visual acuity after treatment. Univariate analysis done, to study the association between risk factors and recurrence of CSCR, showed that patients aged less than 40 and the male sex were significantly associated with recurrence of CSCR. Multivariate logistic regression analysis showed the same two factors to be significantly associated with recurrence of CSCR. 8.37% patients had bilateral CSCR.

Conclusion: The recurrence rate of CSCR in 752 patients, with an average follow-up of 12.11 months was 19.41%. Patients aged less than 40 years had a 1.59 times increased risk of recurrence. Patients of the male sex had a 1.96 times increased risk of recurrence.

Keywords: Central serous chorioretinopathy, Recurrence rate, Risk factors.

INTRODUCTION

Central serous chorioretinopathy (CSCR) is a retinal disorder characterized by an idiopathic, serous, neural, retinal detachment in the macular region. The disease was first recognized by Albrecht von Graefe in 1866 and was termed central recurrent retinitis.¹ The condition was named idiopathic central serous chorioretinopathy by Gass JDM et al in 1967.²

Typically, CSCR affects men aged 20 to 50 years. The disease is seen predominantly in males as compared with females in a ratio of 10:1. This disease is associated with psychological factors; it is found in males with type-A personality, accompanies unusual emotional stress and is occasionally seen with migraine-type headaches. It has been associated with pregnancy, allergic respiratory disease, use of systemic steroids, antibiotics, antihistamines, tobacco and alcohol.

The aim of this study was to determine the recurrence rate of CSCR and risk factors responsible for recurrence of CSCR. Most of the studies done on CSCR have evaluated risk factors for the incidence of CSCR. To our knowledge, there has been no study on the risk factors affecting recurrence of CSCR.

METHODS

The study was designed as a hospital-based retrospective study. All consecutive patients with CSCR during the period January 1999 and December 2008 were included in the study. Patients with less than 1 month follow-up and chronic steroid users were excluded from the study. The diagnosis of CSCR was made clinically using the binocular indirect ophthalmoscope and by biomicroscopic examination of the retina using 78 Diopter lens. Localized neurosensory retinal detachment with no other surrounding abnormalities was diagnosed as CSCR. The medical records of patients with CSCR were retrospectively analyzed. The following data was recorded and analyzed—age, sex, associated systemic diseases, history of medication used, history of CSCR, best corrected visual acuity (BCVA) at each visit, findings of fundus examination at each visit, fundus fluorescein angiography findings including number, location and type of leaks, optical coherence tomography (OCT) findings, including location of serous macular detachment and number of pigment epithelial detachments (PED), form of treatment given (conservative or laser photocoagulation of the

leak), total number of attacks and length of follow-up. Location of the retinal pigment epithelium (RPE) leak was categorized in relation to fovea.

Statistical analysis was performed using SPSS V11. Chi-square test was applied for univariate analysis. Multivariate logistic regression analysis was done for variables with p-value <0.2 in the univariate analysis. Wilcoxon signed ranks test was used to test the statistical significance of change in visual acuity after treatment.

Recurrence was considered as more than one attack of CSCR. Resolution of CSCR was confirmed on the basis of improvement of visual acuity along with resolution of serous macular detachment, based on biomicroscopic and binocular indirect ophthalmoscopic examination of the macula. If after complete resolution of CSCR in terms of signs and symptoms, the patient developed another attack of CSCR (symptomatically and on clinical examination), it was considered as a recurrence. OCT and angiographic confirmation was not always performed.

RESULTS

A total of 815 eyes of 752 patients (413 right eyes and 402 left eyes) were included in this study. There were 652 male patients (86.70%) and 100 female patients (13.29%). The mean age of the patients was 42.16 years (range: 20 to 69 years, median 42 years, SD 8.015). Sixty-three patients (8.37%) had bilateral CSCR (Table 1).

The average follow-up period was 12.11 months (range: 1-132 months, median: 5 months, SD 22.97).

One hundred twenty-one patients (16.09%) had hypertension. However, only 70 patients (9.3%) were on antihypertensive medication. Eighty-three patients (11.3%) had diabetes mellitus. Nineteen patients (0.3%) were on systemic steroids. Three patients had been prescribed steroid drops and three patients were on steroid ointments. Six patients, who had recurrent CSCR, were on systemic steroids as treatment for CSCR by the treating doctors, prior to being referred to our hospital, after which the steroids were discontinued.

The recurrence rate of CSCR in 752 patients with an average follow-up of 12.11 months was 19.41%. Six hundred and fifty-seven eyes (80.50%) had only one attack of CSCR. One hundred and fifty-eight eyes (19.41%) of one hundred and fifty-six patients had more than one attack of CSCR (Table 2). The recurrence rate of CSCR was 13.37% (n = 107) in patients with 6 months and more of follow-up; 11.7% (n = 95) in patients with >1 year follow-up and 3.1% (n = 26) in patients with >5 years follow-up (Table 3).

Table 1: Demographic features of study patients

No. of patients	752
No. of males	652 (86.70%)
No. of females	100 (13.29%)
Mean age (SD)	42.16 years (8.015)
Median age	42 years
Range of age	20 to 69 years

SD: Standard deviation

Eight hundred and fifteen eyes had 1,056 attacks. The mean number of episodes was 2.5 in patients with recurrence.

Considering all the patients (815 eyes), the mean pretreatment visual acuity (VA) was 0.33 logMar units (SD 0.37) and the mean posttreatment VA was 0.15 logMar units (SD 0.27) (Table 4)—a statistically significant improvement (p < 0.001). The results were similar, both in patients with recurrence and without recurrence.

Two hundred and thirty-four OCTs were performed. Two hundred and one eyes (85.89%) showed subfoveal serous macular detachment (SMD) and 33 eyes (14.10%) showed extrafoveal SMD (Figs 1A and B).

Seven hundred and twenty digital fundus fluorescein angiograms (DFA) were performed. Six hundred fifty-five eyes had a RPE leak. The leak was of the inkblot type in 95.94% (Figs 2A to D); and smokestack pattern in 4.05% (Figs 3A to D). Five hundred and nineteen eyes (72.08%) had only 1 leak, while ninety four eyes (13.05%) had two leaks.

Table 2: Recurrence rate of CSCR

No. of attacks	No. of eyes	Percentage
1	657	80.50
2	105	12.9
3	34	4.1
4	12	1.4
5	4	0.4
6	2	0.2
9	1	0.1

Table 3: Recurrence rate of CSCR in patients with 1 to 10 years follow-up

Follow-up in years	No. of patients	No. of eyes	Recurrence rate (%)
1	95	96	11.77
2	73	74	9.07
3	56	57	6.99
4	42	42	5.15
5	26	26	3.1
6	17	17	2.08
7	9	9	1.1
8	8	8	0.98
9	6	6	0.73
10	3	3	0.36

Table 4: Wilcoxon signed ranks test: Change in visual acuity after treatment

Patients (no. of eyes)	Mean pretreatment VA logMar (SD)	Mean posttreatment VA logMar (SD)	p-value
All patients (815 eyes)	0.33 (0.37)	0.15 (0.27)	<0.001
With recurrence (158 eyes)	0.32 (0.36)	0.17 (0.28)	<0.001
Without recurrence (657 eyes)	0.34 (0.38)	0.14 (0.27)	<0.001

VA: Visual acuity; SD: Standard deviation

In relation to the fovea, the leaks were located superior in 38.93%, inferior in 13.89%, temporal in 14.96%, nasal in 23.96% and subfoveal in 8.24%.

Out of the 815 eyes, 514 (63.06%) were treated with green laser photocoagulation to the RPE leak identified on DFA, using 50 micron or 100 micron spot size burns. The end point was mild whitening of the retina at the site of treatment. There were no treatment-related complications, such as laser-induced choroidal neovascularization during follow-up. Three hundred and one eyes (36.93%) were treated conservatively. Conservative treatment meant that the patient did not receive

any medication but was reassured about the nature of the disease and was kept under observation.

One hundred and seven eyes (20.81%) treated with laser photocoagulation and 51 eyes (16.94%) treated conservatively had recurrence of the disease—a difference not found to be statistically significant ($p = 0.2$, on Chi-square test with Yates correction).

Univariate analysis was done to study the association between recurrence of CSCR and various risk factors namely age, sex, presence of diabetes mellitus or hypertension, use of systemic steroids and antihypertensives. Chi-square test was

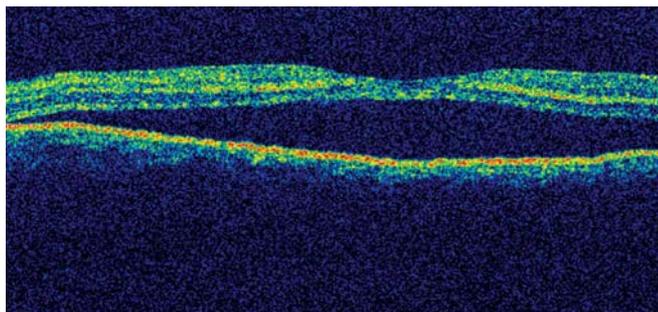


Fig. 1A: An OCT image showing subfoveal serous macular detachment

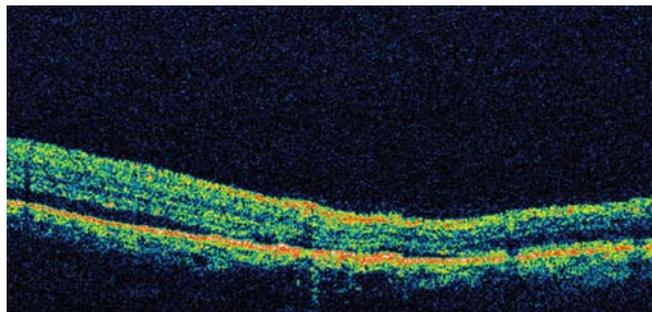
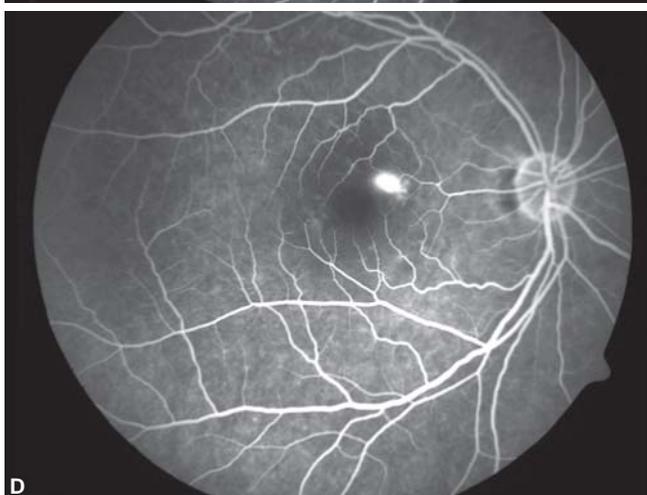
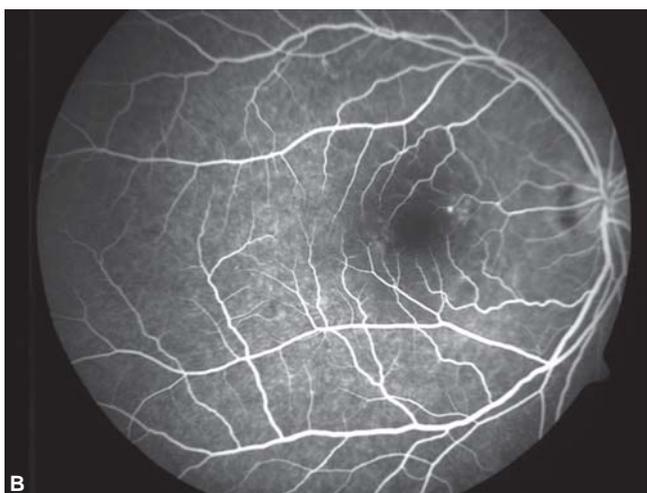
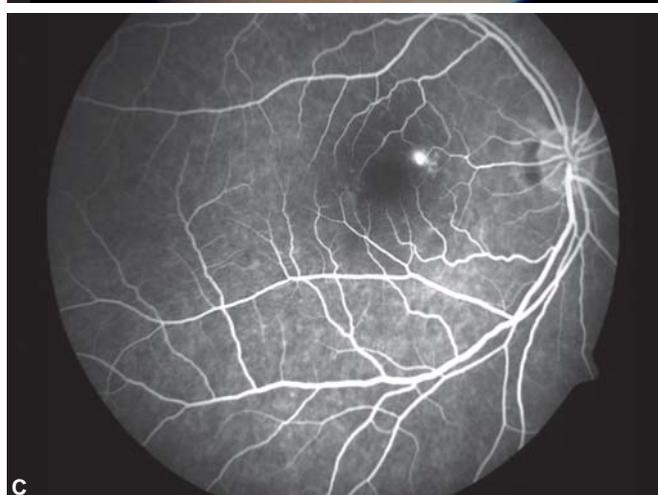
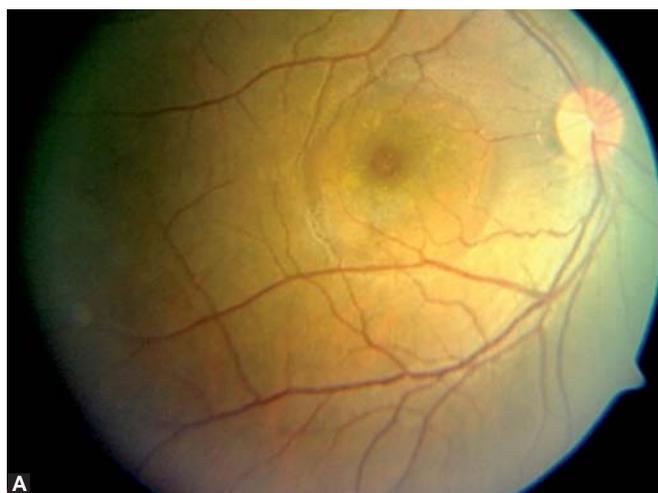


Fig. 1B: An OCT image showing extrafoveal serous macular detachment



Figs 2A to D: Color fundus photograph (A) and corresponding fluorescein angiography images, (B) early, (C) mid, (D) late phase showing ink blot type of RPE leak

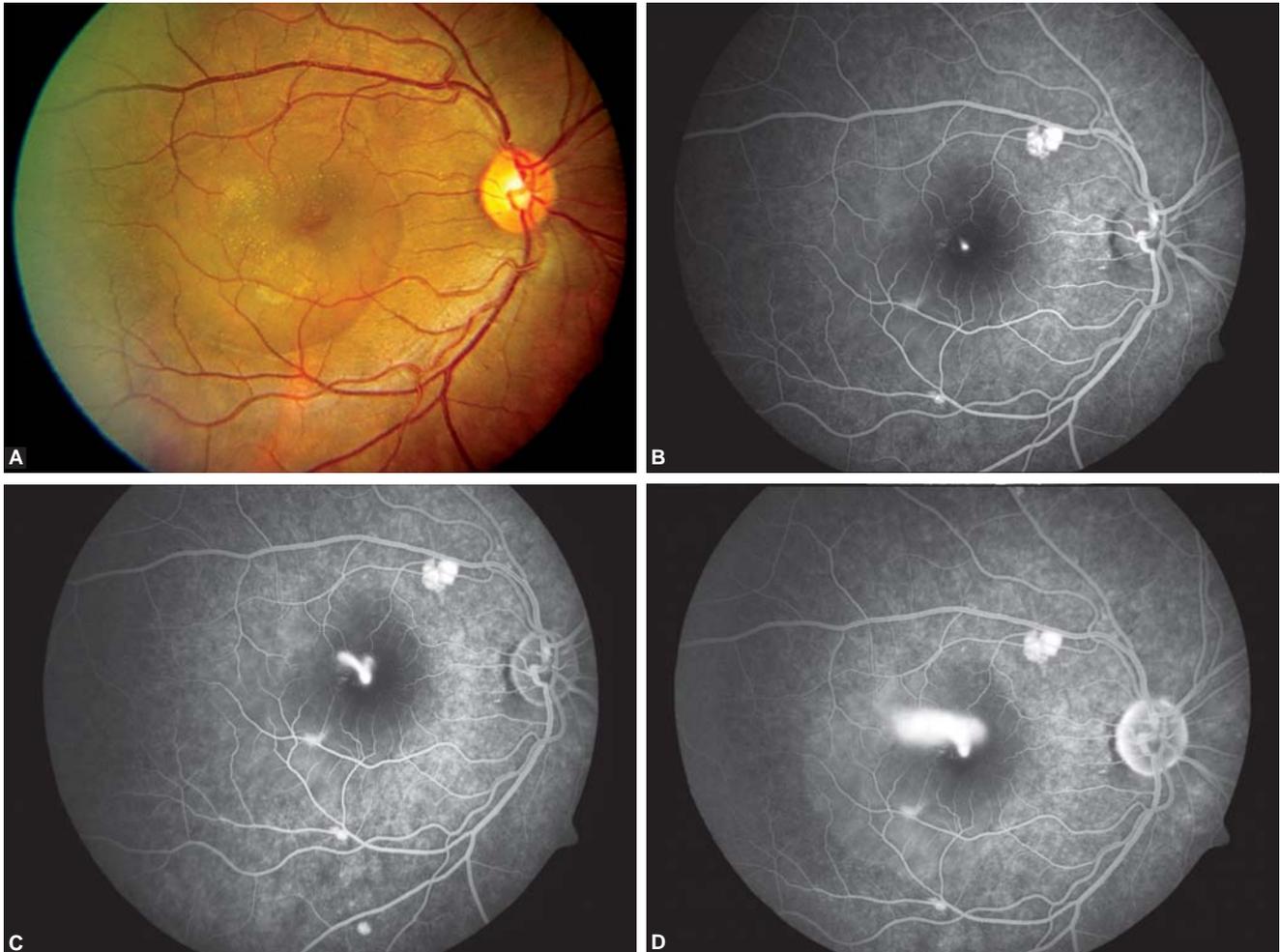
applied for univariate analysis. There was a statistically significant association between the male sex and age less than 40 with recurrence of CSCR (Table 5).

Multivariate logistic regression analysis was done for variables with p-value <0.2 in the univariate analysis, namely age, sex, presence of diabetes mellitus and hypertension. It was found that age less than 40 and male sex was significantly associated with recurrence of CSCR. Patients aged less than

40 years had a 1.59 times increased risk of recurrence of CSCR. Patients of the male sex had a 1.96 times increased risk of recurrence of CSCR (Table 6).

DISCUSSION

The main purpose of the study was to determine the recurrence rate of CSCR and the risk factors responsible for recurrence of CSCR. The recurrence rate of CSCR in our study of 752 patients



Figs 3A to D: Color fundus photograph (A) and corresponding fluorescein angiography images (B) early, (C) mid, (D) late phase showing smoke stack type of RPE leak

Table 5: Univariate analysis—Chi-square test

Variables		Recurrence		Total no.	p-value
		No .	%		
Age (years)	≤40	84	(25.4)	331	0.007
	>40	72	(17.1)		
Sex	Male	144	(22.1)	652	0.029
	Female	12	(12.0)		
Diabetes mellitus	Present	11	(13.3)	83	0.101
	Absent	145	(21.7)		
Hypertension	Present	19	(15.8)	120	0.185
	Absent	137	(21.7)		
Antihypertensives	Taken	14	(20.0)	70	0.995
	Not taken	142	(20.08)		
Systemic steroids	Taken	6	(31.6)	19	0.372
	Not taken	150	(20.5)		

Significant p < 0.05 age and sex

Table 6: Multivariate logistic regression analysis

Variables	No. of patients	Odds ratio	95% confidence interval	p-value
Age <40 years	84	1.597	1.119-2.281	0.010
Male sex	144	1.962	1.041-3.697	0.037

with an average follow-up of 12.11 months was 19.41%. The recurrence rate of CSCR in patients followed up for 1 year and more was 11.77%. Studies by C Mitchell Gilbert,⁴ Anna S Kitzmann⁵ and Gass JDM² reported a recurrence rate of 30%. The two most rigorous retrospective long-term studies by Dellaporta⁶ and Nanjiani⁷ documented recurrences in 50% of patients. The average follow-up in these studies^{4,5} was 16 years. Our patients were all of Indian origin, whereas majority of the patients in these studies were Caucasians. This could possibly be a reason for differences in results. Recurrences often occur within 1 year but may occur up to 10 years after the first episode. Table 7 shows studies comparing recurrence rates in CSCR.

The risk factors for recurrence of CSCR studied were age, sex, presence of diabetes mellitus, hypertension, use of antihypertensives and systemic steroids.

On both multivariate and univariate analysis, the same factors—namely age less than 40 years and male sex—showed a statistically significant association with recurrence of CSCR, with an odds ratio of 1.59 and 1.96 respectively. Haimovici,³ using stepwise logistic regression analysis, identified the use of systemic steroids (odds ratio 37.1), pregnancy (odds ratio 7.1), use of antibiotics, antihistamines, alcohol and allergic respiratory disease as the risk factors for recurrent CSCR.

The risk factors for recurrence may not be the same as those for development of CSCR. One of the most extensive reports on risk factors for CSCR was the work done by Robert A Haimovici.³ In a retrospective case-control study of 312 cases, he has identified several factors which were more likely to be present with recurrent or chronic CSCR. They were previous organ transplantation (odds ratio 5.8), topical steroids (odds ratio 7.7), ulcer medication (odds ratio 3.7) and allergies to medication other than penicillin (odds ratio 2.2). These factors were not noted as causes for recurrence in our series.

The mean age of our patients was 42.16 years (range 20- 69 years). This was comparable with other studies. Yanuzzi et al,⁸ mean of 42 years and Kitzmann et al,⁵ mean of 41 years and range 29-56 years. It has not been reported in a person younger than 20 years. In patients older than 50 years, CSCR does occur, but it needs to be distinguished from age-related macular degeneration.

Of the 752 patients, 652 (86.70%) were males and 100 (13.29%) were females. Similar male preponderance was reported by Kitzman et al⁵ (85%) and Castro-Correia et al⁹ (83.3%). Women with CSR tended to be older than affected men. Quillen,¹⁰ in a study on a series of 51 women with CSR, reported a mean age of 53 years. Stephen LA Perkins,¹¹ in one of the largest series of CSR occurring in women, documented a mean age of 47 years (range 31-71 years). CSCR can occur in the last trimester of pregnancy. It is associated with serofibrinous subretinal fluid in 90% of affected women.¹²

Klein et al¹³ have reported bilaterality in 14 to 30% of cases, while Gilbert et al⁴ reported 14% incidence of bilateral CSCR. In comparison our series had lower incidence of bilaterality (8.37%). This could be due to differences in follow-up or racial composition.

Out of the 720 DFAs performed, 655 eyes had an RPE leak. 72.08% eyes had only one RPE leak. This was comparable to that reported by J Castro Correia⁹ in which 62.7% eyes had one RPE leak. However, Spitznas et al¹⁴ and Gilbert⁴ documented 93 and 80% respectively, of eyes having one RPE leak on DFA. Our series showed 8.24% of leaks to be subfoveal. This was comparable with other studies. Spitznas¹⁴ and Gilbert⁴ documented 11.8% and 17.7% respectively to be subfoveal leaks in their studies.

Studies have shown that the incidence of leakage site to be greatest in the upper nasal quadrant,¹⁴ followed by lower nasal quadrant and the lower temporal quadrant. In our study majority of the leaks were superior to the fovea.

One hundred twenty-one patients (16.09%) had hypertension. However, only 70 patients (9.3%) were on antihypertensive medication. Venkatesh et al,¹⁵ in their study, have shown that patients with CSCR have a tendency toward hypertension compared with normal individuals. Haimovici³ also reported untreated hypertension to be a risk factor for CSCR.

Table 7: Studies comparing recurrence rates in CSCR

Study	Recurrence (%)
Incidence of CSCR in Olmsted County, Minnesota, 1980-2002	
Anna S Kitzmann, Jose S Pulido, MPH, Nancy N, Diehl BS et al ⁵	31
Long-term follow-up of central serous chorioretinopathy	
C Mitchell Gilbert, Sarah L Owens, Patricia D Smith et al ⁴	30
Long-term follow-up of central serous retinopathy	
Nanjiani M ⁷	50
Central serous retinopathy	
Dellaport A ⁶	50
Pathogenesis of disciform detachment of neuroepithelium II	
Idiopathic central serous chorioretinopathy	
Gas JDM ²	30
Current study	19.4

Out of the 752 patients in the study, 19 patients (0.03%) were on systemic steroids. These patients were put on systemic steroids by the treating doctors, prior to being referred to our hospital, after which the steroids were discontinued. In spite of the steroids being discontinued, 6 patients had recurrent CSR. Chronic steroid users were not included in this series. Use of glucocorticosteroids has been identified as a risk factor in several studies.^{16,3}

Our study was significant as it was conducted over a period of 10 years. The number of patients in our study was also significantly large (752) compared to other studies,⁴⁻⁶ that had 68 to 74 patients. Most of the studies have evaluated risk factors for the incidence of CSCR. To our knowledge, this is the only study which has evaluated risk factors for recurrence of CSCR.

We understand the limitations in our study this being retrospective. Since the data was collected from the medical records, lacuna in information is to be expected, especially with regards to psychological stress, etc.

To conclude, the recurrence rate of CSCR in 752 patients with an average follow-up of 12.11 months was 19.41%. Patients aged less than 40 years had a 1.59 times increased risk of recurrence of CSCR. Patients of the male sex had a 1.96 times increased risk of recurrence of CSCR.

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